THE JOURNAL

OF THE

AMERICAN CHEMICAL SOCIETY

VOL. LXII

JANUARY—JUNE

1940

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EASTON, PA.
MACK PRINTING COMPANY
1940

JOURNAL OF THE
AMERICAN CHEMICAL SOCIETY

VOLUME 62 JANUARY 10, 1940 NUMBER 1

[CONTRIBUTION FROM THE AMMONIA DEPARTMENT OF E. I. DU PONT DE NEMOURS & COMPANY, INC.]

Analytical Procedures Employing Karl Fischer Reagent.[1] II. The Determination of Alcoholic Hydroxyl

BY W. M. D. BRYANT, J. MITCHELL, JR., AND DONALD MILTON SMITH

Alcoholic hydroxyl is usually determined acidimetrically by means of acetyl chloride and pyridine[2] or by one of the several acetic anhydride procedures. These methods, however, are lacking in sensitivity where the sample contains considerable amounts of water or acids. Water, for example, reacts mole for mole with acetyl chloride, in competition with alcohols, and necessitates the use of smaller analytical samples in order to maintain the necessary excess of reagent.

In the present research a titrimetric procedure for hydroxyl independent of acidimetry has been developed. This new procedure is useful over a wide range of compositions and is remarkably precise in the presence of large amounts of water or acids. The analysis depends upon the general reaction

$$ROH + CH_3COOH = CH_3COOR + H_2O$$

according to which one mole of water is liberated for each equivalent of hydroxyl esterified. By employing a large excess of acetic acid and making use of boron fluoride as an esterification catalyst,[3] it is possible to shift the equilibrium almost completely in favor of water and ester. A measure of the water formed is obtained by direct titration with Karl Fischer reagent.

(1) This reagent, discussed in detail in the first paper of the series [Smith, Bryant and Mitchell, THIS JOURNAL, **61**, 2407 (1939)], consists of a solution of iodine, sulfur dioxide and pyridine in methanol. It is specific for water.

(2) Smith and Bryant, THIS JOURNAL, **57**, 61 (1935). References covering the acetic anhydride procedures are included.

(3) (a) Bowlus and Nieuwland, *ibid.*, **53**, 3837 (1931); (b) Hinton and Nieuwland, *ibid.*, **54**, 2017 (1932); (c) Hennion, Hinton and Nieuwland, *ibid.*, **55**, 2857 (1933).

The new hydroxyl procedure is applicable to aliphatic and alicyclic alcohols in general, including branched chain types and hydroxy acids, also such aromatic alcohols as have the hydroxyl group attached to an aliphatic side chain. Phenols, however, do not react completely. Some unsaturated terpene alcohols, on the other hand, give results greater than the theoretical.

Differences in the relative esterification rates of aliphatic and strictly aromatic alcohols (*i. e.*, phenols) have made possible a method for differentiating these two classes of compounds. Under the proper conditions aliphatic alcohols are esterified or dehydrated[4] almost completely, while phenols react only to a very small extent. The selective action observed here is probably due as much to differences in the equilibrium constants of the two series, as to purely kinetic differences.

Experimental

Analytical Procedure.—Five to 10 ml. of sample is weighed into a 100-ml. g. s. volumetric flask about one-third filled with dioxane. This mixture is made up to volume with more of the solvent, shaken until homogeneous and finally adjusted after standing at least thirty minutes in a water-bath at 25 ± 1°. Five ml. (using calibrated pipet) of the sample solution is transferred to a 250-ml. g. s. volumetric flask and 20 ml. of the catalyst solution added.[5]

(4) Dehydration of tertiary alcohols to olefins liberates the same amount of water per hydroxyl group as esterification would do, hence it is not necessary to isolate these two effects.

(5) This solution is prepared by dissolving about 100 g. of boron trifluoride gas and 1 or 2 ml. of water in sufficient Merck C. P. glacial acetic acid to make one liter of solution. Boron trifluoride of suitable quality can be obtained in cylinders from the Ohio Chemical Company, Cleveland, Ohio.

The flask is tightly stoppered[6] and together with a control containing 20 ml. of catalyst solution and 5 ml. of dioxane, is placed in an oven or water-bath at 67 ± 2° for two hours.[7] At the end of this time the flasks are removed and allowed to cool to room temperature spontaneously. Five ml. of Baker C. P. pyridine is added to each,[8] and the mixture titrated with Karl Fischer reagent.

After correction for water in the dioxane, catalyst and pyridine, the millimoles of water present after treatment, less the water originally present, are equal to the milliequivalents of free hydroxyl in the sample.

The water originally present may be obtained by titrating 5 ml. of the original dioxane solution with Fischer reagent. A correction must be made for the water initially present in the dioxane as this quantity is usually appreciable. The correction is made on the basis of the volume of dioxane in the aliquot figured with sufficient precision as the difference between the total volume of solution and the volume of concentrated sample employed, neglecting volume changes on mixing.

Analytical Results

The experimental results obtained with a number of alcohols and other hydroxy compounds are given in Table I. In all cases the trade products were used without further purification.

It is interesting to note that aliphatic tertiary alcohols react stoichiometrically.[9] This reaction is undoubtedly due to both esterification and dehydration. The analysis is specific, however, since only one mole of water is released per mole of hydroxyl added.

Phenols do not esterify completely under the conditions of the general procedure. Phenol, pyrogallol and α-naphthol reacted only about 65%. An increase in catalyst concentration from 100 to 300 g. per liter raised the results with phenol to 85%. The substitution of either trimethylacetic or *n*-caproic acid for acetic acid in the catalyst solution had no appreciable effect on the phenol esterification, a recovery of about 60% being obtained in both cases.[10]

Terpenes react differently according to structure. Geraniol and terpineol, the two unsaturated terpenes analyzed, gave results of 109 and 114%, respectively. Borneol, on the other hand, showed 98.4% reaction, checking the analysis by the acetyl chloride–pyridine method.[2]

The precision and accuracy average about ±0.3%, comparing very favorably with the involved acetic anhydride procedures. The stoichiometric accuracy appears to be somewhat better than that of the acetyl chloride–pyridine method,[2] for in all cases noted, with the exception of allyl alcohol and 2-methylbutanol-4, the results were more nearly quantitative.

TABLE I

ANALYTICAL DATA FOR ALCOHOLS AND OTHER HYDROXY COMPOUNDS

Substance	% Hydroxyl compound (various methods)		Complete analysis (using Karl Fischer reagent) % Hydroxyl compound	% Water	% Total
Methanol		(6)[d]	99.0 ± 0.4	0.5	99.5
Ethanol		(4)	99.5 ± .2	.4	99.9
Ethylene glycol[e]		(2)	98.6 ± .2	.7	99.3
n-Propanol[e]		(2)	98.9 ± .4	1.2	100.1
Glycerol[g]		(2)	92.9 ± .1	5.1	98.0
Allyl alcohol[e]	97.2[a]	(4)	96.6 ± .3	1.9	98.5
Isobutanol		(6)	98.8 ± .2	0.9	99.7
t-Butanol[e]		(6)	99.2 ± .3	.8	100.0
2-Methylbutanol-4[f]	97.8[a]	(6)	97.3 ± .4	1.0	98.3
Pentanol-2[f]		(4)	98.3 ± .5	1.6	99.9
2-Methylbutanol-2[f]		(4)	99.3 ± .2	0.9	100.2
2,4-Dimethylpentanol-3		(2)	99.8 ± .3	.2	100.0
Cyclohexanol[e]	95.0[a]	(2)	95.8 ± .2	.0	95.8
Borneol[e]	98.4[a]	(4)	98.4 ± .2	.0	98.4
Benzyl alcohol[e]	97.1[a]	(4)	97.3 ± .2	1.1	98.4
Benzoin[e]	93.1[a]	(4)	97.4 ± .2	0.0	97.4
Glycolic acid[e]	99.9[b]	(4)	100.0 ± .3	.0	100.0
α-Hydroxyisobutyric acid[h]	97.6[b]	(2)	97.5 ± .3	.1	97.6
Ricinoleic acid[i]	58.3[b]	(2)	58.9 ± .0	1.7	60.6
Tartaric acid[g]	94.5[b]	(2)	94.1 ± .4	0.1	94.2
Methyl glycolate		(2)	99.7 ± .2	.1	99.8
Methyl lactate[j]	97.4[c]	(2)	97.5 ± .0	.4	97.9
Ethyl lactate[e]	98.7[c]	(2)	98.5 ± .3	.4	98.9
Ethyl tartrate[e]	94.7[c]	(2)	93.9 ± .2	.0	93.9
Methylcellosolve[k]	93.2[a]	(2)	94.5 ± .2	4.5	99.0

[a] Acetyl chloride–pyridine procedure. [b] Alkali titration. [c] Saponification. [d] Figures in parentheses represent number of determinations. [e] Eastman Chemical. [f] Sharples Solvent Corp. [g] J. T. Baker C. P. [h] American Cyanamide Co. [i] Eimer & Amend Technical. [j] Eastman Practical. [k] Carbide & Carbon.

In Table II are collected results obtained with alcohols containing various quantities of water. In each case the alcohol added was calculated as the difference between the per cent. water found by analysis and 100%. It is interesting to note that reasonably accurate results were obtained with aqueous ethanol samples containing as little as 0.8% ethanol.

The procedure was exactly the same as that described above.

(6) A simple spring clamp (#4799), serving to prevent expulsion of the stopper on heating is furnished by the Precision Scientific Company, 1730 N. Springfield Ave., Chicago, Illinois.

(7) Methanol reacts to completion in one hour at 60°; ethanol in two hours at 60°.

(8) The addition of pyridine just before titration with Karl Fischer reagent is essential. Its probable purpose is to destroy the activity of the catalyst and prevent esterification of the methanol of the Karl Fischer reagent. If the 5 ml. of pyridine is omitted and the activity of the catalyst is not otherwise destroyed, impossibly high titers are obtained.

(9) The tertiary hydroxyl of citric acid, however, is only 35% esterified.

(10) By using acetic anhydride in place of acetic acid, roughly quantitative results were obtained. The end-point was so obscure, because of unusual darkening of the solution, that accurate end-point adjustments were not possible. Checks of ±4% were an average measure of the precision to be expected.

[CONTRIBUTION FROM THE AMMONIA DEPARTMENT OF E. I. DU PONT DE NEMOURS & COMPANY, INC.]

Analytical Procedures Employing Karl Fischer Reagent.[1] III. The Determination of Organic Acids

BY J. MITCHELL, JR., DONALD MILTON SMITH AND W. M. D. BRYANT

The most obvious procedures for the quantitative determination of carboxylic acids are those based on neutralization by strong alkalies. These methods, however, are so general as to be subject to interference from many other types of compounds producing hydrogen ions. For example, where inorganic acids are present, these must be separated or determined separately by specific methods before a measure of the carboxyl group can be obtained by the usual titration with standard base.

In the present investigation a carboxyl procedure independent of ordinary acid–base titrimetry was devised. Its basis is the estimation of water liberated by the reaction $RCOOH + CH_3OH \longrightarrow RCOOCH_3 + H_2O$. This reaction is almost identical with the one used in the authors' hydroxyl procedure.[2] It proved possible to obtain practically stoichiometric conversions of a large number of organic acids to the corresponding esters and water by using a large excess of methanol containing boron fluoride. Nieuwland and his collaborators found the latter substance to be an efficient esterification catalyst.[3] Inasmuch as one mole of water is formed for each equivalent of carboxyl esterified, the water found by titration with Karl Fischer reagent, less that originally present, becomes a measure of the carboxyl content. Strong inorganic acids, with the exception of sulfuric, are not esterified by this procedure. The apparatus requirements are very simple, the entire analysis including the esterification and titration steps being carried out in glass-stoppered flasks.

The new carboxyl procedure is applicable to aliphatic acids generally, including branched chain and hydroxyl substituted types, and also aromatic acids having the carboxyl attached to an aliphatic side-chain. Typical aromatic acids having the carboxyl group attached directly to the ring do not react quantitatively. The heterocyclic furoic acid and the sterically hindered alicyclic camphoric acid also fail to react completely.

Changes in the concentration of the catalyst solution have a marked effect on the esterification of strictly aromatic acids.[3d] An increase, for example, gave results more nearly quantitative. By careful control of this variable it was possible to esterify aliphatic acids without appreciably affecting aromatic acids.

The average precision and accuracy based on comparisons with alkali titration are about $\pm 0.3\%$.

Experimental

Analytical Procedure.—Five to 10 ml. of sample is weighed into a 100-ml. g. s. volumetric flask half-filled with dioxane. The mixture is made up to volume with more dioxane, shaken until homogeneous and allowed to stand at least thirty minutes in a water-bath at 25 ± 1°. Five ml. (using calibrated pipet) of the dioxane solution is placed in a 250-ml. g. s. volumetric flask. To this is added exactly 20 ml. of the catalyst solution.[4] The flask is then placed in a water-bath[5] at 60 ± 1°, and after momentarily raising the stopper to allow for expansion of the included air, is firmly stoppered and maintained at that temperature for one hour.[6] At the end of this period the sample is removed, allowed to cool to room temperature spontaneously, and then titrated with Karl Fischer reagent.[7] A blank is run using 5 ml. of dioxane and 20 ml. of catalyst solution. After correction for water in the dioxane and catalyst, the millimoles of water present after treatment, less the water originally present, are equal to the milliequivalents of free carboxyl in the sample.

The water originally present may be obtained by titrating 5 ml. of the original dioxane solution with Fischer reagent. A correction must be made for the water initially present in the dioxane as this quantity is usually appreciable.

(1) This reagent, discussed in detail in the first paper of the series (Smith, Bryant and Mitchell, THIS JOURNAL, **61**, 2407 (1939)), consists of a solution of iodine, sulfur dioxide, and pyridine in methanol. It is specific for water.

(2) Bryant, Mitchell and Smith, THIS JOURNAL, **62**, 1 (1940).

(3) (a) Bowlus and Nieuwland, *ibid.*, **53**, 3837 (1931); (b) Hinton and Nieuwland, *ibid.*, **54**, 2017 (1932); (c) Hennion, Hinton and Nieuwland, *ibid.*, **55**, 2857 (1933); (d) Sowa and Nieuwland, *ibid.*, **58**, 271 (1936).

(4) This solution is prepared by dissolving 100 g. of boron trifluoride gas and 2 ml. of water in sufficient du Pont synthetic methanol (water content 0.15% or less) to make a final volume of one liter. Boron fluoride of suitable quality may be obtained in cylinders from the Ohio Chemical Co., Cleveland, Ohio.

(5) Smith and Bryant, THIS JOURNAL, **57**, 62 (1935), describe a convenient water-bath.

(6) Acetic and propionic acids react to completion at 25° in one hour, while formic acid requires two hours.

(7) In the presence of the catalyst solution, the iodine color of the reagent may persist during the addition of about the first 15 ml., producing a false end-point. The water included in the catalyst solution is sufficient to permit the addition of 15 ml. of reagent directly. Further addition of reagent produces a normal discharge of the brown color until the true end-point is reached. The false end-point may be avoided altogether if 5 ml. of pyridine of known water content is added just before titration. Unlike the hydroxyl method,[2] this procedure is reliable without the extra pyridine.

TABLE II

ANALYTICAL DATA FOR AQUEOUS ALCOHOL SOLUTIONS

Substance	Wt. % by difference Alcohol	Wt. % by analysis Alcohol	Water	Total
Ethanol	0.8	1.0 ± 0.2	99.2 ± 0.0	100.2
Ethanol	3.9	3.9 ± .2	96.1 ± .1	100.0
Ethanol	7.6	7.4 ± .3	92.4 ± .0	99.8
Ethanol	15.8	15.6 ± .2	84.2 ± .0	99.8
Ethanol	19.4	19.0 ± .2	80.6 ± .2	99.6
Ethanol	38.9	39.0 ± .3	61.1 ± .1	100.1
Isobutanol	8.3	8.3 ± .2	91.7 ± .0	100.0
t-Butanol	16.2	16.0 ± .2	83.8 ± .1	99.8
n-Propanol	17.8	17.9 ± .2	82.2 ± .1	100.1
2-Methylbutanol-4	2.2	2.5 ± .2	97.8 ± .0	100.3
Pentanol	3.5	3.8 ± .2	96.5 ± .1	100.3

The procedure for the approximation of aliphatic alcohols in the presence of aromatic alcohols is based on the use of less concentrated catalyst solutions. Experimental results under various conditions are given in Table III.

TABLE III

ANALYTICAL RESULTS WITH ALCOHOLS USING LESS CONCENTRATED CATALYST SOLUTION

Substance	Percentage of theoretical hydroxyl: 2 hrs. at R. T. (26 ± 1°) a	2 hrs. at R. T. (26 ± 1°) b	2 hrs. at 60° a	2 hrs. at 60° b
Ethanol	25	45	96.8 ± 0.3	99.0 ± 0.0
n-Propanol			98.7 ± .3	
Isobutanol			96.7 ± .3	
t-Butanol	83	93	95.5 ± .4	99.1 ± .4
Glycol			90.6 ± .2	
Glycerol			78.1 ± .2	
Cyclohexanol			55.9 ± .0	
Benzyl alcohol			97.2 ± .4	
Phenol	0.0	2.5	3.9 ± .2	26.6 ± .2
Guaiacol	0.0	2.5	4.5 ± .2	28.2 ± .5

[a] Catalyst concentration 25 g./liter. [b] Catalyst concentration 50 g./liter.

The favorable results obtained with tertiary butanol at room temperature are of interest. These probably were due to dehydration since esterification to this extent seems unlikely.

Conditions which seemed best for the analysis of aliphatic in the presence of aromatic alcohols were those of the third column of figures. Ethanol–phenol mixtures were analyzed by this procedure and the results summarized in Table IV.

TABLE IV

ANALYTICAL RESULTS ON THE DETERMINATION OF ETHANOL IN THE PRESENCE OF PHENOL

% C_6H_5OH added	% C_2H_5OH added	% C_2H_5OH found
93.3	6.7	9.0 ± 0.2
57.0	43.0	43.8 ± .2
11.1	88.9	88.2 ± .1

It is believed that the results obtained with phenol and guaiacol are typical of what may be expected with other phenols and that the degree of differentiation would be much like that in Table IV. As previously noted, using the general catalyst solution, pyrogallol and α-naphthol react to about the same extent as phenol.

Interfering Substances.—The new hydroxyl procedure is unfavorably affected by the presence of a few classes of organic compounds. Aldehydes and ketones react to a considerable extent, *e. g.*, formaldehyde (37% aqueous) and cyclohexanone showed about 70 and 50% reaction, respectively. The reaction with carbonyl compounds in general is probably analogous with that proposed for formaldehyde

$$CH_2O + 2CH_3COOH \longrightarrow (CH_3COO)_2CH_2 + H_2O$$

Acetals and ketals react nearly to completion assuming two moles of water are formed for each mole of sample. For methylal the reaction can be written as

$$CH_2(OCH_3)_2 + 4CH_3OOH \longrightarrow 2CH_3COOCH_3 + (CH_3COO)_2CH_2 + 2H_2O$$

Analyses of methylal, acetal and di-*n*-butyl formal on this basis gave results of 92, 91 and 88%, respectively.

Most amines interfere with the method, by affecting catalyst activity.

Summary

1. A specific quantitative method for the determination of hydroxy compounds has been described. The method is based on quantitative esterification and subsequent titration of the water liberated, using the highly specific Karl Fischer reagent.

2. Analytical results for more than twenty-five hydroxy compounds, principally aliphatic, are tabulated.

3. The method is quantitative for samples containing large excesses of water.

4. Tertiary aliphatic alcohols may be analyzed by this procedure.

5. A quantitative method for the determination of aliphatic alcohols in the presence of phenols is described.

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ble. The correction is made on the basis of the volume of dioxane in the aliquot, figured with sufficient precision as the difference between the total volume of solution and the volume of concentrated sample employed, neglecting volume changes on mixing.

Analytical Results

The experimental results obtained with a group of organic acids are given in Table I. In most cases the results are within 0.3% of those obtained by aqueous caustic titration.

Benzoic and salicylic acids reacted only to the extent of 58 and 19%, respectively; furoic and camphoric, 35 and 75%. Benzilic acid, which should esterify as an aliphatic, reacted only 45%, probably due to steric hindrance.[8]

The solid acids studied in the present research, with the exception of glycolic, phenylacetic and cinnamic acids are not very soluble in dioxane. The original sample should therefore be no larger than 2.5 g. per 100 ml. of dioxane solution.

TABLE I

ANALYTICAL DATA FOR ORGANIC ACIDS

Acid[b]	% Acid (alkali titration)		Complete analysis Using Karl Fischer reagent % Acid	% Water	Total
Formic		(6)[a]	97.2 ± 0.2	2.2	99.4
Acetic[c]		(2)	99.6 ± .2	0.1	99.7
Propionic		(2)	99.8 ± .1	.2	100.0
n-Butyric	99.5	(8)	99.5 ± .4	.5	100.0
i-Butyric	99.5	(6)	99.7 ± .2	.5	100.2
dl-Methylethyl acetic		(2)	95.1 ± .0	.7	95.8
Trimethylacetic		(2)	99.6 ± .0	.4	100.0
n-Caproic	99.1	(6)	99.3 ± .3	.4	99.7
Stearic[d]		(4)	100.3 ± .1	.0	100.3
Succinic[g]		(2)	99.1 ± .5	.7	99.8
Oleic[d]	99.5	(2)	99.2 ± .0	.5	99.7
Linoleic[d]	98.2	(2)	96.5 ± .5	1.2	97.7
Glycolic	99.9	(4)	99.6 ± .2	0.0	99.6
α-Hydroxy-*i*-butyric[f]	97.6	(4)	97.9 ± .5	.1	98.0
Tartaric[g]	94.5	(4)	94.3 ± .5	.1	94.4
Ricinoleic[e]	58.3	(4)	58.4 ± .5	1.7	60.1
Phenylacetic		(2)	100.0 ± .2	0.0	100.0
Cinnamic		(2)	99.7 ± .3	0.0	99.7

[a] Figures in parentheses represent number of determinations. [b] Except where noted, above acids are Eastman Kodak Co. chemicals. [c] Merck glacial c. p. [d] Eimer and Amend pure. [e] Eimer and Amend technical. [f] American Cyanamid Company. [g] J. T. Baker Analyzed c. p.

An increase in catalyst concentration had a marked effect on the esterification of aromatic and heterocyclic acids. Table II shows this change from the regular catalyst solution to a solution three times as strong (300 g. per liter).

(8) Citric acid is about 92% esterified.

TABLE II

ESTERIFICATION USING HIGHER CONCENTRATIONS OF CATALYST

Substance	% Acid esterified: Regular catalyst concn.	High catalyst concn.
Benzoic	58	98.5 ± 0.3
Salicylic	18	67
Anisic		88.5
Phthalic		88
Camphoric	40	46
Furoic	34	83

It is interesting to note that by substituting in the one case glycol and in the other di-isopropylcarbinol for methanol in the catalyst solution and following the conditions of the general procedure, the extent of reaction with benzoic acid was increased to 75% with the glycol solution and decreased to 16% with the di-isopropylcarbinol solution.

A decrease in the concentration of the catalyst solution (25 and 50 g. per liter), while having little effect on the esterification of aliphatic acids, reduced considerably the reaction of aromatic and heterocyclic acids and the sterically hindered camphoric acid. These results are noted in Table III.

TABLE III

ESTERIFICATION USING LOWER CONCENTRATIONS OF CATALYST

Substance	% Acid esterified: Catalyst, 25 g./liter a	b	Catalyst, 50 g./liter a	b
Formic	96.9 ± 0.1	97.7 ± 0.0	97.7 ± 0.0	
Acetic	98.8 ± .0	98.8 ± .0	99.1 ± .2	99.8 ± 0.1
Isobutyric	96.2 ± .0	99.0 ± .2	98.9 ± .2	
Trimethylacetic	31.7 ± .0	95.8 ± .3	52.9 ± .0	96.5 ± 0.3
n-Caproic	98.6 ± .0			
Oleic	95.6 ± .0			
Stearic	100.3 ± .1			
Succinic	87.6 ± .6	99.1 ± .3		
Camphoric	1.3 ± .5			
Benzoic	1.4 ± .8	34.9 ± .3	6.2 ± .0	52.5 ± 0.3
Salicylic	0.0 ± .6	8.4 ± .0	1.1 ± .5	18.4
Furoic	0.9 ± .3			

[a] Conditions: 1 hour at room temperature (26 ± 1°). [b] Conditions: 1 hour at 60°.

Examination of the results in Table III suggests that mixtures of aliphatic and aromatic acids should behave in the same manner as the pure substances. Mixtures of acetic–benzoic and acetic–salicylic acids were analyzed, following the conditions of column 1; *i. e.*, 25 g./l. of catalyst for one hour at room temperature. These results are given in Table IV.

On the basis of Table III, the above procedure may be modified for other mixtures, taking into account the behavior of the pure acids.

TABLE IV

ANALYSIS FOR ACETIC ACID IN THE PRESENCE OF BENZOIC AND SALICYLIC ACIDS

Nature of mixture	% Aromatic acid added	% CH_3COOH added	% CH_3COOH found
Acetic and	89.6	10.4	12.6 ± 0.0
benzoic	50.8	49.2	50.1 ± .1
acids	11.8	88.2	88.1 ± .1
Acetic and	91.3	8.7	9.0 ± .0
salicylic	47.1	52.9	52.9 ± .0
acids	11.7	88.3	87.7 ± .1

Interfering Substances.—Aldehydes and ketones react with the methanol of the catalyst solution presumably to form acetals and ketals:

$$RCHO + 2CH_3OH \longrightarrow RCH(OCH_3)_2 + H_2O$$
$$RCOR' + 2CH_3OH \longrightarrow RR'C(OCH_3)_2 + H_2O$$

In all observed cases, however, the reaction was stoichiometric, so that suitable corrections could readily be made. It is self-evident that substances easily dehydrated interfere with the analysis. Of several classes of substances tried, tertiary alcohols were the only chemicals that were dehydrated sufficiently to affect the method. Tertiary butanol was dehydrated 37% by the above catalyst solution.

Among the strong inorganic acids tried, sulfuric acid was the only one esterified by the catalyst solution. The reaction is quantitative, however, in that one mole of water is formed per mole of the acid: $H_2SO_4 + CH_3OH \longrightarrow CH_3HSO_4 + H_2O$. Other acids, such as benzenesulfonic, phosphoric and hydrochloric, do not interfere with the method.

In the titration of sulfuric acid for water a dioxane solution of the acid should be used. Apparently some charring occurs when concentrated sulfuric acid is titrated directly with Karl Fischer reagent.

Those compounds which fume or volatilize readily, such as hydrochloric acid, are best titrated for water in the presence of an inert solvent.

Boric acid reacts stoichiometrically with the methanol in Karl Fischer reagent, even in the absence of catalyst solution: $H_3BO_3 + 3CH_3OH \longrightarrow (CH_3)_3BO_3 + 3H_2O$.

Anhydrides also interfere with the procedure, probably as follows

$$(RCO)_2O + CH_3OH \longrightarrow RCOOCH_3 + RCOOH$$
$$RCOOH + CH_3OH \longrightarrow RCOOCH_3 + H_2O$$

On this basis the extent of reaction with acetic anhydride was 61% in dioxane solution, but essentially quantitative in methanol solution.

Unsaturated alcohols and hydrocarbons do not interfere with the procedure, as indicated particularly by experiments with allyl alcohol and amylene.

Summary

1. A specific quantitative method for the determination of organic carboxylic acids has been described. The method is based on complete esterification and subsequent titration of the water liberated, using the highly specific Karl Fischer reagent.

2. Analytical results for eighteen acids, principally aliphatic, are tabulated.

3. The effect of changes of catalyst concentration upon esterification has been noted.

4. A method for the estimation of aliphatic acids in the presence of aromatic acids, based on large differences in esterification rate, has been demonstrated for selected cases.

WILMINGTON, DELAWARE RECEIVED SEPTEMBER 26, 1939

[CONTRIBUTION FROM THE BIOCHEMICAL RESEARCH FOUNDATION OF THE FRANKLIN INSTITUTE]

The Reaction between Hydrogen Selenide, Formaldehyde, and Secondary Amines

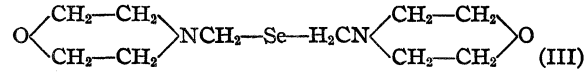
BY ARTHUR H. BINZ, FRANCIS E. REINHART AND HARRY C. WINTER

The formation of substituted *bis*-(aminomethyl) sulfides from secondary amines, formaldehyde, and hydrogen sulfide has been reported by Le Fèvre and Le Fèvre[1] and by Binz and Pence from this Laboratory.[2] The preparation of *bis*-(1-piperidylmethyl) sulfide (II) was described by the former authors; they assumed that the reaction proceeded in two stages, 1-piperidinemethanol (I) being formed in the first step

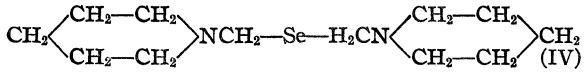
$$2C_5H_{10}NH + 2CH_2O \longrightarrow \underset{(I)}{2C_5H_{10}NCH_2OH} + H_2S \longrightarrow \underset{(II)}{C_5H_{10}NCH_2—S—H_2CNH_{10}C_5}$$

This assumption was confirmed by Binz and Pence, who prepared the same compound, as well as the morpholine analog, by treating the respective aminomethanols with hydrogen sulfide.[3]

By an extension of this reaction, analogous selenides from morpholine and piperidine have been prepared in this Laboratory. Thus 4-morpholinemethanol, or 1-piperidinemethanol, obtained by the action of formaldehyde on the corresponding amine, was found to react readily in ether solution with hydrogen selenide to yield *bis*-(4-morpholylmethyl) selenide (III), or *bis*-(1-piperidylmethyl) selenide (IV). Better yields of compound (III), however, were obtained by saturating an aqueous morpholine solution with hydrogen selenide at 0° and pouring this into cold dilute formaldehyde. Attempts to prepare similar selenides from dimethylamine and diethanolamine gave unstable oils which could not be purified.



(III)



(IV)

After recrystallization from ethyl acetate, compounds (III) and (IV) were found to be quite stable, but unlike the corresponding sulfur derivatives decomposed easily under the combined influence of solvents and air. Selenium was precipitated quantitatively when a warm dilute alcoholic solution of the morpholine selenide was aerated. Colloidal solutions of selenium, which were stable for several days, were obtained when an aqueous suspension of either selenide was treated with an equivalent amount of hydrogen peroxide.

The compounds proved to be highly toxic when injected intravenously into rats, the lethal dose being of the order of 0.012–0.017 g. per kg. of body weight.

(1) Le Fèvre and Le Fèvre, *J. Chem. Soc.*, 1142 (1932).

(2) Binz and Pence, THIS JOURNAL, **61**, 3134 (1939).

(3) For uniformity these authors have named both sulfides as substituted 2-thiapropanes.

Experimental

Hydrogen Selenide.—The hydrogen selenide used in this investigation was prepared by the action of dilute hydrochloric acid on aluminum selenide according to the procedure described by L. Moser.[4] Prior to the generation of the gas, air was removed from the generator and reaction flasks by passing a current of nitrogen through the apparatus for thirty minutes. Because of the toxicity of hydrogen selenide, all unreacted gas was absorbed in a trap containing 20% potassium hydroxide. After completion of the reaction, nitrogen was again passed through the apparatus and traces of hydrogen selenide remaining in the generator were oxidized with hydrogen peroxide.

***bis*-(4-Morpholylmethyl) Selenide (III).**—A solution of morpholine (12 cc.) in water (75 cc.) was cooled in an ice-bath and saturated with hydrogen selenide prepared from aluminum selenide (9 g.). This was poured into a cold solution of 37% formaldehyde (75 cc.) in water (150 cc.). The dense white crystalline precipitate which formed immediately was separated by filtration and recrystallized from ethyl acetate. The yield was 9.1 g. of glossy white plates, melting to a clear liquid at 136–138°. The analytical sample was dried to constant weight at 80° *in vacuo*. The selenium determination was carried out by the microprocedure of Alber and Harand.[5]

Anal. Calcd. for $C_{10}H_{20}O_2N_2Se$: N, 10.0; Se, 28.3. Found: N, 9.9; Se, 28.0.

bis-(4-Morpholylmethyl) selenide was found to be soluble in alcohol and benzene but only slightly soluble in water, decomposing rapidly in the presence of the latter, particularly when hot. When a solution of 0.7842 g. of the compound dissolved in 115 cc. of 80% ethyl alcohol at 40° was shaken in an open flask for fifteen minutes, 98.1% (0.2176 g.) of the total combined selenium precipitated as elementary selenium.

***bis*-(1-Piperidylmethyl) Selenide (IV).**—Piperidine (11.6 cc.) was added slowly with stirring to 37% formaldehyde (20 cc.) cooled in an ice-bath. Anhydrous potassium carbonate (10 g.) was then added and the mixture shaken until the solid dissolved and the solution separated into

(4) Moser, "Reindarstellung von Gasen," Verlag Ferdinand Enke, Stuttgart, 1920, p. 75.

(5) Alber and Harand, *J. Franklin Institute*, **228**, 243–250 (1939).

two layers. The upper layer of 1-piperidinemethanol was separated and dried over anhydrous sodium sulfate.

Crude 1-piperidinemethanol (3 g.) was dissolved in dry ether (30 cc.) and treated with hydrogen selenide obtained from aluminum selenide (1 g.). A slow stream of nitrogen gas was passed through the apparatus during the reaction and continued until the ether had evaporated. The selenide remained as a white crystalline precipitate and was recrystallized by dissolving in ethyl acetate at room temperature and cooling to 0°. After drying *in vacuo* over sulfuric acid, 1.8 g. of glossy white plates, melting at 67°, were obtained.

Anal. Calcd. for $C_{12}H_{24}N_2Se$: N, 10.2; Se, 28.7. Found: N, 10.3; Se, 28.6.

bis-(1-Piperidylmethyl) selenide dissolved readily in the common organic solvents. It was only slightly soluble in water, decomposition occurring in this solvent as in the case of the morpholine analog.

Summary

1. *bis*-(4-Morpholylmethyl) and *bis*-(1-piperidylmethyl) selenides were prepared from hydrogen selenide, formaldehyde, and the corresponding secondary amines. Attempts to prepare stable selenides using dimethylamine and diethanolamine were unsuccessful.

2. Both selenides were found to be very sensitive to oxidizing agents and highly toxic when injected into rats.

PHILADELPHIA, PA. RECEIVED AUGUST 25, 1939

[CONTRIBUTION FROM THE BELL TELEPHONE LABORATORIES, NEW YORK, N. Y.]

Dielectric Evidence of Molecular Rotation in the Crystals of Certain Non-aromatic Compounds*

BY ADDISON H. WHITE AND W. S. BISHOP

A molecular crystal may be considered, as a first approximation, to be a collection of rigid molecules held in a regular arrangement by rather weak intermolecular forces. In 1930 thermal evidence led Pauling to suggest that certain molecules of small moment of inertia are able to rotate in the high-temperature forms of such crystals,[1] the center of gravity of each molecule remaining at or near a point of the appropriate space lattice. He predicted that when the molecule in question is polar the dielectric constant of the high-temperature phase of the crystal should behave like that of a pure polar liquid.[2] This prediction was confirmed by measurement of hydrogen chloride, hydrogen bromide, hydrogen iodide and hydrogen sulfide, whose dielectric constants were found to drop from the high values characteristic of rotating polar molecules at transitions from one solid phase to another, instead of at the freezing points.[3,4,5] By far the greatest number of molecular crystals are organic. Dielectric, volumetric, and thermal measurements of such crystals have more recently revealed similar evidence of the rotation of organic molecules of large moment of inertia, including certain polar derivatives of camphane, cyclohexane and ethane.[6,7,8,9] Dielectric measurements have now been extended to other compounds belonging to these three classes, and show as reported below that the molecules of a surprisingly large number of organic crystals engage in rotational motion nearly or quite as freely as in the corresponding liquids.

In this communication the term "molecular rotation" will be used in the sense in which it has been generally adopted to explain the dielectric behavior of pure polar liquids. Although recent work indicates that the rotation of molecules in liquids is not free,[10] there can be no doubt that its amplitude is far greater than in most solids; *e. g.*, the dielectric constant of nitrobenzene drops from 35.8 to about 3.2 upon freezing.[11] Such a value or lower is characteristic of ordinary organic crystals, in which to a first approximation the rotational motion of the molecules is considered to be an harmonic oscillation.[12]

(*) Published with the financial assistance of an anonymous donor.

(1) Pauling, *Phys. Rev.*, **36**, 430 (1930).

(2) Debye, "Polar Molecules," Chemical Catalog Co., New York, N. Y.

(3) Cone, Denison and Kemp, THIS JOURNAL, **53**, 1278 (1931).

(4) Smyth and Hitchcock, *ibid.*, **55**, 1830 (1933).

(5) Kemp and Denison, *ibid.*, **55**, 251 (1933).

(6) Morgan, Yager and White, *ibid.* **55**, 2171 (1933).

(7) Yager and Morgan, *ibid.*, **57**, 2071 (1935).

(8) White and Morgan, *ibid.*, **57**, 2078 (1935).

(9) White and Morgan, *J. Chem. Phys.*, **5**, 655 (1937).

(10) See, *e. g.*, Debye, *Physik. Z.*, **36**, 100 (1935); *Chem. Rev.*, **19**, 171 (1936).

(11) Smyth and Hitchcock, THIS JOURNAL, **54**, 4631 (1932).

(12) For example, the lattice heat capacity calculated by Lord, Ahlberg and Andrews, *J. Chem. Phys.*, **5**, 649 (1937), for benzene approaches at room temperature the classical value of three translational and three rotational modes of harmonic motion for each molecule.

Preparation of Materials

The sources of compounds not prepared in these laboratories are indicated by the footnotes of the first column of Table I; the remainder of them were prepared as indicated by the references of the third and fifth columns. The thiocamphor prepared by Sen's method contained camphor as an impurity; 16.08% sulfur was found by analysis, as compared with a theoretical content of 19.05%. Among five samples sulfur content was found to decrease steadily with increasing melting point. The optical activity of *l*-camphor and *l*-borneol was checked with a polarimeter. Chlorocyclohexane, bromocyclohexane and camphoricimide were measured as received. Other materials obtained from outside sources were fractionally recrystallized or redistilled, several times when necessary. The purity of the samples measured is indicated in columns two to five of Table I by the comparison of their boiling and melting points with those of the literature. Where the melting point recorded in column four is below room temperature it designates the temperature at which the specimen was observed to solidify in the cell used for dielectric measurement, and is hence not very accurate. Sharp melting points and visible regularities of structure indicated that in the solid state these samples were crystalline rather than amorphous.

Experimental Methods

The equipment used in this work for measurement of the capacity, conductance and temperature of the condenser containing the test specimen, and for control of the temperature, was essentially that described by Morgan and Lowry.[13] The type of cell in which the dielectric properties of each of these compounds were measured is indicated in the last two columns of Table I. "A" specifies that grounded capacity measurements were made with a condenser consisting of three parallel plates of gold-plated brass, which was immersed in the liquid and, where the melting point was below room temperature, in the solid that was formed after sufficient cooling. This condenser is described and illustrated in more detail elsewhere.[9] "B" indicates that the cell illustrated in Fig. 1 was used; it was designed for use with small amounts of material and requires only 6 cc. The cell consists of two concentric gold-plated brass cylinders which are held in place with respect to each other by the shape of the glass container. There is a clearance of only about 0.08 mm. between brass and glass both inside and outside, allowing for differential thermal expansion. Leads consist of small gold-plated brass rods which are silver-soldered to the electrodes and which are rigid enough to permit their use for adjusting the electrodes into identical positions for successive measurements. Since only grounded capacity measurements can be made in this condenser and since the high potential electrode is in direct contact with the inner glass tube, the condenser was calibrated in place in the bath used for temperature control in subsequent measurements. The alterable capacity of this cell is 36.6 $\mu\mu$f, and was found to be reproducible to within about 3%. Although less accurate than a more rigid condenser, it was used for measurement of liquids or of solids freezing below room temperature when only small quantities were available.

(13) Morgan and Lowry, *J. Phys. Chem.*, **34**, 2385 (1930).

C indicates that rectangular sheets of the solid were pressed, using pressures as high as 14,000 lb./sq. in. (1000 atm.). These sheets measured 5.08 × 1.75 cm. and were about 1.2 mm. thick. Comparison of accurately measured densities with those calculated from the weight and dimensions of the pressed sheets indicated that not more than 4% of the volume of such sheets was occupied by voids; where the waxy high-temperature form of a compound existed at room temperature, the volume of voids was negligible. When the sheet was not waxy enough for the gold-plated brass facing plates used in the die to adhere strongly to it, tin-foil electrodes were affixed, using a very thin film of petrolatum as adhesive. These sheets were measured as previously described and illustrated.[9] Sheets of the tetramethylethylene halides sublimed so rapidly at higher temperatures that circular electrodes with a guard ring were provided in an arrangement otherwise similar in principle to the above. When direct capacitance measurements on a pressed disk were thus made, evaporation of that part of the sample covered by the guard ring had no effect on the observed dielectric constant. The use of this method is indicated by D in Table I.

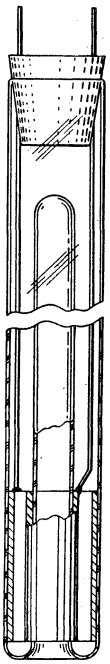


Fig. 1.—Condenser for measurement of small quantities of liquid.

Experimental Results

A summary of the experimental results is included in Table I, in which the compounds are listed more or less in the order of the complexity of their molecular structures. Under t_T° is given the temperature range in which the greater part of the increase of dielectric constant from its low-temperature to its high-temperature value occurs; such an abrupt change of dielectric constant will be designated in this paper as a transition, although the heating curves required to establish isothermal absorption of heat have not been run.[14] The word "none" indicates that no such transition was observed in the solid state. Columns seven and eight, under $\Delta\epsilon_T$, list the dielectric constants observed at the lower and upper limits, respectively, of the transition temperature range t_T°. These values were observed at a frequency of 30 or 100 kc. except in cyclopentanol, where because of anomalous dispersion the 1 kc. value is more representative of the static polarizability due to the rotational motion of the dipoles. Under $\Delta\epsilon_{MP}$ columns nine and ten of Table I record the 100-kc. dielectric constant at the melting point for

(14) Isothermal absorption of heat and abrupt change of density have been observed at the temperature of the discontinuity of dielectric constant in a number of similar crystals (see references 3–9).

TABLE I

	B. p., °C. Obsd.	B. p., °C. Lit.	M. p., °C. Obsd.	M. p., °C. Lit.	$t_T°$	$\Delta\epsilon_T$ From	$\Delta\epsilon_T$ To	$\Delta\epsilon_{MP}$ Solid	$\Delta\epsilon_{MP}$ Liquid	Method Solid	Method Liquid
Tetramethylethylene chloride[a]	...	...	159 to 160	159 to 160[e]	−10 to +4	3.3	4.7	...	...	D	..
Tetramethylethylene bromide[a]	...	...	...	decomp.[e]	+75 to 110	2.9	3.9	...	...	D	..
Cyclopentanol	140.1	141[f,i]	−20	...	−72 to −70	2.87	34.2	27.1	25.5	A, B	A, B
1-Methylcyclopentanol-1	...	...	+34.6	35 to 37[i]	None	..	...	3.06	6.97	A	A
Cyclopentanone[b]	130.7–130.8	130.6[f]	−51	...	None	..	...	2.84	16.3	A	A
1,3-Cyclohexadiene	80.5	80.5[f,k]	−89	−98[f]	−114 to −109	2.66	2.75	2.68	2.66	A	A
Cyclohexene[b]	82.1–82.2	83[f]	−105	−103.7[f]	...	..	...	2.52	2.60	A	A
Methylcyclohexane[b]	100.4	100.8[f]	−129	−126.4[f]	None	..	...	2.28	2.26	A	A
Chlorocyclohexane[b]	...	...	−47	−43.9[g]	−68 to −60[v]	3.0	10.0	10.5	10.9	A	A
l-α-Menthol[b]	...	...	+42.2	+42.5[f]	None	..	...	2.48	3.95	A	A
Cyclohexanone[b]	155.7	155.7[h]	−40	−45[g], −26[h]	−62 to −53	5.1	21.6	20.2	19.9	A	A
2-Methylcyclohexanone-1[b]	164.8–165.2	164.8–165.0[l]	−20 to −15	...	None	..	...	3.66	16.4	A	A
3-Methylcyclohexanone-1[b]	169.3–169.8	168.6–168.9[l]	−89	...	None	..	...	3.53	18.2	A	A
4-Methylcyclohexanone-1[b]	171.3–171.6	171.4–171.5[l]	−41	...	None	..	...	3.29	15.7	A	A
1,4-Cyclohexadione	...	...	+78	+78[m]	+48 to 51	2.81	3.13	...	4.40	C	A
Cyclohexanone oxime[b]	...	...	+89	+89.5 to 90.5[e]	None	..	...	2.74	3.04	A	A
Cyclohexyl fluoroform	107.0	107.0[f]	−85	<−78[n]	−109 to −106	2.86	8.95	9.44	11.9	A	A
α-Hexachlorocyclohexane[b]	...	...	+156	+157[f]	None	..	...	2.91	4.77	A	A
Bromocyclohexane[b]	...	...	−70 to −65	...	None	..	...	2.82	11.0	A	A
Cyclohexylamine[a]	134.1–134.3	134[e]	−21	...	None	..	...	2.63	5.37	A	A
Cyclohexane carboxylic acid[b]	...	...	+31.2	+31[f]	None	..	...	2.50	2.67	B	B
Cyclohexyl adipate[b]	...	...	+35.2 to 35.5	...	None	..	...	2.81	4.84	A	A
o-Cyclohexylphenol[b]	...	...	+54.5 to 55	...	None	..	...	3.09	3.97	A	A
p-Cyclohexylphenol[b]	...	...	+130.6	+132 to 133	None	..	...	2.62	4.42	A	A
d-Camphene[b]	...	...	+39.5 to 41.5	+42.7[f]	−124 to −118	2.14	2.70	2.36	2.33	A	A
l-Camphor	...	...	+180.0	+178.6[e]	−31 to −30	2.91	12.2	...	...	C	..
l-Borneol[c]	...	...	...	...	+71 to 75	2.90	3.54	...	...	C	..
dl-2,3-Camphanedione	...	...	+203	+198 to 202[o]	+45 to 55	2.69	17.7	12.4	16.3	C	A
3-Oxymethylene-*d*-camphor	...	...	74.9 to 75.1	+80 to 81[p]	None	..	...	3.02	13.7	C	B
dl-Bornyl bromide	...	...	+94.6 to 94.8	+91[e,w]	−68 to −61	3.91	9.16	4.91	5.21	C	A
α-Chloro-α′-nitro-*dl*-camphor	...	...	+95.8	+95[e,w]	+45 to 76	5.0	34	31.5	27.7	C	A
3-Cyanocamphor	...	...	+129.3 to 129.5	+127 to 128[q]	+110 to 116	4.0	25	(23)	23	B, C	B
Camphoricimide[d]	...	...	+249	...	+92 to 94	2.91	5.46	5.7	5.5	C	A
dl-Thiocamphor	...	...	138.6 to 139.0	+145[r]	−30 to −10	4.6	11.0	8.8	(8.5)	C	B
3-Nitro-*d*-camphor	...	...	+102.3 to 102.9	+102[s]	+40 to 49	3.2	18.2	...	...	C	..
3-Nitro-*dl*-camphor	...	...	+102.1 to 102.3	+102[s,w]	?	..	21.3	...	...	C	..
3,x-Dichloro-*dl*-camphor	...	...	+71.5 to 71.8	+70 to 77[e,t,w]	?	..	18.0	16.6	14.3	C	A
dl-Thioborneol	...	...	+116 to 117	+120[u]	?	..	4.58	...	...	C	..

[a] Supplied by Fraenkel–Landau. [b] Supplied by Eastman Kodak Co. [c] Supplied by the British Drug Houses. [d] Supplied by Hercules Powder Co. [e] "Beilstein," 4th ed. [f] "International Critical Tables." [g] Handbook of Chemistry and Physics, 12th ed. [h] Supplement Beilstein, 4th ed. [i] Nenitzescu and Ionescu, *C. A.*, **27**, 1329 (1933). [j] Zelinsky and Namjetkin, *Ber.*, **35**, 2683 (1902). [k] "Org. Syn.," Vol. XII, p. 26; Crossley, *J. Chem. Soc.*, **85**, 1416 (1904). [l] Signaigo and Kramer, THIS JOURNAL, **55**, 3326 (1933). [m] Herman, *Ber.*, **16**, 33 (1883). [n] Swarts, *Bull. acad. roy. Belg.*, 399 (1920). [o] Allard, *C. A.*, **28**, 7255 (1934). [p] Bishop, Claisen, and Sinclair, *Ann.*, **281**, 1414 (1894). [q] Lapworth, *J. Chem. Soc.*, **77**, 1058 (1900). [r] Sen, *J. Indian Chem. Soc.*, **12**, 647 (1935). [s] Lowry, *J. Chem. Soc.*, **107**, 1038 (1915). [t] Cazeneuve, *Compt. rend.*, **94**, 731 (1882). [u] Sen, *J. Indian Chem. Soc.*, **12**, 651 (1935). [v] With temperature falling. [w] For an optical isomer.

the solid and liquid states, respectively, as measured in the immediate neighborhood of this temperature, or as determined by extrapolation in cases such as those illustrated in Fig. 11.

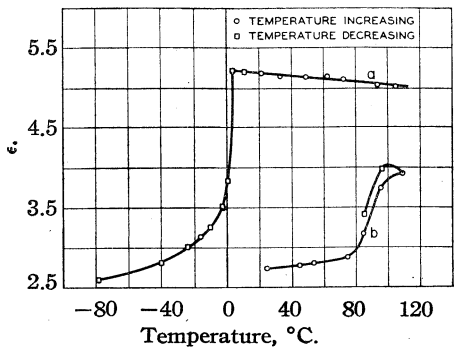


Fig. 2.—Dielectric constant of (a) tetramethylethylene chloride and (b) tetramethylethylene bromide at 100 kc.

Figures 2–13 provide a more complete record of those measurements which constitute evidence that molecular rotation occurs in the crystal. A considerable frequency range, usually 1–100 kc., was covered in this work. Only one measurement is recorded for each temperature except where anomalous dispersion appears, or the spurious effects of electrode polarization capacity are found at low frequency. Total a. c. conductivity also was measured but is reported only where anomalous dispersion and the accompanying dielectric loss are found. The observed conductivities are then used to calculate loss in terms of imaginary dielectric constant ϵ'', which is equal to the product of the ordinary dielectric constant ϵ' by the tangent of the loss angle.

Experimental points in the figures represent

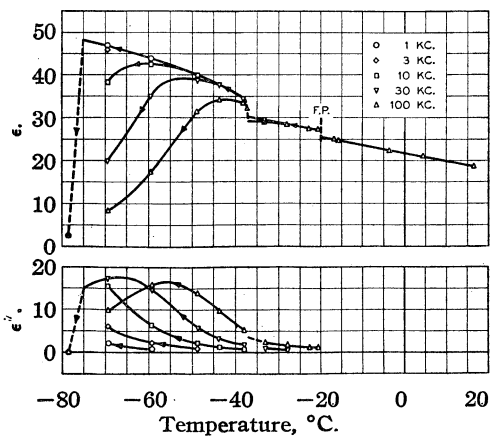


Fig. 3.—Dielectric properties of cyclopentanol as functions of declining temperature.

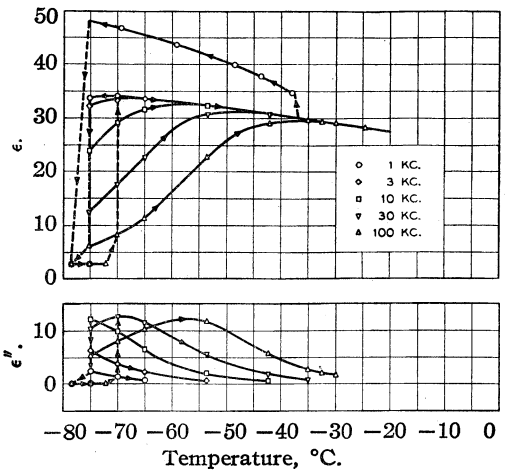


Fig. 4.—Dielectric properties of cyclopentanol as functions of rising temperature.

temperature equilibrium in the sense that each temperature was held constant within 0.1° until the dielectric properties of the sample ceased to change with time. Apparently discontinuous changes of dielectric constant are indicated in the figures by broken lines whose horizontal components measure the interval between successive constant temperatures of measurement. More exact determination of such temperatures of transition is best made with cooling and heating curves.

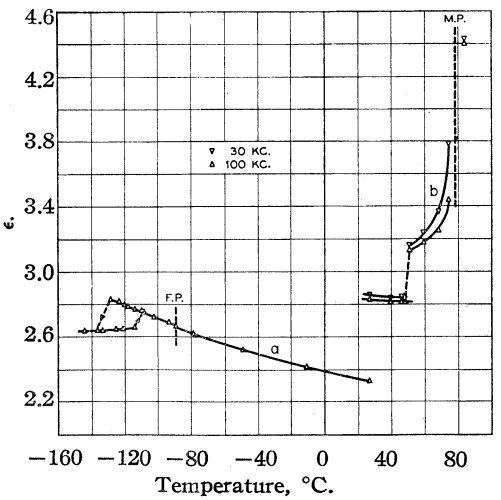


Fig. 5.—Dielectric constant of (a) 1,3-cyclohexadiene and (b) 1,4-cyclohexadione.

Lack of space forbids detailed discussion of the individual experiments except where the figures are not adequately self-explanatory. Inspection of these figures shows, however, that in most cases where measurements of the liquid were obtained, any discontinuity of the dielectric constant curve

at the freezing point is so small as to indicate that the polar molecules are able to rotate about as freely in the crystalline as in the liquid state. Only in 1,4-cyclohexadione (Fig. 5b) and cyclohexyl fluoroform (Fig. 7b) is there an extensive drop of dielectric constant upon freezing; any molecular rotation in these crystals must be considerably restricted as compared with the corresponding liquids.

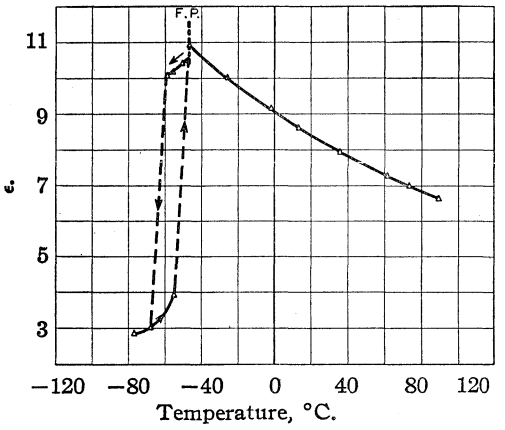


Fig. 6.—Dielectric constant of chlorocyclohexane.

When solid cyclopentanol is cooled through a sequence of constant temperatures, a transition occurs between −36.7 and −37.4°. After cooling to −40.4°, the same transition is observed with rising temperature. The results of only one run are represented in Figs. 3 and 4 by experimental points because the absolute values observed after successive solidifications differed by 5%, due probably to variability in the formation of voids. The data obtained in other runs were used to define the temperature range of each of the transitions more accurately than indicated by the points of Figs. 3 and 4. Immediately below the transition at −37° the dielectric constant at frequencies lower than 30 kc. was found to have risen from about 30 to about 34, and $-d\epsilon/\epsilon dt°$ to have increased from 0.006 to 0.015. No change in the translucent, camphor-like appearance of the solid was visible. To assume that density increases at this transition does not explain the large increase in the negative temperature coefficient of dielectric constant nor the increase of its absolute value, as measured under circumstances where the total number of molecules between the plates of the condenser does not change.

Below −37° an anomalous dispersion involving all or nearly all of the rotational polarization affects dielectric measurements made at frequencies between 1 and 100 kc., as in the supercooled high-temperature form of cyclohexanol.[8] This is evidence that at these temperatures the frequency of rotational motion of the cyclopentanol molecules in the crystal ranges in the neighborhood of 10^6 c. p. s. At −75.2° the frequency of maximum loss is 11.5 kc. and the relaxation time τ calculated according to Debye[2] is 1.30×10^{-6} second.

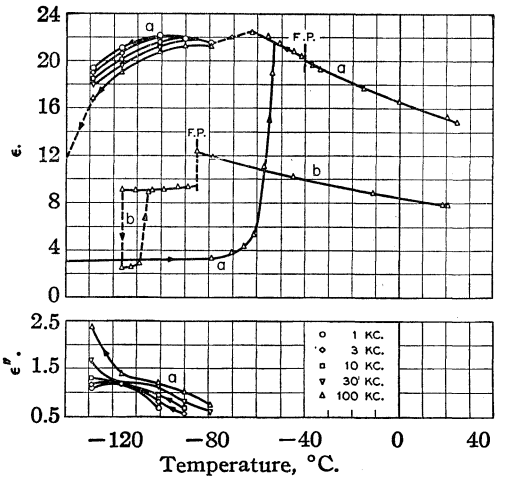


Fig. 7.—Dielectric properties of (a) cyclohexanone and (b) cyclohexyl fluoroform.

Between −75.2 and −78.5° the dielectric constant of cyclopentanol drops abruptly at all frequencies alike to about 2.7. Figure 4 shows that with increasing temperature the solid goes back to a form in which there is again rotational motion of the molecules, the transition occurring between −72 and −70°. At all frequencies, however, the values of ϵ' and ϵ'' are much lower than when −70° was approached from higher temperatures. Upon cooling immediately to −75.2° the transition was not reversed; a complete frequency run at this temperature showed the frequency of maximum loss to be 16 kc., yielding a relaxation time of 1.31×10^{-6} second, about the same as when ϵ' as observed at 1 kc. and −75.2° was 48 instead of 34. Further cooling again produced the transition to the non-rotational form of the solid between −75.2 and −78.5°. From this point temperature was increased regularly, until it became evident as in Fig. 4 that the dielectric constant curve is continuous with that originally observed above −37°, and that with temperature rising from below −75° there is no dielectric evidence of the transition at −37°.

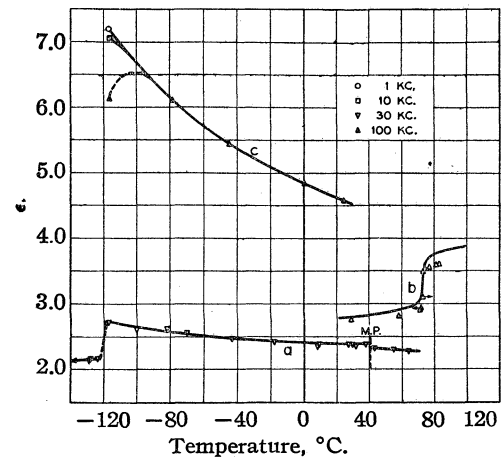


Fig. 8.—Dielectric constant of (a) *d*-camphene, (b) *l*-borneol and (c) *dl*-thioborneol.

l-Borneol and *l*-camphor were measured in order to compare their dielectric behavior with that of the corresponding dextrorotatory compounds. To this end the curves drawn in Figs. 8b and 9b are reproductions of those reported for the *d* compounds by Yager and Morgan,[7] while the points represent experimental values obtained from the *l* isomers. An arrow attached to an experimental point represents the direction of temperature change before and after its observation. The similarity of dielectric constant and transition temperature exhibited by the *d* and *l* forms of each of these two compounds shows as expected that the forces acting between molecules are of identical symmetry and magnitude in crystals of optically active isomers.

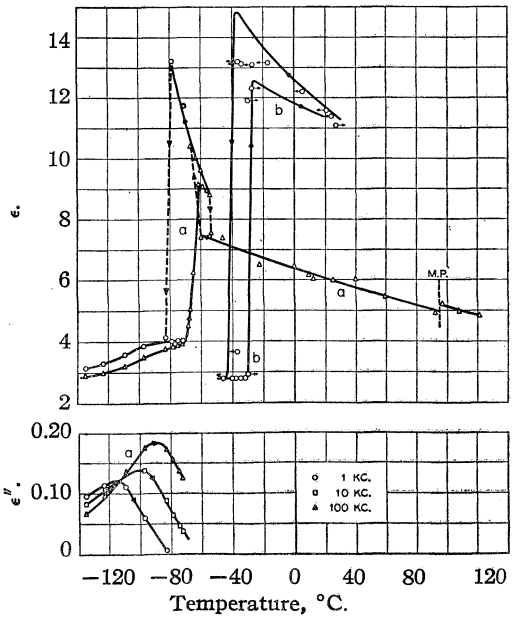


Fig. 9.—Dielectric properties of (a) *dl*-bornyl bromide and (b) *l*-camphor.

Since the behavior of *dl*-bornyl bromide is very complicated, the temperature range in which the transitions occur is illustrated in Fig. 10 on a larger scale than in Fig. 9a. With falling temperature the first transition, from what will be called Phase I to Phase II, occurred between −60.1 and −66.5°. Dielectric constant and its negative temperature coefficient increased greatly, much as in cyclopentanol. When the temperature was increased before converting to the non-rotating form, hysteresis appeared and the transition from

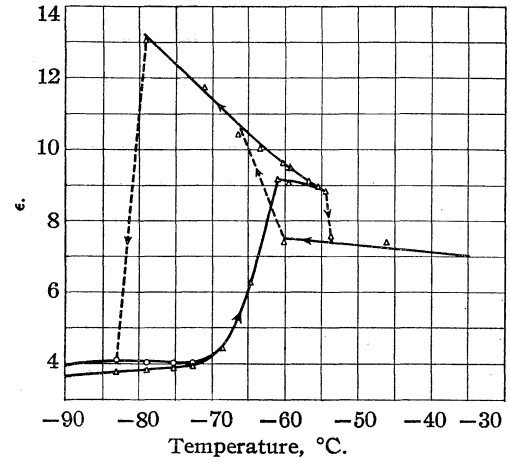


Fig. 10.—Dielectric constant of *dl*-bornyl bromide in region of transitions.

Phase II to Phase I was found between −54.5 and −53.7°. Upon cooling again, dielectric constant fell on the curve of Phase II as indicated by points at −71.1 and −79.1°. The transformation to Phase III was characterized by an abrupt fall of dielectric constant from 13 to about 4 between −79.1 and −83.0°. Evidence of a residual molecular rotation in Phase III was found in the high value of its dielectric constant and the anomalous dispersion which caused the high-frequency dielectric constant to drop to 2.9 at −135°. After reversing the direction of temperature change, dielectric constant rose rapidly but with a measurable temperature coefficient between −70 and −61°. The value to which it rose was 9.16, showing that this transition was from Phase III to Phase II rather than to Phase I

The failure of the dielectric constant of *dl*-thiocamphor to return to its original value with rising temperature, as shown in Fig. 11a, is not a

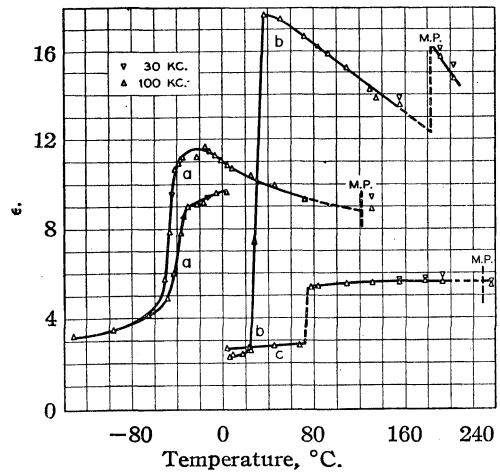


Fig. 11.—Dielectric constant of (a) *dl*-thiocamphor, (b) *dl*-2,3-camphanedione and (c) camphoric imide.

real effect. It was found that the waxy sheets originally pressed had been shattered by the embrittlement and the presumably large density change which occurred when the sample went over to the low-temperature form, leaving voids which were not eliminated when the transition was reversed, because of the lack of constraint along the edge of the sheets. When the specimens which had been through this temperature cycle were pressed again, dielectric constant returned to its original value of 11.0.

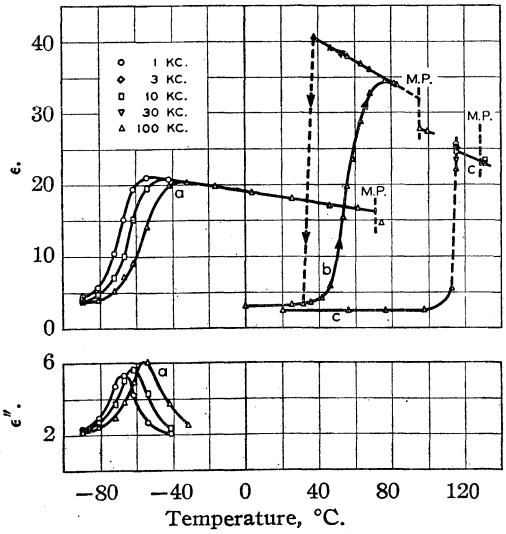


Fig. 12.—Dielectric properties of (a) 3,x-dichloro-*dl*-camphor, (b) α-chloro-α'-nitro-*dl*-camphor and (c) 3-cyanocamphor.

The dielectric constant of 3-nitro-*dl*-camphor at room temperature is not very different from that of the 3-nitro-*d*-camphor in the high-temperature form, as may be seen in Fig. 13. Upon cooling

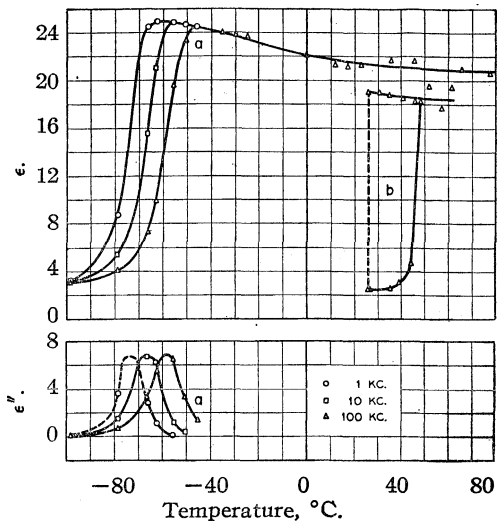


Fig. 13.—Dielectric properties of (a) 3-nitro-*dl*-camphor and (b) 3-nitro-*d*-camphor.

to low temperature there was no transition at which dielectric constant fell at all frequencies alike to a low value indicative of no molecular rotation. Anomalous dispersion appeared instead, eliminating at −98.7° practically all effect of molecular rotation on the dielectric constant at frequencies as low as 1 kc. This presumably means only that the relaxation time of the rotational motion of the molecules is much longer than 10^{-3} second at this temperature. Two other crystalline compounds in which dielectric constant similarly falls off with anomalous dispersion rather than at a transition are 3,x-dichloro-*dl*-camphor (Fig. 12a) and *dl*-thioborneol (Fig. 8c).

Discussion of Results

Taken all together these measurements and those previously reported[6,7,8,9] constitute convincing evidence that extensive rotational motion of large organic molecules is much more commonly found in crystals than has been suspected. It is also evident that this ability of the molecule to rotate in the crystal lattice is much more frequently found among the derivatives of cyclic polymethylenes than among the generality of organic compounds, whose polarizations have normally been found to be so low in the solid state as to be ascribed to distortional effects only. Inspection of Table I indicates that among the

cyclic polymethylene derivatives the attachment of a large substituent to the ring inhibits molecular rotation, as in cyclohexyl adipate, the cyclohexylphenols, and cyclohexane carboxylic acid. Even the substitution of one methyl group for a hydrogen atom has the same effect in such cases as the methylcyclohexanones and 1-methylcyclopentanol-1. There is no satisfactory correlation of ability to rotate or of transition temperature with either the dipole moment or the moment of inertia of the molecule.

Among the compounds of Table I molecular rotation in the crystal is much more noticeably correlated with the gross physical properties of the crystal than with the chemical structure of the molecule. Crystals in which there is no molecular rotation at room temperature are relatively hard and brittle; those in which the molecules rotate at room temperature are soft and waxy. When one of these compounds is solidified from the melt in a test-tube, the formation of a semi-transparent mass having an appearance similar to that of camphor is characteristic of molecular rotation; the transition to the form in which there is no such rotation is marked by the rise of opacity, possibly because of shattering due to change of density. Perhaps the most significant physical characteristic of the crystals in which we have found molecular rotation is their low heat of fusion, as roughly observed by the rapidity with which a large sample is able to freeze at a temperature only a few degrees below its melting point. Since the crystal does not "freeze" with respect to rotational motion until the transition temperature is reached, a low heat of fusion is to be expected, as has been pointed out by Clusius.[15]

Pirsch[16] reports that molecules of approximately spherical shape are found to produce crystals of much lower heats of fusion than molecules of roughly circular or linear shape. He suggests that this may result from the small ratio of surface to volume in a sphere, which means that the effectiveness of interatomic forces in producing intermolecular forces is low, relative to the number of atoms, in molecules of roughly spherical shape. Among such compounds cited by Pirsch for their large cryoscopic constants and correspondingly low heats of fusion are camphorquinone (2,3-camphanedione), camphor, borneol, bornyl chloride, bornyl bromide, and camphene, all of which we have found to exhibit molecular rotation immediately below the melting point. In these cases at least Pirsch's explanation of low heat of fusion may be modified by saying that at the melting point the crystal freezes with respect to translational motion of the molecules only; the intermolecular forces are so small, or, at least, so symmetrical, that the crystal does not "freeze" with respect to rotational motion until the transition temperature is reached. Hence the change of entropy which ordinarily would occur at the freezing point alone is divided between the freezing point and the transition temperature.

The other camphane derivatives and the tetramethylethylene halides in which we have observed molecular rotation are spherical in the sense in which Pirsch uses the term. However, cyclopentanol, ethylene cyanide and the many cyclohexane derivatives which exhibit a similar freedom of molecular rotation in the crystal, are not even approximately spherical. Pirsch[17] has noted that certain cyclohexane and cyclopentane derivatives exhibit much lower heats of fusion than do other circular compounds. The heat of fusion of 406 calories per mole observed in cyclohexanol[18] and that of 940 calories per mole reported for ethylene cyanide[19] fall on the curve of heat of fusion against temperature which Pirsch characterizes as that of spherical molecules.[19] On the other hand, such a spherical molecule as *t*-butyl alcohol shows no dielectric evidence of molecular rotation in the crystal,[20] while its heat of fusion of about 1600 cal./mole[19] is fully twice as high as that indicated by Pirsch's curve for spherical molecules without rings. Pirsch cites other spherical molecules of anomalously large heat of fusion.[17] It appears likely that among these non-aromatic compounds very low heat of fusion is more immediately associated with the ability of a molecule to rotate in the crystal lattice than with its spherical shape. For rotation in the crystal to be possible, however, a certain degree of either spherical or circular geometrical symmetry obviously is required of the molecule, and its center of figure should not be displaced too far from its center of gravity. The approximately spherical symmetry of the molecules of the cam-

(15) Clusius, *Z. Elektrochem.*, **39**, 598 (1933).
(16) Pirsch, *Angew. Chem.*, **51**, 73 (1938).
(17) Reference 16, footnote 14.
(18) Kelley, THIS JOURNAL, **51**, 1400 (1929).
(19) "International Critical Tables," McGraw-Hill Book Co., Inc., New York, N. Y.
(20) Smyth and McNeight, THIS JOURNAL, **58**, 1597 (1936).

phane derivatives and the tetramethylethylene halides indicates that they rotate about all three axes in the solid state. It has been suggested that internal motion of atoms unrestrained by valence forces may produce in ethylene cyanide[9] and the cyclohexane derivatives[8] sufficient time-average molecular symmetry to account for their rotation about three Cartesian axes in the crystal. Since this suggestion was made, there has been an accumulation of evidence that internal motion about the single carbon-to-carbon bond is not as free as was then supposed,[21] although no other explanation of the dipole moments of ethylene chloride[22] and ethylene cyanide[23] has yet appeared. Finbak and Hassel interpret their X-ray measurements of solid cyclohexane derivatives in terms of molecular rotation about only one axis, although the nearest distance of approach of methylene groups of neighboring molecules thus calculated is anomalously large.[24]

(21) See, *e. g.*, Kistiakowsky and Nazmi, *J. Chem. Phys.*, **6**, 18 (1938).

(22) See, *e. g.*, Lennard-Jones and Pike, *Trans. Faraday Soc.*, **30**, 830 (1934).

(23) Williams, *Z. physik. Chem.*, **138A**, 75 (1928).

The authors are indebted to Dr. S. O. Morgan for his helpful advice in connection with this work; to Dr. B. S. Biggs for the preparation of cyclohexyl fluoroform; and to the Hercules Powder Company for the sample of camphoricimide which they kindly supplied us.

Summary

Dielectric evidence of the rotation of polar molecules has been observed in the crystals of two derivatives of ethane, one derivative of cyclopentane, five derivatives of cyclohexane, and thirteen derivatives of camphane. In most of these solids dielectric constant rises abruptly at a transition, as temperature is increased, to a value characteristic of polar liquids. A relatively symmetrical gravimetric and volumetric distribution of atoms around the center of gravity of the molecule evidently facilitates its rotation in the crystal.

(24) Finbak and Hassel, *Z. physik. Chem.*, **40B**, 391 (1938).

NEW YORK, N. Y. RECEIVED AUGUST 24, 1939

[CONTRIBUTION FROM THE BELL TELEPHONE LABORATORIES, NEW YORK, N. Y.]

Dielectric Evidence of Molecular Rotation in the Crystals of Certain Benzene Derivatives*

BY ADDISON H. WHITE, B. S. BIGGS AND S. O. MORGAN

This paper presents dielectric measurements which show that molecular rotation may occur in the crystalline form of benzene derivatives as well as in aliphatic compounds, provided certain requirements of symmetry are met. The use of dielectric constant data as evidence of the existence of molecular rotation[1] is based on the fact, now well established, that a dielectric constant higher than the refraction value (that equal to the square of the optical refractive index) in a homogeneous, non-conducting organic material arises from the orientation or rotational motion of polar molecules or groups. Since the refractive index for organic compounds rarely exceeds 1.7, the excess of dielectric constant over about 3 is a good measure of the extent to which orientation of dipoles is contributing thereto. There is little tendency to question such a statement as it applies to the dielectric constant of organic liquids whose molecules have been shown by dipole moment measurements to be polar. It has become evident from the work of Smyth and his associates and from papers from this Laboratory that the same view can be carried over to organic solids having large molecules.

Baker and Smyth have presented evidence of rotation in rod-like molecules,[2] in comparatively spherical molecules,[3] and in intermediate "pear-shaped" molecules.[3] The earlier work from this Laboratory on camphor compounds[4,5] and ethane derivatives[6] has been extended to include other members of these series. The work reported in the present paper represents an extension of the ideas of the importance of symmetry gained from our earlier work to a new class of compounds, substi-

* Published with the financial assistance of an anonymous donor.

(1) The term "molecular rotation" will be used in the sense in which it has been generally adopted to explain the dielectric behavior of polar liquids.

(2) Baker and Smyth, THIS JOURNAL, **60**, 1229 (1938).

(3) Baker and Smyth, *ibid.*, **61**, 2063, 2798 (1939).

(4) Yager and Morgan, *ibid.*, **57**, 2071 (1935).

(5) White and Morgan, *ibid.*, **57**, 2078 (1935).

(6) White and Morgan, *J. Chem. Phys.*, **5**, 655 (1937).

tuted benzenes, which are geometrically symmetrical about one axis, but electrically assymmetrical.

Experimental Methods

The apparatus and methods employed were similar to those described elsewhere.[7,8] Tin-foil electrodes were affixed to pressed sheets of each compound, using a very thin film of petrolatum as adhesive. Measurements of such solid sheets and of the corresponding liquids were made in the cells of Fig. 2 and Fig. 1, respectively, of a previous paper.[6] The density of the sheets at room temperature was determined roughly from their weights and dimensions. As an example of the accuracy of this procedure, the densities of hexamethylbenzene and hexachlorobenzene thus measured are 1.05 and 1.96, respectively; the corresponding densities calculated from X-ray data are 1.035 and 2.044.[9] Although such density measurements as the former are often in error because of voids in the sample, they determine the actual number of molecules per cc. of the specimen upon which dielectric measurements are made and are thus more appropriate than the true density for the calculation of molar polarization.

Preparation of Materials.—The substances marked E. K. in Table I were obtained from the Eastman Kodak Company. The liquids were fractionally distilled and a middle fraction taken for measurement. The solids were recrystallized from a non-polar solvent (usually petroleum ether, 30–60° range) before use. The other compounds were all prepared in this Laboratory. All are pure materials with the exception of the trichloro-*m*-xylene and trichloro-*o*-xylene, which were distillation fractions from chlorination products obtained by direct chlorination of the respective hydrocarbons.

3,4,5-Trichloro-*o*-xylene was obtained by chlorination of *o*-xylene and fractionation of the product. Of the two possible trichloro-*o*-xylenes the 3,4,6- melts at 48° and the 3,4,5- at 96°. The fraction boiling at 269–270° goes completely solid on being cooled and melts at 94–96°. It is therefore rather pure 3,4,5-trichloro-*o*-xylene.

The trichloro-*m*-xylene studied was that obtained by fractionally distilling the product of chlorination of *m*-xylene. The fraction boiling between 250 and 260° was recrystallized from alcohol and then from cold petroleum ether. The compound separates in long, glistening waxy needles melting at 95°.

3-Nitro-4,5-dichloro-*o*-xylene and 5-nitro-3,4-dichloro-*o*-xylene were prepared from the corresponding dichloro-*o*-xylenes by the method of Hinkel.[10] The 4,5-dichloro compound could not be obtained completely free of isomers and the resulting nitro compound melted at 82° rather than at 78°, its recorded melting point. This 5-nitro compound probably contained a small amount of the higher melting 3-nitro-4,5-dichloro-*o*-xylene in solid solution.

Pentachloroethylbenzene was prepared by chlorination of ethylbenzene in carbon tetrachloride solution with antimony pentachloride as catalyst. It was fractionally distilled, the 300° fraction being recrystallized from alcohol several times and finally crystallized from heptane. The melting point recorded in Beilstein is in error. The value consistently obtained here was 56° and this is in agreement with that reported by E. I. du Pont de Nemours & Company.[11] Because of the wide discrepancy between the recorded melting points the material was analyzed.

Anal. Calcd. for $C_8H_5Cl_5$: C, 34.53; H, 1.78. Found: C, 34.28; H, 1.87.

Pentaethylacetophenone is apparently a new compound. It was prepared from pentaethylbenzene and acetyl chloride by the Friedel–Crafts reaction, heptane being used as the reaction medium. The aluminum chloride addition compound was decomposed in the usual manner and sufficient benzene was added to keep the crystalline product in solution. The benzene solution was washed with dilute hydrochloric acid, with sodium carbonate solution, and finally with water. The solvent was then allowed to evaporate from an open dish. The crystalline residue was recrystallized twice from alcohol and finally from heptane. It crystallizes in thick, colorless needles which melt at 141°.

Anal. Calcd. for $C_{18}H_{28}O$: C, 83.00; H, 10.84. Found: C, 83.15; H, 10.74.

Pentamethylnitrobenzene and *o*-dinitrotetramethylbenzene were prepared by the methods of Smith and Taylor, and Smith and Harris, respectively.[12,13]

Experimental Results

A summary of the dielectric properties of some of the benzene derivatives which were measured is provided in Table I. A (+) in the third column indicates that rotation of the molecule is observed in the crystalline solid and a (−) that it is not. The last column gives data on the circumstances attending the cessation of molecular rotation, *i. e.*, whether it ceases at the melting point (m. p.), at a transition point (t. p.) or with anomalous dispersion (a. d.).[14] The measurements on compounds which show evidence of molecular rotation in the solid are represented in Figs. 1 to 13. When anomalous dispersion appeared measurements were made at the frequencies of 1, 3, 10, 30, 100 kc. The dielectric loss in regions of anomalous dispersion is represented in terms of the imaginary part ϵ'' of the complex dielectric constant,[15] which is equal to the product of real dielectric constant ϵ by the tangent of the loss angle. The generally negligible d. c. conductivity was not subtracted from the total a. c. conductivity in calculating ϵ''.

(7) Morgan and Lowry, *J. Phys. Chem.*, **34**, 2385 (1930).

(8) White and Morgan, *J. Chem. Phys.*, **5**, 655 (1937).

(9) Lonsdale, *Proc. Roy. Soc.* (London), **123**, 494 (1929); **133**, 536 (1931).

(10) Hinkel, Ayling and Bevan, *J. Chem. Soc.*, 1874 (1928).

(11) French Patent 814,479.

(12) Smith and Taylor, THIS JOURNAL, **57**, 2400 (1935).

(13) Smith and Harris, *ibid.*, **57**, 1289 (1935).

(14) The temperature given in connection with those materials having anomalous dispersion is that at which the relaxation time τ is 10^{-6} second.

(15) Debye, "Polar Molecules," The Chemical Catalog Co., New York, N. Y., 1929, pp. 92–94.

Discussion of Results

The data supply two kinds of evidence of molecular rotation in the crystal: (1) the dielectric constant of the solid behaves like that of the corresponding liquid, and (2) among these solids, ϵ may be correlated with dipole moment of the molecule.

The figures show that with one exception the dielectric constant of the solid at the highest temperature measured is higher than that of the liquid in those cases where the latter has been observed. As among non-aromatic compounds,[4,5,6] this is taken to be evidence that the molecules rotate with much the same freedom in the solid as in the liquid.

Since no determination of the corresponding dipole moments has been found in literature, the fifth column of Table I lists values estimated by vectorial addition for some of these compounds, assuming the moment of the methyl radical to be $+0.4\ D$ and of the chlorine atom $-1.5\ D$.[16] In 3,4,5-trichloro-*o*-xylene the presence of an unsubstituted hydrogen atom probably leads to a considerably lower dipole moment than that estimated as above. The dielectric constant of 1,2,3-trimethyl-4,5,6-trichlorobenzene will be shown below to suffer an unusually large reduction due probably to intermolecular action. Otherwise the correlation between dielectric constant and calculated dipole moment is good in spite of the tendency of density and intermolecular action to mask it. Since a permanent dipole cannot affect the dielectric constant except through rotational motion, this correlation is convincing evidence that the molecules of all of these solids engage in such motion.

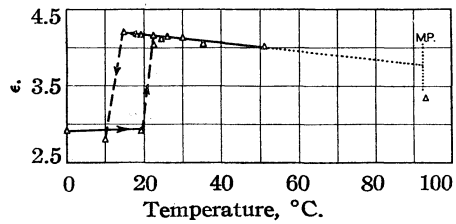


Fig. 1.—Dielectric constant of trichloro-*m*-xylene at 100 kc.

The abrupt rise of ϵ with temperature between 19 and 22° exhibited in Fig. 1 by trichloro-*m*-xylene is typical of a transition marking the onset of molecular rotation. As among the non-aromatic transition compounds, the solid is brittle below the transition temperature and quite waxy above it. Above 50° the specimen sheets became so waxy as to deform in the condenser, and hence could not be measured accurately. Extrapolation of the observed curve to the melting point indicates that ϵ is at least as high after solidification as before and hence that molecular rotation is about as extensive in the solid as in the liquid.

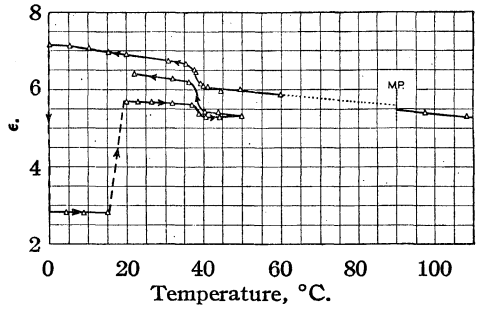


Fig. 2.—Dielectric constant of 3,4,5-trichloro-*o*-xylene at 100 kc.

Figure 2 portrays the complicated behavior of 3,4,5-trichloro-*o*-xylene. Waxiness again prevented measurement of sheets above 60°, but extrapolation indicates that ϵ does not change much at the freezing point and hence that the molecules of the crystal are rotating. Upon cooling through a declining sequence of constant temperatures, a transition appears between 40 and 36°, at which ϵ rises by about 0.5. With further cooling the transition to the brittle non-rotating form of the crystal had occurred after the sample had been left at −0.2° for one hour. The corresponding rise of ϵ with heating occurs between 15 and 20°; the value of ϵ at which the rise ceases is, however, much lower than expected. Figure 2 shows that after heating to 50°, ϵ returned at 25° much more nearly to its original value. This behavior may be explained by the formation of voids upon transformation to the low temperature form; such voids would be at least partially eliminated at temperatures where the material is very waxy.

The dielectric constant of 3.4 found in 5-nitro-3,4-dichloro-*o*-xylene at 0° as shown in Fig. 3 is enough higher than the refraction value to indicate some molecular rotation even at this low temperature. The dielectric constant rises progressively as temperature increases, particularly between 50 and 64°. Above the latter temperature the specimen became so waxy that no further measurement of sheets could be made. After measuring the liquid the material was therefore allowed to solidify with the condenser for liquids immersed in

(16) Smyth, "Dielectric Constant and Molecular Structure," Chem. Catalog Co., New York, N. Y., 1930, pp. 106–114.

it. Although such measurements are accurate only for temperatures near the melting point of the solid, the essential continuity of the ϵ curves for liquid and solid indicates that the freedom of molecular rotation is approximately the same in the solid and liquid phases. In this condenser the reverse transition to the low temperature form had not occurred after the temperature of the sample had remained in the neighborhood of 30° for several days.

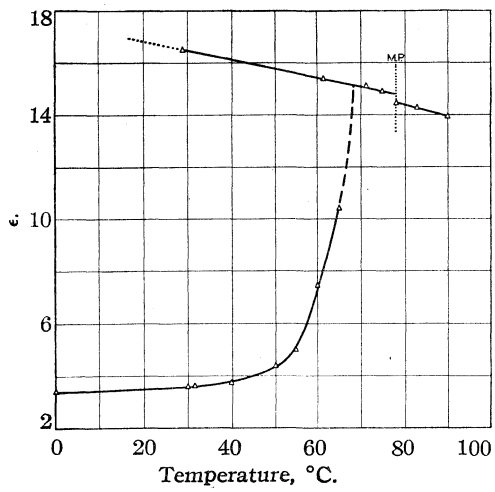


Fig. 3.—Dielectric constant of 5-nitro-3,4-dichloro-*o*-xylene at 100 kc.

The behavior of the isomer of this compound, 3-nitro-4,5-dichloro-*o*-xylene, is striking by contrast; at 111°, only six degrees below its melting point, ϵ is 3.02, which is evidence of no molecular rotation in the crystal. Its nitro group lies between chlorine and methyl radicals, while in the isomer the adjacent methyl is replaced with a hydrogen atom.

Figure 4 shows the gradual rise of the dielectric constant of *o*-dinitrotetramethylbenzene. The abrupt completion of this rise at 154° leaves the dielectric constant of the solid as extrapolated to the melting point much lower than that of the liquid. The behavior of this compound is consistent with the onset of a considerable degree of rotational motion between 100 and 154°, but it is evident that there is a further increase of such motion at the melting point. There was no great degree of waxiness to be observed above 154°; electrode polarization capacity prevented measurement at temperatures higher than 165°.

The behavior illustrated in Figs. 1 to 3 and to some extent in Fig. 4 is very similar to that usually observed in the many non-aromatic compounds

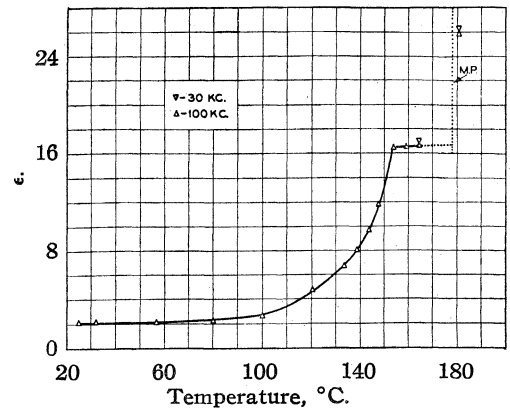


Fig. 4.—Dielectric constant of *o*-dinitrotetramethylbenzene at 30 and 100 kc.

in which there is molecular rotation below the freezing point. Dielectric constant rises more or less sharply at what appears to be a transition of the solid from one crystalline form to another. With cooling, the corresponding fall of ϵ often occurs at a lower temperature, producing a temperature hysteresis loop. The dielectric constant is independent of frequency through the range measured except for electrode polarization effects such as in Fig. 4 at 164°. There are no dielectric loss maxima. Above the transition temperature these materials are waxy; pressed sheets or solidified melts are very translucent. Below the transition temperature the same materials are brittle; the progress of the transformation to the low temperature form often may be observed as a growth of opaque regions in the translucent matrix of the high temperature form. There is evidence of a considerable change of density at such transitions. The molar volume estimated from the weight and dimensions of sheets of 3,4,5-trichloro-*o*-xylene pressed below the transition temperature was 136 cc.; when the sheets were pressed above the transition temperature, the molar volume was 143 cc. The actual difference in molar volume of the rotating and non-rotating forms is undoubtedly even greater since the apparent molar volume of the low temperature form is the more likely to be enhanced by voids in the sheet.

Although the evidence of molecular rotation below the freezing point as exhibited in Figs. 5 to 13 is equally good, the behavior of these solids is otherwise strikingly different from that of the compounds discussed above. Dielectric constant rises gradually from its low temperature value, and through a different temperature range for each frequency of measurement. There is no tem-

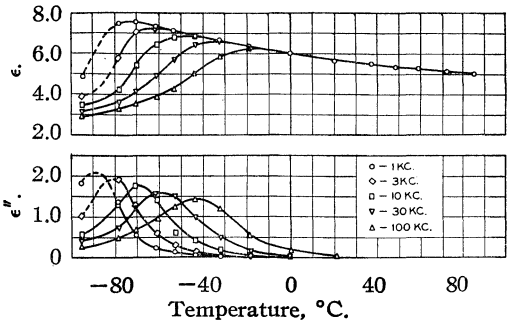


Fig. 5.—Dielectric properties of pentamethylchlorobenzene.

perature hysteresis. For any given frequency the rise of dielectric constant is accompanied by a maximum of dielectric loss as a function of temperature. This temperature behavior of ϵ and ϵ'' is, of course, typical of anomalous dispersion. Although the dielectric constants of these materials are high at room temperature, the solids are so brittle that they can be powdered easily, and the pressed sheets are opaque.

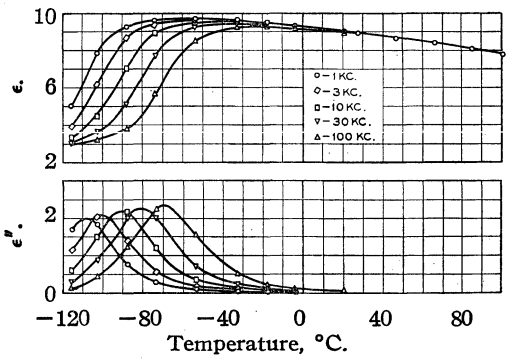


Fig. 6.—Dielectric properties of 1,2,3,4-tetramethyl-5,6-dichlorobenzene.

In Fig. 8 the static dielectric constant of 1,2,3-trimethyl-4,5,6-trichlorobenzene falls gradually over a temperature range of fully 120°, but the behavior of this compound does not otherwise resemble that of the solids which show sharp transitions; its pressed sheets are brittle, opaque, and their density is 1.48, agreeing with the value 1.49 in the isomer, 1,2,4-trimethyl-3,5,6-trichlorobenzene. Furthermore, these two isomers exhibit in Figs. 7 and 8 the same general temperature range of anomalous dispersion.

Several derivatives of camphane, 3-nitro-*dl*-camphor for example, have also exhibited no transition of the static dielectric constant,[17] the rotational polarization disappearing with anoma-

(17) White and Bishop. THIS JOURNAL, 62, 8 (1940).

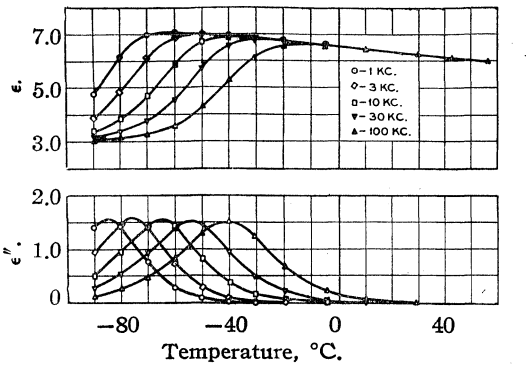


Fig. 7.—Dielectric properties of 1,2,4-trimethyl-3,5,6-trichlorobenzene as measured by W. A. Yager.

lous dispersion as temperature is reduced. In each such case, however, the waxiness and translucence of the material clearly indicate that it belongs to the same class as the high temperature forms of the transition dielectrics; there was some evidence that the failure of the transition to appear was due to the presence of solid solutions of optical isomers or to the existence of the high temperature form in a metastable state at temperatures below that of its presumed transition. If the compounds of Figs. 5 to 13 are existing in a metastable state at any temperature, not the slightest evidence of such behavior has been found.

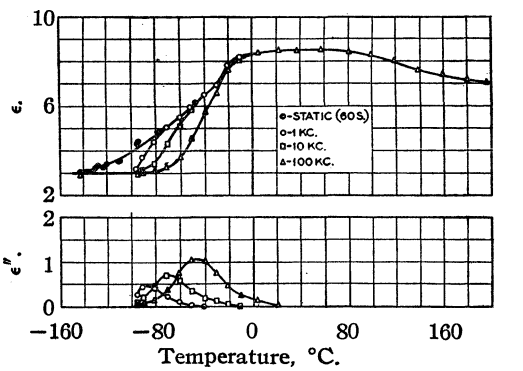


Fig. 8.—Dielectric properties of 1,2,3-trimethyl-4,5,6-trichlorobenzene.

In the following discussion the dielectric constant observed at frequencies so low that the rotational polarization is unaffected by anomalous dispersion will be designated the static dielectric constant ϵ_s. Figure 5 shows the curve of ϵ_s *vs.* $t°$ for pentamethylchlorobenzene to be concave upward, as in most polar liquids and in many solids in which dipole rotation is contributing to the dielectric constant. In 1,2,3,4-tetramethyl-5,6-

dichlorobenzene and 1,2,4-trimethyl-3,5,6-trichlorobenzene the corresponding curves are shown in Figs. 6 and 7 to be concave downward through the measured temperature range. In Fig. 8 this trend reaches its logical conclusion with the most unsymmetrical of the hexasubstituted methylchlorobenzenes when ϵ_s, after becoming almost independent of temperature from +70 to +20°, starts to decline with falling temperature. At −70° anomalous dispersion begins to affect the measurements at frequencies as low as 1 kc.; below this temperature ϵ was measured ballistically, using a charging time of sixty seconds.[18] The results are recorded in Fig. 8 with filled circles and probably represent ϵ_s down to about −100°, below which even the sixty-second ballistic measurements may be affected by anomalous dispersion.

The behavior of the maxima of curves of ϵ'' is consistent with the course of ϵ_s in the several isomers. This maximum should be proportional to the difference between the static and refraction values of the dielectric constant ($\epsilon_s - \epsilon_\infty$). Since ϵ_∞ changes only very slightly with temperature, the height of the maxima of ϵ'' should increase or decrease with ϵ_s. Figure 5 shows a pronounced increase of ϵ'' maxima with declining temperature, while Fig. 8 shows an even more striking decrease.

A reasonable explanation of the reduction of the rotational polarizability of a condensed phase below that of the corresponding gas is found in Debye's theory of hindered rotation, in which this reduction is ascribed to the restraining force of intermolecular action.[19] The sinusoidal potential function which he chooses to represent the effect of this interaction on a given molecule is inadequate for the explanation of the behavior of 1,2,3-trimethyl-4,5,6-trichlorobenzene, however, since it leads to a static polarizability which continually increases with declining temperature, and since without added assumptions it does not account for anomalous dispersion. These difficulties are eliminated by a model recently proposed,[20] in which the rotational motion is from one to another of two equilibrium orientations of different potential energy, with the frequency and temperature range of anomalous dispersion determined by the height of the intervening potential

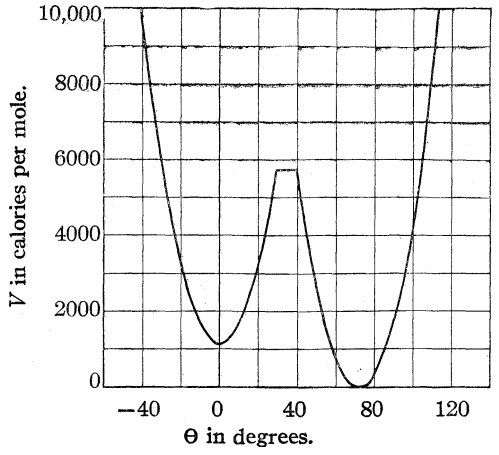


Fig. 9.—Potential function assumed for rotational motion of 1,2,3-trimethyl-4,5,6-trichlorobenzene molecule.

hill.[21,22] The potential function of Fig. 9 is an example showing how such an hypothesis can account for the observed dielectric properties of 1,2,3-trimethyl-4,5,6-trichlorobenzene. After inferring from the shape of this molecule that the rotation is about only one axis, the curve of Fig. 9 represents an assumed angular variation of the potential energy of interaction of a given molecule with all of its neighbors. This interaction is taken to be independent of both temperature and time. As actually drawn the equilibrium orientations are represented as minima in parabolic potential valleys. The polarization due to harmonic torsional vibration of the dipole in either of these valleys is independent of temperature and, at frequencies below about 10^{11} cps., of frequency. In a mass of randomly oriented microcrystals and with an estimated dipole of 3.8 *D*, the molar polarization due to this motion would amount to about 4.5 cc. At −195° (78°K.) practically all of a statistical assemblage of such molecules lie in the valley centered at $\theta = 72°$ and there is no additional contribution to the polarization due to rotational motion from one to the other of the valleys. As the temperature rises, statistical equilibrium permits increasing numbers of molecules to occupy the potential valley centered at 0°; application of an external field modifies this distribution and thus produces a static rotational polarization P_r in accordance with[20]

$$P_r = \frac{2\pi N_\mu^2 (1 - \cos \beta)}{9kT \cosh^2 (E/2kT)} \qquad (1)$$

(18) E. J. Murphy, *Trans. Electrochem. Soc.*, **45**, 133 (1934).

(19) Debye, *Physik. Z.*, **36**, 100 (1935); *Chem. Rev.*, **19**, 171 (1936).

(20) White, *J. Chem. Phys.*, **7**, 58 (1939).

(21) Frank, *Trans. Faraday Soc.*, **32**, 1634 (1936); Eyring, *J. Chem. Phys.*, **4**, 283 (1936).

(22) Mueller, Report of the Committee on Electrical Insulation of the Division of Engineering and Industrial Research of the National Research Council, 1935, p. 11.

N is Avogadro's number; μ is the dipole moment of 3.8 D; β is the angle of 72° between equilibrium orientations; and E is the difference between the energies of the two equilibrium orientations, in this case 7.8×10^{-14} erg per molecule or 1130 cal. per mole.

At temperatures above −100° the total molar polarization was derived from the observed values of static dielectric constant, employing at all temperatures the molar volume of 151 cc. observed in the sheets at 25°; in this method of measurement the number of molecules between the electrodes of the condenser is independent of temperature. After subtracting the entire polarization of 58.5 cc. observed at −195° and 100 kc., the remainder is represented as rotational polarization P_r by the circles in Fig. 10. P_r as calcu-

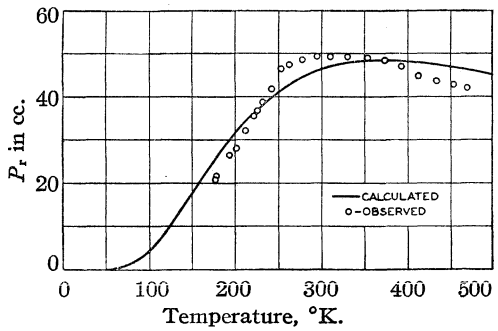


Fig. 10.—Rotational polarization of 1,2,3-trimethyl-4,5,6-trichlorobenzene.

lated by equation (1) is shown by the smooth curve. Despite the use of two adjustable parameters in the calculation, the similarity of the temperature variation of the observed and theoretical curves over a 300° range is significant in exhibiting the ability of the model to account qualitatively for the behavior of ϵ_s in 1,2,3-trimethyl-4,5,6-trichlorobenzene. In passing it may be noted that 72° is not altogether an arbitrary choice for β, since the interval between potential valleys for a truly hexagonal molecule should be 60°.

The height of the potential hill in Fig. 9 determines the time required to establish an equilibrium distribution of molecular orientations between the two potential valleys, and hence may be estimated from the observed principal relaxation time τ where

$$\tau = \frac{\epsilon_\infty + 2}{\epsilon_s + 2} \frac{1}{2\pi f_m} \qquad (2)$$

ϵ_∞ being the dielectric constant at frequencies too high (or temperatures too low) for any rotational

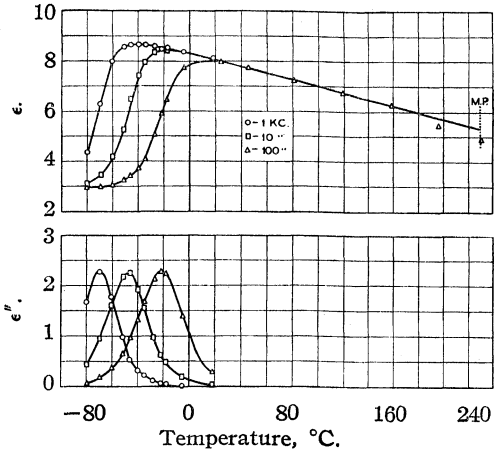


Fig. 11.—Dielectric properties of tetrachloro-*o*-xylene.

contribution, and f_m being at any given temperature the frequency at which $\epsilon = (1/2)(\epsilon_s + \epsilon_\infty)$. According to the Eyring–Frank theory of anomalous dispersion[21]

$$\frac{1}{\tau} = 5 \times 10^{11} e^{-V_0/kT} \qquad (3)$$

where V_0 is the height of the potential hill (above $V = 0$) and the factor 5×10^{11} is the frequency of torsional vibration in either potential valley, estimating the molecular moment of inertia to be 2.5×10^{-37} g.-cm.^{2}. Hence a potential hill V_0 of 3.97×10^{-13} erg per molecule or 5740 cal. per mole accounts for the observed relaxation time of 10^{-6} second at −52.5°. The value thus calculated for V_0 is undoubtedly artificial, for the model of Fig. 9 is analogous to chemical activation in one degree of freedom, while as Frank points out[21] there should be activation in many degrees of freedom in a crystal or liquid. Using $V_0 = 3.97 \times 10^{-13}$ erg, the relaxation time calculated from equation (3) is therefore not as sensitive to temperature as that observed in Fig. 8.

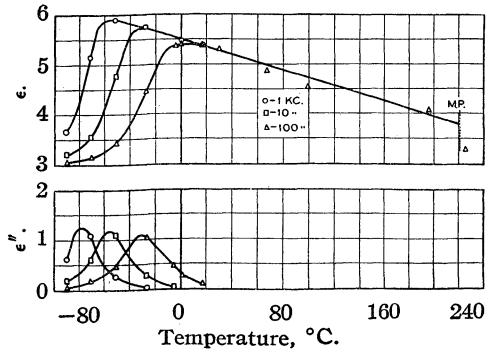


Fig. 12.—Dielectric properties of tetrachloro-*m*-xylene.

Potential functions similar to that of Fig. 9, but with the ratio V_0/E so large that the region of positive $d\epsilon_s/dt$ could not be observed at frequencies as high as 1 kc., are capable of accounting for both the reduction factors and the anomalous dispersion of the other compounds illustrated in Figs. 5 to 13. Once the idea of two or more potential minima is admitted to account for anomalous dispersion, it is difficult to avoid the conclusion that the energies of these minima should in general differ in crystals composed of polar molecules.

With the exception of 1,2,3,5-tetramethyl-4,6-dichlorobenzene, Figs. 5 to 13 include dielectric measurements on all possible polar hexasubstituted methylchlorobenzenes. Since the rotational polarization of each of these compounds is subject to anomalous dispersion, it is of interest to correlate molecular structure with some temperature characterizing the rise of the dispersion. To this end the temperature t_1 at which $\tau = 10^{-6}$ second was obtained by interpolation from the dielectric data for each of these compounds. The results are listed in the sixth column of Table I. They appear to exclude dipole interaction as a determining factor; t_1 declines if anything with increasing dipole moment. Figure 14 shows, however, that considerable regularity appears when t_1 is plotted against the number of chlorine atoms in the molecule, indicating in terms of the theory[21] that the height of the potential

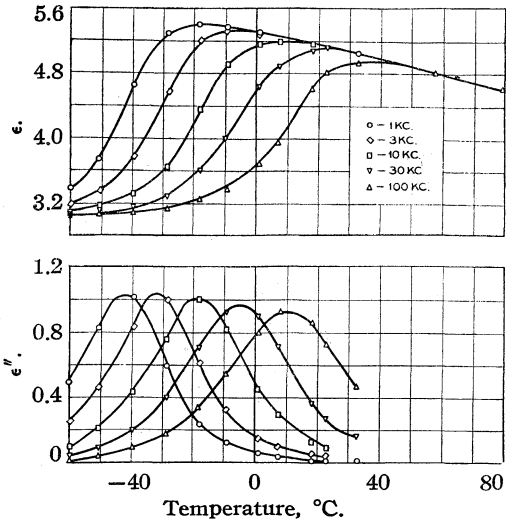


Fig. 13.—Dielectric properties of methylpentachlorobenzene.

hill between equilibrium orientations is increased by replacing a methyl radical in a molecule with a chlorine. The points fall within 7° of the straight line of Fig. 14 for each case except that of pentamethylchlorobenzene, whose point lies 53° above the line. A clue to the cause of its anomalous behavior is found in its crystal habit; it crystallizes from alcohol in plates, while all other members of this series crystallize in fine needles. Hexamethylbenzene, whose system is triclinic,[9] crystallizes from alcohol in plates; while hexachlorobenzene, whose system is monoclinic,[9]

TABLE I

Compound	M. p., °C.	Rotation in solid	Dielectric constant of solid at 20° and calcd. dipole moment		Temp. below which rotation ceases, °C.	
Methylpentachlorobenzene	+224	+	5.2	1.9	+11	a. d.
Tetrachloro-*m*-xylene	+223	+	5.3	1.9	−29	a. d.
Tetrachloro-*o*-xylene	+228	+	8.0	3.3	−26	a. d.
1,2,3-Trimethyl-4,5,6-trichlorobenzene	+225	+	8.5	3.8	−52	a. d.
1,2,4-Trimethyl-3,5,6-trichlorobenzene	+210	+	6.3	1.9	−44	a. d.
1,2,3,4-Tetramethyl-5,6-dichlorobenzene	+193	+	9.1	3.3	−74	a. d.
1,2,3,5-Tetramethyl-4,6-dichlorobenzene	+190	+	6.5			a. d.
Pentamethylchlorobenzene	+154	+	5.7	1.9	−47	a. d.
Trichloro-*m*-xylene	+ 94–95	+	4.1 (30°)	1.8	20–22	t. p.
3,4,5-Trichloro-*o*-xylene	+ 94–96	+	6.9 (30°)	3.6	15–20	t. p.
Pentamethylnitrobenzene	+154	−	3.2			m. p.
2,4,6-Trimethylnitrobenzene, E. K.	+ 44	−	3.0			m. p.
1,2,3,4-Tetramethyl-5,6-dinitrobenzene	+178	+	3.0 (16.5 at +160°)		+150	t. p.
2,4,6-Trimethyldinitrobenzene, E. K.	+ 85	−	3.0_5			m. p.
5-Nitro-3,4-dichloro-*o*-xylene	+ 82	+	3.6 (15.0 at +70°)			
3-Nitro-4,5-dichloro-*o*-xylene	+117	−	3.0			
Ethylpentachlorobenzene	+ 56	−	2.8_5			m. p.
Pentaethylacetophenone	+141	−	2.6_5			m. p.
1,2,3,4-Tetraethyl-5,6-dinitrobenzene	+116	−	2.7			m. p.
1,2,3,4-Tetrachlorobenzene, E. K.	+ 45	−	3.2			m. p.
4,5-Dichloro-*o*-xylene	+ 76	−	2.9_4			m. p.
o-Dinitrobenzene, E. K.	+117	−	3.5			m. p.

crystallizes in fine needles. Although attempts to grow large single crystals for goniometric measurement have failed, it is reasonable to suppose that all compounds represented in Fig. 14 crystallize in the monoclinic system except pentamethylchlorobenzene, whose crystal is triclinic. Any regularity of behavior of t_1 would certainly be destroyed by such a change of crystal system.

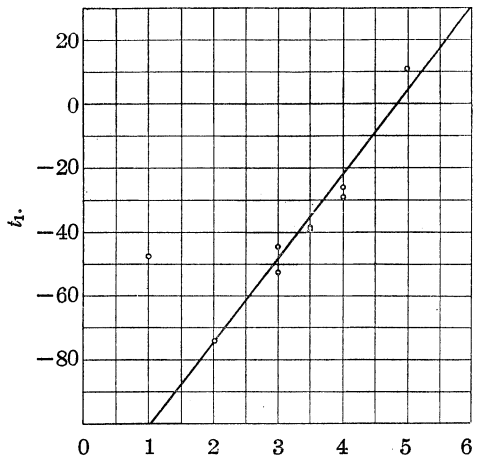


Fig. 14.—Temperature t at which $\tau = 10^{-6}$ seconds *vs.* number of chlorine atoms in hexasubstituted methylchlorobenzenes.

One striking feature of these results is the regular behavior of the relaxation time of 1,2,3-trimethyl-4,5,6-trichlorobenzene in the face of the very large reduction of ϵ_s. This argues in favor of a model in which the reduction factor and t_1 are determined by intrinsically independent features of the potential function, as in Fig. 9.

As a further test of the relation exhibited by Fig. 14, an equimolecular solid solution of methyl pentachlorobenzene and 1,2,3,4-tetramethyl-5,6-dichlorobenzene was prepared. This mixture was first melted and then cooled very slowly through the freezing range, in order to produce as far as possible an equilibrium distribution of the two molecular species throughout the specimen. The dielectric properties of pressed sheets of this solid solution are represented in Fig. 15. The value of t_1 thus observed is −38°, which as represented by the square in Fig. 14 is about what would be expected of a hexasubstituted methylchlorobenzene crystal each of whose molecules contained 3.5 chlorine atoms. Furthermore, the distribution of relaxation times about the principal value is not noticeably broader in the mixture than in the pure crystals, as may be seen by comparing the ratios $\epsilon''_m/(\epsilon_s - \epsilon_\infty)$, where ϵ''_m is the maximum value of ϵ'' at the temperature in question.[23] In the ideal case of a dielectric all of whose molecules have the same relaxation time, this ratio is 0.50; the observed values are 0.42 in methylpentachlorobenzene, 0.35 in 1,2,3,4-tetramethyl-5,6-dichlorobenzene, and 0.34 in the mixture. If any property of the individual molecule, such as moment of inertia, were of controlling importance in determining the frequency with which rotational motion could occur, a broadening of the distribution of relaxation times or possibly two separate principal relaxation times would have been expected in this solid solution. The absence of any such detectable inertia effect is, on the other hand, to be expected if these molecules pass over the potential hill classically as suggested by Frank[21] instead of passing through it in the quantum-mechanical tunnel effect as suggested by Mueller.[22]

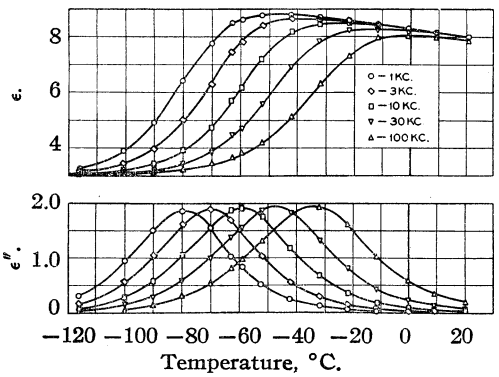


Fig. 15.—Dielectric properties of equimolecular mixture of 1,2,3,4-tetramethyl-5,6-dichlorobenzene and methylpentachlorobenzene.

Among the compounds of Figs. 1 to 4, in whose crystals molecular rotation sets in at a transition, only *o*-dinitrotetramethylbenzene is completely substituted. Among the compounds of Figs. 5 to 13, where there is molecular rotation but no transition, all are completely substituted. Diagrams of these molecules have been drawn to scale.[24] While it is difficult to evaluate the volumetric symmetry about the molecular center of gravity from such a drawing, the hexasubstituted compounds are in general much more symmetrical than the pentasubstituted, with 1,2,3-trimethyl-4,5,6-trichlorobenzene and *o*-dinitrotetramethylbenzene falling close to the dividing line. The

(23) Yager, *Physics*, **7**, 434 (1936).

(24) The procedure was similar to that employed by Smyth in his diagram of *o*-dichlorobenzene, reference 16, p. 111.

appearance of transitions in pentasubstituted benzenes and the derivatives of camphane, cyclohexane and ethane may be pictured in terms of the reduction of rotational energy with declining temperature, which eventually permits the crystal to collapse into a dense form in which "interlocking" of molecules eliminates their rotation without changing the closest distance of approach of the peripheral atoms of nearest neighbors. The more symmetrical hexasubstituted benzene molecules appear to require about the same amount of space in the crystal whether they rotate or not. Hence when the energy (or frequency) of molecular rotation is reduced with the temperature, there is little or no tendency for the crystal to collapse into a denser form. At room temperature the molar volume of tetrachloro-*o*-xylene is about 145 cc., while that of the high-temperature form of 3,4,5-trichloro-*o*-xylene is 143 cc., indicating that when rotating the volume required by corresponding hexa- and pentasubstituted molecules is about the same. At almost the same temperature but in the absence of rotation, the molecules of 3,4,5-trichloro-*o*-xylene require a molar volume of only about 136 cc.

The above explanation of the absence of transitions in certain crystals whose molecules rotate is obviously incomplete. Anomalous dispersion in the 1–100 kc. frequency range has been observed in a number of derivatives of camphane and cyclohexane,[5,6] although usually a transition is also found or there is reason to suspect that the state is one of metastable equilibrium.

Further evidence of the influence of symmetry in determining the ability of molecules to rotate is supplied by the negative results for other compounds in Table I. For example, pentamethylnitrobenzene differs from pentamethylchlorobenzene in that the nitro group is larger than chlorine and in that it projects out of the plane of the flat hexagonal ring. These factors apparently result in a sufficient distortion of the symmetry of the molecule or in sufficient interference between nitro groups of neighboring molecules to prevent rotation. The table shows that ethylpentachlorobenzene also is not sufficiently symmetrical to permit rotation. Consideration of models indicates that the ethyl group projects out of the plane of the ring more than the nitro group and thus that rotation is less likely. Pentaethylacetophenone also illustrates the requirement that the symmetry be in the plane of the ring. The decrease in symmetry in going to the tetrasubstituted compounds is so great that no rotation is to be expected among them. For the 1,2,3,4-tetrachlorobenzene, the most asymmetrical, and for the 4,5-dichloro-*o*-xylene, the most symmetrical tetra-substituted compound, there is no molecular rotation.

The authors are indebted to Mr. W. A. Yager for making his measurements of 1,2,4-trimethyl-3,5,6-trichlorobenzene available to them.

Summary

The dielectric data supply two kinds of evidence of molecular rotation in certain aromatic crystals: (1) the dielectric constant of the solid behaves like that of the corresponding liquid, and (2) among these solids, ϵ may be correlated with the dipole moment of the molecule. Although each of the molecules involved possesses considerable volumetric symmetry about one axis through its center of gravity, the less symmetrical of them cease rotating abruptly at transitions, while the more symmetrical exhibit reduced frequency of rotation but no transitions as temperature declines. Among the symmetrical hexasubstituted methylchlorobenzenes, the temperature at which the relaxation time reaches a given value depends with one exception on the number of chlorine atoms per molecule. A function recently proposed by one of the authors to describe the interaction of a molecule with its neighbors is used to explain the peculiar temperature variation of the static polarization of 1,2,3-trimethyl-4,5,6-trichlorobenzene.

NEW YORK, N. Y. RECEIVED AUGUST 24, 1939

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF WASHINGTON]

The Partial Vapor Pressures of Water and Ammonia from the System Water–Phosphoric Acid–Ammonia

BY CLAYTON S. HUEY AND H. V. TARTAR

Introduction

This investigation of the ammonium orthophosphates was undertaken because of the growing importance of these salts commercially and the lack of precise information concerning their behavior.

Even such a fundamental property as the extent of hydrolysis of solutions of these salts has been investigated only partially previous to this work. Ball[1] measured the acidity of solutions of mono- and diammonium phosphates. Buchanan and Winner,[2] when studying the solubility of the above salts, found that only the latter was hydrolyzed. Ross, Merz and Jacob[3] discuss the dissociation of the three ammonium orthophosphates both in solution and in the solid form. The hydrolysis of solutions of the related compounds, disodium ammonium phosphate ($Na_2NH_4PO_4$) and sodium ammonium hydrogen phosphate ($NaNH_4HPO_4$), was investigated by Abbott and Bray.[4]

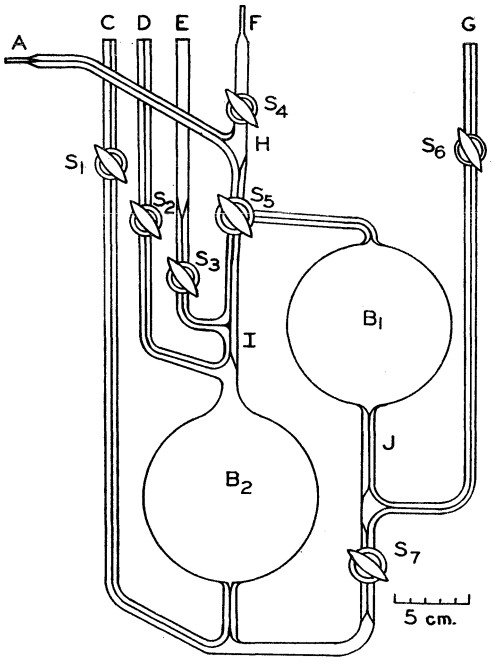


Fig. 1.—Sketch of the vapor pressure apparatus.

(1) Ball, THIS JOURNAL, **52**, 3901 (1930).
(2) Buchanan and Winner, *J. Ind. Eng. Chem.*, **12**, 448 (1920).
(3) Ross, Merz and Jacob, *ibid.*, **21**, 286 (1929).
(4) Abbott and Bray, THIS JOURNAL, **31**, 729 (1909).

The dissociation pressures of some of the salts of this system have been studied by Warren[5] (mono-, di- and tri-ammonium phosphates), by Britzke and Dunaev[6] (diammonium phosphate) and by de Passille[7] (di- and tri-ammonium phosphates). The present work supplies the dissociation pressures of ammonia and water from triammonium phosphate trihydrate, $(NH_4)_3PO_4 \cdot 3H_2O$.

Vapor Pressure Apparatus

A static method for measuring vapor pressure was devised which permitted the determination of the composition of the two phases in equilibrium. The principal part of the equipment was the Pyrex glass apparatus shown in Fig. 1. The bulbs B_1 and B_2 were of 500 and 700 ml. capacity, respectively. The apparatus was supported by a frame made of brass angle strips, the bulbs resting on brass rings covered with rubber tubing. The frame was fastened in the thermostat at two points only so that it could be rocked about an almost vertical axis through the center of B_1. Bulb B_2 could then be moved through an arc of approximately 1.3 cm. twice per second by an eccentric arm from an electric motor. The glass tubing H to A and the rubber tube connection at A were wrapped with auxiliary heating coils to maintain a temperature somewhat higher than that of the thermostat. The volume of B_1 from S_5 to a mark on J was determined carefully. A scale fastened to tube J was calibrated in terms of the volume of the tube.

The operation of the apparatus was typically as follows: B_1, from S_5 to G to B_2, was filled with mercury through G. Then B_2 was rinsed with carbon dioxide-free air. Next the desired solution was added through C and the apparatus submerged in the water-bath to bring the water level just above S_5. After reaching temperature equilibrium, S_2 was opened momentarily to reduce the inside pressure to atmospheric and the apparatus rocked to establish equilibrium between the liquid and vapor in B_2; this required from twelve hours to several days, the longer time being when solid phases were present. The temperature of the water-bath was maintained to $\pm 0.005°$ at 35° and below and to $\pm 0.015°$ above that range.

To remove the vapor sample for analysis, the mercury was allowed to flow (about 30 ml./min.) from B_1 to B_2, being displaced by the vapor from B_2 through S_5. The mercury was stopped in J to permit the determination of the volume of the sample, which was finally removed (by displacement to H with mercury from G) through the absorption train connected to A after the temperature of the water-bath was raised about 1° to prevent condensation.

(5) Warren, *ibid.*, **49**, 1904 (1927).
(6) Britzke and Dunaev, *J. Chem. Ind. U. S. S. R.*, **5**, 161 (1928).
(7) De Passille, *Compt. rend.*, **199**, 356 (1934).

Tube A was finally washed with a stream of purified air admitted at S_4.

The absorption train consisted of a small tube filled with barium oxide desiccant, for absorbing water, and the ammonia absorber which was made of two 125-ml. Erlenmeyer flasks fitted with glass tubes so that the gas stream bubbled through the liquid. Following this was a Mariotte flask adjusted to maintain the pressure at A a little below atmospheric. The rubber connections at F, A and between the water and ammonia absorbers were treated as suggested by Pregl.[8]

After absorption of the vapor sample, the temperature of the water-bath was lowered to its original value and a portion of liquid removed from B_2, by displacement with mercury, through S_2 into a weighed sampling bulb attached at D. Any liquid in the capillary tube outside the stopcock on the sampling bulb was removed and the bulb wiped and weighed. The long tube on the sampling bulb was broken under an excess of sulfuric acid, the liquid then diluted to volume in a volumetric flask and suitable aliquots taken for the determination of ammonia and phosphate content.

Reagents

The preparation and purification of the materials used in this research which are not specified elsewhere were as follows.

Phosphoric Acid.—A "reagent" grade phosphoric acid (85% H_3PO_4) was concentrated to near 97% and crystallized by seeding with a few crystals of the acid. The crystals were separated by centrifuging in porcelain cups, and dissolved in water to make a stock solution which contained approximately 45% phosphoric acid. This solution was diluted to the desired strength, as needed. A check on the purity of this acid solution was obtained by analyzing three of the diluted solutions both gravimetrically for phosphate content and acidimetrically, the two methods agreeing within the limits of experimental error. The stock solution was also found to be free of reducing substances.[9]

Diammonium Phosphate.—A "C. P." grade of diammonium phosphate was recrystallized twice, and dissolved in water to give an approximately saturated solution. Since there was loss of ammonia from the solutions during recrystallization, the stock solution was analyzed for both ammonia and phosphate content, and ammonia added until the analyses showed a value of two for the molar ratio of ammonia to phosphate ion. This solution was diluted suitably for use in the experiments on the hydrolysis of diammonium phosphate.

Ammonia.—The gas from a tank of liquid ammonia was led through a barium oxide tube before use to remove any water which might have been present.

Water.—The water used was distilled through a block tin condenser and stored in a tin tank. Its specific resistance was approximately 10^6 ohms, without removal of the carbon dioxide.

Ammonium Chloride.—This salt was purified by recrystallization.

Mercury.—The mercury was cleaned by allowing it to drop through a column of dilute nitric acid, in the conventional apparatus.

Analytical Methods, Calculation and Accuracy of Vapor Pressure Determinations

Determination of Water in the Vapor Phase.—A microtechnique was employed. A Kuhlmann balance and microabsorption tubes of the type described by Kemmerer and Hallett[10] were used. The method of weighing was essentially that described by Pregl,[11] except that only a single wiping with a slightly damp chamois was made.

The final choice of barium oxide as a desiccant in the absorption tube was reached after aluminum oxide, calcium oxide and potassium hydroxide had been found unsatisfactory. The barium oxide was pulverized and packed in the absorption tubes in layers separated by Pyrex fiber. The flow of the gas stream through the absorption train was 5 ml. per min., the maximum rate that could be used safely.

The increase in weight of the barium oxide was taken as the weight of water in the sample except at temperatures above 25°. In these cases, a correction was made for the vapor pressure of mercury; at 50° this correction was 0.057 mg.

Determination of Ammonia in the Vapor Phase.—Slightly acidulated water or 4% boric acid solution was used as an absorbent for ammonia. Forty ml. of the former was used and the ammonia content determined directly by Nesslerization[12] when the ammonia pressure was less than 0.3 mm. The lowest pressure that could be measured by this method was about 0.002 mm.

Twenty-five or 50 ml. of the boric acid solution was used for the higher pressures of ammonia, and the quantity determined by titrating with standard hydrochloric acid, using brom phenol blue indicator. The end-point of this titration was determined in such a manner as to obviate the effect of the salts and water on the indicator. This was accomplished through the use of a solution of ammonium chloride of the same normality as the hydrochloric acid. For each titration a similar amount of the boric acid solution was treated in just the same way as the portion with the sample, except that ammonium chloride solution was added in place of the acid, until the sample showed approximately the color of the end-point. Then standard acid was added to the duplicate until the colors matched, and this volume subtracted from the volume of acid added to the sample. This corrected volume represented the acid equivalent to the ammonia in the sample. The end-point was checked by adding more acid to one solution, and matching the color again by adding to the other. Usually the correction amounted to a few tenths of a ml. of 0.015 *N* acid. Under these conditions the color change caused by 0.01 ml. of the standard acid could be seen.

Determination of Ammonia in Solution.—The method of distillation from an alkaline solution into 4% boric acid solution, as used by Markley and Hann,[13] was employed.

(8) Roth, "Quantitative Organic Microanalysis of Fritz Pregl," 3rd English Edition, P. Blakiston's Son and Co., Inc., Philadelphia, Penna., 1937, p. 26.

(9) Collins, Farr, Rofin, Spencer and Wichers, *Ind. Eng. Chem.*, **19**, 1369 (1927).

(10) Kemmerer and Hallett, *Ind. Eng. Chem.*, **19**, 173 (1927).

(11) Roth, *loc. cit.*, p. 43.

(12) Hillebrand and Lundell, "Applied Inorganic Analysis," John Wiley and Sons, Inc., New York, N. Y., 1929, p. 642.

(13) Markley and Hann, *J. Assoc. Off. Agr. Chem.*, **8**, 455 (1925).

The same principle of color matching, as applied in the previous determination, was utilized here.

Determination of Phosphoric Acid.—The phosphate analyses were performed by a double precipitation of magnesium ammonium phosphate and final ignition to magnesium pyrophosphate ($Mg_2P_2O_7$).[14] The phosphoric acid was titrated as a dibasic acid using phenolphthalein indicator.[15]

Standardization of Hydrochloric Acid.—This reagent was standardized using phenolphthalein indicator with carbonate-free sodium hydroxide, using recrystallized potassium biphthalate[16] as the primary standard.

Calculations and Constants Used.—Use was made of the perfect gas law to calculate partial pressures from the number of moles, analytically determined, of ammonia or water vapor. The value of the gas constant R was taken to be 1.9864 cal. The weighings were corrected to values *in vacuo* except in the case of solutions whose densities were unknown.

Accuracy of the Vapor Pressure Determinations.—Numerous determinations of the vapor pressure of water were made at 25° to develop the details of the procedure. The average of nine determinations was 23.778 mm.; average deviation was 0.018 mm.; the deviation of the mean from the accepted value[17] was −0.001 mm.

The partial pressures of ammonia and water from several aqueous solutions of ammonia were determined at 25° in an early part of this research to test the method. While the results were not as consistent as those obtained after the technique of the various operations had been improved, the data are shown in Table I, to indicate the accuracy at this stage of development.

TABLE I

A COMPARISON OF THE PARTIAL PRESSURES OF AMMONIA AND WATER FROM AQUEOUS SOLUTIONS OF AMMONIA AT 25° WITH THOSE PUBLISHED PREVIOUSLY

Ammonia in soln., %	Found, partial press. of ammonia, mm.	Found, partial press. of water, mm.	Calculated, partial pressure, mm. Ammonia de Wijs[a]	Ammonia Perman[b]	Water Wilson[c]	Water Perman[b]
3.959	32.77	22.80	32.6[d]		22.68	
2.016	16.13		15.91	15.8	23.22	23.0
2.012	15.78	22.78	15.88	15.7	23.22	23.0
1.997	16.01	23.57	15.76	15.6	23.22	23.0
2.008	16.11	22.98	15.85	15.7	23.22	23.0
2.008	16.06	23.07	15.85	15.7	23.22	23.0

[a] De Wijs, Thesis, Delft, 1923; "International Critical Tables," Vol. III, p. 259. [b] Perman, *J. Chem. Soc.*, **83**, 1168 (1903). [c] Wilson, *Univ. Ill. Exp. Sta., Bull.* 146 (1925). [d] This value was obtained by extrapolating de Wijs' curve with the aid of data from Morgan and Maass.[18]

To ascertain whether or not ammonia was absorbed by the barium oxide in the water absorption tube, the following experiment was performed. The barium oxide from one of these tubes, which had been used for six determinations and through which approximately 0.4 millimole of ammonia had passed, was divided into two parts, and each analyzed for ammonia. The part of the barium oxide which had absorbed the water in those six determinations, *i. e.* the front end, showed no ammonia, and the rest of it showed 6.5×10^{-8} millimole. The molar ratio of ammonia to barium oxide in the latter portion of the tube was calculated and found to be 1.9×10^{-4}. Hence absorption of ammonia by the barium oxide was considered to be negligible. The small residues of ammonia left in the barium oxide from each determination would introduce a very small error, since successive determinations were made on solutions with the same, or nearly the same, pressures of ammonia, and were made under similar conditions, thus making the residues approximately the same each time.

An estimate of the reliability and accuracy of the method was obtained from the last data taken, namely, those recorded in Table IV. The average deviation of the thirteen individual points from the straight line determined by the method of least squares was found to be 0.09 mm. for the water pressure and 0.03 mm. for the ammonia pressure, with about 60% of the variation due to four values in the first case, and two in the latter.

Partial Pressures of Ammonia and Water from Solutions of the Ammonium Orthophosphates at 25°.—Owing to hydrolysis, solutions of the secondary and tertiary ammonium phosphates would be expected to exhibit a pressure of ammonia. To study the extent of this reaction, solutions of phosphoric acid were titrated with anhydrous ammonia, and the partial pressures of both ammonia and water above the solutions determined at 25° as a function of the composition of the solution. The results of these experiments are shown in Table II, and graphically in Fig. 2.

Kabulkov and Zagwosdkin[19] have published the only available data with which these may be compared. Their values for the partial pressure of water from the 1.0 and 0.25 M solutions are 23.2 and 23.6 mm., respectively; the corresponding results reported herein are 23.16 and 23.55 mm.

A noteworthy point in Fig. 2 is on Curve E, where R equals 3. The fact that no break in the value of the ammonia pressure occurs here shows that triammonium phosphate is practically completely hydrolyzed in this solution.

Hydrolysis of Diammonium Hydrogen Phosphate at 25°.—Diammonium phosphate undergoes the following hydrolytic reaction

$$(NH_4)_2HPO_4 + H_2O \rightleftarrows NH_4OH + NH_4H_2PO_4 \quad (1)$$

(14) Hillebrand and Lundell, *loc. cit.*, p. 563.

(15) Kolthoff and Sandell, "Textbook of Quantitative Inorganic Analysis," The Macmillan Co., New York, N. Y., 1936, p. 533.

(16) Kolthoff and Sandell, *loc. cit.*, p. 524.

(17) "International Critical Tables," Vol. III, McGraw-Hill Book Co., Inc., New York, N. Y., 1928, p. 212.

(18) Morgan and Maass, *Can. J. Research*, **5**, 162 (1931).

(19) Kabulkov and Zagwosdkin, *Z. anorg. allgem. Chem.*, **224**, 315 (1935).

TABLE II

PARTIAL PRESSURES OF AMMONIA AND WATER FROM SOLUTIONS OF THE AMMONIUM ORTHOPHOSPHATES AT 25°

Phosphate ion, molality	R[a]	Partial pressures in mm. Water	Ammonia
0.9971	0	23.16	0
	0	23.15	0
	0.4860		<0.002
	0.4860		< .002
	1.067	23.10	< .002
	1.239	23.11	< .002
	1.469		.002
	1.469		.002
	1.469		.002
	1.605		.003
	1.762	23.09	.003
	1.854	23.14	.037
	2.086		1.81
	2.091	23.10	
	2.278		4.70
	2.530		8.77
	2.879	22.78	14.73
0.5010	1.274		0.002
	1.532	23.49	.003
	1.689	23.36	.003
	1.940		.089
	2.052	23.30	.53
	2.401	23.19	3.27
	2.719	23.10	5.74
	2.719	23.12	5.75
	3.299	23.03	9.92
	3.593	22.96	12.36
0.2501	0	23.53	0
	0	23.57	0
	1.281		<0.002
	1.444		< .002
	1.617	23.55	< .002
	1.886		.039
	2.030	23.49	.22
	2.076	23.54	.36
	2.225	23.37	.80
	2.388	23.38	1.42
	2.627	23.24	2.22
	2.832	23.24	2.91
	2.994	23.33	3.46
	2.994	23.36	3.47

[a] R represents the molar ratio of ammonia to phosphate ion.

The hydrolysis constant is defined by the equation

$$K_h = k_w/K_a K_b \qquad (2)$$

and can be formulated in terms of the experimental values as follows. We have

$$K_w = a_{H^+} a_{OH^-}/a_{H_2O}$$
$$K_a = a_{H^+} a_{HPO_4^{--}}/a_{H_2PO_4^-}$$
$$K_b = a_{NH_4^+} a_{OH^-}/a_{NH_4OH}$$

and substituting in equation (2) we obtain

$$K_h = \frac{a_{H_2PO_4^-} a_{NH_4OH}}{a_{HPO_4^{--}} a_{NH_4^+} a_{H_2O}}$$

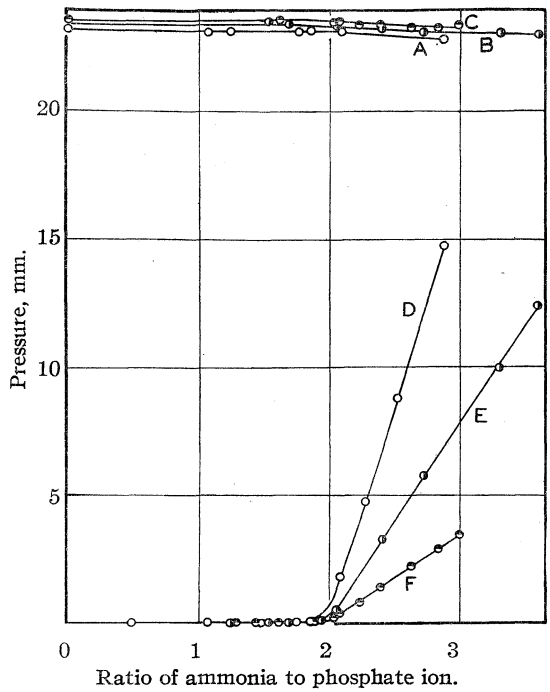


Fig. 2.—Partial pressures of ammonia and water from solutions of the ammonium orthophosphates at 25°. Curves A, B and C represent the partial pressure of water from solutions whose phosphate ion molalities are 1.0, 0.5 and 0.25, respectively. Curves D, E and F show the partial pressures of ammonia from the same solutions, respectively.

Consider a solution of diammonium hydrogen phosphate, of molality M_2, of which X is the fraction hydrolyzed. Then at equilibrium the molality of the $H_2PO_4^-$ ion and also that of the ammonium hydroxide is XM_2; also the molalities of the HPO_4^- and NH_4^+ ions are $(1 - X)M_2$ and $(2 - X)M_2$, respectively, assuming no appreciable ionization of the ammonium hydroxide. Then

$$K_h = \frac{X^2}{(1 - X)(2 - X)} \frac{\gamma_{H_2PO_4^-}\gamma_{NH_4OH}}{\gamma_{HPO_4^{--}}\gamma_{NH_4^+} a_{H_2O}}$$

Letting

$$K_h' = \frac{X^2}{(1 - X)(2 - X)} \qquad (3)$$

and expressing in logarithmic form

$$\log K_h = \log K_h' + \log \frac{\gamma_{H_2PO_4^-}\gamma_{NH_4OH}}{\gamma_{HPO_4^{--}}\gamma_{NH_4^+} a_{H_2O}}$$

Use was made of a correction factor similar to the Debye and Hückel expression for the activities of ions for evaluating the last term of the preceding equation. Doing this we obtain

$$\log \frac{\gamma_{H_2PO_4^-}}{\gamma_{HPO_4^{--}}\gamma_{NH_4^+}} = \frac{4A\sqrt{\mu}}{1 + B\sqrt{\mu}}$$

A has the value 0.506 at 25° and B is a semi-

TABLE III

HYDROLYSIS OF DIAMMONIUM HYDROGEN PHOSPHATE AT 25°

Diammonium hydrogen phosphate molality, (M_2)	Partial press., mm. Water	Ammonia	M_0	X	$-\log K_h'$	μ	$-\log K_h^*$
5.007	21.13	1.019	0.07784	0.01555	3.9076	14.86	2.067
5.007	21.24	0.959	.07328	.01463	3.9607	14.87	2.119
2.745		.667	.05089	.01854	3.7528	8.133	2.053
2.219	22.32	.618	.04705	.02120	3.6342	6.564	1.989
1.662		.474	.03600	.02166	3.6153	4.919	2.045
1.662	22.32						
1.104	22.74	.352	.02664	.02413	3.5200	3.259	2.068
0.9211		.325	.02468	.02673	3.4294	2.714	2.030
.4011		.144	.01077	.02685	3.4257	1.182	2.276

empirical constant related to the ionic radius, a, by the relation $B = 0.327 \times 10^8 a$, when the difference between the molality and normality is negligible.

Next, a quantity K_h^* was defined by the equation

$$\log K_h^* = \log K_h' + \frac{4A\sqrt{\mu}}{1 + B\sqrt{\mu}} \qquad (4)$$

If $\log K_h^*$ is plotted against μ, the ionic strength, the intercept at zero ionic strength is the logarithm of the hydrolysis constant.

The following procedure was employed to evaluate K_h'. Suppose that a membrane were available which would permit the passage of ammonia but which would be impermeable to water vapor. If this membrane were placed between a solution of diammonium phosphate and water, ammonia would distil from the former to the latter until the activity of the ammonia would become the same in all three phases. Let a_0 represent the activity and M_0 the molality of un-ionized ammonia in the ammonia solution. Let P_0 represent the partial pressure of ammonia. The ammonia solution would exhibit the equilibria

$$NH_{3(g)} \rightleftarrows NH_{3(soln.)}$$

$$NH_{3(soln.)} + H_2O \rightleftarrows NH_4OH$$

$$K_0 = \frac{(a_{NH_4OH})}{(a_{NH_3(soln.)})(a_{H_2O})}$$

$$NH_4OH \rightleftarrows NH_4^+ + OH^-$$

Then

$$a_0 = M_0\gamma_0 = (a_{NH_3(soln.)}) + (a_{NH_4OH}) = (a_{NH_3(soln.)})(1 + K_0 a_{H_2O})$$

and since the activity of ammonia in solution is proportional to its partial pressure above the solution

$$a_0 = M_0\gamma_0 = P_0K_2(1 + K_0a_{H_2O})$$

Therefore, the activity of the un-ionized ammonia in both solutions would be directly proportional to the pressure of ammonia, if the activity of water were the same in the two cases.

The value of M_0, the molality of un-ionized ammonia in the water solution, was calculated by using P_0, the ionization constant of ammonium hydroxide, and the pressure–composition curve for ammonia in water.[20] Since the activity of the un-ionized ammonia was essentially the same in the two solutions, M_0 was also taken as equal to XM_2, the molality of the un-ionized ammonia in the diammonium phosphate solution. This was based on two approximations: first, that the activity coefficients of the un-ionized ammonia in the two solutions were the same, and, second, that the activities of water in the two solutions were the same. X was calculated from this value of M_0 and the analytically determined M_2. These values were introduced into equation (3) and K_h' computed.

The molality of diammonium phosphate was varied approximately from 5.0 to 0.4 and the measured values of P_0 plotted against M_2. These values are shown in Table III, and graphically in Fig. 3, Curve A. Curve B gives the corresponding values of the partial pressure of water, with the addition of three values in the dilute solution from Fig. 2.

Table III also includes the calculated values for $-\log K_h^*$, arbitrarily taking B in equation (4) to be 0.84. No trend is apparent in the values of $-\log K_h^*$; the best value is probably 2.053 ($K_h^* = 8.86 \times 10^{-3}$), the average of the values given omitting the last one for the most dilute solution because of its evident inconsistency. K_h was found to be 8.87×10^{-3}, using the values 10^{-14} for K_w, 6.226×10^{-8} for K_a[21] and 1.81×10^{-5} for K_b.[22] Since the arbitrarily chosen value of B influenced the magnitude of K_h, the agree-

(20) The values for the partial pressures of ammonia from the ammonia–water solutions were those of de Wijs (see Note *a*, Table I).

(21) Nims, THIS JOURNAL, **55**, 1946 (1933).

(22) "International Crit. Tables," Vol. VII, McGraw-Hill Book Co., Inc., New York, N. Y., 1926, p. 240.

ment of the two values for this constant is not a complete check on the validity of the present work. Using the value 0.84 for B, however, the average ionic radius was calculated to be 2.56×10^{-8} cm., slightly lower than similarly obtained values[23] yet nevertheless quite reasonable. Hence the agreement of the value of K_h obtained from our experimental data with that calculated from the defining equation (2) is deemed to be satisfactory.

Dissociation Pressures of Triammonium Phosphate Trihydrate from 25 to 50°.—The measurement of the dissociation pressures corresponding to the reaction

$$(NH_4)_3PO_4 \cdot 3H_2O(s) \rightleftharpoons (NH_4)_2HPO_4(s) + 3H_2O(g) + NH_3(g) \quad (5)$$

was accomplished by preparing a solution saturated with respect to both solids and measuring the partial pressures of ammonia and water exerted by this solution over the temperature range 25 to 50°. This solution was prepared by adding gaseous ammonia to the 45% phosphoric acid solution until the above solids were present.

The phase rule shows that during the addition of ammonia the composition of the solution and the partial pressures of ammonia and water will not change as long as both triammonium phosphate trihydrate and diammonium phosphate are in equilibrium with the solution. This constancy of the partial pressures with changing total composition was taken as the chief criterion for determining when the two solid phases were present. The solubility curves of the system, known approximately at these temperatures[24,2] served to locate the approximate composition of the solution at this equilibrium. When nearly enough ammonia had been added to give the above equilibrium mixture, a vapor pressure determination was made, more ammonia or 45% phosphoric acid added, and the determination repeated, until at least two successive experiments gave the same values for the partial pressures. Proceeding in this manner, four determinations at 50° gave essentially the same partial pressures when the ammonia content of the mixture was varied about 3.2%. This variation was calculated from the weight of solution added and the time during which ammonia was added through a calibrated Venturi meter.

(23) Dole, "Principles of Experimental and Theoretical Electrochemistry," McGraw-Hill Book Co., Inc., New York, N. Y., 1935, p. 302.

(24) D'Ans and Schreiner, *Z. physik. Chem.*, **75**, 95 (1911); Parker, *J. Phys. Chem.*, **18**, 653 (1914); Jänecke, *Z. physik. Chem.*, **127**, 71 (1927); **A177**, 7 (1936).

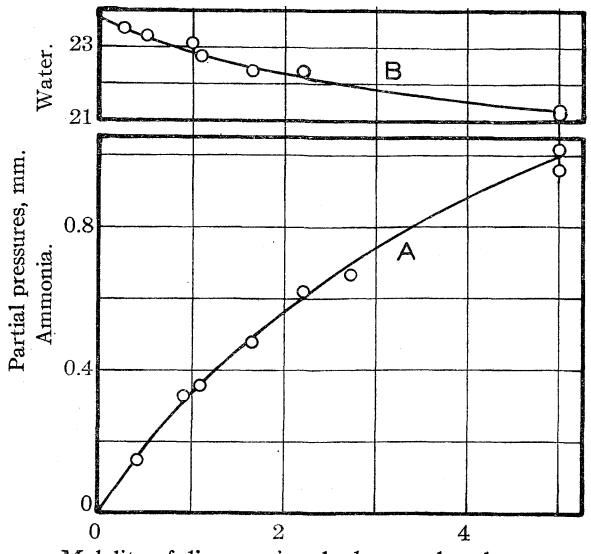


Fig. 3.—The hydrolysis of diammonium phosphate at 25°.

Then the temperature variations of the partial pressures were determined by changing the temperature of the apparatus to the values 40, 45, 35, 30, 25, 20 and 25°, respectively. The data obtained are given in Table IV. Figure 4 shows a graph of the logarithm of the pressure against the reciprocal of the absolute temperature.

TABLE IV

DISSOCIATION PRESSURES OF TRIAMMONIUM PHOSPHATE TRIHYDRATE FROM 25 TO 50°

Temp., °A.	Partial press., mm. Water	Ammonia	ΔR[a] %	$-\log K_p$	$K_p \cdot 10^7$	$\Delta F°$ calcd.	ΔS calcd.
298.14	21.26	3.995					
298.14	21.11	3.995					
298.14	21.14	4.012	+1.0	6.9440	1.138	9469	151.5
303.16	28.10	5.958		6.4017	3.966	8877	149.0
308.14	37.04	8.825		5.8714	13.45	8275	146.6
313.14	48.34	12.84					
313.14	48.39	12.82					
313.14	48.48	12.85	+0.5	5.3600	43.65	7677	144.3
318.14	62.89	18.55		4.8591	138.3	7071	142.0
323.14	80.51	26.39					
323.14	80.50	26.27	−0.1				
323.14	80.33	26.39	−3.0				
323.14	80.45	26.50	−0.1	4.3853	411.8	6482	139.8

[a] ΔR represents the increase in the value of the ratio of ammonia to phosphoric acid in the mixture from the value in the experiment immediately preceding the one for which the value is tabulated.

From the average values at each temperature the following equations were calculated by the method of least squares, where the pressures are

in mm. of mercury and T is the absolute temperature.

$$\log_{10}P_{NH_3} = (-3161.3/T) + 11.2045 \quad (25 \text{ to } 50°)$$
$$\log_{10}P_{H_2O} = (-2239.0/T) + 8.8353 \quad (25 \text{ to } 50°)$$

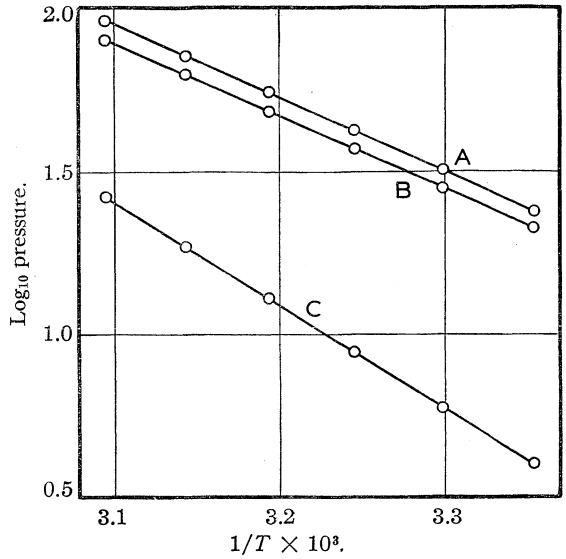


Fig. 4.—The dissociation pressures of triammonium phosphate trihydrate from 25 to 50°. Curve A shows the vapor pressure of pure water. Curves B and C represent the partial pressures of water and ammonia, respectively.

For equation (5) the following well-known thermodynamic quantities were evaluated

$$K_p = (P_{H_2O})^3(P_{NH_3})$$
$$\log_{10}K_p = (-\Delta H/2.3026RT) + C$$
$$\Delta F° = -RT \log_e K_p$$
$$\Delta S = \Delta H/T$$

The following equations were derived from the above after converting the unit of pressure to the atmosphere

$$\log_{10}K_p = (-9878.4/T) + 26.1870$$
$$\Delta F° = 45{,}183 - 119.78\ T \text{ cal.}$$
$$\Delta H = 4.518 \cdot 10^4 \text{ cal.}$$

The values of $\log_{10}K_p$, K_p, $\Delta F°$ and ΔS, which were computed directly from the experimental values, are listed in the last four columns of Table IV.

Samples of the solution were removed at both 25 and 50° and subsequently analyzed. The results of these analyses are given in Table V.

TABLE V

COMPARISON OF THE ANALYSIS OF THE SOLUTIONS SATURATED WITH DIAMMONIUM PHOSPHATE AND TRIAMMONIUM PHOSPHATE TRIHYDRATE AT 25 AND 50°

Temp., °C.	Found, % Ammonia in soln.	Found, % Phosphoric acid in soln.	Calcd., % Ammonia in soln.	Calcd., % Phosphoric acid in soln.	Source
25	10.79	30.08	11.03	31.0	D'Ans and
25	10.79	30.38			Schreiner[25]
50	12.08	34.10	12.7	34.7	Jänecke[26]

It is believed that the discrepancies in Table V are not due to lack of attainment of equilibrium conditions, because of the constancy of the ammonia pressure found. Whether or not the analytical values were in error due to a mistake in sampling is difficult to judge. On the other hand, the values of Jänecke are the result of an interpolation and can only be considered as approximate.

Parker's[24] investigation at 25° throws no light on this particular point and apparently is in error in this region. At least his data for this range are at variance with those of other investigations,[25,2] which are in fair agreement. None of these, however, except that of D'Ans and Schreiner, has included this point.

Summary

1. A method for determining the partial pressures of ammonia and water from solutions has been developed.

2. The partial pressures of these gases were measured at 25° from solutions of orthophosphoric acid containing varying amounts of ammonia.

3. These partial pressures were determined at 25° for solutions of diammonium phosphate of varying molality, and the hydrolysis constant of this salt was calculated.

4. The dissociation pressures of ammonia and water for the reaction: $(NH_4)_3PO_4 \cdot 3H_2O(s) \rightleftarrows (NH_4)_2HPO_4(s) + 3H_2O(g) + NH_3(g)$ were measured over the temperature range from 25 to 50°. From these measurements K_p, $\Delta F°$, ΔS and ΔH were computed for this reaction.

SEATTLE, WASHINGTON RECEIVED JULY 5, 1939

(25) D'Ans and Schreiner, *Z. physik. Chem.*, **75**, 95 (1911).
(26) Jänecke, *ibid.*, **A177**, 7 (1936).

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, PASADENA, CALIFORNIA, NO. 741]

The Extraction of Ferric Iron from Hydrochloric Acid Solutions by Dichloroethyl Ether and the Formula of the Iron Compound in the Ether

BY JOSEPH AXELROD AND ERNEST H. SWIFT

Introduction

Although the extraction of ferric iron from hydrochloric acid solutions by ethyl ether has been an analytical procedure for over fifty years, only recently has the use of other than ethyl ether been investigated; furthermore, although there have been studies of the molecular condition of anhydrous ferric chloride in ethyl ether[1,2] only very recently does there appear to have been any experimental investigations to establish the molecular nature of the iron compound in the ether phase obtained in the extraction process.[3] Dodson, Forney and Swift[4] have shown recently that isopropyl ether possesses certain advantages over ethyl ether for the extraction of ferric iron from hydrochloric acid solutions, and unpublished experiments by Dodson have shown that the ferric chloride in the isopropyl ether phase was associated with hydrogen chloride. He found that with high initial concentrations of acid and of iron in the aqueous phase, two ether phases separated and obtained ratios of hydrogen chloride to ferric chloride of 1.25 and 1.32 in the two ether phases. In addition, it seemed necessary to assume polymerization of the iron in the ether layer in order to explain the dependence of the distribution ratio upon the concentration of iron.

This paper presents the results of studies of, first, the distribution of ferric iron between hydrochloric acid solutions and dichloroethyl ether, and, second, the nature of the ferric iron compound in the ether phase. Preliminary experiments by Mr. John Gates had shown that the mutual solubilities of this ether with hydrochloric acid solutions are small so that extractions are practical with even quite concentrated acid solutions, and, in addition, so little acid passes into the ether phase that conditions are favorable for studying the association of hydrogen chloride with the iron. Dichloroethyl ether also has a practical advantage over either ethyl or isopropyl ether for the extraction of iron in that it separates as the lower phase when shaken with hydrochloric acid solutions and repeated extractions from a single separatory funnel are therefore possible.

The Distribution of Iron between Dichloroethyl Ether and Hydrochloric Acid Solutions

Experimental.—The β,β'-dichloroethyl ether was a redistilled grade. It was found to have a boiling range of less than 3° and gave a negative test for peroxide. It was used repeatedly, being washed and distilled each time. Various solutions of ferric chloride in hydrochloric acid were prepared; both reagent grade hexahydrate and anhydrous sublimed ferric chloride were used. Standard solutions of sodium thiosulfate, ammonium thiocyanate, silver nitrate, hydrochloric acid and sodium hydroxide were prepared and standardized by conventional methods.

The distribution data were obtained by shaking equal volumes of the ether with iron and hydrochloric solutions of the desired concentrations in a thermostat at 25° for from thirty to sixty minutes in order to obtain thermal equilibrium. The equilibrium of the iron between the two phases appeared to be established very rapidly. The probable accuracy of the distribution ratios is indicated by the reproducibility of duplicate experiments and the conformity of the points to the curves of Fig. 1. The separatory funnel was then allowed to stand in the thermostat until the two layers separated and the ether layer drawn off. Duplicate twenty-five ml. portions of the acid phase were pipetted into conical flasks, the acid concentration made approximately one normal and the iron determined iodometrically.[5] Where the amount of iron present was small, a 0.01 normal thiosulfate solution was used. Duplicate twenty-five ml. portions of the ether phase were shaken with twenty-five ml. portions of water, the water layer separated and the iron determined as above. Experiments showed that the hydrochloric acid and iron were quantitatively extracted from the ether layer by an equal volume of water. In Table I below is shown the initial concentration of the acid in the aqueous phase and the acid concentration after equilibrium had been established. This latter value was calculated by correcting the original acid concentration for the hydrogen chloride dissolved as such and as $HFeCl_4$ by the ether, for dilution of the aqueous phase by dissolved ether, and for concentration by the water passing into the ether phase. The solubility of ether in 7.5 formal hydrochloric acid and in a solution 7.5 formal in hydrochloric acid and 1 formal in ferric chloride was found to be substantially the same. It should be

(1) E. Beckmann, *Z. physik. Chem.*, **46**, 860 (1903).

(2) Forster, Cooper and Yarrow, *J. Chem. Soc.*, **111**, 810 (1917).

(3) Not until after this article was prepared for publication did the work of Kato and Isii, *Sci. Papers Inst. Phys. Chem. Research (Tokyo)*, **36**, 82–96 (1939), on the molecular formula of the iron compound in ethyl ether come to the attention of the authors. As the result of analytical and absorption spectra studies of the ether phase these investigators assign the compound in ethyl ether the formula $2[FeCl_3 \cdot HCl] \cdot 9H_2O \cdot 15(C_2H_5)_2O$.

(4) Dodson, Forney and Swift, THIS JOURNAL, **58**, 2573 (1936).

(5) Swift, THIS JOURNAL, **51**, 2682 (1929).

pointed out that the acid concentrations given are formal, not molal, concentrations as there is undoubted association of the iron and acid in the aqueous phase.[6]

The results of the distribution experiments are collected in Table I and curves showing the percentage extraction at various acid concentrations are shown in Fig. 1.

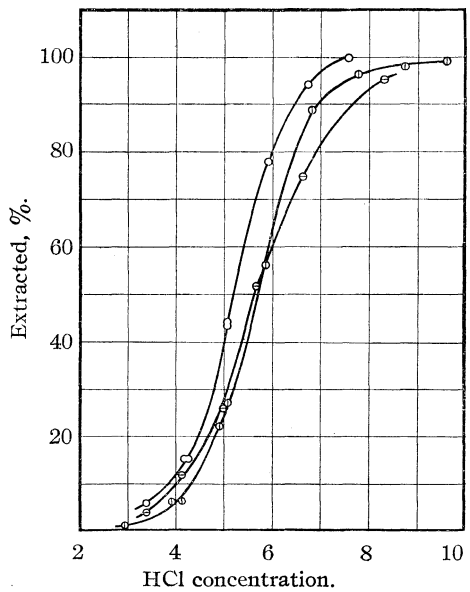


Fig. 1.—Iron extracted into dichloroethyl ether from HCl solutions: ○, initial iron concentration, 0.01 *F*; ⊕, initial iron concentration, 0.07 *F*; ⊖, initial iron concentration, 0.57 *F*.

An inspection of the data of Table I and the curves of Fig. 1 shows that, over the concentration range studied, the extraction of the iron by dichloroethyl ether becomes more effective the higher the hydrochloric acid concentration. This was confirmed by preliminary experiments which extended to 11.5 formal acid without showing any evidence of a decrease in the distribution ratio. This is contrary to the results of Dodson, Forney and Swift which show regions of maximum extraction at approximately 6 and 8 formal acid for ethyl and for isopropyl ether, respectively, and indicates that in the aqueous phase there is a continuous increase with increasing acid concentration of the concentration of the molecular compound passing into the ether phase.

The curves also show that dichloroethyl ether can be used for the practical extraction of iron from solutions in which the hydrochloric acid concentration is greater than seven formal. Mention should be made, however, that the time required for the separation of the two phases is somewhat longer than for either ethyl or isopropyl ether.

(6) Complex acids such as $HFeCl_4 \cdot 2H_2O$ and $H_2FeCl_5 \cdot 4H_2O$ have been prepared, as have salts such as $KFeCl_4$. In addition, studies of the heat of solution of ferric chloride in hydrochloric acid solutions show evidence of such compound formation. Kangro and Flugge, *Z. physik. Chem.*, **A175**, 187 (1935).

TABLE I

THE DISTRIBUTION OF FERRIC IRON BETWEEN HYDROCHLORIC ACID SOLUTIONS AND DICHLOROETHYL ETHER

HCl (moles/liter) aqueous layer Initial	HCl (moles/liter) aqueous layer Final	Iron (moles/liter) aqueous layer Initial	Distribution ratio $\frac{Fe(ether)}{Fe(H_2O)}$	Extracted, %
3.45	3.42	0.00895	0.065	6.0
4.24	4.19	.00895	.187	15.4
4.31	4.26	.00895	.186	15.4
5.17	5.10	.00895	.820	44.5
5.17	5.10	.00895	.795	43.6
6.03	5.93	.00895	3.64	78.0
6.90	6.77	.00895	17.8	94.5
7.75	7.58	.00895	...	>99.8
2.99	2.97	.0720	0.013	1.26
4.00	3.95	.0720	.066	6.1
4.20	4.14	.0720	.071	6.5
5.00	4.93	.0720	.294	22.3
5.17	5.09	.0720	.379	27.1
5.99	5.88	.0720	1.32	56.4
7.00	6.84	.0720	7.74	88.2
7.99	7.80	.0720	29.8	96.6
9.00	8.75	.0720	51	98.0
9.99	9.65	.0720	132	99.2
3.45	3.40	.574	0.043	4.05
4.24	4.15	.574	.136	11.9
5.17	5.02	.574	.350	26.0
6.03	5.66	.574	1.06	52.0
6.90	6.64	.574	2.88	75.0
8.63	8.33	.574	19.4	95.4

The unexpected behavior of the lower portion of the curve for the solutions 0.57 formal in iron may be due to the ferric iron causing an abnormal increase in the ionic strength of the solutions. When a large fraction of the iron is extracted into the ether, this effect diminishes and the upper portion of the curve conforms more nearly to the other two.

The Determination of the Formula of the Iron Compound in the Ether Phase.—In the determination of the formula of the iron in the ether phase the analytical procedure was essentially as follows, although minor refinements and modifications were made as the experiments progressed. Equal volumes of the ether and the iron–hydrochloric acid solutions were shaken together, allowed to separate and the ether layer was analyzed for chloride by shaking it with an equal volume of water, removing the water layer, adding an excess of standard silver nitrate, coagulating the precipitate, and titrating the excess silver nitrate

with a standard thiocyanate solution. A second portion of the ether layer was analyzed for acid and ferric iron by similarly shaking it with an equal volume of water, separating the water layer, titrating it with standard hydroxide until the ferric hydroxide could be coagulated by heating, then again titrating with the hydroxide to a phenolphthalein end-point. The titrated solution was then made approximately one normal in hydrochloric acid and the iron determined iodometrically. The amount of hydrogen chloride passing into the ether layer from pure hydrochloric acid solutions of various concentrations was determined by separate experiments and this amount subtracted from the total amount found with the iron extracts. The analytical data have been collected and are shown in Table II below; also the molecular ratios of chloride and of acid to iron in the ether phase are calculated and tabulated. It was not at first thought necessary to entirely free the water extracts (containing the iron and acid) from ether before heating the solution for the acid titration; however, upon heating 100 ml. of water with a small amount of the ether for an hour it was found that an acidity had developed roughly equivalent to one per cent. of the acid found in the previous analyses. In the last two experiments the water extracts were separated from the ether and then filtered through paper filters before making the titration for acid, thus removing suspended droplets of ether.

TABLE II

ANALYSES OF THE ETHER EXTRACTS

Concentration (moles liter)			Ratios	
Fe^{III}	Cl^-	$H^+ + 3Fe^{III}$	Cl^-/Fe^{III}	H^+/Fe^{III}
Initial HCl concentration, 6.2 formal. Solubility of HCl in ether, 0.0022 formal				
0.3059	1.232	1.237	4.03	1.05
.3065	1.233	1.227	4.02	1.00
.2961	1.187	1.206	4.01	1.07
Initial HCl concentration, 7.1 formal. Solubility of HCl in ether, 0.0032 formal				
0.2114	0.8481	0.8580	4.01	1.06
.2117	.8570	.8563	4.05	1.04
.2111	.8455	.8578	4.01	1.06
Initial HCl concentration, 8.2 formal. Solubility of HCl in ether, 0.0077 formal				
0.1527	0.6123	0.6157	4.01	1.03
.1537	.6124	.6206	3.98	1.04
.1535	...	.6185	..	1.03
.1541	.6169	.6157	4.00	0.997
.1544	.6160	.6181	3.99	1.000

From the data of Table II it is seen that, exclusive of water and ether, the formula of the iron compound can be written as $HFeCl_4$. The closeness of the agreement of the ratios with this formula makes it appear reasonable to conclude that no other complex with a higher ratio of chloride to iron exists in appreciable amounts in the ether.

As Schwarz and Meyer[7] in their study of the various chloro acids found that they could not prepare anhydrous $HFeCl_4$, and as the evaporation of ethyl ether extracts containing iron gives evidence of more water than that normally dissolving in the ether, attempts were made to analyze dichloroethyl ether extracts for their water content. The presence of hydrogen chloride and ferric chloride cause interference with most chemical methods, so, in spite of obvious decomposition in the ether solution during the process, a distillation method was used. A 100-ml. round-bottomed flask was sealed to a fractionating column connected by a ground-glass joint to a condenser which drained into a 15-ml. graduated centrifuge tube initially containing 5 ml. of petroleum ether. Decomposition in the solution in the distilling flask began after approximately 40% of the water was collected and by the time complete recovery was obtained (as shown by the analysis of artificially prepared solutions) a dark viscous mixture was left. Probably because of this decomposition the analysis of the artificial solutions of known content gave an excess of water which was independent of the amount of water originally present and varied in volume from 0.62 to 1.05 ml. with an average value of 0.89 ml.; this volume was subtracted from the total volume of water obtained in the subsequent distillation, as was also the volume of water found to be dissolved by the ether from pure hydrochloric acid solutions. Hydrogen chloride also was distilled over and collected with the water; therefore, the distillate was titrated to determine the acid concentration and the volume corrected accordingly. The data obtained from analyses of ether extracts of iron from 7.5 formal hydrochloric acid solutions are shown in Table III. In the first column are shown the millimoles of iron present in the 50.0 ml. of ether solution; in column two is shown the total volume of water obtained by the distillation procedure outlined above; in column three the corrected volume; and in the last column the calculated molal ratio of water to iron.

The data of Table III show that from four to five molecules of water are associated with each

(7) Schwarz and Meyer, *Z. anorg. allgem. Chem.*, **166**, 190 (1927).

TABLE III

DETERMINATION OF WATER IN THE ETHER EXTRACT

Initial volume of ether, 50.0 ml.

Fe^{III} present (millimoles)	Total H_2O recov., ml.	Corrected H_2O, ml.	Ratio: H_2O/Fe
37.8	4.97	3.11	4.56
39.8	5.4	3.41	4.76
40.3	5.4	3.40	4.68
39.8	5.1	3.11	4.34
38.6	5.13	3.06	4.40
40.7	5.23	3.32	4.53
40.6	5.21	3.22	4.40
		Mean	4.52

molecule of iron. The average ratio is 4.52; this value and the formula assigned to the iron compound in the ethyl ether phase by Kato and Isii[3] suggests the possibility that at least two iron atoms are associated in the molecule existing in the ether phase; however, because of the large corrections applied in obtaining the water volumes, and because a water determination was made with only one concentration of acid and of iron, too great significance should not be placed on the ratio values.

No attempt was made to determine the extent to which the ether may be associated with the iron compound. That there may be such association is indicated by the fact that the compounds $FeCl_3 \cdot (C_2H_5)_2O$[2] and $FeCl_3 \cdot HCl \cdot 2(C_2H_5)_2O$[8] have been prepared, and by the results of Kato and Isii. Although the first of the compounds mentioned is stated to be immediately decomposed by water, this does not preclude the possibility of the existence in an ether solution of a mixed compound containing both water and ether molecules. Because of the uncertainty regarding the association of ether molecules, an exact formulation of the compound or its structure cannot be made. It seems probable that the four chlorides are bonded tetrahedrally to the iron and that the waters are held by hydrogen bonds to the chlorides. As previously stated, Schwarz and Meyer could not prepare anhydrous $HFeCl_4$, which indicates that these hydrogen bonds are needed to stabilize the tetrahedral complex.

(8) Houben and Fischer, *J. prakt. Chem.*, **123**, 89 (1929).

Acknowledgment: The authors are greatly indebted to Mr. John Gates and Mr. R. C. Jones for carrying out an extensive series of preliminary experiments. These experiments were of value in showing the dependence of the distribution ratio on the acid concentration and in establishing the ratio of acid and of chloride to iron in the ether solution.

Summary

The distribution of ferric iron between hydrochloric acid solutions and β,β'-dichloroethyl ether has been studied for various concentrations of acid and iron. Dichloroethyl ether can be used for the quantitative extraction of ferric iron from solutions greater than 7 formal in hydrochloric acid.

Chemical analyses of the ether solution have shown that one molecule of hydrochloric acid and from four to five molecules of water are present for each molecule of iron present in the ether layer. Neglecting polymerization and the possible presence of ether in the molecule, the empirical formula can be written as $HFeCl_4 \cdot 4\text{–}5H_2O$.

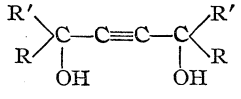
PASADENA, CALIFORNIA RECEIVED OCTOBER 16, 1939

[CONTRIBUTION FROM RÖHM AND HAAS COMPANY, INC.]

Cycli-Alkylation of Aromatic Compounds by the Friedel and Crafts Reaction

BY HERMAN ALEXANDER BRUSON AND JOHN W. KROEGER

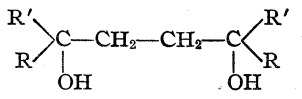
The method recently described by Kazarian[1] for preparing acetylenic alcohols by the interaction of calcium carbide, potassium hydroxide and a ketone, has made more readily available, many acetylenic tertiary glycols heretofore obtainable only with considerable difficulty and expense. These acetylenic tertiary glycols have the general formula (I)



I

Upon catalytic hydrogenation with Raney nickel at 60–85° and 100 lb. pressure/square inch (7 atm.), the acetylenic bond of these glycols can be completely saturated with hydrogen, thus making available in quantity 1,4-ditertiary glycols (II) having unique interest for further synthetic work.

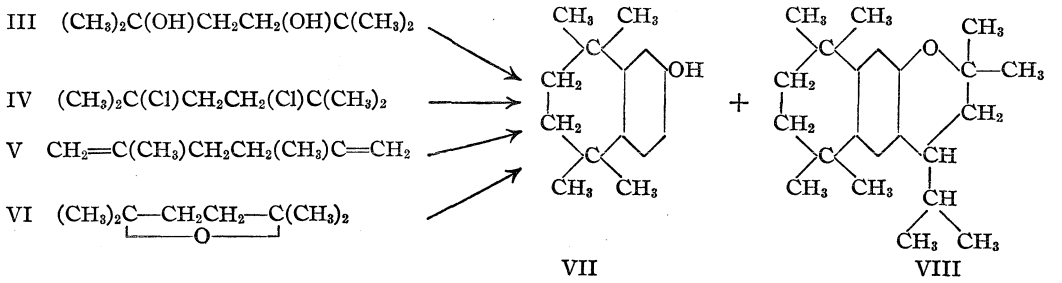
(1) Kazarian, *J. Gen. Chem.* (*U. S. S. R.*), **4**, 1347 (1934), *C. A.* **29**, 3978 (1935); Russian Patent 41,516 (1935), *C. A.* **30**, 8241 (1936); *J. Gen. Chem.* (*U. S. S. R.*), **7**, 956 (1937), *C. A.* **31**, 5320 (1937).



II

The glycol in which R and R′ are each methyl groups, namely, 2,5-dimethylhexane-2,5-diol (III) and a number of its derivatives, namely, 2,5-dichloro-2,5-dimethylhexane (IV), 2,5-dimethyl-1,5-hexadiene (V), and 2,2,5,5-tetramethyl-tetrahydrofuran (VI), were each condensed with various aromatic compounds in the presence of anhydrous aluminum chloride, boron trifluoride, and sulfuric acid as the condensing agents.

Reactions with Phenols and Aluminum Chloride.—It was found that phenol condenses with compounds III, IV, V, and VI in the presence of anhydrous aluminum chloride to give, in each case, the same crystalline compound, m. p. 145°, which is a tetramethyltetrahydronaphthol derivative having the configuration (VII). A small amount of a crystalline non-phenolic compound, m. p. 240–241°, was also isolated, which appears to be a benzo-chromane derivative (VIII). The reactions involved may be formulated as shown



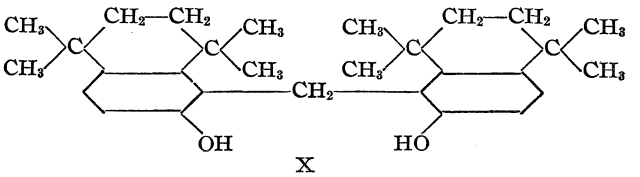
VII VIII

In accordance with known alkylation reactions of phenol with tertiary aliphatic alcohols, tertiary alkyl halides, or tertiary olefins to yield para tertiary alkylphenols, it is very probable that compounds III, IV and V first alkylate phenol in the para position to form mono-alkyl derivatives which immediately undergo either cyclo-dehydration, cyclo-dehydro-halogenation or cyclo-addition, respectively, to form the β-naphthol derivative (VII) which, in turn, may react with another molecule of the alkylating agent to form the chromane derivative (VIII). In the case of compound (VI), the furan ring must open up for cyclo-dehydration to occur. In no case was it possible to isolate the open chain mono-alkylation products, nor was there any evidence of the presence of a diphenolic alkane which could conceivably be formed.

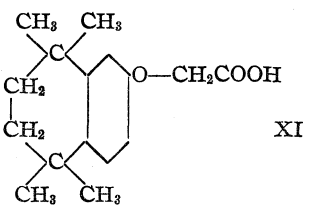
Since alkylation with these compounds proceeds at each end of a difunctionally reactive open chain to form a new cycle by attachment of a saturated divalent alkyl group to the aromatic nucleus, it is proposed that the term "*cycli-alkylation*" be applied to this form of condensation reaction.[2]

Upon oxidation with potassium permanganate, compound (VII) yielded 1,1,4,4-tetramethyladipic acid, (IX), thus proving that no rearrangement of the entering group had occurred during the condensation with aluminum chloride. Attempts to definitely establish the position of the hydroxyl group in (VII) through conversion to a hydroxyphthalic acid by oxidation of the hydroaromatic ring with fused potassium hydroxide were unsuccessful. However, like β-naphthol, compound (VII) condenses readily with formaldehyde in acid solution to yield a crystalline methylene dinaphthol derivative (X) melting at 232°.

With chloroacetic acid in sodium hydroxide solution, compound (VII) yields an oxyacetic acid derivative (XI) melting at 164–165°. The same compound is obtained by condensing (IV) in the presence of aluminum chloride with phenoxyacetic acid. Similarly, ethylation of (VII) gives an ethyl ether, b. p. 132° (5 mm.), identical with the



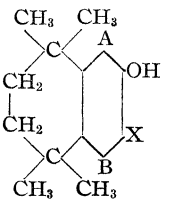
X



XI

(2) The term "*cyclo*-alkylation" already has been applied to reactions involving the introduction of a monovalent cyclo-aliphatic group, such as cyclohexyl, cyclopentyl, etc., into an aromatic nucleus, and is, of course, quite different from the above concept.

TABLE I



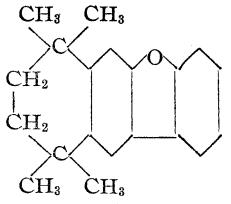
Phenol used	Values of X	A	B	Formula	M. p., °C.	Analyses, % Calculated C	H	Found C	H
Phenol	H	H	H	$C_{14}H_{20}O$	145	82.29	9.87	81.92	9.34
o-Cresol	CH_3	H	H	$C_{15}H_{22}O$	125.5–126	82.50	10.16	82.18	9.88
m-Cresol	H	H	CH_3	$C_{15}H_{22}O$	134–135	82.50	10.16	82.51	9.84
2,6-Dimethylphenol	CH_3	CH_3	H	$C_{16}H_{24}O$	164.5	82.69	10.42	81.72	9.58[a]
Pyrocatechol	OH	H	H	$C_{14}H_{20}O_2$	182–183	76.38	9.15	76.84	9.11
o-Phenylphenol	C_6H_5	H	H	$C_{20}H_{24}O$	98	85.66	8.63	85.46	8.17
o-Cyclohexylphenol	C_6H_{11}	H	H	$C_{20}H_{30}O$	109–110	83.8	10.58	83.07	10.60
o-Chlorophenol	Cl	H	H	$C_{14}H_{19}OCl$	103.5–104	Cl, 14.86		Cl, 15.1	
m-HO–C_6H_4–O–CH_2CH_2–O–CH_2CH_2Cl (1)	H	H	$C_4H_9O_2Cl$	$C_{13}H_{27}O_3Cl$	107–108	66.2	8.34	66.15	8.06
						Cl, 10.85		Cl, 10.65	
m-HO–C_6H_4–O–CH_2CH_2–O–CH_2CH_2Cl (2)	H	H	$C_4H_9O_2Cl$	$C_{13}H_{27}O_3Cl$	71–75	66.2	8.34	65.67	8.12
						Cl, 10.85		Cl, 10.65	

[a] This compound rapidly oxidizes in the air, which accounts for the low analysis.

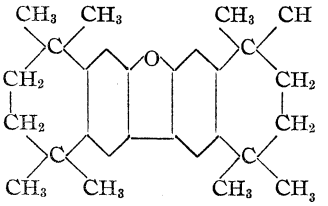
compound obtained by condensing (IV) with phenetole.

Most aromatic ethers, such as phenetole, guaiacol, ethyl *p*-cresyl ether, diphenyl ether, phenoxyacetic acid, and *m*-hydroxyphenoxyethoxy ethyl chloride, $HOC_6H_4OCH_2CH_2OCH_2CH_2Cl$, condense in the presence of aluminum chloride with compound (IV), so as to introduce one additional cycle in a manner analogous to that of phenol. The ether-phenol last mentioned gave two isomers, one, m. p. 107–108°, and the other, m. p. 71–75°.

Diphenylene oxide, however, gave both a monocycli-alkylated and a di-cycli-alkylated compound, represented, respectively, by the probable formulas (XII) and (XIII).



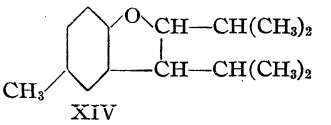
XII



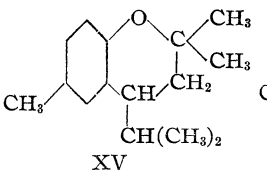
XIII

The following phenols were each condensed with (IV) in the presence of anhydrous aluminum chloride to produce the corresponding analogs of (VII), the properties of which are given in Table I.

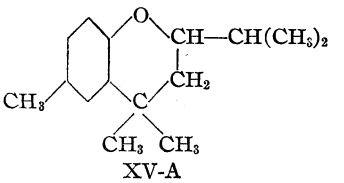
p-Cresol, however, reacted with 2,5-dichloro-2,5-dimethylhexane and aluminum chloride to give a mixture of two isomeric ether-like compounds having the empirical formula $C_{15}H_{22}O$, one of which is a liquid of faint minty odor, b. p. 107–108° (1 mm.), the other a crystalline compound, m. p. 100–101°. These compounds are believed to be coumaranes or chromanes which may be tentatively represented as (XIV), (XV) or (XV-A). A small quantity of a di-cycli-alkylated derivative, m. p. 193–195°, also was isolated.



XIV



XV

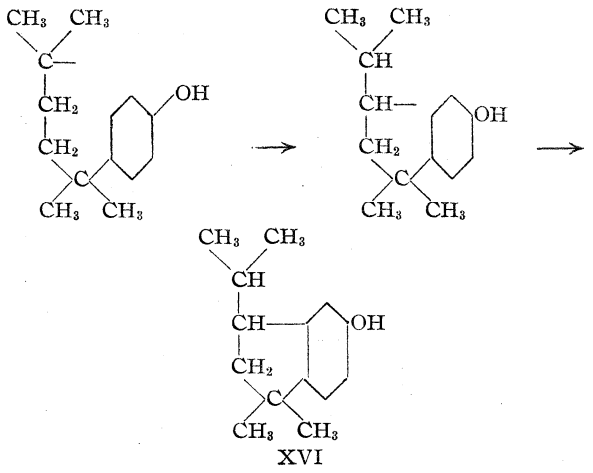


XV-A

Reactions with Sulfuric Acid or Boron Trifluoride.—In all of the above condensations, aluminum chloride was used as the condensing agent. When the aluminum chloride was replaced by sulfuric acid or boron trifluoride, phenol condensed with compounds (III), (V) or (VI) to give not the tetramethyltetrahydronaphthol (VII) but a phenolic compound isomeric therewith melting at 97–98°. This substance gave a crystalline oxyacetic acid derivative, m. p. 112–113°. It did not give a crystalline derivative with formaldehyde, nor did it yield any identifiable acid upon oxidation with permanganate. It is believed to be a hydroxy-indane[3] derivative (XVI) formed by rearrangement of the cycli-alkylating group, rather than an *alpha* isomer of compound (VII).

The formation of such a compound would result from the internal stabilization of an intermediate such as that shown below.

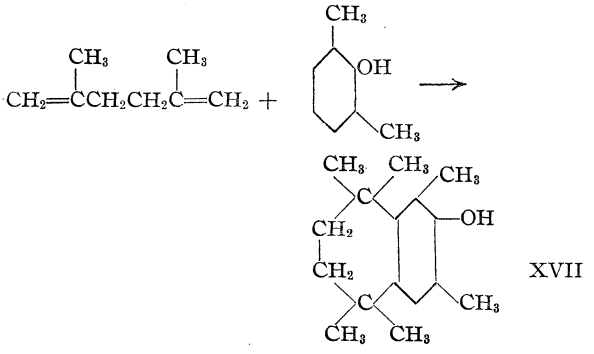
(3) Niederl, Niederl and Reznick, THIS JOURNAL, **58**, 657 (1936).



XVI

The net result of this stabilization is a shifting of a hydrogen atom from a secondary to a tertiary carbon atom[4] followed by ring closure on the depleted carbon atom.

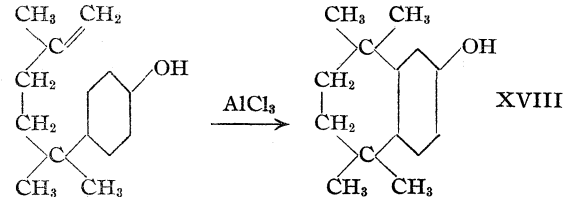
The possibility that compound (XVI) might be an *alpha* isomer of (VII) appears to be unlikely, since if the entering cycli-alkylene group did not rearrange, then a compound such as 2,6-dimethylphenol should condense to give only one compound (XVII), regardless of which catalyst was used.



XVII

However, 2,6-dimethylphenol behaves like phenol and gives two isomers, one with aluminum chloride (m. p. 165°) and the other with sulfuric acid (liquid, b. p. 156° (6 mm.)) as catalyst. Since two isomers are obtained, isomerism must occur in the entering group, unless the methyl groups of the phenol nucleus itself are assumed to wander. This appears unlikely under the conditions used.

That the second isomer in the case of phenol and of 2,6-dimethylphenol is not an open-chain para-substituted phenol, but a bicyclic structure, is shown by the fact that these compounds are unchanged by heating with aluminum chloride. If they had an open chain structure, aluminum chloride should cause cyclization to the higher melting isomer, as follows

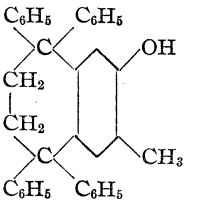


XVIII

It has already been pointed out that in the alkylation of aromatic compounds with olefins, sulfuric acid shows a greater tendency to bring about rearrangements than does aluminum chloride.[5] The hydroxy-indane compound (XVI) was not obtained when aluminum chloride was employed as the condensing agent under a wide variety of conditions.

When boron trifluoride was used as a catalyst at 90° for condensing *p*-cresol and (V), the liquid isomer (XIV) previously mentioned, together with a crystalline di-cycli-alkylated product (XVIII) melting at 193–195°, was obtained. At 0°, however, the rearranging tendencies of boron trifluoride are greatly reduced, phenol, for example, reacting with (V) to give the tetramethyltetrahydronaphthol (VII), together with the hydroxyindane (XVI) and the benzochromane (VIII).

Reactions with Other Cycli-alkylating Compounds.—It was of interest to investigate the action of phenols in the presence of aluminum chloride upon 1,1,4,4-tetraphenylbutane-1,4-diol (made from benzophenone, calcium carbide and potassium hydroxide, followed by catalytic hydrogenation), since this compound might undergo internal ring closure before appreciable cycli-alkylation occurred. The reaction with phenol, or *o*-chlorophenol, led mainly to dehydration of the glycol with formation of 1,1,4,4-tetraphenyl-1,3-butadiene. With *o*-cresol, however, the reaction yielded, in addition to 1,1,4,4-tetraphenyl-1,3-butadiene, a definite compound, m. p. 330–332°, the analysis of which corresponds to the probable structure (XIX).



XIX

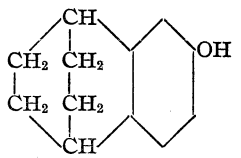
(4) Whitmore, THIS JOURNAL, **54**, 3274 (1932).

(5) Ipatieff, Pines and Schmerling, Printed Abstracts of 96th Meeting, Am. Chem. Soc., Sept. 5–9, 1938, Organic Division, p. 9.

TABLE II

Reacting thiophenol	Catalyst used	R	Alkylating agent	M. p., °C.	Formula of product	Analyses, % Calculated C	H	S	Found C	H	S
Thiophenol	$AlCl_3$	..	IV	79–80	$C_{20}H_{26}S_2$	72.7	7.94	19.4	72.80	7.96	19.35
o-Thiocresol	$AlCl_3$	CH_3	IV	75–76	$C_{22}H_{30}S_2$	73.8	8.45	17.9	73.88	8.29	17.83
o-Thiocresol	BF_3	CH_3	V	75–76	$C_{22}H_{30}S_2$	73.8	8.45	17.9	...	..	...
m-Thiocresol	$AlCl_3$	CH_3	IV	105–106	$C_{22}H_{30}S_2$	73.8	8.45	17.9	73.86	8.30	17.90
m-Thiocresol	$AlCl_3$	CH_3	V	105–106	$C_{22}H_{30}S_2$	73.8	8.45	17.9	...	..	...
p-Thiocresol	$AlCl_3$	CH_3	IV	128–129	$C_{22}H_{30}S_2$	73.8	8.45	17.9	73.80	8.48	17.85

An attempt was made to obtain a compound with an internal bridge such as shown in formula (XX) by condensing phenol in the presence of anhydrous aluminum chloride with 1,4-dichlorocyclohexane.

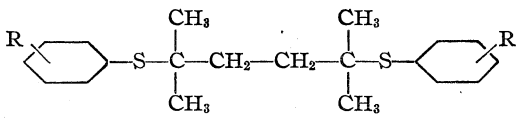


XX

A phenolic crystalline substance was obtained which melted at 124–127° and contained 0.35% chlorine. It appears probable that this is the desired compound (XX) in impure condition.

Finally, it should be pointed out that secondary aliphatic 1,4-glycols condense with phenol in the presence of 77% sulfuric acid to cycli-alkylate the aromatic nucleus. For example, 2,5-dihydroxyhexane and phenol gave a liquid phenolic product which appears to be a hydroxyindane derivative. 1,4-Dihydroxybutane, however, did not condense with phenol in the presence of 77% sulfuric acid to give tetrahydronaphthol.

Condensation with Thiophenols.—In contrast to phenol and its homologs, the thiophenols condense with compounds (IV) or (V) to form dithio ethers, instead of undergoing cycli-alkylation. The same dithio ethers are obtained, regardless of whether aluminum chloride or boron trifluoride is used as the catalyst. These dithio ethers are beautifully crystalline compounds of the general formula (XXI).

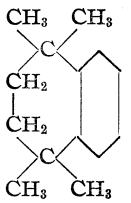


XXI

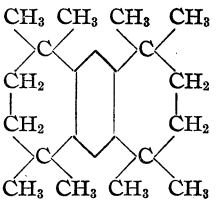
Their properties are given in Table II.

The unusual tendency for olefins and thiophenols to condense even in the absence of catalysts to form thiophenol ethers already has been pointed out by Ipatieff, Pines and Friedman,[6] and may thus account for the non-formation of cycli-alkylation products.

Cycli-alkylation of Aromatic Hydrocarbons.—The condensation of 2,5-dichloro-2,5-dimethylhexane with benzene in the presence of anhydrous aluminum chloride yields a liquid mono- and a crystalline di-cycli-alkylation product, (XXII) and (XXIII), respectively.



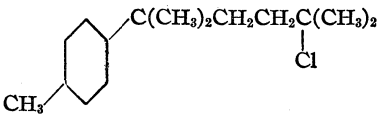
XXII

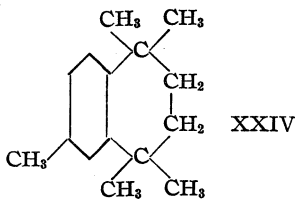


XXIII

It is assumed that the entering group in the case of hydrocarbons has the same configuration as in the case of phenols, since there was no difference in the method of preparation. The analytical data checked the formulas given.

When only catalytic quantities of aluminum chloride are used, nearly quantitative yields of compound (XXIII) are obtained. Larger amounts of aluminum chloride favor the formation of the mono-cycli-alkylation product. Toluene, however, gave only a liquid mono-cycli-alkylation product. It already has been pointed out[7] that in the cyclo-dehydration of *m*-$CH_3C_6H_4CH_2CH_2CH_2C(CH_3)_2OH$ ring closure occurs so that the entering group takes a position as far removed as possible from the substituent already present in the ring. It is highly probable that in the case of





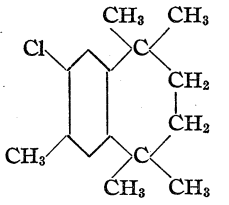
XXIV

(6) Ipatieff, Pines and Friedman, THIS JOURNAL, **60**, 2731 (1938).

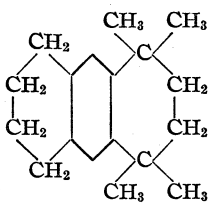
(7) Bogert, Davidson and Apfelbaum, *ibid.*, **56**, 959 (1934).

toluene the entering group is first introduced into the para position and immediately undergoes cyclo-dehydrohalogenation to give the mono-cycli-alkylation product (XXIV).

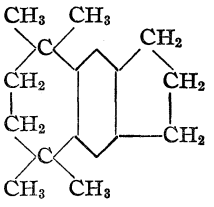
o-Chlorotoluene, tetralin and hydrindene each give crystalline mono-cycli-alkylation products with (IV) in the presence of aluminum chloride. These compounds may be represented by formulas (XXV), (XXVI) and (XXVII), respectively.



XXV

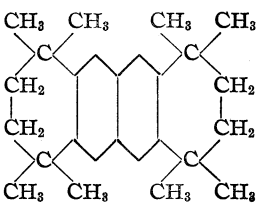


XXVI

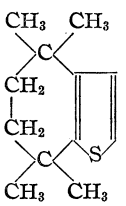


XXVII

Naphthalene, however, gave only a di-cycli-alkylated derivative. The high melting point of this compound (319–320°) and the tendency for naphthalene to alkylate first in the beta position, is indicative that the compound is probably a hydronaphthacene derivative (XXVIII).



XXVIII



XXIX

On the other hand, thiophene condenses with (IV) in the presence of stannic chloride as catalyst, to give only a mono-cycli-alkylation product (XXIX), which is believed to be a tetramethyltetrahydrobenzothiophene.

Although the exact formulas of these compounds have not as yet been proved, it is none the less certain that this simple method of introducing hydroaromatic rings into aromatic compounds may be of unusual interest at the present time, in connection with the synthesis of higher polynuclear structures in vitamin and hormone research.

Experimental

Preparation of Intermediates

2,5-Dimethyl-3-hexyn-2,5-diol.[1]—Technical calcium carbide (20–35 mesh, 80%) was powdered by grinding with benzene in a ball mill. Seven hundred grams of this suspension, containing 1.75 moles of calcium carbide, was diluted with 800 g. of benzene, and 196 g. (3.50 moles) of powdered potassium hydroxide was added. The mixture was stirred vigorously, while 305 g. of acetone (5.25 moles) was added during seven hours. The temperature was held at 21–24° by external cooling and by controlling the rate of addition of the acetone.

Stirring was continued for ninety-six hours at about 20°; then the pasty mass was hydrolyzed by slow addition of 750–800 g. of 37% hydrochloric acid, which left the mixture neutral or faintly acid. The aqueous layer was discarded and the organic layer was heated to boiling and filtered. The clear yellow filtrate deposited 183 g. of 2,5-dimethyl-3-hexyn-2,5-diol on cooling. This was filtered off and washed with a little benzene; then the combined filtrate and washings were distilled to recover the remaining glycol, b. p. 115–140° (30 mm.), 60 g. The total yield of white, crystalline product was 243 g. or 98%. The material was pure enough for preparative purposes. A sample recrystallized from petroleum ether melted at 94–95° and had the following analysis: calcd. for $C_8H_{14}O_2$: C, 67.55; H, 9.93. Found: C, 67.47; H, 10.09.

(III) 2,5-Dimethylhexane-2,5-diol.—This compound was prepared by hydrogenating 2,5-dimethyl-3-hexyn-2,5-diol dissolved in water or alcohol at 60–85° under 100 lb./square inch (7 atm.) pressure of hydrogen in the presence of Raney nickel. The product was obtained in excellent purity by simply evaporating the solvent *in vacuo*, m. p. (·$6H_2O$) 38°, m. p. (anhydrous) 88–89°; yield 95–99%.[8]

(IV) 2,5-Dichloro-2,5-dimethylhexane.—III was dissolved in concentrated hydrochloric acid and the solution was saturated with hydrogen chloride at room temperature. During this last operation, the product crystallized as small, white leaflets. This was filtered off, washed thoroughly with water, finally with a little methanol, then air-dried or dried *in vacuo*. The yield was quantitative. The dichloride melted at 63–64° and had a strong menthol-like odor.[9]

(V) 2,5-Dimethyl-1,5-hexadiene.—This compound was prepared by the usual Grignard technique from methallyl chloride and magnesium[10] in a molar ratio of 2 to 1, b. p. 114.5° (763 mm.).

(VI) 2,2,5,5-Tetramethyltetrahydrofuran.—This compound was obtained, together with a small amount of 2,5-dimethyl-2,4-hexadiene, by distilling (III) in the presence of 3% of aniline hydrobromide. It boiled at 112–114° (768 mm.).[9]

Cycli-alkylated Products

(VII) 5,5,8,8-Tetramethyl-5,6,7,8-tetrahydro-2-naphthol. (a) (From phenol and IV).—Twenty-nine grams of phenol, 55 g. of (IV) and 3 g. of anhydrous aluminum

(8) Dupont, *Ann. chim. phys.*, (8) **30**, 485 (1913); *C. A.*, **8**, 1579 (1914).

(9) Henry, *Compt. rend.*, **143**, 497 (1906).

(10) Schales, *Ber.*, **70**, 117 (1937).

chloride were suspended and partly dissolved in 30 g. of petroleum ether (b. p. 90–100°). This mixture was stirred at room temperature for about one hour or until the first vigorous evolution of hydrogen chloride had abated. The suspension was then heated on a steam-bath for two hours, 2 g. of aluminum chloride added, and heating continued for two hours more. The product was stirred with cold, dilute hydrochloric acid, and the light gray crystalline tetrahydronaphthol derivative which separated was filtered off (42 g.). Evaporation of the organic layer gave an additional 6 g.; total yield, 48 g., 80%.

The product was recrystallized to constant melting point from petroleum ether or benzene, and separated as long, thick, colorless prisms, m. p. 145.0–145.2° (uncorr.). It gave an emerald-green color with alcoholic ferric chloride, and had a hydroxyl number of 279.9; calculated value, 275. The oxyacetic acid derivative (XI) melted at 164–165°. *Anal.* Calcd. for $C_{16}H_{22}O_3$: C, 73.23; H, 8.46. Found: C, 73.08; H, 8.48.

The ethyl ether boiled at 132° (5 mm.). *Anal.* Calcd. for $C_{16}H_{24}O$: C, 82.70; H, 10.42. Found: C, 81.91; H, 10.06.

Attempted oxidation of this ether with dilute nitric acid gave a crystalline yellow mono-nitro derivative, m. p. 106–108°. *Anal.* Calcd. for $C_{16}H_{23}O_3N$: C, 69.3; H, 8.37; N, 5.05. Found: C, 68.90; H, 7.92; N, 5.70.

(X), m. p. 232°, was prepared by condensing the substituted naphthol with aqueous formaldehyde in the presence of hydrochloric acid. *Anal.* Calcd. for $C_{29}H_{40}O$: C, 82.79; H, 9.59. Found: C, 82.91; H, 9.30.

Oxidation of (VII) with neutral potassium permanganate gave a small quantity of 1,1,4,4-tetramethyladipic acid, m. p. 190–193° (uncorr.). *Anal.* Calcd. for $C_{10}H_{18}O_4$: C, 59.36; H, 8.97. Found: C, 58.73; H, 8.05.

From the combined recrystallization liquors of several preparations of (VII), a small amount of a disubstituted derivative, the benzochromane (VIII) was isolated. This crystallized from petroleum ether in large, oblique hexahedra, m. p. 240–241°. Its hydroxyl number was zero. *Anal.* Calcd. for $C_{22}H_{34}O$: C, 84.00; H, 10.90. Found: C, 84.42; H, 10.68.

(b) **(From Phenol and III).**—Twenty-one grams of (III), 54 g. of phenol, and 50 g. of anhydrous aluminum chloride were suspended in 200 cc. of petroleum naphtha and stirred at 85–90° for eight hours. The mixture was hydrolyzed with cold, dilute hydrochloric acid, then the organic layer was taken up in benzene, washed with 5% sodium carbonate solution, and distilled. The fraction boiling from 150–165° (3 mm.) weighed 21 g. and crystallized on standing. Recrystallization from petroleum ether gave the pure compound, m. p. 145°.

(c) **(From Phenol and VI).**—Thirteen grams of phenol, 12.8 g. of (VI) and 13 g. of aluminum chloride were suspended in 30 g. of petroleum ether (b. p. 90–100°) and cooled for five minutes. The mixture was then stirred at room temperature for five hours and refluxed for two hours. The mixture was then hydrolyzed and filtered, giving 16 g. of crude product. After one recrystallization from petroleum ether, it melted at 143–145°.

(d) **(From Phenol and V).**—Forty grams of phenol and 4 g. of anhydrous aluminum chloride were suspended in 20 g. of 90–100° petroleum ether and cooled to 0° or below. Forty-four grams of (V) was then added slowly with stirring, while the temperature was kept below 0°. The temperature was then allowed to rise slowly, the mixture was stirred at 25° for sixteen hours, and finally at 50° for one hour. The product was worked up as in (b). The fraction boiling from 128–150° (1 mm.) crystallized partly. On recrystallization from petroleum ether, the solid melted at 145°.

Mixed melting points of products (a), (b), (c) and (d) showed no depressions.

(XI) **5,5,8,8-Tetramethyl-5,6,7,8-tetrahydro-2-naphthoxyacetic Acid.**—Four grams of (IV), 3.5 g. of phenoxyacetic acid, and 3.5 g. of anhydrous aluminum chloride were suspended in 30 g. of ethylene dichloride and stirred for one hour at room temperature. The mixture next was refluxed for five hours and then hydrolyzed with dilute hydrochloric acid. The organic layer was separated and the solvent was evaporated by a stream of air, leaving 5.5 g. of greenish crystals. The solid was dissolved in petroleum ether and boiled with Norite for an hour. On cooling, the product separated in glistening white plates. A second crystallization from petroleum ether and two from 33% alcohol gave the pure compound, m. p. 164–165°. The melting point was not raised by the last recrystallization, and showed no depression when mixed with the oxyacetic acid derivative prepared by heating chloroacetic acid with an aqueous sodium hydroxide solution of (VII).

The properties of other substituted naphthols prepared in the manner described in (a) above are given in Table I.

***m*-Hydroxyphenoxyethoxyethyl Chloride.**—This compound was obtained as a crystalline solid, m. p. 46–47°, by condensing resorcinol in aqueous potassium carbonate solution with β,β'-dichlorodiethyl ether.[11]

Six grams of *m*-hydroxyphenoxyethoxyethyl chloride, 5 g. of (IV) and 0.5 g. of anhydrous aluminum chloride were mixed and heated at 65° for four hours. Hydrolysis with dilute hydrochloric acid gave a dough-like mass which crystallized partly on macerating with water. The organic material was dissolved in 90–100° petroleum ether, and cooled, giving crystals which melted at 102–103°. Concentration of the mother liquor gave a second compound, m. p. 69–71°. Both these compounds were recrystallized twice more and the first was decolorized with Norite. The final melting points were 107–108° and 71–75°, respectively.

(XVI) **1,1-Dimethyl-3-isopropyl-5-hydroxyindane.**—Twenty-five grams of phenol and 54.5 g. of (III) were melted together and the melt was dropped slowly into 96 g. of 77% sulfuric acid, which was well stirred and held at 10°. The temperature was allowed to rise slowly to 35°, the mixture was stirred at room temperature for twenty-two hours, and at 85–95° for one hour, then was poured into 200 ml. of cold water. The oil was extracted with benzene, washed with water and dilute sodium carbonate solution, and distilled. The fraction boiling from 145–170° (5 mm.) (b. p. 160–165° (5 mm.)), weighing 30 g., solidified on standing. After several recrystallizations from petroleum ether, the pure compound was obtained as tiny needles, m. p. 97–98°. *Anal.* Calcd. for $C_{14}H_{20}O$: C, 82.29; H, 9.87. Found: C, 82.60; H, 9.70.

(11) Bruson, U. S. Patent 2,098,204 (1937).

This compound, like (VII), gave an emerald-green color with alcoholic ferric chloride, and formed a sparingly soluble sodium salt when dissolved in warm 10% sodium hydroxide. It did not give a crystalline methylene derivative with formaldehyde, but treatment of the sodium salt with chloroacetic acid gave an oxyacetic acid derivative, m. p. 112–113°. It was unchanged by warming with aluminum chloride in petroleum ether.

2,6-Dimethylphenol was condensed similarly with 2,5-dimethylhexane-2,5-diol in the presence of 77% sulfuric acid to give a compound of b. p. 156° (6 mm.). *Anal.* Calcd. for $C_{16}H_{24}O$: C, 82.69; H, 10.42. Found: C, 82.66; H, 10.34.

(XIX) 5,5,8,8-Tetraphenyl-3-methyl-5,6,7,8-tetrahydro-2-naphthol.—Eight grams of 1,1,4,4-tetraphenylbutane-1,4-diol, 10 g. of *o*-cresol, and 8 g. of anhydrous aluminum chloride were suspended in 100 ml. of petroleum ether (b. p. 30–60°) and refluxed for fourteen hours. After hydrolysis with 200 ml. of dilute hydrochloric acid, the product was filtered out (6 g.). Two recrystallizations from toluene gave the pure compound, m. p. 330–332°, as glistening, white needles. *Anal.* Calcd. for $C_{35}H_{30}O$: C, 90.08; H, 6.48. Found: C, 89.81; H, 5.94.

Evaporation of the mother liquors gave a small amount of 1,1,4,4-tetraphenyl-1,3-butadiene. After several recrystallizations from toluene, it was obtained as pale violet needles, m. p. 195–196° (uncorr.). *Anal.* Calcd. for $C_{28}H_{22}$: C, 93.80; H, 6.19. Found: C, 93.67; H, 6.24.

(XX) 5,8-Endoethylene-5,6,7,8-tetrahydro-2-naphthol (?).—Fourteen grams of 1,4-dichlorocyclohexane (*cis* and *trans*), 8 g. of phenol, 1 g. of aluminum chloride, and 20 g. of petroleum ether were stirred for a half hour and refluxed for six hours; 9 g. of aluminum chloride was added and the mixture was stirred for four hours, then hydrolyzed with ice and hydrochloric acid. The organic layer was washed and distilled and the fraction boiling from 110–180° (3 mm.) was saved. Two recrystallizations from di-isobutylene gave white needles, m. p. 124–127°. *Anal.* Calcd. for $C_{12}H_{14}O$: C, 82.70; H, 8.10. Found: C, 81.00; H, 8.77; Cl, 0.35%.

2,5-Dimethylhexane-2,5-bis-(*p*-tolyl sulfide).—Nine g. of (IV), 6.2 g. of *p*-thiocresol, and 1.0 g. of anhydrous aluminum chloride were suspended and partly dissolved in 30 g. of petroleum ether (b. p. 90–100°), and refluxed for four hours. The product was hydrolyzed with dilute hydrochloric acid and the organic layer was cooled and evaporated to give 4 g. of the crystalline dithio ether. This was recrystallized to constant melting point from petroleum ether, giving long, white needles, m. p. 128–129°. Data on this compound and other dithio ethers prepared in the same manner are given in Table II. The compounds were insoluble in hot 5% sodium hydroxide.

(XXII) 1,1,4,4-Tetramethyl-1,2,3,4-tetrahydronaphthalene.—Thirty-six grams of (IV) was dissolved in 78 g. of benzene and stirred at 30° or lower, while 16 g. of anhydrous aluminum chloride was added in small portions. The thick suspension was then stirred at room temperature for twenty-one hours, refluxed for two hours, and poured into ice and dilute hydrochloric acid. The organic layer was washed with water and dilute sodium carbonate solution and distilled. A 61% yield (22.5 g.) of crude (XXII) was obtained, boiling from 95–125° (4 mm.). The pure compound was a water-white oil and had the following properties: b. p. 82–84° (3 mm.); 248° (760 mm.); $n^{27}D$ 1.5278; d^{27}_4 0.9482; MR_D calcd., 61.06; found, 61.09.

(XXIII) 1,1,4,4,5,5,8,8-Octamethyl-1,2,3,4,5,6,7,8-octahydroanthracene.—Thirty-six grams of (IV), 78 g. of benzene, and 1 g. of anhydrous aluminum chloride were stirred and refluxed for four hours. The product was hydrolyzed without cooling by adding warm, dilute hydrochloric acid; then the hot organic layer was separated and chilled. The substituted anthracene separated in large, white prisms which were filtered off and the filtrate was evaporated to recover the remainder (total, 26 g.). It was purified by recrystallization to constant melting point from benzene or carbon tetrachloride–methanol mixture (2:1) and melted at 220–222° (uncorr.). In the evaporation mentioned above, a small amount of oil remained, which contained 3.5 g. of the substituted naphthalene (XXII).

When treated with nitric and sulfuric acids (2:1), this compound formed a nitro derivative, m. p. 259–261°.

(XXVI) 1,1,4,4-Tetramethyl-1,2,3,4,5,6,7,8-octahydroanthracene.—Thirteen grams of tetralin, 18 g. of (IV) and 1 g. of anhydrous aluminum chloride were suspended in 30 g. of petroleum ether (b. p. 90–100°) and refluxed for five hours. The product was hydrolyzed with ice-cold, dilute hydrochloric acid, filtered, then the organic layer was taken up in benzene, washed and distilled. Two fractionations gave 7 g. of yellow sirup boiling from 150–160° (4 mm.) which crystallized on standing for four days. The solid was recrystallized four times from methanol containing a few drops of ethyl acetate, m. p. 90–91°.

(XXVII) 5,5,8,8-Tetramethyl-5,6,7,8-tetrahydro-β-naphthindane.—Fifteen grams of hydrindene, 18 g. of (IV) and 1 g. of aluminum chloride were suspended in 30 g. of petroleum ether and stirred at room temperature for two hours. The mixture was then refluxed for four hours and worked up as in the previous experiment. The fraction boiling from 110–150° (3 mm.) weighed 3 g. and crystallized in the receiver. The product was recrystallized four times from a mixture of methanol and ethyl acetate and finally separated as large square plates, m. p. 93–94°.

(XXVIII) 1,1,4,4,7,7,10,10-Octamethyl-1,2,3,4,7,8,9,10-octahydronaphthacene.—Thirty-eight grams of naphthalene, 55 g. of (IV) and 5 g. of aluminum chloride were suspended in 100 g. of petroleum ether (b. p. 90–100°) and refluxed for four hours. The product was hydrolyzed with cold, dilute hydrochloric acid and filtered. The crystalline solid was then washed with four 50-cc. portions of cold benzene to remove unchanged naphthalene, and air-dried; yield, 42 g., 80.5%. Two recrystallizations from toluene gave the pure product in the form of beautiful white needles, m. p. 319–320°.

Other hydrocarbons prepared in this way are described in Table III.

(XXIX) Thiophene and (IV).—Nine grams of (IV) and 8.4 g. of thiophene were dissolved in 30 g. of petroleum ether and 2.0 g. of anhydrous stannic chloride was slowly dropped in. The solution was stirred for one hour at room temperature, refluxed for three hours, then the product hydrolyzed, washed, filtered from a trace of black impurity, and distilled. The fraction boiling from 90–130° (6 mm.) was saved and redistilled. The pure compound had a boiling point of 94° (6 mm.). *Anal.* Calcd. for

TABLE III

Hydrocarbon used	Formula	M. p. or b. p., °C.	Analyses, % Calculated C	Calculated H	Found C	Found H
Benzene (mono)	XXII $C_{14}H_{20}$	B. 82–84 (3 mm.)	89.29	10.72	89.44	10.32
Benzene (di)	XXIII $C_{22}H_{34}$[a]	M. 221–222	88.5	11.5	88.50	12.02
Toluene	XXIV $C_{15}H_{22}$	B. 95 (4 mm.)	89.1	10.95	88.85	11.07
o-Chlorotoluene	XXV $C_{15}H_{21}Cl$	M. 104–105	76.07	8.95	76.28	8.75
			Cl, 14.98		14.70	
Tetralin	XXVI $C_{18}H_{26}$	M. 90–91	89.2	10.82	89.25	11.18
Hydrindene	XXVII $C_{17}H_{24}$	M. 93–94	89.4	10.61	88.71	10.70
Naphthalene (di)	XXVIII $C_{26}H_{36}$[b]	M. 319–320	89.59	10.42	90.05	10.35

[a] Molecular weight (Rast): calcd., 298; found, 286. [b] Molecular weight (Rast): calcd., 348; found, 342.

$C_{12}H_{18}S$: C, 74.17; H, 9.34; S, 16.48. Found: C, 74.46; H, 9.70; S, 16.20.

***p*-Cresol and IV.**—Thirty-three grams of *p*-cresol, 55 g. of (IV) and 3 g. of aluminum chloride were suspended and partly dissolved in 50 g. of petroleum ether. The mixture was then stirred for a half hour at room temperature and at 85–90° for two hours. Two grams of aluminum chloride was added and heating and stirring was continued for two hours more. The product was hydrolyzed, washed and distilled. The fraction boiling from 91–115° (2 mm.) (26.5 g.) gave the liquid isomer (A) as a water-white oil, having a pleasant, minty odor. It had the following properties: b. p. 107–108° (1 mm.); $n^{25}D$ 1.5137; d^{25}_4 0.953.

The fraction boiling from 115–140° (2 mm.) (6 g.) crystallized partly when diluted with petroleum ether and chilled. Recrystallization to constant melting point gave small prisms, m. p. 100–101° (B).

The above experiment was repeated, using (V) as a cycli-alkylating agent and boron trifluoride as a catalyst. Small amounts of the liquid isomer (A) and a disubstituted derivative (C) melting at 193–195° were obtained. The analytical data are as follows: calcd. for $C_{15}H_{22}O$ (XIV and XV): C, 82.50; H, 10.16. Found (A): C, 83.02; H, 10.09. Found (B): C, 82.81; H, 9.92. Calcd. for the disubstituted derivative (C); $C_{23}H_{36}O$: C, 84.07; H, 11.05. Found: C, 84.27; H, 10.81.

Diphenylene Oxide and IV.—Nine grams of (IV), 8.5 g. of diphenylene oxide, and 1 g. of anhydrous aluminum chloride were suspended in 30 g. of petroleum ether (b. p. 30–60°) and stirred for eight and one-half hours at room temperature. The mixture was then refluxed for one hour, hydrolyzed, washed and distilled. The fraction boiling from 170–240° (4 mm.) (5.5 g.) was a thick yellow sirup (XII) and was analyzed. Calcd. for $C_{20}H_{22}O$: C, 86.27; H, 7.97. Found: C, 86.91; H, 8.38. From this it appeared the compound (XII) was contained in this fraction.

The residue of the above distillation was recrystallized three times from an ethyl acetate–methanol mixture as colorless crystals, m. p. 201–202°. *Anal.* (XIII) Calculated for $C_{28}H_{36}O$: C, 86.53; H, 9.34. Found: C, 87.00; H, 9.50.

Acknowledgment.—We are indebted to Dr. C. W. Nash of this Company for microdeterminations of carbon, hydrogen, sulfur and chlorine.

Summary

1. Di-tertiary 1,4-glycols condense in the presence of aluminum chloride with aromatic hydrocarbons, phenols, or phenol ethers, so as to introduce a new hydroaromatic cycle into the aromatic nucleus. The use of boron trifluoride or of 77% sulfuric acid as condensing agent in place of aluminum chloride, gives isomers of the above compounds. Phenols which are blocked in the para-position give chromanes or coumaranes.

2. Similar condensation products are obtained by using di-tertiary 1,4-dichlorides, 1,5-diolefins, and 2,2,5,5-tetraalkyltetrahydrofurans in place of the 1,4-glycols.

3. Thiophenols behave differently from phenols and give diaryl dithio ethers. Thiophene takes up a hydroaromatic cycle.

4. Certain aromatics, notably benzene, naphthalene and diphenylene oxide, readily take up two hydroaromatic cycles.

5. The term "cycli-alkylation" has been proposed for these reactions.

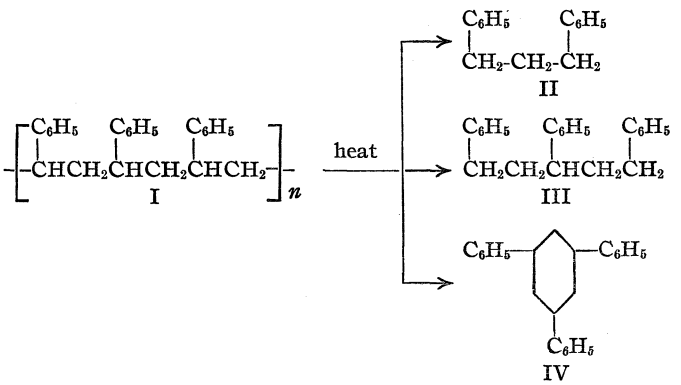
PHILADELPHIA, PA. RECEIVED OCTOBER 19, 1939

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

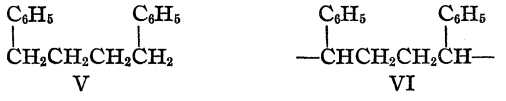
The Structure of Vinyl Polymers. VIII.[1] Polystyrene and Some of its Derivatives

BY C. S. MARVEL AND NEIL S. MOON

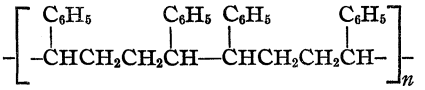
The destructive distillation of polystyrene (I) has been shown by Staudinger and Steinhofer[2] to produce a rather complex mixture of hydrocarbons from which, among other things, 1,3-diphenylpropane (II), 1,3,5-triphenylpentane (III) and 1,3,5-triphenylbenzene (IV) have been isolated and identified. These products furnish excellent evidence that the aryl groups are on alternate carbon atoms in the polymer chain (I).[3]



Midgley, Henne and Leicester[4] found that treatment of styrene with sodium and alcohol yielded 1,4-diphenylbutane (V) and a polymer of styrene which appeared to be identical with that obtained by the polymerization of styrene in the presence of peroxides.

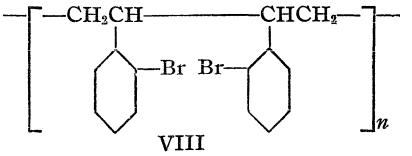


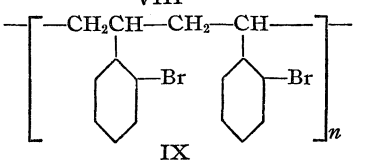
The formation of 1,4-diphenylbutane in this reaction was interpreted as evidence that the biradical (VI) was an intermediate in the polymerization of styrene and that polystyrene might have the "head to head, tail to tail" type of structure (VII).

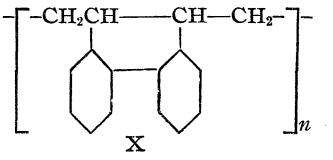


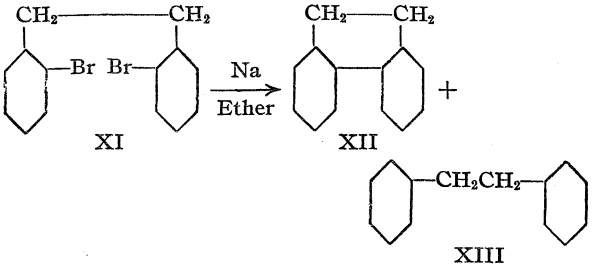
In the present work we have prepared a number of derivatives of styrene containing various functional groups both in the ring and in the side chain with the aim of producing polymers whose chemical reactions would be useful in determining the relative positions of the aryl groups in the polymer chain. Ortho-, meta- and para-bromostyrenes were synthesized and polymerized. Meta- and para-bromostyrenes have been reported previously[5] but the ortho-compound apparently is new. It was prepared readily by dehydration of *o*-bromophenylmethylcarbinol. All three of these bromostyrenes polymerized more readily than styrene itself to give hard, brittle, colorless, transparent products which gradually assumed an amber color on aging for a few months.

A poly-*o*-bromostyrene which has the 1,2-arrangement (VIII) of the aryl groups along the polymer chain should react with metals to give a dihydrophenanthrene (X) type of polymer in a manner similar to









(1) For the seventh communication in this series, see THIS JOURNAL, **61**, 3244 (1939).

(2) Staudinger and Steinhofer, *Ann.*, **517**, 35 (1935).

(3) Allen (Gibson Island Conference on Synthetic Resins, July 12, 1939) reported the identification of toluene and isopropenylbenzene as products of the pyrolysis of polystyrene. The formation of isopropenylbenzene is most readily explained on the basis of structure I for this polymer.

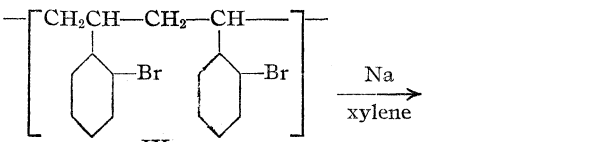
(4) Midgley, Henne and Leicester, THIS JOURNAL, **58**, 1961 (1936).

(5) Ziegler and Tiemann, *Ber.*, **55**, 3414 (1922); Quelet, *Bull. soc. chim.*, (4) **45**, 75 (1929); Brown and Marvel, THIS JOURNAL, **59**, 1176 (1937).

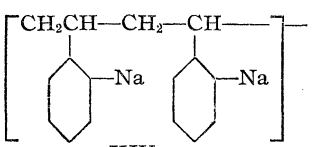
the conversion of 1,2-di-(*o*-bromophenyl)-ethane (XI) to dihydrophenanthrene (XII). Kenner and Wilson[6] have shown that at least a 12% yield of cyclic product results from the action of sodium on 1,2-di-(*o*-bromophenyl)-ethane although debromination to 1,2-diphenylethane (XIII) accounts for most of the product.

When poly-*o*-bromostyrene in dioxane solution was treated with zinc, very little halogen was removed. Neither did copper remove halogen from a nitrobenzene solution of the polymer. Sodium did remove halogen from the hot solution of the polymer in benzene or toluene and when xylene was used as a solvent, the removal of halogen became essentially quantitative. The viscosity of the solution did not change appreciably during this treatment, showing that the polymeric material was not coupling to give a higher molecular weight product and there was no separation from solution as should occur if cross linking of chains had occurred. These facts led to the belief that ring closure must be taking place. However, it was impossible to obtain any evidence of a cyclization reaction. Oxidation of the debrominated polymer gave neither diphenic acid nor a phenanthraquinone derivative. Dehydrogenation and cracking of the polymer over hot selenium gave no phenanthrene derivatives.

The reaction of poly-*p*-bromostyrene in xylene solution with sodium was next tried. This polymer was as readily debrominated by the treatment as the ortho compound and there was no evidence of cross linking in the reaction. Obviously, then, sodium had reacted with these two polybromostyrenes to give polymeric organometallic materials (XIV) which were hydrolyzed by water during the subsequent steps in the working up of the reaction mixtures. This was confirmed by treating the reaction mixture of poly-*o*-bromostyrene and sodium in xylene with dry carbon dioxide. Some alkali soluble material was



IX

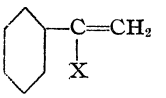


XIV

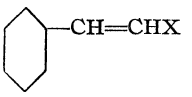
(6) Kenner and Wilson, *J. Chem. Soc.*, 1108 (1927).

produced showing that carbonation had taken place. It seems probable that the *o*-bromophenyl groups are on alternate carbon atoms in the chain (IX) for this formation of the sodium derivative to proceed so smoothly. If the aryl groups are on adjacent carbon atoms (VIII) in the polymer chains some evidence that a Wurtz–Fittig reaction had occurred should have been found.

α-Chlorostyrene (XV, X = Cl) was prepared by the method of Dufraisse and Viel[7] and attempts



XV



XVI

were made to polymerize it with heat, ultraviolet light, benzoyl peroxide, ascaridole, stannic chloride and the boron fluoride complex with ethyl acetate. No polymer was obtained although the boron fluoride catalyst did convert α-chlorostyrene into 1,3,5-triphenylbenzene (IV).

α-Methoxystyrene[8] (XV, X = OCH_3), β-bromostyrene (XVI, X = Br), α-acetoxystyrene (XV, X = $OCOCH_3$) and β-acetoxystyrene[9] (XVI, X = $OCOCH_3$) failed to give polymers with peroxide catalysts or under the influence of ultraviolet light. β-Nitrostyrene (XVI, X = NO_2) was polymerized by the method of Vorländer and Herrmann[10] but the polymer was too insoluble to permit the attack of any reagents.

Experimental

o-Bromophenylmethylcarbinol.—A suspension of methylmagnesium chloride was prepared by passing commercial methyl chloride, dried by passing through a calcium chloride tower, into ice cold anhydrous ether covering 100 g. of magnesium turnings. When the ether was saturated with methyl chloride the cooling bath was removed and the temperature of the mixture allowed to rise to room temperature. Usually the reaction between methyl chloride and the magnesium started readily when this was done. Occasionally it was necessary to repeat the cooling and saturating with methyl chloride. Once the reaction had started another 500 cc. of dry ether was added and methyl chloride was slowly passed into the mixture until the magnesium had dissolved. A grayish precipitate separated during the reaction. If the loss of ether became too great more was added to the reaction mixture.

When the formation of the Grignard reagent was complete, a solution of 600 g. of *o*-bromobenzaldehyde in 1200 cc. of dry ether was added slowly to the cooled solution. After all of the aldehyde had been added, the reaction mixture was warmed slowly and finally refluxed gently for

(7) Dufraisse and Viel, *Bull. soc. chim.*, (4) **37**, 874 (1925).

(8) Lauer and Spielman, THIS JOURNAL, **55**, 4923 (1933).

(9) V. Auwers and Eisenlohr, *J. prakt. Chem.*, (2) **82**, 100 (1910).

(10) Vorländer and Herrmann, *Abhandlung der Naturforschenden Gesellschaft zu Halle*, **21**, 251 (1899); *Chem. Centr.*, **70**, I, 730 (1899).

about an hour. Usually the addition product separated from solution at this stage but if it did not appear the reaction mixture was allowed to stand until it did separate. The reaction mixture was then worked up in the usual manner. The yield was 568 g. (87%) of a colorless, viscous liquid boiling at 91–98° (2 mm.). A sample was redistilled for analysis. It boiled at 108.5° (6.5 mm.); d^{27}_{27} 1.470; $n^{20}D$ 1.5702; $n^{25}D$ 1.5678.

Anal. Calcd. for C_8H_9OBr: C, 47.76; H, 4.51. Found: C, 47.39, 47.99; H, 4.40, 4.51.

When methylmagnesium iodide was used in place of methylmagnesium chloride, the product was red and it seemed impossible to remove iodine completely even by washing with sodium bisulfite, as the red color always reappeared when the product was heated.

o-Bromostyrene.—In a 50-cc. Claisen flask were placed 30 g. of *o*-bromophenylmethylcarbinol, 5 g. of freshly fused and powdered potassium acid sulfate and 0.3 g. of hydroquinone. The mixture was heated under a pressure of 21–30 mm. in an oil-bath at 155–160°. To the distillate was added a little hydroquinone and ether, the water was separated, the ether dried and the mixture distilled. The yield was 9 g. (33%) of product of b. p. 60–65° (3 mm.); 65° (4 mm.); d^{27}_{27} 1.468; $n^{25}D$ 1.5893.

Anal. Calcd. for C_8H_7Br: C, 52.47; H, 3.86. Found: C, 52.75; H, 4.22.

The product was slightly lachrymatory and polymerized on standing even in the presence of hydroquinone.

o-Bromo-α-chloroethylbenzene.—This was prepared by adding dropwise 201 g. of *o*-bromophenylmethylcarbinol to 292 g. of thionyl chloride in the cold. After the evolution of hydrogen chloride and sulfur dioxide had slowed down, the reaction mixture was warmed to 50° for about an hour. Distillation gave 183 g. (83%) of a product boiling at 63–65° (2 mm.). A sample purified by redistillation had the following constants: d^{20}_{20} 1.499; $n^{20}D$ 1.5693.

Anal. Calcd. for C_8H_8BrCl: C, 43.77; H, 3.67. Found: C, 43.70; H, 3.77.

Attempts to remove hydrogen chloride from this product by treatment with quinoline were ineffective.

Poly-o-bromostyrene.—*o*-Bromostyrene containing 1–2% of hydroquinone polymerized slowly and a solid product was obtained in a matter of months. Heating alone or especially in the presence of peroxides such as benzoyl peroxide greatly accelerated the polymerization. Freshly distilled *o*-bromostyrene was polymerized in three to five minutes at 175°, whereas at 160° several hours were required to produce the same result.

Most of the polymer used in these experiments was produced by adding 0.2% of benzoyl peroxide to *o*-bromostyrene and heating the mixture to about 140–150° in an oil-bath. The reaction was exothermic and once started proceeded rapidly. It was complete in a few minutes. The end-point could be detected by noting the cessation of the evolution of bubbles. The product as first formed was a hard, brittle, colorless transparent mass. Even if the *o*-bromostyrene used was yellow, the polymer was colorless. On standing, however, an amber color developed in the polymer in a few months.

The polymer was soluble in benzene, toluene, xylene, dioxane and nitrobenzene. It was insoluble in ether, ethyl and methyl alcohols, ethyl acetate, glacial acetic acid and acetone. By dissolving the polymer in benzene or dioxane and pouring this solution into a large excess of ether or methyl alcohol, a colorless amorphous powder was obtained.

A sample of polymer prepared at 140–150° in the presence of benzoyl peroxide had an approximate molecular weight of 24,000 as indicated by viscosity measurements[11]; $n^{25}D$ 1.6333 ± 0.003.[12]

Anal. Calcd. for $(C_8H_7Br)_x$: Br, 43.67. Found: Br, 43.35, 43.73.

Poly-m- and p-Bromostyrenes.—These products were prepared in the same general manner and their properties were essentially the same as recorded for poly-*o*-bromostyrene. Dr. H. R. Moulton of the American Optical Company has kindly determined the refractive indices of these two polymers for us. The meta isomer has a refractive index of 1.63 and the para isomer 1.62.

Reaction of Poly-o-bromostyrene with Metals.—A solution of 1 g. of poly-*o*-bromostyrene in 500 cc. of dioxane was refluxed for seven days with 5 g. of activated zinc.[13] The solution took on an orange-yellow color. About half of the dioxane was removed by distillation and the remaining solution was filtered to remove the zinc. The polymer was precipitated as a buff powder by pouring this solution into water. Analysis of the polymer showed 35.54 and 35.37% bromine remaining.

An attempt to carry out an Ullmann reaction by treating 1 g. of poly-*o*-bromostyrene in 500 cc. of nitrobenzene with 3 g. of copper bronze produced a black, tarry intractable material.

Boiling a solution of 5 g. of poly-*o*-bromostyrene in 2 liters of dry benzene with an excess of clean sodium shavings for fifty hours gave a polymer which contained 37.59–36.99% bromine. After three days of treatment in boiling toluene a polymer was formed containing 34.62–35.54% bromine. Using boiling xylene with sodium, almost complete removal of bromine resulted in 300 to 400 hours. The details of such an experiment follow.

A solution of 2 g. of poly-*o*-bromostyrene in 1 liter of dry technical xylene (which had been purified by refluxing with sodium followed by distillation) was refluxed in an all-glass apparatus with about 7 g. of freshly sliced, clean sodium. The reaction mixture turned yellow in about an hour and gradually assumed an orange color and became somewhat opaque. After about three hundred hours of boiling, part of the xylene was distilled and water was added carefully to destroy the excess sodium. The mixture was then steam distilled to remove the remaining xylene. The polymer which remained was a white or gray, porous, brittle mass. It was dissolved in dioxane and precipitated by pouring the solution into water. The polymer was analyzed for bromine and all of the solutions were saved and analyzed for bromide ion. Many experiments were performed before the time necessary for the removal of bromine was found. In three hundred

(11) Staudinger, "Die hochmolekularen organischen Verbindungen," J. Springer, Berlin, 1932.

(12) This determination was made by Dr. M. L. Willard to whom we are indebted for permission to include it in this publication.

(13) Marvel, Sample and Roy, THIS JOURNAL, **61**, 3241 (1939).

hours 97% removal of bromine was obtained and in a four hundred and fifty hour run 100% of the bromine was removed.

Carbonation of the Reaction Product of Sodium and Poly-*o*-bromostyrene.—A solution of 15 g. of poly-*o*-bromostyrene in 1 liter of xylene was heated under a reflux condenser for twenty days with 50 g. of sodium. Solid carbon dioxide was then introduced into the reaction mixture. The excess sodium was removed mechanically, the xylene by steam distillation and the insoluble polymer by filtration. The water layer (about 1.5 liters) on acidification gave about 0.23 g. of acidic material. The water layer was then made alkaline, concentrated to about 300 cc. and again acidified. About 1.5 g. of acidic material was obtained. This fraction was a very complex mixture and melted over the range of 90–225°. There was some crystalline material which must have been formed by degradation of the polymer. The neutral equivalent was 76–78.

Anal. Found: C, 69.54; H, 5.87; Br, none.

No definite products were isolated but the experiment did establish the fact that an alkali metal derivative was formed by the reaction of sodium and the poly-*o*-bromostyrene.

Attempts to Oxidize the Debrominated Polymer.—The debrominated polymer was treated with hot chromic acid in glacial acetic acid, with hot nitric acid and with potassium dichromate in dilute sulfuric acid but none of these procedures gave products which could be characterized.

Heating 2 g. of the debrominated polymer with 6 g. of selenium to 400° for twenty hours gave no crystalline products but only gummy solids and brownish powders.

Action of Sodium on Poly-*p*-bromostyrene.—A reaction mixture containing 2.5 g. of poly-*p*-bromostyrene, 1 liter of xylene and 4.7 g. of sodium was heated under a reflux condenser for about five hundred and fifty hours as described for the ortho isomer. Analysis of the water solution showed that 99% of the bromine was removed. The polymer remaining was soluble in xylene and dioxane.

α-Chlorostyrene and Boron Trifluoride–Ethyl Acetate Complex.—A reaction mixture containing 2 cc. of α-chlorostyrene, 3 drops of boron trifluoride–ethyl acetate complex[14] and 2 cc. of ethyl alcohol was sealed and set aside. After two years a mass of long plate-like crystals had separated. The tube was opened and these crystals were recrystallized from absolute alcohol. They melted at 171.5–173.5° whereas the 1,3,5-triphenylbenzene is reported to melt at 172°.[15]

Anal. Calcd. for $C_{24}H_{18}$: C, 94.07; H, 5.93. Found: C, 93.90; H, 6.01.

Other attempts to polymerize α-chlorostyrene with ultraviolet light, benzoyl peroxide, ascaridole, anhydrous stannic chloride and large amounts of the boron trifluoride–ethyl acetate complex[14] gave colored products but no definite polymeric compounds. In one experiment α-chlorostyrene was heated to 130–140° with ascaridole and an impure 1,3,5-triphenylbenzene was obtained.

α-Acetoxystyrene.—Several attempts to add acetic acid to phenylacetylene under various conditions failed to give this product. It was then prepared from styrene bromohydrin obtained by the method of Read and Reid.[16] To 181 g. of styrene bromohydrin was added in small portions 141 g. of acetyl chloride.[17] Heat was evolved during the addition. The reaction mixture was refluxed for ten hours after the addition was complete and then allowed to stand overnight. The excess acetyl chloride was destroyed by pouring the mixture on cracked ice. The organic layer was collected in ether, separated, washed with sodium bicarbonate solution, dried and distilled. The yield was 199.5 g. (91%) of a product of b. p. 105–107° (3 mm.); d^{20}_{20} 1.386; $n^{20}D$ 1.5380.

Anal. Calcd. for $C_{10}H_{11}O_2Br$: C, 49.40; H, 4.56. Found: C, 49.59; H, 4.63.

A mixture of 48.6 g. of α-acetoxy-β-bromoethylbenzene, 51.5 g. of quinoline and 0.2 g. of hydroquinone was heated to 145–155° for one hour and then distilled under reduced pressure. The yield of product boiling at 80–90° (2 mm.) was 49 g. The quinoline was removed by washing with dilute hydrochloric acid and the product was then fractionated several times through a modified Widmer column. Some decomposition occurred during distillation and analysis of the product showed it to be slightly impure. The yield of product was about 11 g. (34%) boiling at 87.5–89.5° (3.5 mm.); 57.5–58° (0.5 mm.); d^{20}_{20} 1.074; $n^{20}D$ 1.5533.

Anal. Calcd. for $C_{10}H_{10}O_2$: C, 74.04; H, 6.21. Found: C, 72.84; H, 6.41.

The dibromide was prepared by treating a sample of the above product with bromine in dry carbon tetrachloride. After recrystallization from 95% ethyl alcohol the dibromide melted at 93.5–94.5°.

Anal. Calcd. for $C_{10}H_{10}O_2Br_2$: C, 37.20; H, 3.13. Found: C, 37.23; H, 3.20.

Attempts to Polymerize Various α- and β-Substituted Styrenes.—A variety of catalysts under different conditions were used with α- and β-acetoxystyrene, β-bromostyrene and α-methoxystyrene but no true polymers were obtained. Details of the experiments are therefore not recorded.

Summary

1. Poly-*o*-bromostyrene prepared by peroxide polymerization reacted with sodium in boiling xylene to give replacement of bromine by sodium and no evidence for a Wurtz–Fittig reaction was obtained. This indicates a 1,3-structure for the polymer.

2. Poly-*p*-bromostyrene also reacted with sodium in xylene to give complete removal of halogen without cross linking the polymer chains.

3. α-Chlorostyrene under the influence of boron trifluoride was slowly converted to 1,3,5-triphenylbenzene.

4. α-Acetoxystyrene has been prepared from

(14) Morgan and Taylor, *Chemistry and Industry*, **50**, 869 (1931).
(15) Odell and Hines, THIS JOURNAL, **35**, 81 (1913).
(16) Read and Reid, *J. Chem. Soc.*, 1488 (1928).
(17) The authors are indebted to the Bakelite Corporation for generous samples of styrene.

styrene bromohydrin by acetylation and dehydrohalogenation.

5. Attempts to polymerize a variety of α- and β-substituted styrenes have been unsuccessful.

URBANA, ILLINOIS RECEIVED NOVEMBER 13, 1939

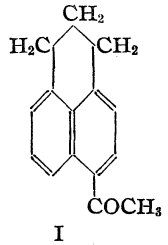
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Further Observations on the Use of Hydrogen Fluoride in Acylations and Cyclizations

BY LOUIS F. FIESER AND E. B. HERSHBERG[1]

In a first paper[2] on this subject it was reported that acenaphthene can be acylated smoothly by reaction with various free acids, acid anhydrides and acid chlorides in the presence of liquid anhydrous hydrogen fluoride at room temperature. Under the same conditions, entirely negative results were obtained with benzene, naphthalene, phenanthrene, anthracene and 1,2-benzanthracene. These observations have now been extended, partly in the hope of casting further light on the remarkable specificity of acenaphthene in the reaction, and partly to see if any additional examples could be found of unusual orientations of practical synthetic value, as encountered in the acetylation of the above hydrocarbon by the hydrogen fluoride method.[2] We may state at the outset that no such applications have been discovered and that the theoretical interpretation still seems obscure.

Two other aromatic hydrocarbons which, like acenaphthene, contain an alicyclic side ring, have been found amenable to acylation under the above conditions. Perinaphthane reacted fairly readily with either acetic acid or acetic anhydride to give as the chief product a substance identified as the 4-aceto derivative I by oxidative degradation.



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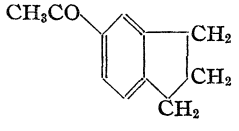


II

The orientation is thus the same as in the benzoylation of the hydrocarbon by the Friedel and Crafts (Perrier) method.[3] Satisfactory condensation also occurred in the presence of hydrogen fluoride between hydrindene and either acetic acid or benzoyl chloride, and again substitution took the normal course and gave the 5-derivatives, such as II. The direct substitution of an α-naphthoyl group in the 4-position of hydrindene would give a known ketone[4] which is easily convertible into cholanthrene, but the total ketonic reaction product obtained with α-naphthoic acid and hydrogen fluoride yielded no hydrocarbon on pyrolysis and afforded on purification a crystalline substance which evidently is the 5-derivative.

It was next found that certain of the hydrocarbons which do not react at room temperature and atmospheric pressure can be acylated by conducting the condensation in an iron pressure vessel under reflux at temperatures up to that of the steam-bath. The acetylation of acenaphthene under these conditions was investigated for comparison and because of the usefulness in syntheses of the 1-aceto compound made available by this reaction. The condensation proceeded smoothly and 1-acetoacenaphthene was obtained in even better yield (37%) than at room temperature. The ketone was converted through the acid to the new 1-acenaphthaldehyde by the Rosenmund reaction. Using the pressure apparatus naphthalene and acetic anhydride gave a mixture of the α- and β-aceto compounds somewhat richer in the β-isomer than that obtained by the Friedel and Crafts method in carbon bisulfide solution[5]; the hydrocarbon did not react with succinic anhydride at moderate temperatures and tar formation occurred on attempting to push the reaction. At 50–55° phenanthrene and acetic anhydride gave a mixture from which the 2- and 3-acetyl compounds were isolated, as with aluminum chloride.[6] A condensation of the hydrocarbon with crotonic acid was also effected giving an oil which appears to be a mixture of isomeric methylketo-

(1) Research Fellow on funds from the National Cancer Institute and the Eli Lilly Company.

(2) Fieser and Hershberg, THIS JOURNAL, **61**, 1272 (1939).

(3) Fieser and Hershberg, *ibid.*, **60**, 1658 (1938).

(4) Fieser and Seligman, *ibid.*, **57**, 2174 (1935).

(5) Fieser, Holmes and Newman, *ibid.*, **58**, 1055 (1936).

(6) Mosettig and van de Kamp, *ibid.*, **52**, 3704 (1930).

cyclopentenophenanthrenes. The special susceptibility shown by acenaphthene, perinaphthane and hydrindene in the acylation reaction, while still appearing rather remarkable, is thus seen to be a matter of degree rather than of kind.

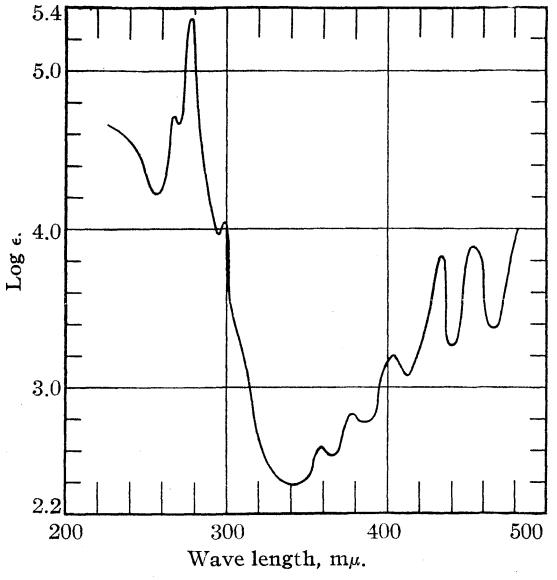
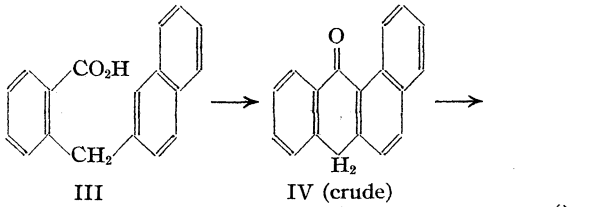
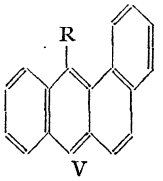


Fig. 1.—1′,10-Dimethyl-2,3-benzanthracene in absolute alcohol. Principal maxima in mμ (log ε values in parentheses): 278 (5.33), 299 (4.03), 359 (2.61), 378 (2.82), 403 (3.20), 433 (3.82), 454 (3.90).

The hydrogen fluoride method[2] of cyclizing aromatic compounds with acidic side chains has found many useful applications.[7] In view of the success in the preparation of 1,2-benz-10-anthrones by this method in a condition suitable for the introduction of 10-alkyl substituents by the Grignard reaction,[2] we have investigated this possible route to 9-alkyl-1,2-benzanthracenes, with particular reference to the unknown 1′,9-dimethyl compound. *o*-(β-Naphthylmethyl)-benzoic acid (III) was found to undergo rapid cyclization in hydrogen fluoride at room temperature, but the anthrone IV proved to be a very sensitive substance and was not isolated as such. By pumping the mixture to dryness decomposition and isomerization attendant upon the manipulation of the material was minimized, and on treating the crude residue with Grignard reagent it was possible to obtain substituted hydrocarbons in significant if low yields. The known 9-methyl-1,2-benzanthracene[8] was isolated in 14% yield, and the 9-allyl compound was obtained in 35% yield.

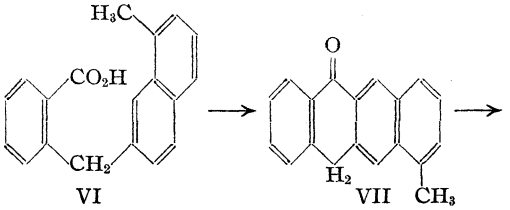


III IV (crude)

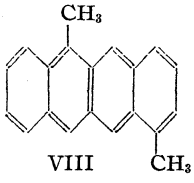


V

These results seemed sufficiently promising to warrant a further attempt to synthesize 1′,9-dimethyl-1,2-benzanthracene from the previously described intermediate VI.[9] It had been established that on cyclization with zinc chloride and acetic anhydride this acid gives a 1,2-benzanthranyl-10-acetate, but this could not be converted satisfactorily into the corresponding anthrone. On using hydrogen fluoride in the hope of obtaining the anthrone directly we were surprised to find that ring closure largely takes the alternate course and gives chiefly the naphthacene derivative VII and only a very small amount of the angular isomer (characterized as the quinone). The anthrone VII, like the parent substance,[10] is stable in the ketonic form and easily purified, and on reaction with methylmagnesium chloride it gave a hydrocarbon which crystallized either in bronze plates or in the form of fiery red needles of striking beauty.



VI VII



VIII

That the substance has the linear rather than the angular structure was at once apparent from the ultraviolet absorption spectrum, kindly de-

(7) For additional examples, see (a) Fieser and Johnson, THIS JOURNAL, **61**, 1647 (1939); (b) Fieser and Cason, *ibid.*, **61**, 1740 (1939); (c) Fieser, Joshel and Seligman, *ibid.*, **61**, 2134 (1939); (d) Fieser and Joshel, *ibid.*, **61**, 2959 (1939); (e) Calcott, Tinker and Linch, U. S. Patent 2,174,118 (1939).

(8) Newman, THIS JOURNAL, **59**, 1003 (1937); Cook, Robinson and Goulden, *J. Chem. Soc.*, 393 (1937).

(9) Fieser and Seligman, THIS JOURNAL, **60**, 170 (1938).

(10) Fieser, *ibid.*, **53**, 2329 (1931).

termined by Mr. D. M. Bowen. The curve (Fig. 1) bears no resemblance to that of 1,2-benzanthracene but corresponds well in form with the absorption curve of naphthacene as reported by Radulescu and co-workers[11] and by Clar.[12] Compared with the parent hydrocarbon, the maxima for the dimethyl compound VIII are shifted about 7–8 mμ (av.) in the direction of longer wave lengths. The extinction coefficients found for VIII correspond with the values for naphthacene given by Clar rather than the distinctly lower values reported by Radulescu. Chemical evidence for the linear structure was also obtained, for the anthrone VII gave on oxidation a quinone isomeric with the known 1′-methyl-1,2-benzanthraquinone[9] and exhibiting the resistance to alkaline hydrosulfite characteristic of naphthacenequinone.[10]

Experimental Part[13]

3-Acetoperinaphthane (I).—A mixture of 10 g. of perinaphthane[3] in 5 cc. of dry ether, 6.1 g. of acetic anhydride, and 200 g. of hydrogen fluoride was stirred mechanically for sixty hours at room temperature, fresh hydrogen fluoride being added to replace that lost by evaporation. The solution was then evaporated on the steam-bath and the product taken up in benzene, washed with dilute alkali, and distilled. A fore-run of 1.3 g. (perinaphthane) was collected up to 160° (2 mm.) and the ketone fraction boiled at 170–175°; yield 9.1 g. (71%).

Anal. Calcd. for $C_{15}H_{14}O$: C, 85.69; H, 6.72. Found: C, 85.28; H, 6.66.

Acetic acid gave similar results. Trial runs with no solvent to serve as a diluent were less satisfactory.

The ketone forms an easily dissociated picrate in ether–ligroin and no complex was obtained in methanol.

The **trinitrobenzene derivative** separated from methanol in yellow needles of m. p. 114–114.5°.

Anal. Calcd. for $C_{15}H_{14}O \cdot C_6H_3O_6N_3$: N, 10.22. Found: N, 9.82.

Oxidation to **4-aceto-1,8-naphthalic anhydride** was accomplished by warming a solution of 1.0 g. of the ketone and 7.5 g. of anhydrous sodium dichromate in 25 cc. of acetic acid to 75–90° until the first vigorous reaction was over and then refluxing for two hours. The anhydride slowly separated after cooling and three crystallizations from benzene–ligroin gave yellow micro-needles, m. p. 193–195°. The substance has been reported as melting at 189°[14] or 191–192°[15]; the 2-aceto isomer[7b] melts considerably higher.

3-Perinaphthoic acid was obtained by shaking the ketone with potassium hypochlorite solution until dissolved. The acid after four crystallizations from benzene–ligroin formed pale yellow needles, m. p. 188.4–189°.

Anal. Calcd. for $C_{14}H_{12}O_2$: C, 79.25; H, 5.70. Found: C, 78.89; H, 5.83.

Acylation of Hydrindene. (a) 5-Aceto Compound.—From 46.4 g. of hydrindene, 27 g. of acetic acid, and 600 g. of hydrogen fluoride there was obtained after a reaction time of sixty-four hours at room temperature 46.2 g. (73%) of 5-acetohydrindene, b. p. 134–137° (8 mm.). A 2-g. portion of the material, oxidized with hot hypochlorite solution, gave 1.3 g. of hydrindene-5-carboxylic acid, m. p. 172–178°; recrystallized from dilute alcohol, m. p. 179.5–181.5° (compare 178–179°[16]; the 4-isomer melts at 152.5–153.5°).[17]

(b) **Benzoylation.**—Treated with one equivalent of benzoyl chloride and excess hydrogen fluoride at room temperature for thirty-six hours, 11.6 g. of hydrindene gave 16.5 g. (75%) of a colorless ketone, b. p. 203–204° (8 mm.) and 1.75 g. of benzoic acid was recovered from the alkaline extract. The material seems to consist very largely of 5-benzoylhydrindene, for 1.0 g. of the ketone treated with hydroxylamine in pyridine–alcohol gave 1.1 g. of once crystallized oxime which, after a second crystallization from benzene–ligroin, melted at 149–152° (compare 153–154°).[18]

(c) **5-(α-Naphthoyl)-hydrindene** was prepared as above from the hydrocarbon (7 g.) and α-naphthoic acid (9.8 g.). After seventy-two hours at room temperature, 2.1 g. of α-naphthoic acid was recovered and the ketone, b. p. 255–265° (8 mm.), obtained as a pale yellow oil amounted to 11.0 g. (90%, allowing for the recovered acid). The oil crystallized after standing for several weeks and on recrystallization from ether–petroleum ether it formed rosets of colorless needles, m. p. 71–72°.

Anal. Calcd. for $C_{20}H_{16}O$: C, 88.21; H, 5.92. Found: C, 88.23; H, 6.14.

Pyrolysis of the total distilled ketone under conditions suited for the Elbs reaction gave only tars and no cholanthrene could be detected.

Acetylation of Acenaphthene under Pressure.—The reaction vessel used was a welded steel cylinder with 1/8 in. (3-mm.) walls. This was connected to a stainless steel condenser tube carrying a glass water jacket by means of a wrought steel union with a brass seat (large stainless steel unions could not be as easily disconnected after exposure to hydrogen fluoride). A tee connection at the top of the condenser tube carried a 200-lb. (13 atm.) pressure gage, but this did not withstand corrosion very well and was used only in pilot runs and then disconnected and a plug substituted. To the horizontal opening of the tee connection there was fitted a stainless steel needle valve leading, through a second wrought steel union, to a steel receiver which could be closed by a separate brass needle valve. A mixture of 61.6 g. of acenaphthene, 22 cc. of acetic anhydride, and 120 g. of hydrogen fluoride was heated in this pressure vessel under reflux on the steam-bath for one and one-half hours at a gage pressure of 60 lb. (4 atm.). The hydrogen fluoride was then allowed to distill into the receiver and the residue was taken up in

(11) Radulescu, Ostrogovich and Barbulescu, *Ber.*, **64**, 2240 (1931).
(12) Clar, *ibid.*, **65**, 503 (1932).
(13) All melting points are corrected. Microanalyses by Lyon Southworth and Herbert S. Wight.
(14) Graebe and Haas, *Ann.*, **327**, 94 (1903).
(15) Dziewonski and Piasecki, *Bull. intern. acad. polon. sci. classe sci. math. nat.*, A, 287 (1932).
(16) Von Braun, Kirschbaum and Schuhmann, *Ber.*, **53**, 1155 (1920).
(17) Fieser and Seligman, THIS JOURNAL, **59**, 394 (1937).
(18) Borsche and Pommer, *Ber.*, **54**, 102 (1921).

benzene, washed thoroughly but rapidly with water in a glass separatory funnel and distilled. The total ketone fraction, b. p. 190–200° at 6 mm., weighed 54.7 g. (78%) and on two crystallizations from methanol afforded 23.6 g. of 1-acetoacenaphthene, m. p. 103–104.5°, and 2.3 g., m. p. 101.5–104.5° (yield, 37%). A fore-run of 6.7 g. consisted largely of acenaphthene.

1-Acenaphthaldehyde.—A solution of 7.5 g. of 1-acenaphthoyl chloride in 75 cc. of xylene, to which was added 0.35 g. of 2% palladium catalyst on barium sulfate and 0.075 cc. of the quinoline–sulfur reagent,[19] was stirred mechanically at 150–160° while passing in hydrogen. The evolution of hydrogen chloride continued for five and one-half hours, when 88% of the theoretical amount had been produced. After filtration and removal of the solvent at reduced pressure the product was distilled and the crude aldehyde (5 g., b. p. 150–165° at 2 mm.) dissolved in ether–benzene and stirred overnight with 75 cc. of saturated sodium bisulfite solution. The solid addition product was collected by centrifugation and decomposed with sodium carbonate solution, giving 4.5 g. (72%) of aldehyde, m. p. 93–99°. After five crystallizations from ether–roleum ether, the substance formed faintly yellowish dles, m. p. 99.5–100.5°.

Anal. Calcd. for $C_{13}H_{10}O$: C, 85.72; H, 5.54. Found: C, 85.29; H, 5.56.

β-Naphthaldehyde was obtained by the same procedure in 84% yield.

Naphthalene and Acetic Anhydride.—The hydrocarbon (12.8 g.) and anhydride (10.2 g.) were heated with hydrogen fluoride (100 g.) in the pressure bomb at 50–60° for sixty-eight hours. Distillation of the recovered and washed product gave a small fore-run of naphthalene and 4.9 g. of acetonaphthalene mixture, b. p. 155–165° (9 mm.). Oxidation with hypochlorite afforded 4.7 g. of naphthoic acid mixture, m. p. 145–168°, and on two crystallizations from dilute alcohol 2.9 g. of β-naphthoic acid, m. p. 182–184°, was obtained.

Phenanthrene and Acetic Anhydride.—From 35.6 g. of phenanthrene, 11 cc. of the anhydride, and 150 g. of hydrogen fluoride heated one hundred hours at 50–55° there was obtained 25.8 g. of recovered hydrocarbon and 9.3 g. (77% based on material consumed) of ketone, b. p. 180–210° (3 mm.). Crystallization from ether and from benzene–ligroin afforded 1.2 g. of 2-acetophenanthrene, m. p. 144–145°; the mother material when purified from methanol gave 3.6 g. of the 3-isomer, m. p. 70.5–71.5°. The latter substance gave a large depression when mixed with 9-acetophenanthrene (m. p. 74°).

Phenanthrene (17.8 g.) and crotonic acid in equivalent amounts were heated with hydrogen fluoride (100 g.) for forty-three hours at 40–50 lb. (3 atm.) pressure. The reagent was evaporated, the product taken up in benzene, and the blue organic layer washed with alkali and distilled, giving 8.4 g. of phenanthrene, b. p. 140–200° (2 mm.), and 6.4 g. of ketone, b. p. 210–240°. The redistilled material was an orange oil, b. p. 215–225° (2 mm.).

Anal. Calcd. for $C_{18}H_{14}O$: C, 87.78; H, 5.73. Found: C, 87.42; H, 5.88.

(19) Rosenmund and Zetzsche, *Ber.*, **54**, 425 (1921).

o-(β-Naphthoyl)-benzoic acid was prepared from 29 g. of β-bromonaphthalene and 23 g. of phthalic anhydride by the Grignard procedure[20] in 37% yield. It crystallized from benzene in small needles containing combined solvent; this complex melted at 129–131° with loss of benzene, resolidified and melted at 166–167° (compare 168°).[20]

Anal. Calcd. for $C_{18}H_{12}O_3 \cdot {}^1/_2C_6H_6$: C, 80.00; H, 4.79. Found: C, 80.14; H, 5.01.

o-(β-Naphthylmethyl)-benzoic Acid (III).—The keto acid (9 g.) was refluxed for sixteen hours with 200 cc. of water containing 20 g. of sodium hydroxide, 12 g. of zinc dust and a trace of copper sulfate. Capryl alcohol (2–3 cc.) was helpful in preventing foaming and was distilled off prior to filtration and acidification. The product was taken up in ether–benzene and the solution extracted with soda; precipitation gave 7.3 g. (97%) of good acid, m. p. 134–138°. After two crystallizations from dilute acetic acid the substance formed glistening white leaflets melting at 134–136°, and remelting after solidification at 139.5–140°.

Anal. Calcd. for $C_{18}H_{14}O_2$: C, 82.42; H, 5.34. Found: C, 82.59; H, 5.47.

The acid was previously prepared in poor yield by another method by King[21] (m. p. 136–137°).

9-Methyl-1,2-benzanthracene.—The best procedure found consisted in dissolving 2.5 g. of the acid III in 18 g. of hydrogen fluoride in a platinum cylinder, allowing the solution to stand at room temperature for one hour, and removing the reagent by placing the cylinder in a large glass test-tube and evaporating at the water pump. An ethereal solution of methylmagnesium chloride from 2.5 g. of metal was then added to the residue in the platinum container and after suitable time for reaction the mixture was worked up in the usual manner[22] and the hydrocarbon obtained as bright yellow prisms, m. p. 136–137.5°; yield 0.32 g. (14%). This did not depress the melting point of Newman's material.[8]

9-Allyl-1,2-benzanthracene was prepared from 3.8 g. of III as above but allowing only twenty minutes for cyclization before evaporating the hydrogen fluoride and adding the Grignard reagent (16 g. allyl bromide). The yield of hydrocarbon, m. p. 111–115°, was 1.4 g. (35%). The purified substance separated from ligroin in pale yellow aggregates, m. p. 115–116°.

Anal. Calcd. for $C_{21}H_{16}$: C, 94.00; H, 6.01. Found: C, 94.26; H, 6.23.

o-(8-Methyl-2-naphthylmethyl)-benzoic Acid (VI).[9]—In repeating the previous synthesis **1-methyl-7-bromonaphthalene** was prepared from 100 g. of the dihydride according to Fieser and Seligman,[9] and after fractionation the naphthalene derivative was isolated from the mixture as the **trinitrobenzene derivative.** The complex forms yellow blades from methanol, m. p. 92.5–93°.

Anal. Calcd. for $C_{11}H_9Br \cdot C_6H_3O_6N_3$: N, 9.70. Found: N, 9.35.

This was cleaved by reduction with stannous chloride in hydrochloric acid, giving 10.9 g. of pure 1-methyl-7-

(20) Weizmann, Bergmann and Bergmann, *J. Chem. Soc.*, 1367 (1935).

(21) King, THIS JOURNAL, **49**, 562 (1927).

(22) Fieser and Hershberg, *ibid.*, **59**, 1028 (1937).

bromonaphthalene (liquid). On reaction with magnesium and then phthalic anhydride, this afforded 11.4 g. of hydrated keto acid, m. p. 110–120° (76%, assuming the substance to be a monohydrate). Reduction as above gave the acid VI, m. p. 142–143.5°, in 60% yield.

1'-Methyl-2,3-benz-10-anthrone (VII).—One gram of the methylnaphthylmethylbenzoic acid VII was treated with hydrogen fluoride at room temperature and after seven minutes was poured onto ice and the light yellow solid was quickly collected and washed. A portion was crystallized from acetone and obtained in two polymorphic forms of the same m. p. 174–176°. Prisms separated when a saturated solution was cooled rapidly in the ice box, while slow crystallization at room temperature gave rise to needles. Recrystallized slowly, the anthrone formed pale yellow needles, melting at 175–176° when heated slowly but liquefying when immersed in a bath at 171°.

Anal. Calcd. for $C_{19}H_{14}O$: C, 88.35; H, 5.46. Found: C, 88.80; H, 5.63.

With alcoholic alkali the anthrone gives a characteristic[10] purplish color which fades on shaking with air.

1'-Methyl-2,3-benzanthraquinone was obtained by oxidation of 100 mg. of the anthrone with 55 mg. of chromic anhydride in acetic acid. The substance crystallized from this solvent in orange-yellow needles, m. p. 227–229°. It gave no red color with aqueous hydrosulfite–alkali.

Anal. Calcd. for $C_{19}H_{12}O_2$: C, 83.80; H, 4.45. Found: C, 83.68; H, 4.66.

1',10-Dimethyl-2,3-benzanthracene (VIII).—After treatment of the crude anthrone VII with excess methylmagnesium chloride the collected product was passed in benzene solution through a tower charged with alumina mixed with Super-cel. On slow crystallization from absolute alcohol the hydrocarbon then formed brilliant, fiery red needles, m. p. 138–139°. When the alcoholic solution is cooled rapidly by cooling in ice the hydrocarbon separates in another modification which forms small, bronze-colored plates. This form melts when inserted in a bath at 133° and then solidifies and remelts at the higher temperature. The solution in concentrated sulfuric acid is olive-green.

Anal. Calcd. for $C_{20}H_{16}$: C, 93.71; H, 6.29. Found: C, 93.82; H, 6.35.

The **picrate** forms purplish-black needles from absolute alcohol, m. p. 164–165°.

Anal. Calcd. for $C_{20}H_{16}\cdot C_6H_3O_7N_3$: N, 8.66. Found: N, 8.59.

The **trinitrobenzene derivative** resembles the picrate in appearance, m. p. 166.5–167.5° (absolute alcohol).

Anal. Calcd. for $C_{20}H_{16}\cdot C_6H_3O_6N_3$: N, 8.94. Found: N, 9.04.

When the total crude product of cyclization was treated with Grignard reagent there was obtained in addition to the hydrocarbon a small amount of 1'-methyl-1,2-benzanthraquinone.[9]

Summary

Perinaphthane and hydrindene can be acetylated in the presence of hydrogen fluoride at room temperature, and the acylation of naphthalene and phenanthrene can be accomplished in a pressure bomb at somewhat higher temperatures.

9-Methyl- and 9-allyl-1,2-benzanthracene were synthesized successfully by cyclizing *o*-(β-naphthylmethyl)-benzoic acid with hydrogen fluoride and treating the crude anthrone with Grignard reagent, but when this process was applied to *o*-(8-methyl-2-naphthylmethyl)-benzoic acid ring closure occurred chiefly in the alternate direction, giving rise to the linear isomer. 1',10-Dimethyl-2,3-benzanthracene exists in two modifications, one of which has a striking red color.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASSACHUSETTS

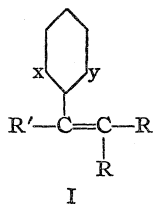
RECEIVED NOVEMBER 2, 1939

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

Restricted Rotation in Aryl Olefins. I. Preparation and Resolution of β-Chloro-β-(2,4,6-trimethyl-3-bromophenyl)-α-methylacrylic Acid

BY ROGER ADAMS AND M. W. MILLER[1]

Molecular dissymmetry due to restricted rotation between the ring and the olefinic carbon in appropriately substituted aryl olefins of types I and II was postulated in a previous communication.[2] Synthetic difficulties in preparing such compounds proved to be great and no procedure was found which gave successful results. The



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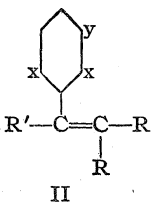


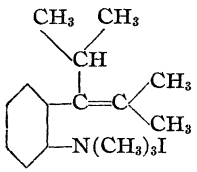
II

introduction of an atom or group other than hydrogen for the R' was complicated when R, x and y represented substituents other than hydrogen.

(1) Portion of a thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy in chemistry; Eastman Kodak Fellow, 1939–1940.

(2) Maxwell and Adams, THIS JOURNAL, **52**, 2960 (1930).

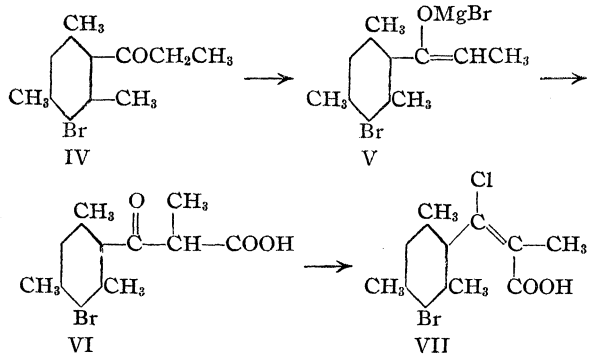
In the last few years several compounds have been prepared in which restricted rotation between an aryl group and an aliphatic nitrogen or carbon atom has been demonstrated.[3] The probability of resolution of properly substituted aryl olefins was thus made to appear more likely. Just recently, Mills and Dazeley[4] have succeeded in synthesizing and resolving *o*-(β,β-dimethyl-α-isopropylvinyl)-phenyltrimethylammonium iodide (III), thus verifying the correctness of the original



III

postulation. They observed also that a hydrogen atom on the olefin carbon not attached to the ring resulted in a compound which they were unable to obtain in enantiomorphic forms.

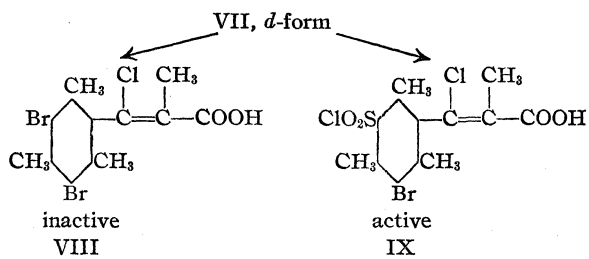
Search has been continued in this Laboratory to find a procedure for synthesizing molecules of types I and II, especially a procedure which would make feasible the preparation of several closely related compounds and thus allow a study of the effect of different groups around the point of restricted rotation. Such a procedure has now been devised. The first compound to be prepared and resolved is β-chloro-β-(2,4,6-trimethyl-3-bromophenyl)-α-methylacrylic acid. In its synthesis, advantage has been taken of the reports of Kohler[5] that hindered ketones react with ethylmagnesium bromide to give ethane and the magnesium bromide derivative of the enol form, and the observation by Kohler and Baltzly as well as by Fuson, Fugate and Fisher[6] that such enol magnesium bromides and carbon dioxide give β-ketonic acids. Thus, bromopropiomesitylene (IV) gives the magnesium bromide derivative (V), which carbonates to α-methyl-(2,4,6-trimethyl-3-bromobenzoyl)-acetic acid (VI). Molecules of the type shown by VI enolize with great ease and it was possible, therefore, to convert the keto acid (VI) by means of a mixture of phosphorus pentachloride and phosphorus oxy-



IV V VI VII

chloride into the chloro olefin (VII), β-chloro-β-(2,4,6-trimethyl-3-bromophenyl)-α-methylacrylic acid. Although VII should exist in *cis* and *trans* forms, only one of these isomers was obtained. This isomer was resolved readily through the quinine salt. The *d*-form from the less soluble salt gave $[\alpha]^{20}D$ +52.6° in ethanol and proved to be surprisingly stable. The *l*-form also was isolated. The optical activity of the *d*-form was not changed by refluxing for fifteen hours in ethanol or twelve hours in glacial acetic acid. A very rigid restriction of rotation in this molecule was thus demonstrated.

The necessity for unsymmetrical substitution in the benzene ring in order to produce asymmetry in VII was proved by bromination and by preparing a sulfonyl chloride derivative of the optically active forms. Bromination resulted in symmetrical substitution with formation of an optically inactive dibromo compound (VIII), identical with that prepared by bromination of the racemic form of VII. Chlorosulfonic acid, on the other hand, gave a molecule with unsymmetrical substitution which proved to be the optically active chlorosulfonyl derivative (IX).



VIII IX

The reactions by which VII was prepared are peculiarly suitable for synthesizing molecules in which the atoms or groups substituted in the benzene ring and on the olefin linkage may be varied. A study of such molecules and others containing two points of restricted rotation is now under way.

(3) Mills and Elliott, *J. Chem. Soc.*, 1291 (1928); Mills, *Trans. Faraday Soc.*, **26**, 431 (1930); Mills and Breckenridge, *J. Chem. Soc.*, 2209 (1932); Mills and Kelham, *ibid.*, 274 (1937).

(4) Mills and Dazeley, *J. Chem. Soc.*, 460 (1939).

(5) Kohler and Tishler, THIS JOURNAL, **54**, 1594 (1932); Kohler, Tishler and Potter, *ibid.*, **57**, 2517 (1935); Kohler and Sonnichsen, *ibid.*, **60**, 2650 (1938).

(6) Kohler and Baltzly, *ibid.*, **54**, 4015 (1932); Fuson, Fugate and Fisher, *ibid.*, **61**, 2362 (1939).

Experimental

Bromopropiomesitylene.—To a mechanically stirred mixture of 300 g. of carbon disulfide, 100 g. of bromomesitylene and 140 g. of aluminum chloride, was added 65 g. of propionic anhydride at such a rate that the solvent refluxed gently. After completion of the addition, stirring was continued for two hours and the reaction product was then poured into iced hydrochloric acid. The carbon disulfide layer was separated, the solvent removed and the residual oil dissolved in ether. This solution was washed with hydrochloric acid, water and finally with aqueous sodium carbonate. The product was a colorless liquid, b. p. 127–129° (3 mm.), $n^{20}D$ 1.5490, d^{24}_{24} 1.2956.

Anal. Calcd. for $C_{12}H_{15}OBr$: C, 56.50; H, 5.88. Found: C, 56.47; H, 6.08.

Dinitrobromomesitylene.—The structure of bromopropiomesitylene was proved by cleavage of the propionyl group with sirupy phosphoric acid[7] and nitration of the product to dinitrobromomesitylene. Following the same nitration procedure, bromomesitylene was converted to an identical product.

A mixture of 50 cc. of sirupy phosphoric acid and 5 g. of bromopropiomesitylene was refluxed for twelve hours and then steam distilled. The distillate was extracted with ether and the ether removed. The oil thus obtained was added slowly to 25 cc. of ice cold fuming nitric acid. After standing for twenty minutes, the mixture was poured on ice. The product was purified by crystallization from ethanol, m. p. 199.5–201.5° (cor.). Fittig and Storer[8] report m. p. of 189–190°.

Anal. Calcd. for $C_9H_9O_4N_2Br$: C, 37.37; H, 3.12. Found: C, 37.60; H, 3.31.

Bromomagnesium Enolate of Bromopropiomesitylene (V); α-Methyl-(2,4,6-trimethyl-3-bromobenzoyl)-acetic Acid (VI).—A solution of 25 g. of bromopropiomesitylene in 25 cc. of dry ether was added to 100 cc. of an ether solution containing slightly over one mole equivalent of ethylmagnesium bromide. The mixture was refluxed for thirty minutes, then transferred to a catalytic hydrogenation apparatus, cooled in an ice-bath, and carbon dioxide passed in at a pressure of 2–3 atm. After forty-five minutes, the temperature was allowed to come to that of the room and addition of carbon dioxide continued for six hours.

The reaction mixture was then chilled in an ice-bath, and poured slowly into iced hydrochloric acid. The ether layer was extracted with aqueous sodium carbonate and the aqueous extract acidified with iced hydrochloric acid. The product was purified by crystallization from benzene; white crystals, m. p. 123–124° (cor.) with decomposition. The crude product was satisfactory for conversion to the chloro compound; yield 15 g. (51%).

Anal. Calcd. for $C_{13}H_{15}O_3Br$: C, 52.17; H, 5.02. Found: C, 52.39; H, 5.55.

β-Chloro-β-(2,4,6-trimethyl-3-bromophenyl)-α-methylacrylic Acid (VII).—To a solution of 10 g. of α-methyl-(2,4,6-trimethyl-3-bromobenzoyl)-acetic acid in 50 cc. of ice cold phosphorus oxychloride, was added 25 g. of phosphorus pentachloride.[9] After warming on a steam cone for one hour, the solution was cooled and poured on 300 g. of ice. The product separated as an oil which solidified on standing. It was purified by crystallization from petroleum ether (b. p. 60–110°) as white crystals, m. p. 157–158° (cor.); yield 5.6 g. (53%).

Anal. Calcd. for $C_{13}H_{14}O_2BrCl$: C, 49.12; H, 4.42; neut. equiv., 317.5. Found: C, 48.95; H, 4.58; neut. equiv., 317, 314.

β-Chloro-β-(2,4,6-trimethyl-3-bromo-5-chlorosulfonylphenyl)-α-methylacrylic Acid (IX).—To 5 cc. of chlorosulfonic acid cooled to −10° was added slowly 0.20 g. of β-chloro-β-(2,4,6-trimethyl-3-bromophenyl)-α-methylacrylic acid. The reaction mixture was allowed to warm to room temperature and then poured on ice. The yellow solid was purified by recrystallization from petroleum ether (b. p. 60–110°): white crystals, m. p. 188–189° (cor.); yield 0.14 g. (53%).

Anal. Calcd. for $C_{13}H_{13}O_4BrCl_2S$: C, 37.59; H, 3.13. Found: C, 37.94; H, 3.26.

β-Chloro-β-(2,4,6-trimethyl-3,5-dibromophenyl)-α-methylacrylic Acid (VIII).—A mixture of 0.2 g. of β-chloro-β-(2,4,6-trimethyl-3-bromophenyl)-α-methylacrylic acid and 0.5 cc. of liquid bromine (cooled to 0°) was allowed to stand for twenty minutes. The excess bromine was evaporated and the residue treated with aqueous sodium bisulfite. The cream colored solid was purified by crystallization from ethanol; white needles, m. p. 228–229° (cor.).

Anal. Calcd. for $C_{13}H_{13}O_2Br_2Cl$: C, 39.39; H, 3.28. Found: C, 39.26; H, 3.26.

Resolution of β-Chloro-β-(2,4,6-trimethyl-3-bromophenyl)-α-methylacrylic Acid.—A solution of 10 g. of β-chloro-β-(2,4,6-trimethyl-3-bromophenyl)-α-methylacrylic acid in 75 cc. of warm absolute ethanol was added to a solution of 10 g. of quinine in 75 cc. of warm absolute ethanol. After filtration and cooling, 8.45 g. of salt (fraction A) crystallized. Evaporation of the filtrate to 100 cc. and cooling gave an additional 5.34 g. of salt (fraction B). The filtrate from the second fraction was diluted with 50 cc. of water whereupon 3.2 g. of oil separated (fraction C). Decantation of the solvent and slow evaporation yielded an additional crop of crystals (fraction D).

Fraction A was twice recrystallized from ethanol after which a constant rotation had been reached.

Rotation. Less soluble salt (*l*B·*d*A) 0.0995 g. made up to 25 cc. in absolute ethanol at 20° gave αD −0.37; *l*, 2; $[\alpha]^{20}D$ −46.8°.

Anal. Calcd. for $C_{33}H_{38}O_4N_2BrCl$: C, 61.73; H, 5.92. Found: C, 61.82; H, 6.05.

***d*-β-Chloro-β-(2,4,6-trimethyl-3-bromophenyl)-α-methylacrylic Acid.**—To a suspension of 5.2 g. of the purified salt (fraction A) in 100 cc. of water was added 10 cc. of concentrated hydrochloric acid. After stirring for thirty minutes, the product was filtered and washed with 5% hydrochloric acid until quinine-free and then with water. The product (2.4 g.) was purified by recrystallization twice from petroleum ether (b. p. 60–110°). Its rotation was the same after each crystallization; white crystals, m. p. 155–156° (cor.).

Rotation. (*d*-acid) 0.0998 g. made up to 25 cc. with absolute ethanol at 20° gave αD +0.42; *l*, 2; $[\alpha]^{20}D$

(7) Klages and Lickroth, *Ber.*, **32**, 1549 (1899).
(8) Fittig and Storer, *Ann.*, **147**, 8 (1868).
(9) Perkin, *J. Chem. Soc.*, **49**, 157 (1886).

+52.6°. 0.1008 g. made up to 25 cc. with glacial acetic acid at 20° gave α_D +0.56; *l*, 2; $[\alpha]^{20}D$ +69.4°.

Anal. Calcd. for $C_{13}H_{14}OBrCl$: C, 49.12; H, 4.42. Found: C, 49.04; H, 4.04.

Decomposition of the oily fraction C in a similar manner gave *l*-acid which after two crystallizations gave a constant rotation; white crystals, m. p. 155–156° (cor.).

Rotation. (*l*-acid) 0.0994 g. made up to 25 cc. with absolute ethanol at 20° gave α_D −0.43; *l*, 2; $[\alpha]^{20}D$ −54°.

Anal. Calcd. for $C_{13}H_{14}O_2BrCl$: C, 49.12; H, 4.42. Found: C, 49.62; H, 4.52.

Racemization Experiments.—The *d*-acid was refluxed in absolute ethanol for fifteen hours and in glacial acetic acid for twelve hours with no change in rotation in either case.

Bromination of *d*- + *l*-Acids: *dl*-β-Chloro-β-(2,4,6-trimethyl-3,5-dibromophenyl)-α-methylacrylic Acid.—The procedure for bromination was exactly that used in bromination of the racemic compound. The product was optically inactive and proved to be identical with the dibromo compound previously prepared; white needles, m. p. 228–229° (cor.). Bromination of the *l*-acid gave the same compound.

Action of Chlorosulfonic Acid on *d*- and *l*-Acids. Preparation of *d*- and *l*-β-Chloro-β-(2,4,6-trimethyl-3-bromo-5-chlorosulfonylphenyl)-α-methylacrylic Acids.—The procedure in these preparations was identical with that used for the racemic acid. Both *d*- and *l*-forms consisted of white crystals from petroleum ether (b. p. 60–100°), m. p. 183–184° (cor.).

Rotation. (derivative from *d*-acid) 0.1018 g. made up to 25 cc. with benzene at 20° gave α_D −0.07; *l*, 2; $[\alpha]^{20}D$ −8.6°.

Anal. Calcd. for $C_{13}H_{13}O_4BrCl_2S$: C, 37.59; H, 3.13. Found: C, 37.96; H, 3.29.

Rotation. (derivative from *l*-acid) 0.1002 g. made up to 25 cc. with benzene at 20° gave α_D +0.08; *l*, 2; $[\alpha]^{20}D$ +10.0°.

Summary

1. β-Chloro-β-(2,4,6-trimethyl-3-bromophenyl)-α-methylacrylic acid has been synthesized. This substance was resolved into its enantiomorphic forms. They proved to be very stable to racemization.

2. The asymmetry of the molecule is undoubtedly due to restricted rotation between the carbon of the benzene ring and the olefinic carbon to which it is attached. Necessity for unsymmetrical substitution in the benzene ring was demonstrated by bromination of the active acids and introduction of a chlorosulfonyl group. Bromination which results in a dibromo compound with symmetrical substitution gave an inactive product. Chlorosulfonic acid, on the other hand, which results in a molecule still containing an unsymmetrically substituted benzene, gave an optically active product.

3. This compound is typical of a general class of aryl olefins which should be capable of resolution.

URBANA, ILLINOIS RECEIVED NOVEMBER 8, 1939

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

The Synthesis of 1,3-Diphenyldihydroisobenzofurans, 1,3-Diphenylisobenzofurans and *o*-Dibenzoylbenzenes from the Diene Addition Products to Dibenzoylethylene

BY ROGER ADAMS AND MARVIN H. GOLD[1]

In a recent paper, the addition of 1,4-dimethylbutadiene to *trans*-dibenzoylethylene was described and a number of the reaction products of this substance was prepared.[2] A more systematic study is now under way on the diene addition products to dibenzoyl and substituted dibenzoyl ethylenes. In this communication will be reported the substances formed by the action of butadiene, 2,3-dimethylbutadiene, and cyclopentadiene on dibenzoylethylene, and the transformations of these substances.

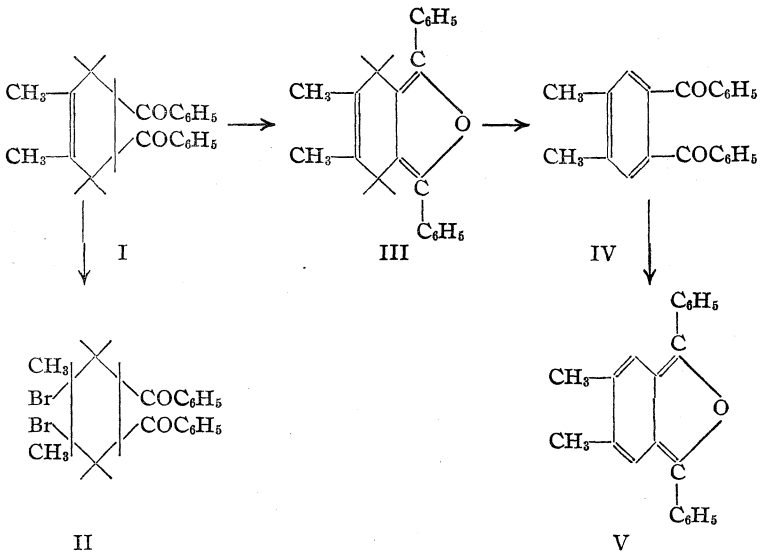
2,3-Dimethylbutadiene and *trans*-dibenzoylethylene react to give a quantitative yield of 1,2-dimethyl-4,5-dibenzoylcyclohexene (I), which adds a mole of bromine to give the expected dibromide (II).

The cyclohexene (I) is converted, by means of a few drops of sirupy phosphoric acid in acetic anhydride, into 1,3-diphenyl-5,6-dimethyl-4,7-dihydroisobenzofuran (III).

Compound III, on treatment with two molecules of bromine followed by sodium acetate in acetic acid, gives an excellent yield of 1,2-dimethyl-4,5-dibenzoylbenzene (IV). The exact mechanism of this reaction was not determined but it is probable that one mole of bromine adds to the cyclohexene double bond and one mole to the 1,4-position in the furan conjugated system

(1) An abstract of a thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry.

(2) Adams and Geissman, THIS JOURNAL, **61**, 2083 (1939).

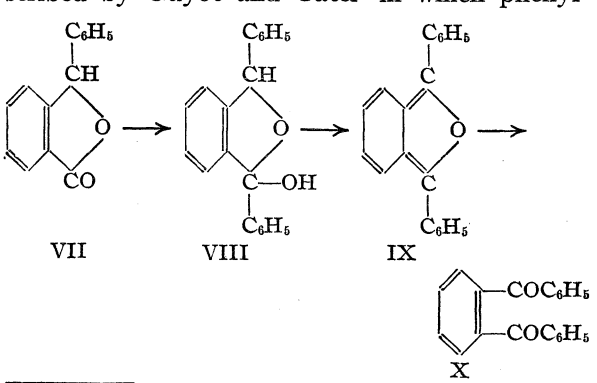


molecule of bromine to compound III was isolated and then treated with sodium acetate, a mixture of the *o*-dibenzoylbenzene (IV) and the isobenzofuran (V) was obtained.

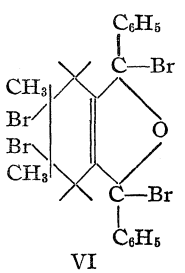
Butadiene in place of 2,3-dimethylbutadiene adds equally well to *trans*-dibenzoylethylene and by analogous reactions to those just described, compounds corresponding to I, II, III, IV, and V without the methyl groups were synthesized.

o-Dibenzoylbenzene and certain of its derivatives are known compounds but none of the methods of preparation is entirely satisfactory. A brief review of these methods is pertinent. It was first prepared by oxidation of *o*-dibenzylbenzene resulting as one of the products from the action of zinc dust on a mixture of benzyl chloride and benzene.[4] Beis[5] obtained it as one of the products from the reaction of phenylmagnesium bromide on N-phenylphthalimide. Bruhat and Thomas[6] used the Grignard reagent from *o*-diiodobenzene and two moles of benzonitrile followed by hydrolysis. Blicke and Patelski[3b,7] condensed *o*-benzoylbenzonitrile with phenylmagnesium bromide followed by hydrolysis. Clar, John and Hawran[8] replaced the two chlorines in *o*-phthalyl chloride with phenyl groups by the action of phenylmagnesium bromide.

The procedure most frequently used and unquestionably superior to the others is that described by Guyot and Catel[9] in which phenyl-



(VI). Two hydrogen bromides are then eliminated to form the benzene ring with simultaneous hy-



drolysis of the brominated furan ring to give two benzoyl groups.

o-Dibenzoylbenzene and one or two of its derivatives have been converted into 1,3-diphenylisobenzofuran by means of zinc dust and acetic acid.[3] This reaction, however, has not been extensively studied since the isobenzofurans have been in general more easily obtained than the *o*-dibenzoylbenzenes and have served as intermediates in the preparation of the latter compounds. Since in the reactions described in this paper the *o*-dibenzoylbenzenes are more easily obtained than the isobenzofurans, the conversion of the former to the latter was investigated. It was found that activated zinc and ethanolic sodium hydroxide was a superior reagent and resulted in a quantitative conversion of IV to the 1,3-diphenyl-5,6-dimethylisobenzofuran (V). The time of reduction of the *o*-dibenzoylbenzenes varies with the activity of the zinc dust.

If the product formed by the addition of one

(3) (a) Boyd and Ladhams, *J. Chem. Soc.*, 2089 (1928); (b) Blicke and Patelski, THIS JOURNAL, **58**, 273 (1936).

(4) Zincke, *Ber.*, **6**, 119 (1873); **9**, 31 (1876).
(5) Beis, *Compt. rend.*, **143**, 430 (1906).
(6) Bruhat and Thomas, *Compt. rend.*, **183**, 297 (1926).
(7) Blicke and Patelski, THIS JOURNAL, **58**, 559 (1936).
(8) Clar, John and Hawran, *Ber.*, **62**, 940 (1929).
(9) Guyot and Catel, *Compt. rend.*, **140**, 1348 (1905).

phthalide (VII) was condensed with phenylmagnesium bromide. The initial product (VIII) was transformed by hydrochloric acid or acetic acid to 1,3-diphenylisobenzofuran (IX) which, on oxidation with chromic acid, gave *o*-dibenzoylbenzene (X).

The method for preparing *o*-dibenzoylbenzene through the butadiene addition to dibenzoylethylene unquestionably is better than these just described. It has the further advantage of being readily applicable to certain substituted dibenzoylbenzenes which would be very difficult to prepare by the other methods.

Thus, by using reasonably accessible 2,3-disubstituted butadienes and substituted dibenzoylethylenes, 4,5-dialkyl or diaryl 1,2-dibenzoyl or substituted 1,2-dibenzoylbenzenes can be synthesized.

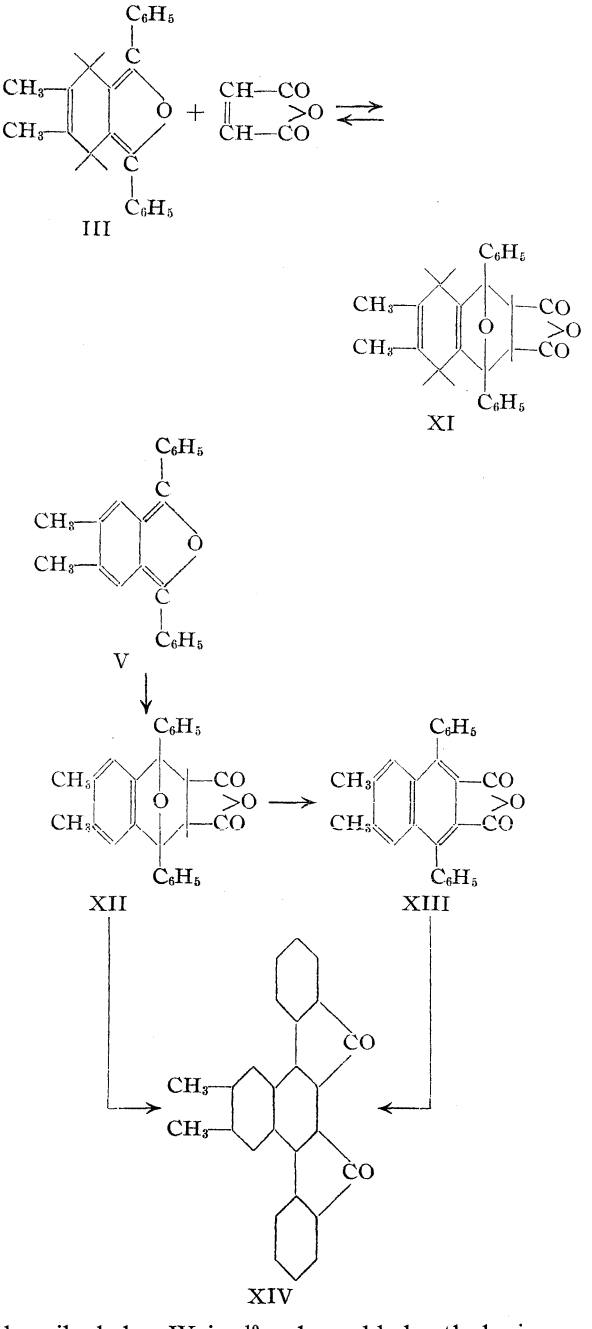
1,3-Diphenylisobenzofurans previously have been made by three processes: (1) the reduction of *o*-dibenzoylbenzenes by means of zinc and acetic acid,[3a,b] (2) the action of sulfuric acid on phthalins,[3b] (3) the action of arylmagnesium halides on aryl phthalides.[9] The unsubstituted compound has been made by the action of phenylmagnesium bromide on *o*-cyanobenzaldehyde.[3b] Since *o*-dibenzoylbenzenes can now be produced readily, the reduction of this type of compound seems the best procedure for arriving at the 1,3-diphenylisobenzofurans.

No 1,3-diphenyl-4,7-dihydroisobenzofurans (III) have been described previously.

The 1,3-diphenyl-4,7-dihydroisobenzofurans and the 1,3-diphenylisobenzofurans show marked fluorescence in dilute solution. The former are sometimes fluorescent even in the solid state. A quantitative study of the fluorescence of a series of these substances is now under way.

The isobenzofurans are useful as intermediates in various syntheses since they contain an active diene conjugated system. They add various compounds of the α,β-unsaturated carbonyl type. Thus, 1,3-diphenyl-5,6-dimethylisobenzofuran (V) is converted with maleic anhydride to 1,4-diphenyl-1,4-oxido-6,7-dimethyl-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylic acid anhydride (XII). The dihydroisobenzofurans also contain a similar active conjugated system but the reaction with maleic anhydride is so readily reversible that isolation of pure products was not accomplished (III $\rightleftarrows$ XI).

Additions of this type (V $\rightarrow$ XII) have been



described by Weiss,[10] who added ethyl cinnamate, indene, maleic anhydride and acrolein to 1,3-diphenylisobenzofuran, and maleic anhydride and acrolein to 1,3-di-α-naphthylisobenzofuran.

Barnett[11] added maleic anhydride and *p*-benzoquinone to 1,3-diphenylisobenzofuran and Dufraisse[12] *p*-benzoquinone and naphthoquinone.

(10) Weiss and Beller, *Monatsh.*, **61**, 143 (1932); Weiss and Abeles, *ibid.*, **61**, 162 (1932); Weiss and Kaltes, *ibid.*, **65**, 351 (1935); Weiss, *ibid.*, **71**, 6 (1937).

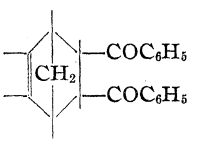
(11) Barnett, *J. Chem. Soc.*, 1326 (1935).

(12) Dufraisse and Compagnon, *Compt. rend.*, **207**, 585 (1938); Dufraisse and Priou, *Bull. soc. chim.*, [5] **5**, 502, 611 (1938).

By treatment of these adducts with hydrogen chloride, napthalene derivatives are produced and the adducts or the corresponding napthalenes are converted by sulfuric acid to 1,2,3,4-dibenzoylenenaphthalenes. Thus, the adduct (XII) is converted by hydrogen chloride to 1,4-diphenyl-6,7-dimethyl-2,3-naphthalic anhydride (XIII) and by sulfuric acid to 6,7-dimethyl-1,2,3,4-dibenzoylenenaphthalene (XIV).

Because of the ease with which many 1,3-diphenylisobenzofurans can now be made, satisfactory syntheses of 1,4-diaryl or substituted diaryl 6,7-dialkyl or diaryl 2,3-mono- or disubstituted naphthalenes are made available. A further study is being made of the scope of these preparative procedures.

When cyclopentadiene was added to *trans*-dibenzoylethylene, a compound presumably with structure XV was produced.



XV

This isomer must represent a molecule in which the benzoyl groups are *trans* or on opposite sides of the ring. A second isomer with the two benzoyl groups on the same side was obtained by addition of cyclopentadiene to *cis*-dibenzoylethylene. Neither of these adducts could be converted to furans by the procedure used for the cyclohexene derivatives.

Experimental

1,2-Dimethyl-4,5-dibenzoylcyclohexene.—To a solution of 40 g. of *trans*-dibenzoylethylene[13] in 200 cc. of absolute ethanol was added 35 g. of crude 2,3-dimethylbutadiene (unredistilled dehydration product of pinacol with 48% hydrobromic acid). The mixture was refluxed for three hours on the steam cone and allowed to cool, whereupon the product crystallized; yield 54 g. Purifications by recrystallization from 95% ethanol gave large plate-like prisms, m. p. 111–111.5° (corr.). On the first recrystallization 1.5 g. of a less soluble product remained undissolved in the hot ethanol and was identified as the corresponding dihydroisobenzofuran described in a subsequent procedure. The adduct gives a lemon yellow color in concentrated sulfuric acid.

Anal. Calcd. for $C_{22}H_{22}O_2$: C, 83.02; H, 6.92. Found: C, 82.92; H, 7.05.

cis-Dibenzoylethylene gives the same 2,3-dimethylbutadiene adduct.

Anal. Calcd. for $C_{22}H_{22}O_2$: C, 83.02; H, 6.92. Found: C, 82.92; H, 7.05.

(13) Lutz, THIS JOURNAL, **52**, 3434 (1930).

1,2-Dimethyl-4,5-dibenzoylcyclohexene Monodinitrophenylhydrazone.—The product separated from an ethanol solution of the reactants after standing overnight: orange crystals from ethanol; m. p. 226–228° (corr.) with decomposition.

Anal. Calcd. for $C_{28}H_{26}O_5N_4$: N, 11.25. Found: N, 11.20.

1,2-Dimethyl-1,2-dibromo-4,5-dibenzoylcyclohexane.—The addition product was prepared in glacial acetic acid: small white crystals from ethanol or petroleum ether (b. p. 60–110°); m. p. 170–171° (corr.) with decomposition.

Anal. Calcd. for $C_{22}H_{22}O_2Br_2$: C, 55.23; H, 4.60. Found: C, 55.37; H, 4.86.

1,3-Diphenyl-5,6-dimethyl-4,7-dihydroisobenzofuran.—To a nearly boiling solution of 5 g. of 1,2-dimethyl-4,5-dibenzoylcyclohexene in 75 cc. of acetic anhydride was added a few drops of sirupy phosphoric acid. The mixture was allowed to reflux for ten minutes, although the product started to come out after the first minute or two. After cooling the solution, the product was filtered, washed with water and recrystallized from benzene: yellowish-green fluorescent crystals, m. p. 225–226° (corr.); yield 4.7 g. (99%).

Anal. Calcd. for $C_{22}H_{20}O$: C, 88.00; H, 6.67. Found: C, 87.82; H, 6.79.

The furan exhibited a blue fluorescence in solution in organic solvents. With concentrated sulfuric acid, it gives an orange-brown color.

1,2-Dimethyl-4,5-dibenzoylbenzene.—A solution of 5 cc. of bromine in 30 cc. of glacial acetic acid was added slowly to a boiling suspension of 15 g. of 1,3-diphenyl-5,6-dimethyl-4,7-dihydroisobenzofuran in 200 cc. of acetic acid, 30 g. of sodium acetate and 15 cc. of water. Within a few minutes the bromine was completely absorbed and all of the furan dissolved. Reflux was continued for five minutes and then the solution was poured directly into 500–600 cc. of hot water, after which it was allowed to cool slowly for several hours. The product was filtered, dissolved in 300 cc. of ethanol and decolorized with norit: small white rectangular plates from ethanol, m. p. 143–144° (corr.); yield 14.2 g. (90%). The product gave a violet color in concentrated sulfuric acid.

Anal. Calcd. for $C_{22}H_{18}O_2$: C, 84.07; H, 5.73. Found: C, 83.81; H, 5.93.

2-Methyl-4,5-dibenzoylbenzoic Acid.—To a mixture of 25 cc. of pyridine, 35 cc. of water, 5 g. of potassium permanganate and 1 cc. of 10% aqueous sodium hydroxide was added 2 g. of 1,2-dimethyl-4,5-dibenzoylbenzene. The solution was refluxed for thirty minutes after which time all the permanganate was reduced. The solution was cooled, acidified with sulfuric acid and the manganese dioxide reduced with sodium bisulfite. The white precipitate was filtered, dissolved in 50 cc. of 5% aqueous sodium hydroxide, again filtered and reprecipitated with dilute sulfuric acid. The product was purified by recrystallization from benzene: small white crystals, m. p. 196–197° (corr.); yield 1.4 g. (64%).

Anal. Calcd. for $C_{22}H_{16}O_4$: C, 76.74; H, 4.65; neut. equiv., 344. Found: C, 76.50; H, 4.77; neut. equiv., 340.

1,3-Diphenyl-5,6-dimethylisobenzofuran.—A mixture of 3 g. of 1,2-dimethyl-4,5-dibenzoylbenzene, 3 g. of sodium hydroxide and 75 cc. of 95% ethanol was refluxed until the solution had turned dark brownish-red in color (usually about forty-five minutes). Then 3 g. of active zinc dust (prepared by suspending zinc dust in dilute hydrochloric acid, stirring well for one minute, decanting and washing with water until free of acid) was added and refluxing continued until the red solution became light yellow (usually five to forty-five minutes, depending on the activity of the zinc dust). The reaction should be discontinued as soon as the yellow color has appeared, otherwise the reduction proceeds too far. The hot solution was next filtered and poured into 70 cc. of glacial acetic acid and stirred to help precipitation. Within half a minute, the furan started to come out of solution. About 10 cc. of water was then added to ensure complete precipitation and the mixture was digested for about five minutes on the hot plate before allowing to cool. The product was purified from benzene or acetone: orange-yellow needles, m. p. 187–188° (corr.); yield 2.8 g. (97%).

Anal. Calcd. for $C_{22}H_{18}O$: C, 88.58; H, 6.04. Found: C, 88.13; H, 6.01.

The product exhibited a brilliant blue-green fluorescence in solution in organic solvents. It gave a reddish-orange color in concentrated sulfuric acid.

When an ethanolic solution of the benzofuran was illuminated by a strong lamp for a few days, it was reconverted completely to the 1,2-dimethyl-4,5-dibenzoylbenzene.[14]

A second procedure for preparing 1,3-diphenyl-5,6-dimethylisobenzofuran is from 1,3-diphenyl-5,6-dimethyl-5,6-dibromo-4,5,6,7-tetrahydroisobenzofuran. A solution of 1 g. of the dibromo compound in 30 cc. of glacial acetic acid and 10 cc. of acetic anhydride was heated nearly to boiling, then 8 g. of anhydrous sodium acetate and 10 cc. of glacial acetic acid was added, and the mixture refluxed for one-half hour. Upon cooling, the 1,3-diphenyl-5,6-dimethylisobenzofuran separated as yellow needles; yield 0.3 g. The mother liquor was then heated nearly to boiling and water was added until just turbid. Upon cooling, 0.36 g. of 1,2-dimethyl-4,5-dibenzoylbenzene precipitated.

1,3-Diphenyl-5,6-dibromo-5,6-dimethyl-4,5,6,7-tetrahydroisobenzofuran.—To a solution of 1 g. of 1,3-diphenyl-5,6-dimethyl-4,7-dihydroisobenzofuran in 80 cc. of chloroform was added a solution of 0.17 cc. of bromine in 15 cc. of chloroform over a period of ten minutes. The resulting solution was then evaporated to about 10 cc. and 5 cc. of petroleum ether (b. p. 60–110°) was added. The immediate precipitate consisting of unchanged dihydroisobenzofuran was filtered and the solution concentrated until the dibromo derivative crystallized. It was purified by recrystallization from ethanol: small light yellow crystals, m. p. 155–156° (corr.) with decomposition; yield 0.58 g. (38%; 60% based on unrecovered dihydroisobenzofuran).

Anal. Calcd. for $C_{22}H_{20}OBr_2$: C, 57.39; H, 4.35. Found: C, 57.76; H, 4.68.

1,4-Diphenyl-1,4-oxido-6,7-dimethyl-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylic Anhydride.—To a solution of 1.5 g. of 1,3-diphenyl-5,6-dimethylisobenzofuran in 75 cc. of benzene was added 0.5 g. of powdered maleic anhydride. Upon the addition of the anhydride there was a brilliant flash of red color which immediately disappeared, leaving a colorless solution which no longer fluoresced. The product soon separated. Purified from toluene, it gave tiny white crystals, m. p. (sealed tube) 254–255° (corr.) with decomposition; yield 2 g. (quant.).

Anal. Calcd. for $C_{26}H_{20}O_4$: C, 78.78; H, 5.05. Found: C, 78.65; H, 5.38.

The product gave a lemon yellow color in concentrated sulfuric acid.

1,4-Diphenyl-6,7-dimethyl-2,3-naphthalic Anhydride.—A suspension of 2 g. of the oxido compound in 150 cc. of absolute methanol was saturated with dry hydrogen chloride and then refluxed for two hours, while a slow stream of the hydrogen chloride was kept continuously bubbling through the reaction mixture. The oxido compound rapidly dissolved and the solution exhibited a faint fluorescence. After evaporation to dryness, 25 cc. of water, 5 g. of sodium hydroxide and 100 cc. of ethanol were added and the mixture refluxed for four hours. The solution was then cooled and acidified to congo red. The resulting white precipitate was filtered and dissolved in 10% aqueous sodium hydroxide, filtered and reprecipitated with acid. Upon purification by recrystallization from benzene, it gave tiny white crystals, m. p. 324–325° (corr.) with decomposition and some sublimation; yield 1.3 g. (68%).

Anal. Calcd. for $C_{26}H_{18}O_3$: C, 82.80; H, 4.76. Found: C, 83.06; H, 4.85.

The product gave a greenish-yellow color in concentrated sulfuric acid.

6,7-Dimethyl-1,2,3,4-dibenzoylenenaphthalene.—A mixture of 10 cc. of concentrated sulfuric acid and 0.5 g. of 1,4-diphenyl-1,4-oxido-6,7-dimethyl-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylic anhydride was allowed to stand for three and one-half hours. After this time the solution, which had turned from a light yellow to a deep green, was poured over 30 g. of ice. The red precipitate was purified by recrystallization from boiling acetic acid: tiny red needles, m. p. >325°; yield 0.2 g.

Anal. Calcd. for $C_{26}H_{16}O_2$: C, 86.67; H, 4.44. Found: C, 86.58; H, 4.56.

4,5-Dibenzoylcyclohexene.—To a cooled solution of 15 g. (1.5 moles) of butadiene in 200 cc. of benzene was added 40 g. of *trans*-dibenzoylethylene. The mixture was heated in a pressure bomb for two hours at 100°. The benzene was evaporated to 75 cc. and 125 cc. of methanol was added. Upon cooling, the product separated. It was purified by crystallization from ethanol: fine white crystals, m. p. 111.5–112° (corr.); yield 49 g. (quant.).

Anal. Calcd. for $C_{20}H_{18}O_2$: C, 82.75; H, 6.21. Found: C, 82.81; H, 6.47.

1,2-Dibromo-4,5-dibenzoylcyclohexane.—The procedure used was the same as for the bromination of the dimethyl homolog. The product was obtained in 90% yield and was purified from petroleum ether (b. p. 60–110°): small white crystals, m. p. 148–149° (corr.).

Anal. Calcd. for $C_{20}H_{18}O_2Br_2$: C, 53.33; H, 4.00. Found: C, 53.61; H, 4.22.

(14) Guyot and Catel, *Bull. soc. chim.*, [3] **35**, 1127 (1906).

1,3-Diphenyl-4,7-dihydroisobenzofuran.—The procedure used was that employed for preparation of the dimethyl compound: yellowish-green crystals from petroleum ether (b. p. 60–110°), m. p. 120–121° (corr.); yield 99%.

Anal. Calcd. for $C_{20}H_{16}O$: C, 88.23; H, 5.88. Found: C, 88.04; H, 6.28.

1,3 - Diphenyl - 5,6 - dibromo - 4,5,6,7 - tetrahydroisobenzofuran.—To a solution of 4 g. of 1,3-diphenyl-4,7-dihydroisobenzofuran in 30 cc. of glacial acetic acid was added dropwise a solution of 0.76 cc. of bromine in 10 cc. of acetic acid. The mixture was cooled and 4 g. (67%) of product separated. It was purified by crystallization from petroleum ether (b. p. 60–110°): yellow crystals, m. p. 150–151° (corr.) with decomposition.

Anal. Calcd. for $C_{20}H_{16}OBr_2$: C, 55.55; H, 3.72. Found: C, 55.01; H, 3.77.

This compound is relatively unstable and consequently difficult to obtain in an absolutely pure state. For this reason, the analysis does not agree with the theoretical as closely as is usually expected.

***o*-Dibenzoylbenzene.**—This was prepared in the same manner as the 4,5-dimethyl derivative; yield 85%. It was purified by recrystallization from ethanol or petroleum ether (b. p. 60–110°): white crystals, m. p. 145–146° (corr.); previously reported melting points are Zincke,[4] 145–146°; Beis,[5] 149°; Bruhat and Thomas,[6] 148°; Boyd and Ladhams,[3a] 145°.

1,3-Diphenylisobenzofuran.—This was prepared in the same manner as the dimethyl homolog. After the zinc dust reduction of 1 g. of dibenzoylbenzene, the filtered solution was treated with 5 cc. of concentrated hydrochloric acid with stirring. In a few seconds, the product separated in the form of yellow flakes. The product was purified by crystallization from petroleum ether (b. p. 60–110°): yellow crystals, m. p. 125–126° (corr.); yield 69%; previously reported melting points, Guyot and Catel,[9] 125°; Boyd and Ladhams,[3a] 120–125°.

Addition of Maleic Anhydride to 1,3-Diphenyl-4,7-dihydroisobenzofuran and to 1,3-Diphenyl-5,6-dimethyl-4,7-dihydroisobenzofuran.—These addition reactions were carried out in benzene solution. Mixing of the reactants was followed immediately by formation of an orange-red color which slowly faded. The characterisric fluorescence of the furans disappeared after refluxing for a short time. By concentration of the solvent products crystallized which, however, could not be purified owing to reversal to the furan and maleic anhydride.

2,3 - Dibenzoyl - 1,4 - endomethylene - 1,2,3,4 - tetrahydrobenzene.—To a solution of 10 g. of *trans*-dibenzoylethylene in 45 cc. of dry benzene was added 10 g. of cyclopentadiene. Heat was evolved and the yellow color faded. The mixture was refluxed for several hours, then well cooled, whereupon an oil separated. Concentration to a small volume, addition of ethanol, scratching and cooling resulted in the formation of crystals. These were purified by recrystallization from methanol: white crystals, m. p. 78–79° (corr.); yield 11 g. (89%).

Anal. Calcd. for $C_{21}H_{18}O_2$: C, 83.11; H, 5.96. Found: C, 83.00; H, 6.15.

A solution of 0.5 g. of *cis*-dibenzoylethylene in 15 cc. of absolute ethanol was refluxed with 1 g. of cyclopentadiene for four hours. This gave white needles on cooling. Purified by recrystallization from ethanol, m. p. 160–161° (corr.). This compound was a second isomer.

Anal. Calcd. for $C_{21}H_{18}O_2$: C, 83.11; H, 5.96. Found: C, 82.70; H, 6.12.

Summary

New and unusually satisfactory methods for preparing dihydroisobenzofurans, isobenzofurans and *o*-dibenzoylbenzenes are described.

Butadiene and 2,3-dimethylbutadiene have been condensed with *trans*-dibenzoylethylene to give 4,5-dibenzoylcyclohexene and its 1,2-dimethyl derivative. These dibenzoyl compounds are quantitatively converted by means of a little phosphoric acid in acetic anhydride to dihydroisobenzofurans. These, in turn, by bromine and sodium acetate give excellent yields of *o*-dibenzoylbenzenes.

It has been shown that the *o*-dibenzoylbenzenes can be converted quantitatively to isobenzofurans by ethanolic sodium hydroxide and activated zinc dust.

Both the dihydroisobenzofurans and the isobenzofurans add maleic anhydride and the adducts of the latter may be converted to naphthalene derivatives.

Cyclopentadiene also adds to *trans*- and *cis*-dibenzoylethylenes with formation of isomeric adducts.

URBANA, ILLINOIS RECEIVED NOVEMBER 10, 1939

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF DUKE UNIVERSITY]

Condensations Brought about by Bases. VIII. The Conversion of Ethyl Benzoyldimethylacetate to Ethyl Benzoate and Ethyl Isobutyryl-isobutyrate in the Presence of Sodium Ethoxide and Triphenylmethane. The Reversibility of the Claisen Type of Condensation[1]

BY CHARLES R. HAUSER AND BOYD E. HUDSON, JR.

Recently[2] it was shown that ethyl isobutyrate condenses with ethyl benzoate in the presence of sodium triphenylmethyl to form ethyl benzoyldimethylacetate, but in order to obtain this product it was necessary to stop the reaction by acidification within a short time (thirty minutes). When the reaction mixture was allowed to stand for several days before acidification no ethyl benzoyldimethylacetate could be isolated. This indicated that ethyl benzoyldimethylacetate, although first formed by the condensation of ethyl isobutyrate with ethyl benzoate, was cleaved later by the sodium ethoxide and triphenylmethane which were produced during the reaction. This has now been definitely established.

It has been found that ethyl benzoyldimethylacetate (synthesized from the enolate of ethyl isobutyrate and benzoyl chloride[3]) on standing in ether solution with sodium ethoxide and triphenylmethane at room temperature decomposes completely within five days. On working up the reaction mixture after this time, none of the original ethyl benzoyldimethylacetate could be isolated; instead ethyl benzoate and ethyl isobutyryl-isobutyrate were obtained.

The condensation of ethyl isobutyrate with ethyl benzoate, in the presence of sodium triphenylmethyl, to form ethyl benzoyldimethylacetate, as well as the cleavage of the latter and the condensation of ethyl isobutyrate with itself, may be represented by the following equations.

(I) $H—C(CH_3)_2COOC_2H_5 + (C_6H_5)_3CNa \rightleftharpoons Na[C(CH_3)_2COOC_2H_5] + (C_6H_5)_3CH$

(II) $C_6H_5COOC_2H_5 + Na[C(CH_3)_2COOC_2H_5] \rightleftharpoons$
Component A Component B
$C_6H_5C(ONa)(OC_2H_5)C(CH_3)_2COOC_2H_5 \rightleftharpoons C_6H_5COC(CH_3)_2COOC_2H_5 + NaOC_2H_5$

(III) $H—C(CH_3)_2COOC_2H_5 +$
Component A
$Na[C(CH_3)_2COOC_2H_5] \rightleftharpoons$
Component B
$H—C(CH_3)_2C(ONa)(OC_2H_5)C(CH_3)_2COOC_2H_5 \rightleftharpoons H—C(CH_3)_2COC(CH_3)_2COOC_2H_5 + NaOC_2H_5$

These reactions are regarded as essentially ionic.[4] The ethyl isobutyrate is converted into its sodium derivative (enolate) by means of sodium triphenylmethyl as represented by equation (I). The anion of the sodium enolate is undoubtedly a resonance structure, its two resonance forms being represented by (IV) (a) and (b); the mesomeric form of the anion may be represented by (c).

(IV)
(a) $(CH_3)_2\overset{\ominus}{C}—COOC_2H_5$
(b) $(CH_3)_2C=\underset{\ominus}{C}(O)OC_2H_5$
(c) $CH_3—\overset{\ominus}{C}(—O)—C(CH_3)(OC_2H_5)$

The condensations represented by equations (II) and (III) may be considered to involve the addition of the enolate anion to the carbon atoms of the carbonyl groups of the esters, ethyl benzoate and ethyl isobutyrate, to form intermediate anions with the charge on the oxygen atoms; the intermediate anions release ethoxide ion giving the β-keto esters.

When equimolar quantities of ethyl isobutyrate, ethyl benzoate and sodium triphenylmethyl are used, reaction (II) at first predominates over reaction (III). This is the case even though the ethyl isobutyrate and the sodium triphenylmethyl are allowed to react for a few minutes before adding the ethyl benzoate. After a time, however, reaction (III) becomes predominant, reaction (II) being reversed completely. This illustrates the reversibility of the Claisen type of condensation.[5]

The fact that reaction (II) at first predominates was anticipated on the basis that not only is the carbonyl group of ethyl benzoate probably more reactive than that of ethyl isobutyrate, but the

(1) This work was supported in part by a grant from the Duke University Research Council.

(2) Renfrow and Hauser, THIS JOURNAL, **60**, 463 (1938).

(3) Hauser and Renfrow, "Organic Syntheses," Vol. XIX, John Wiley and Sons, New York, N. Y., 1939, p. 43. See also Hudson, Dick and Hauser, THIS JOURNAL, **60**, 1961 (1938).

(4) See (a) Hauser and Renfrow, *ibid.*, **59**, 1823 (1937); (b) Hauser, *ibid.*, **60**, 1957 (1938).

(5) In this connection see Dieckmann, *Ber.*, **33**, 2670 (1900); *ibid.*, **41**, 1260 (1908); see also Arndt and Loewe, *ibid.*, **71**, 1636 (1938).

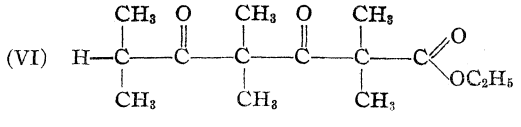
concentration of the latter, which may serve as component A, is much lower than that of ethyl benzoate; this is so because most of the ethyl isobutyrate is soon converted by the sodium triphenylmethyl into its enolate which is incapable of serving as component A.

The reason why ethyl benzoyldimethylacetate, in the presence of sodium ethoxide and triphenylmethane, is converted completely into ethyl benzoate and ethyl isobutyryl-isobutyrate is not entirely clear, but this change appears to be connected with the capacity for enolization of the latter and its existence in the reaction mixture in the form of its enolate. The formation of this enolate from the reactants used may be illustrated thus

$$\text{(V)}\quad 2C_6H_5COC(CH_3)_2COOC_2H_5 + NaOC_2H_5 \xrightarrow{(C_6H_5)_3CH} 2C_6H_5COOC_2H_5 + Na[C(CH_3)_2COC(CH_3)_2COOC_2H_5]$$

The formation of ethyl isobutyryl-isobutyrate from ethyl benzoyldimethylacetate presumably involves the cleavage of the latter and the condensation of two isobutyrate residues as represented in (III). The reversal of equation (II) gives the enolate of ethyl isobutyrate but apparently the only way the free ester, required for reaction (III), could be formed from ethyl benzoyldimethylacetate is by the reaction of the enolate of ethyl isobutyrate (formed by the reversal of II) with the proton donor, triphenylmethane (the reverse of reaction I). This gives the strong base sodium triphenylmethyl, which readily can convert the ethyl isobutyryl-isobutyrate as it is formed in reaction (III) into its enolate.

Experimental evidence has been obtained that at least most of the ethyl isobutyryl-isobutyrate, produced by the action of sodium ethoxide on ethyl benzoyldimethylacetate in the presence of triphenylmethane, is in the form of its enolate. The evidence has been obtained as follows. The reaction mixture of ethyl benzoyldimethylacetate, sodium ethoxide and triphenylmethane, after standing five days (during which time the cleavage is complete) was treated with isobutyryl chloride. On working up the resulting mixture, there was obtained, in addition to ethyl benzoate and ethyl isobutyryl-isobutyrate, a 32% yield of the compound represented by formula (VI).



Presumably, compound (VI) could have resulted only if the ethyl isobutyryl-isobutyrate were in the form of its enolate,[6] since the free β-keto ester does not condense with acid chlorides. Previously,[6] a yield of 46% of compound (VI) has been obtained from the enolate of pure ethyl isobutyryl-isobutyrate and isobutyryl chloride. Judging from this yield of compound (VI), it would appear that most of the ethyl isobutyryl-isobutyrate obtained from ethyl benzoyldimethylacetate (in the presence of sodium ethoxide and triphenylmethane) was in the form of its enolate. The passage from ethyl benzoyldimethylacetate (which is incapable of enolizing) to the enolate anion of ethyl isobutyryl-isobutyrate, which is a resonance structure, might furnish a driving force for the reaction.[7]

That the proton donor, triphenylmethane, is necessary for the conversion of ethyl benzoyldimethylacetate to ethyl benzoate and ethyl isobutyryl-isobutyrate is shown by the fact that the former ester may be recovered unchanged after standing for five days with sodium ethoxide in ether. Stronger proton donors, such as water or alcohol, cause ethyl benzoyldimethylacetate to be cleaved into acids or esters.[8]

In connection with the results presented above it is of interest to consider the reaction of sodium ethoxide with certain other β-keto esters. Dieckmann[5] reported that ethyl α,α-diethylacetoacetate with sodium ethoxide gave the acetyl derivative of this β-keto ester. We have obtained similar results with ethyl α,α-dimethylacetoacetate (VII). In the presence of sodium ethoxide, compound (VII) gave a good yield of ethyl isobutyrate, a fair yield of ethyl γ-acetyl-α,α-dimethylacetoacetate (VIII), and some ethyl acetate; also, some unchanged compound (VII) was recovered.

$CH_3COC(CH_3)_2COOC_2H_5$
(VII)
$CH_3COCH_2COC(CH_3)_2COOC_2H_5$
(VIII)

It is assumed that compound (VII), in the presence of sodium ethoxide, is cleaved to form ethyl

(6) Similar evidence has been obtained that the ethyl isobutyryl-isobutyrate, produced by the self-condensation of ethyl isobutyrate by means of sodium triphenylmethyl, is in the form of its sodium enolate. See Hudson and Hauser, THIS JOURNAL, **61**, 3567 (1939).

(7) The over-all reaction may depend upon the relative acidities (including the "activities" of the carbonyl groups) and basicities of the starting materials and of the products formed.

(8) In the presence of sodium ethoxide and alcohol, β-keto esters undergo "ester cleavage" giving two moles of ester (see ref. 5). Ethyl benzoyldimethylacetate in the presence of aqueous sodium hydroxide probably forms sodium benzoate and ethyl isobutyrate, the latter undergoing hydrolysis giving sodium isobutyrate.

acetate and the sodium enolate of ethyl isobutyrate. The latter, which is a strong base, immediately enolizes unchanged ethyl α,α-dimethylacetoacetate (VII). The enolate thus produced condenses with the ethyl acetate formed by the cleavage of (VII) giving compound (VIII) which is converted into its enolate by sodium ethoxide.

It is of interest to note that no appreciable amount of ethyl acetoacetate, which might have resulted by the self-condensation of the ethyl acetate, was obtained from the reaction. This is in agreement with theoretical considerations. One should expect that the enolate of ethyl isobutyrate, practically as rapidly as it is formed, should enolize unchanged ethyl α,α-dimethylacetoacetate (VII) rather than the ethyl acetate. The keto ester is not only the stronger acid but it is present in higher concentration than ethyl acetate, since the equilibrium of the cleavage reaction is probably far on the side of the unchanged β-keto-ester.

Finally, it should be noted that the original keto-ester, ethyl α,α-dimethylacetoacetate (VII), is not enolized appreciably by sodium ethoxide, whereas the final keto-ester, ethyl γ-acetyl-α,α-dimethylacetoacetate (VIII), is enolized by this base.

Experimental[9]

The Reaction of Ethyl Benzoyldimethylacetate with Sodium Ethoxide in the Presence of Triphenylmethane.—A solution of sodium triphenylmethyl was prepared as described previously[10,11] from 63 g. of triphenylchloromethane (m. p. 112–113°), 1500 cc. of dry ether (dried with sodium), and 2000 g. of 1% sodium amalgam. The average concentration of the base in solutions prepared from recrystallized[12] triphenylchloromethane has been found to be about 0.13 mole per liter. Approximately 1150 cc. of this solution was delivered by means of a nitrogen siphon to a previously calibrated 2-liter Pyrex glass-stoppered bottle filled with dry nitrogen. By means of a bent tube, an atmosphere of dry nitrogen was maintained in the bottle while the solution was neutralized with absolute alcohol[13] from a siphon-filled buret. The red color of the sodium triphenylmethyl became lighter as the alcohol was added, and finally, on the addition of a single drop of alcohol, there was a definite color change from orange to light yellow. This was considered to be the equivalence point of the neutralization. To this suspension of sodium ethoxide in an ether solution of triphenylmethane was added 33 g. (0.15 mole) of ethyl benzoyldimethylacetate (b. p. 146–148°) prepared from the enolate of ethyl isobutyrate and benzoyl chloride.[3] The stopper was lubricated with a little "Lubriseal," inserted immediately, and clamped in place. The mixture was allowed to stand for two weeks at room temperature with occasional shaking. At the end of that time, the stopper was removed and the mixture poured with vigorous shaking into 25 cc. of glacial acetic acid. The resulting mixture was extracted once with water and twice with 300-cc. portions of 10% sodium carbonate solution. The ether solution was dried with anhydrous sodium sulfate followed by "Drierite." The solution was filtered and the ether distilled off until the volume of the residue was approximately 75 cc. The residue was chilled overnight in the refrigerator and the supernatant solution decanted from the crystallized triphenylmethane, the latter being washed with a little ether and the washings added to the solution. After a final removal of ether by distillation at atmospheric pressure, the remaining liquid was vacuum-distilled, collecting up to 180° at 18 mm., at which point triphenylmethane began coming over. The distillate was redistilled and yielded 18 g. of material, presumably a mixture of ethyl benzoate and ethyl isobutyryl-isobutyrate, boiling at 96–116° at 18 mm. No ethyl benzoyldimethylacetate could be recovered. The fraction obtained was hydrolyzed by refluxing with 200 cc. of 8% potassium hydroxide; at the end of five hours, 8 g. additional alkali was added and refluxing continued three hours longer. The resulting mixture was cooled and extracted with four 50-cc. portions of ether. The combined ether extract was washed with a small quantity of water and dried with anhydrous sodium sulfate. The ether was distilled off. The residue yielded, on distillation at atmospheric pressure, 0.5 g. of di-isopropyl ketone boiling at 123–126°, which is the boiling point recorded previously[14] for this ketone. An additional 0.5 g. of the ketone boiling a few degrees above and below this range was obtained. The semicarbazone of the ketone melted at 159–160° in agreement with the melting point reported by Hauser and Renfrow.[4a] The alkaline solution, after the ether extraction, was boiled to remove dissolved ether. When cool, it was acidified with excess hydrochloric acid and chilled in the refrigerator. The precipitated benzoic acid was filtered by suction and air-dried; yield, 9.0 g., m. p. 118–120°. After one recrystallization from water, the melting point was 121–122° and was not lowered by the addition of an authentic specimen of benzoic acid.

A similar experiment was carried out using 10 g. (0.045 mole) of ethyl benzoyldimethylacetate and the corresponding amount of neutralized sodium triphenylmethyl solution. The reaction mixture was allowed to stand only five days and on working up yielded a fraction boiling at 91–111° at 15 mm. and weighing 6.0 g. There was no evidence of unchanged ethyl benzoyldimethylacetate.

Treatment of the Reaction Mixture of Ethyl Benzoyldimethylacetate, Sodium Ethoxide, and Triphenylmethane with Isobutyryl Chloride.—A suspension of sodium ethoxide in an ether solution of triphenylmethane was prepared as described above by neutralizing 1050 cc. of sodium triphenylmethyl solution (containing about 0.14 mole of base) with alcohol. To this suspension was added 30 g.

(9) All melting points and boiling points given are corrected.

(10) Renfrow and Hauser, "Organic Syntheses," Vol. XIX, John Wiley and Sons, Inc., New York, N. Y., 1939, p. 83.

(11) Hauser and Renfrow, THIS JOURNAL, **59**, 1825 (1937).

(12) See ref. 10, p. 84, note 1.

(13) Prepared by the method of Lund and Bjerrum, *Ber.*, **64**, 210 (1931).

(14) See ref. (4a) p. 1826.

(0.136 mole) of ethyl benzoyldimethylacetate, the bottle being stoppered and allowed to stand five days at room temperature with occasional shaking. At the end of that time, the mixture was poured into a solution of 17.5 g. (0.16 mole) of isobutyryl chloride (Eastman Kodak Co.) in 500 cc. of dry ether vigorously agitated by a mechanical stirrer. After the mixture had stood an hour in a closed vessel, 3 cc. of glacial acetic acid was added and the mixture extracted with water. The resulting ether solution was washed with 10% sodium carbonate solution and dried with anhydrous sodium sulfate followed by "Drierite." The solution was filtered and most of the ether distilled off. The residue was chilled overnight in the refrigerator and the crystallized triphenylmethane filtered off and washed with a small quantity of ether, the washings being added to the filtrate. After the ether was removed by distillation at atmospheric pressure, the filtrate was distilled at 15 mm., a fraction boiling up to 50° and another boiling from 50–180° being collected. The low-boiling fraction (approximately 3 g.) consisted presumably of ethyl isobutyrate (probably formed from isobutyryl chloride and sodium ethoxide); on redistillation at atmospheric pressure it boiled at 110–120°. The higher boiling material was refractionated at 15 mm., the following fractions being obtained: (a) 95–115° at 15 mm., 17.8 g.; (b) 115–130° at 15 mm., 2 g.; (c) 130–140° at 15 mm., 5.5 g. (Most of this fraction distilled at 135–138°.)

Fraction (a) was shown to be a mixture of ethyl benzoate and ethyl isobutyryl-isobutyrate by hydrolysis as described in the preceding experiment. A yield of 5.5 g. of benzoic acid (m. p. 121–122°) and 1 g. of di-isopropyl ketone (b. p. 115–125°) was obtained. The latter was converted into its semicarbazone, which melted at 158–159°.

Fraction (c) undoubtedly consisted largely of ethyl 2,2,4,-4,6-pentamethyl-3,5-diketoheptanoate, which boils at 136–138° at 15 mm.[6] It was cyclized to hexamethylphloroglucinol, which was identified by the mixed melting point method.[6] The yield (5.5 g.) of the heptanoate obtained corresponds to 32% of the theoretical amount, based on the quantity of ethyl benzoyldimethylacetate used.

Preparation of Ethyl Benzoyldimethylacetate by the Oxidation of Ethyl β-Phenyl-β-hydroxypivalate.—Fifty grams of ethyl β-phenyl-β-hydroxypivalate[15] (m. p. 39–40°) was dissolved in 100 cc. of glacial acetic acid on a water-bath. The solution was maintained at 80–100° while 17.3 g. (a 15% excess over the equivalent quantity) of chromic anhydride was added in 0.5-g. portions. After each addition, the mixture was stirred until reaction was complete and no chromic anhydride remained on the bottom of the flask. When all the chromic anhydride had been added, the solution was heated on the water-bath an hour longer, at the end of which time it was poured into 500 cc. of water and shaken vigorously. The resulting mixture was extracted with three 100-cc. portions of ether. The combined ether extract was washed once with water and several times with 10% sodium carbonate solution, and was dried with anhydrous sodium sulfate followed by "Drierite." The solution was filtered and the ether was removed by distillation at atmospheric pressure. The residue was vacuum-distilled and the portion of ethyl benzoyldimethylacetate boiling at 146–148° at 15 mm. collected; yield, 36 g., 72% of the theoretical amount.

Treatment of Ethyl Benzoyldimethylacetate with Sodium Ethoxide in the Absence of Proton Donors.—Fifteen grams (0.068 mole) of ethyl benzoyldimethylacetate, prepared by the oxidation of ethyl β-phenyl-β-hydroxypivalate, was dissolved in 500 cc. of dry ether and added to 4.65 g. (0.068 mole) of alcohol-free sodium ethoxide contained in a glass-stoppered flask. Several pieces of glass tubing 1 cm. long were dropped in the flask, and a glass stopper well lubricated with "Lubriseal" was inserted and clamped in place. The flask was shaken vigorously until all the caked sodium ethoxide was changed to a fine suspension. The reaction mixture was allowed to stand for five days with occasional shaking. At the end of that time, the mixture was poured with vigorous shaking into 5 cc. of glacial acetic acid, extracted with water, and washed twice with 10% sodium carbonate solution. The resulting ether solution was dried with anhydrous sodium sulfate followed by "Drierite." The solution was filtered and the ether distilled off. The residue was vacuum-distilled at 15 mm., yielding two fractions, 90–115° (2.3 g.) and 140–148° (9.8 g.). The lower boiling fraction was presumably a mixture of ethyl isobutyryl-isobutyrate and ethyl benzoate. The higher boiling fraction was shown to be ethyl benzoyldimethylacetate by conversion into its isoxazolone, which melted at 69–70° in agreement with the melting point reported in the literature.[16] The recovered ethyl benzoyldimethylacetate (9.8 g.) represents 65% of the initial quantity and 81% of the recovered products. These results indicate that ethyl benzoyldimethylacetate is essentially unaffected by sodium ethoxide in the absence of appreciable quantities of proton donors.

Reaction of Ethyl α,α-Dimethylacetoacetate with Sodium Ethoxide.—A solution of 50 g. (0.136 mole) of ethyl α,α-dimethylacetoacetate[17] (b. p. 75–76° at 15 mm.) in 1000 cc. of dry ether was added to 22 g. (0.32 mole) of alcohol-free sodium ethoxide contained in a glass stoppered flask. The flask was stoppered and allowed to stand three days with frequent shaking. At the end of that time, the mixture was acidified with 25 cc. of glacial acetic acid and extracted with water. The resulting ether solution was washed three times with 10% sodium carbonate solution and dried with anhydrous sodium sulfate. Ether was removed up to 40°. The remaining liquid was distilled through a short Widmer column up to 120°. Redistillation of the distillate and vacuum fractionation of the residue gave the following fractions:

(a)	60–80° at atm. press.	3.5 g. ethyl acetate (b. p. 77°)
(b)	80–108° at atm. press.	1.5 g. mid-fraction
(c)	108–112° at atm. press.	18.5 g. ethyl isobutyrate (b. p. 111°)
(d)	up to 75° at 15 mm.	1.2 g. mid-fraction
(e)	75–80° at 15 mm.	3.5 g. unchanged ethyl α,-α-dimethylacetoacetate
(f)	80–95° at 15 mm.	1.4 g. mid-fraction
(g)	95–121° at 15 mm.	3.5 g. largely ethyl γ-acetyl α,α-dimethylacetoacetate
(h)	121–123° at 15 mm.	5.3 g. ethyl γ-acetyl α,α-dimethylacetoacetate

(15) Blaise and Hermann, *Ann. chim. phys.*, [8] **23**, 532 (1911).

(16) See ref. 2, p. 464.

(17) Frankland and Duppa, *Ann.*, **138**, 328 (1866).

Ferric chloride tests with fractions (d) and (e) were negative, with fraction (f) faintly positive, and with fractions (g) and (h), strongly positive. Fraction (g) was shown to consist largely of ethyl γ-acetyl-α,α-dimethylacetoacetate by conversion (by means of concentrated ammonia) into the lactam of 2,2-dimethyl-3-keto-5-amino-4-hexenecarboxylic acid, melting at 139–140°; this is the melting point reported in the literature[18] for this lactam. Fraction (h) presumably consisted entirely of ethyl γ-acetyl-α,α-dimethylacetoacetate.

Summary

1. In the presence of sodium ethoxide and triphenylmethane, ethyl benzoyldimethylacetate is converted completely into ethyl benzoate and ethyl isobutyryl-isobutyrate, the latter being converted into its enolate.

2. In the complete absence of proton donors, ethyl benzoyldimethylacetate is apparently stable toward sodium ethoxide.

3. In the presence of sodium ethoxide, α,α-dimethylacetoacetic ester is converted into γ-acetyl-α,α-dimethylacetoacetic ester and ethyl isobutyrate.

4. These results illustrate the reversibility of the Claisen type of condensation.

5. The mechanisms for these reactions are discussed.

(18) See Conrad and Gast, *Ber.*, **31**, 1342 (1898).

DURHAM, NORTH CAROLINA RECEIVED OCTOBER 30, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

The Synthesis of Certain Oligosaccharide Acetates in the Mannose Series[1]

BY DELBERT D. REYNOLDS AND WM. LLOYD EVANS

In a recent publication, the authors[2] discussed certain improvements in the well-known Königs and Knorr reaction as it was applied to the synthesis of α- and β-gentiobiose octaacetates. Our present paper contains an account of the first successful use of this reaction in the synthesis of certain acetates in the mannose series of saccharides.

Several epimeric pairs of mono- and disaccharides have been prepared by other workers and the properties of these compounds have been studied carefully. As far as the authors are aware such an epimeric pair in the trisaccharide series has never been reported. Anticipating the interesting problems that would arise from such a synthesis, acetobromogentiobiose was condensed with β-*d*-mannose-1,2,3,4-tetraacetate, a reaction which gave rise to 6-β-gentiobiosido-β-*d*-mannose hendekaacetate. This new hendekaacetate and that of 6-β-gentiobiosido-β-*d*-glucose prepared by Helferich and co-workers[3] make available the first known epimeric pair of trisaccharides. An application of Hudson's isorotation rules has been made to these two compounds.

By another application of the improved Königs and Knorr reaction, 6-β-*d*-glucosido-α-*d*-mannose octaacetate was prepared by the condensation of acetobromoglucose with α-*d*-mannose-1,2,3,4-tetraacetate. This method of preparing this disaccharide is to be preferred to the oxidation of gentiobial by the procedure of Bergmann and Schotte[4] which was utilized previously in this Laboratory[5]; the new method involves fewer steps and gives higher yields.

During the progress of this work it became necessary to prepare ethyl gentiobioside heptaacetate, the synthesis of which is herein described, together with an application of the isorotation rules to its rotation.

Experimental Part

Purification of Reagents.—Chloroform was purified by the method described in an earlier paper.[2] The mannose was prepared according to the method of Levene.[6] Acetobromogentiobiose was prepared from gentiobiose octaacetate by the method of Brauns.[7]

6 - Trityl - β - *d* - mannose - 1,2,3,4 - tetraacetate.—The method of Helferich and Leete[8] was modified in such a way that the yield of 6-trityl-β-*d*-mannose-1,2,3,4-tetraacetate was doubled. One hundred grams of dry mannose and trityl chloride (161 g.) were added to anhydrous pyridine (500 cc.). The mixture was shaken in a thermostat at 50° until solution was complete (four hours). Without cooling, three hundred cc. of acetic anhydride was then

(1) Abstracted from a Thesis presented by Delbert D. Reynolds to the Graduate School of The Ohio State University in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

(2) D. D. Reynolds and W. L. Evans, THIS JOURNAL, **60**, 2559 (1938).

(3) B. Helferich and R. Gootz, *Ber.*, **64**, 109 (1931); B. Helferich and W. Schaefer, *Ann.*, **450**, 236 (1926).

(4) M. Bergmann and H. Schotte, *Ber.* **54**, 440 (1921).

(5) H. J. Dauben and W. L. Evans, THIS JOURNAL, **60**, 886 (1938).

(6) P. A. Levene, *J. Biol. Chem.*, **108**, 419 (1935).

(7) D. H. Brauns, THIS JOURNAL, **49**, 3170 (1927).

(8) B. Helferich and J. Leete, *Ber.*, **62**, 1552 (1929).

added in one portion. After standing at room temperature for about eighteen hours, the reaction mixture was poured slowly into seven liters of mechanically stirred ice water. The reaction product separated as a white amorphous solid. The water was changed twice in order to remove the pyridine. The crude product was separated by filtration, washed well with cold water and dried in the open air. It was then dissolved in hot 95% ethanol, decolorized with Carboraffin and the β-isomer allowed to crystallize. It was recrystallized from the same solvent; yield 150 g.; m. p. 204–206° (corr.).

β - *d* - Mannose - 1,2,3,4 - tetraacetate.—β - *d* - Mannose-1,2,3,4-tetraacetate was prepared according to the directions of Helferich and Leete[8] except for the method of crystallization.

Forty-six grams of 6-trityl-β-*d*-mannose-1,2,3,4-tetraacetate was dissolved in glacial acetic acid (200 cc.) by warming on a water-bath. The solution was cooled to 10°. Acetic acid (18 cc.) saturated with hydrogen bromide at 0° was added and the solution shaken for about forty-five seconds. The trityl bromide was removed at once by filtration and the filtrate poured into one liter of cold water. The tetraacetate was extracted with chloroform (250 cc.). The chloroform layer was washed twice with ice water and then dried over anhydrous sodium sulfate. After filtration, the chloroform was partially removed by a stream of dry air. The last traces were removed under reduced pressure. Anhydrous ether (100 cc.) was added and the sirup rubbed with a glass rod. Crystallization took place instantaneously. The product was purified by dissolving it in a minimum amount of U. S. P. chloroform and then adding anhydrous ether until crystallization began; yield 19.3 g.; m. p. 135.5–136.5° (corr.).

6-β-Gentiobiosido-β-*d*-mannose Hendekaacetate.—Sixteen grams (1.2 mol) of β-*d*-mannose-1,2,3,4-tetraacetate, silver oxide (26 g.), Drierite (100 g.) preheated at 240° for two hours, and dry, alcohol-free chloroform (150 cc.) were placed in a 500 cc. three-necked, round-bottomed flask equipped with a mercury-sealed mechanical stirrer, a calcium chloride drying tube and a dropping funnel. The flask was wrapped in black paper. The contents of the flask were stirred for about one hour to ensure the complete absence of water. Iodine (5 g.) was then added to the reaction mixture. Acetobromogentiobiose[7] (26.6 g., 1 mol) was dissolved in dry, alcohol-free chloroform (100 cc.) and then added through the dropping funnel to the reaction mixture over a course of about one hour. The stirring was then continued for an additional twenty-four hours. The reaction mixture was filtered through a layer of "Filter-Cel" and the residue washed well with U. S. P. chloroform. The filtrate was blown down by a stream of dry air and finally concentrated to a sirup under reduced pressure. The sirup was then dissolved in 95% ethanol. Crystallization began after a short time at room temperature. After standing in the refrigerator overnight, the crystals were filtered and dried; yield 27 g. (73.4%), m. p. 116–118° (corr.); after six recrystallizations, m. p. 122–123° (corr.) and $[\alpha]^{25}D$ −21.02° (*c*, 3.92; *l*, 2; $CHCl_3$).

Anal. Calcd. for $C_{18}H_{21}O_{16}(COCH_3)_{11}$: (a) acetyl, 11.39 cc. of 0.1 *N* sodium hydroxide per 100 mg. sample; C, 49.66; H, 5.63; mol. wt., 966. Found: (b) acetyl, 11.41 and 11.42; C, 48.55; H, 5.62; mol. wt., by Rast method, 935 and 1000.

Ethyl Gentiobioside Heptaacetate.—The preparation of 6-β-gentiobiosido-β-*d*-mannose hendekaacetate was repeated several times. In one instance crystalline ethyl gentiobioside heptaacetate was isolated as a result of insufficiently purified chloroform. Ethyl gentiobioside heptaacetate has not been recorded in the literature. For identification and characterization, it has been prepared by the method described for 6-β-gentiobiosido-β-*d*-mannose hendekaacetate. A mixture of absolute ethanol (100 cc.), silver oxide (10 g.), Drierite (50 g.) and dry chloroform (75 cc.) was stirred for one hour. One gram of iodine was added. Acetobromogentiobiose (15 g.) was dissolved in dry chloroform (25 cc.) and then added to the reaction mixture over a period of about one hour. After stirring for twenty-four hours, the reaction mixture was treated as previously described for 6-β-gentiobiosido-β-*d*-mannose hendekaacetate. Crystallization began as soon as the chloroform was removed. The product was filtered and recrystallized from 95% ethanol; yield 11.7 g. (82%) m. p. 158–159° (corr.); $[\alpha]^{25}D$ −23.06° (*c*, 4.12; *l*, 2; $CHCl_3$).

Anal. Calcd. for $C_{14}H_{19}O_{11}(COCH_3)_7$; acetyl, 10.54 cc. of 0.1 *N* sodium hydroxide per 100 mg. of sample. Found: acetyl, 10.51 cc.

6-Trityl-α-*d*-mannose-1,2,3,4-tetraacetate.—A mixture of dry mannose (20 g.), trityl chloride (32.2 g.) and anhydrous pyridine (100 cc.) was shaken mechanically at room temperature. Solution was effected within four hours. The solution was placed in the refrigerator at 0° for fifteen hours and then poured slowly into two liters of mechanically stirred ice water. This water was changed three times. The granular precipitate was then filtered and dried, after which it was dissolved in pyridine and placed in the refrigerator for twelve hours. It was then kept at a temperature of 0–5° while 60 cc. of acetic anhydride was added and then placed in the refrigerator overnight. Ice water was added to turbidity and the solution poured slowly into three liters of mechanically stirred ice water. The water was changed twice. The dried precipitate (48 g.) was taken up in absolute ethanol (300 cc.), decolorized with Carboraffin and filtered. Crystallization began when the solution was blown down by a stream of dry air; yield 15 g. After one recrystallization $[\alpha]D$ +73.5° ($CHCl_3$); m. p. 123–124° (corr.).

6-β-*d*-Glucosido-α-*d*-mannose Octaacetate.—6-Trityl-α-*d*-mannose-1,2,3,4-tetraacetate (34 g.) was dissolved in glacial acetic acid (100 cc.). After cooling to 10° a saturated solution of hydrogen bromide in glacial acetic acid (18 cc.) was added. The solution was shaken for about one minute, filtered and the filtrate poured into one liter of water (25°). This water was stirred for one hour, in order to dissolve the α-*d*-mannose-1,2,3,4-tetraacetate and then filtered. The filtrate was extracted with U. S. P. chloroform (500 cc.), the chloroform portion washed three times with three 400-cc. portions of ice water, dried over anhydrous sodium sulfate and blown down to a sirup. This sirup was finally concentrated under reduced pressure and taken up in anhydrous alcohol-free chloroform.

To this chloroform solution were added Drierite (15 g.), and silver oxide (8 g.). After stirring for one-half hour,

iodine (0.5 g.) was added and then acetobromoglucose (8 g.), dissolved in anhydrous alcohol-free chloroform (35 cc.), was added over a course of one hour. The apparatus used was the same as that for the preparation of 6-β-gentiobiosido-β-*d*-mannose hendekaacetate. The reaction mixture was stirred for a total of twenty-four hours, filtered and concentrated to a sirup. This sirup was dissolved in 95% ethanol (50 cc.) and placed in the refrigerator. Crystallization began immediately; yield 6 g. (45.5%); after one recrystallization $[\alpha]_D$ +26.01° (*c*, 2.96; *l*, 2; $CHCl_3$), the same value as that recorded by Dauben and Evans.[5]

Discussion

The isorotation rules of Hudson[9] afford a means of arriving at the approximate rotation of the trisaccharide acetate. If it is assumed that the epimeric difference of the molecular rotation between 6-β-gentiobiosido-β-*d*-glucose hendekaacetate and 6-β-gentiobiosido-β-*d*-mannose hendekaacetate has the same value as that between β-*d*-glucose pentaacetate and β-*d*-mannose pentaacetate under the experimental conditions indicated by the symbol, $[\alpha]^{25}D$, then by the relation

$$[\alpha_A]M_A[10] - [\alpha_B]M_B = [\alpha_{A'}]M_{A'} - [\alpha_{B'}]M_{B'}$$

it is possible to calculate the approximate rotation of 6-β-gentiobiosido-β-*d*-mannose hendekaacetate (B) from the known values of the molecular rotations of 6-β-gentiobiosido-β-*d*-glucose hendekaacetate (A),[3] β-*d*-glucose pentaacetate (A)[11] and β-*d*-mannose pentaacetate (B)[11] all measurements referring to chloroform solutions. Thus

$$\begin{aligned}[\alpha_B]M_B &= [\alpha_A]M_A - [\alpha_{A'}]M_{A'} + [\alpha_{B'}]M_{B'}\\ &= (-7728) - (1482) + (-9828)\\ &= -19{,}038\\ \therefore [\alpha_B] &= -19.7^\circ \text{ (The observed value is } -21.0^\circ.)\end{aligned}$$

Hudson[12] and Isbell[13] have shown previously that the values for the epimeric difference in the α-derivatives of the mannose series are entirely different from those of the β-derivatives. This is illustrated for the acetates in Table I.

Haworth and Hirst[14] have pointed out that the values of "the epimeric differences required by Hudson's scheme are not found in 4-glucosidomannose octaacetate and cellobiose octaacetate." However, it may be observed from Table I, as was shown by Dauben and Evans,[5] that the epimeric differences of α-gentiobiose octaacetate and 6-β-*d*-glucosido-α-*d*-mannose octaacetate agree very well with that of α-*d*-glucose pentaacetate and α-*d*-mannose pentaacetate. Further observation shows that the epimeric difference for 6-β-gentiobiosido-β-*d*-glucose hendekaacetate and the newly synthesized 6-β-gentiobiosido-β-*d*-mannose hendekaacetate agree in a satisfactory way with that of β-*d*-glucose pentaacetate and β-*d*-mannose pentaacetate. It thus appears that the epimeric relationships hold for the 6-linked sugar acetates, although they fail for the 4-linked acetates. Since the epimeric difference is twice the rotational value of carbon 2, the farther the glucosido portion is removed from carbon 2 the less influence it seems to have on the value of the epimeric difference.

TABLE I

EPIMERIC DIFFERENCES OF MOLECULAR ROTATION IN THE GLUCOSE AND MANNOSE SERIES

Sugar acetates	$[\alpha]_D$	Mol. epimeric diff.
α-Glucose pentaacetate	+101.6°	
α-Mannose pentaacetate	+ 55.0°	+18,200
α-Gentiobiose octaacetate	+ 52.4°	
α-6-Glucosidomannose octaacetate	+ 26.0°	+17,900
α-Cellobiose octaacetate	+ 42.0	
α-4-Glucosidomannose octaacetate	+ 36.2	+ 3,260
β-Glucose pentaacetate	+ 3.8	
β-Mannose pentaacetate	− 25.2	+11,300
β-Gentiobiosido-β-*d*-glucose hendekaacetate	− 8.0	
β-Gentiobiosido-β-*d*-mannose hendekaacetate	− 21.0	+12,600
β-Cellobiose octaacetate	− 14.6	
β-4-Glucosidomannose octaacetate	− 13.0	− 1,940

The rotation of the new β-ethyl gentiobioside heptaacetate may be calculated from the known values for

β-methylgentiobioside heptaacetate[15] ($[M]_D$ = (−18.9)-(650) = −12.300)

β-methylglucoside tetraacetate[16] ($[M]_D$ = (−18.3)(362) = −6600)

β-ethylglucoside tetraacetate[17] ($[M]_D$ = (−22.7)(374) = −8535)

The isorotation rules give the augmentation of the molecular rotation from the methyl to the ethyl compound as 8535−6600 = 1935; hence

(9) C. S. Hudson, "Rapports sur les Hydrates de Carbone, Dixième Conférence de l'Union Internationale de Chimie," 1930, p. 59.

(10) *M* = Molecular weight.
$[\alpha_A]M_A$ = Molecular rotation of 6-β-gentiobiosido-β-*d*-glucose hendekaacetate.
$[\alpha_B]M_B$ = Molecular rotation of 6-β-gentiobiosido-β-*d*-mannose hendekaacetate.
$[\alpha_{A'}]M_{A'}$ = Molecular rotation of β-*d*-glucose pentaacetate.
$[\alpha_{B'}]M_{B'}$ = Molecular rotation of β-*d*-mannose pentaacetate.

(11) Hudson, "Scientific Papers of the Bureau of Standards," No. 533.

(12) Hudson, THIS JOURNAL, **48**, 1424, 1434 (1926).

(13) Isbell, *Bur. Standards J. Research*, **5**, 1179 (1930).

(14) W. Haworth and E. Hirst, *J. Chem. Soc.*, 2631 (1930).

(15) Hudson and Johnson, THIS JOURNAL, **39**, 1272 (1917).

(16) Hudson and Dale, *ibid.*, **37**, 1264 (1915).

(17) Ferguson, *ibid.*, **54**, 4086 (1932).

the $[\alpha]_D$ value for β-ethylgentiobioside heptaacetate is calculated to be $(-12{,}300-1935)/664 = -21.4°$, which agrees satisfactorily with the observed value, $-23.1°$.

Acknowledgment.—The authors wish to acknowledge the assistance given by William G. Dauben and Harold D. McDowell during the progress of this work.

Summary

1. A new crystalline 6-β-gentiobiosido-β-*d*-mannose hendekaacetate has been synthesized by the improved Königs and Knorr reaction and its physical properties determined. This is the first time that a crystalline 6-linked oligosaccharide acetate containing mannose has been synthesized by this method.

2. The epimeric difference relationships of the new 6-β-gentiobiosido-β-*d*-mannose hendekaacetate and the known 6-β-gentiobiosido-β-*d*-glucose hendekaacetate have been correlated with others of the mannose series. The specific rotation as calculated by Hudson's rules is $-19.7°$. The observed specific rotation is $[\alpha]^{25}D$ $-21.0°$. It has been pointed out that the values of the epimeric differences as required by Hudson's scheme seem to hold for 6-linked sugars although they do not hold for 4-linked sugars.

3. The known 6-β-*d*-glucosido-α-*d*-mannose octaacetate has been made more available by the improved Königs and Knorr reaction. Its preparation represents the second synthesis of a crystalline 6-linked oligosaccharide acetate containing a mannose unit.

4. Ethylgentiobioside heptaacetate has been synthesized and its physical properties determined, m. p. 158–159° (corr.); $[\alpha]^{25}D$ $-23.1°$. This rotation agrees with that which is calculated $(-21.4°)$ from Hudson's rules.

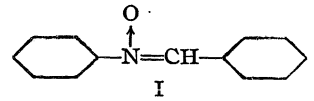
COLUMBUS, OHIO RECEIVED OCTOBER 11, 1939

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

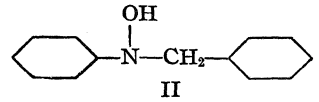
Secondary Amines from Nitro Compounds

BY WILLIAM S. EMERSON AND H. W. MOHRMAN

Since most aromatic primary amines are prepared by the reduction of nitro compounds, it seemed possible that the procedure for reductive alkylation of these amines[1] could be adapted to apply directly to the original nitro compounds. Vavon and Crajcinovic,[2] reduced a mixture of nitrobenzene and benzaldehyde with hydrogen and platinum. By suitably interrupting the reduction they obtained the nitrone I or the alkylarylhydroxylamine II.



I



II

They postulated the course of the reaction as (1) reduction of the nitrobenzene to phenylhydroxylamine, (2) condensation of the phenylhydroxylamine with the benzaldehyde to give the nitrone I and (3) reduction of the nitrone to the substituted hydroxylamine II.

In order to obtain secondary amines it, therefore, appeared necessary to determine satisfactory conditions for the reduction of the hydroxylamine II. From the work of Major[3] it seemed likely that hydrogen and a catalyst would be suitable. He reduced *p*-nitrophenol with hydrogen and platinum in acetone solution to obtain good yields of *p*-hydroxy-N-isopropylaniline. Later he extended the reaction to obtain N,N′-diisopropyl-*p*-phenylenediamine in good yield from *p*-nitroaniline, but states he was unable to obtain alkylation with nitrobenzene and acetone or with *p*-nitrophenol and formaldehyde or acetaldehyde. Benzaldehyde, however, gave *p*-hydroxydibenzylaniline with *p*-nitrophenol. For these reactions Major postulated the same mechanism as that proposed by Vavon and Crajcinovic.

We have found that when an alcoholic solution of an aromatic nitro compound and an aldehyde is reduced with hydrogen and Raney nickel in the presence of sodium acetate as a condensing agent, the corresponding secondary amine is formed in good yield. The reaction is apparently general

(1) Emerson and Walters, THIS JOURNAL, **60**, 2023 (1938); Emerson and Robb, *ibid.*, **61**, 3145 (1939).

(2) Vavon and Crajcinovic, *Compt. rend.*, **187**, 420 (1928).

(3) Major, THIS JOURNAL, **53**, 1901, 2803, 4373 (1931); *Chem. Abs.*, **29**, 178 (1935) (U. S. Patent 1,978,433).

TABLE I

N-ALKYLARYLAMINES

Amine	Yield, %		Derivative	M. p. of deriv., °C.	Recorded m. p., °C.
N-Methylaniline		50	*p*-Bromobenzenesulfonamide	92	92[a]
N-Ethylaniline	57	63	*p*-Bromobenzenesulfonamide	91	91[a]
N-*n*-Butylaniline	94	96	*p*-Bromobenzenesulfonamide	86–87	87[a]
N-*n*-Amylaniline		84	*m*-Nitrobenzenesulfonamide	74–75	74–75[b]
N-*n*-Heptylaniline		40	*p*-Bromobenzenesulfonamide	115	115[b]
N-Benzylaniline		33	Hydrochloride	210–212	214–216[c]
N-*n*-Butyl-*p*-anisidine		31	*p*-Bromobenzenesulfonamide	72–73	
N-*n*-Butyl-α-naphthylamine		60	*p*-Chlorobenzamide	242–243	
N-*n*-Amyl-α-naphthylamine		43	*p*-Bromobenzamide	226–227	
N-*n*-Butyl-*p*-toluidine	40	85	Hydrochloride	148–149	148–149[d]
N-*n*-Heptyl-*p*-toluidine		35	*p*-Bromobenzenesulfonamide	52.0–52.5	

[a] Marvel and Smith, THIS JOURNAL, **45**, 2696 (1923). [b] See footnote (1). [c] Brand, *Ber.*, **42**, 3460 (1909). [d] Wagner' THIS JOURNAL, **55**, 724 (1933).

TABLE II

PROPERTIES OF AMINES

Amine	B. p., °C.	Mm.	d^{20}_{20}	$n^{20}D$	Deriv.	Analyses, % Calcd.	Found
N-*n*-Butyl-*p*-anisidine					*p*-Bromobenzenesulfonamide	Br, 20.06	20.45
N-*n*-Butyl-α-naphthylamine					*p*-Chlorobenzamide	Cl, 10.50	10.62
N-*n*-Amyl-α-naphthylamine	136–146	4	1.102	1.6460	*p*-Bromobenzamide	Br, 20.18	20.17
N-*n*-Heptyl-*p*-toluidine	135–150	4	0.906	1.5055	*p*-Bromobenzenesulfonamide	Br, 18.89	18.54
N,N-Di-*n*-butyl-*p*-toluidine	295–296[a]		.976	1.5514	Picrate, m. p. 186–187°	N, 12.50	12.84
N,N-Di-*n*-heptyl-*p*-toluidine	175–200	2.5	.943	1.5089	Hydrochloride, m. p. 136°	Cl, 10.43	10.53

[a] By Siwoloboff method. Hill and Donleavy, *Ind. Eng. Chem.*, **13**, 504 (1921), give 283–285°/755 mm.

for aromatic nitro compounds and aliphatic or aromatic aldehydes. Our results are summarized in Table I.

Experimental

General Procedure.—All of the reactions were carried out in a machine for catalytic reduction[4] using Raney nickel[5] as the catalyst. In each experiment 0.1 mole of the nitro compound, 0.3 mole of the aldehyde and 2.0 g. of sodium acetate were dissolved in 150 cc. of alcohol. From 3.0 to 6.0 g. of Raney nickel was then added and the mixture placed in the machine at an initial pressure of 40 lb. It was shaken until no more hydrogen was absorbed, usually from twelve to twenty-four hours, 0.42 to 0.62 mole of hydrogen being taken up. After the catalyst had been removed by filtration, the solvent was distilled on the steam-bath. The remaining oil was steam distilled and the residue or distillate, depending on the amine, fractionated to obtain the pure product.

N-Alkylarylamines.—Using the general procedure described above, we have prepared twelve N-alkylarylamines in yields of from 31 to 96%. The compounds prepared, yields, and derivatives used in their identification are shown in Table I. Four of these amines are new and their characterization is summarized in Table II. In all cases except the toluidines the yield of tertiary amine was negligible. No appreciable quantity of high boiling material was isolated except in the case of N-*n*-amylaniline where there was 1.5 cc. of a high boiling oil.

In the case of *p*-nitrotoluene appreciable quantities of the tertiary amines were formed: 53% of N,N-di-*n*-butyl-*p*-toluidine in the first butyraldehyde run and 34% of N,N-di-*n*-heptyl-*p*-toluidine in the heptaldehyde run. The latter is a new compound and is included in Table II. Since our constants for N,N-di-*n*-butyl-*p*-toluidine differ from those previously recorded, this compound is also in Table II.

(4) Adams and Voorhees, "Org. Syntheses," Coll. Vol. I, 1932, p. 53.

(5) Covert and Adkins, THIS JOURNAL, **54**, 4116 (1932).

Summary

A procedure has been developed for preparing N-alkylarylamines from aromatic nitro compounds in 31 to 96% yields by treating an alcoholic solution of the nitro compound and an aldehyde with hydrogen and Raney nickel in the presence of sodium acetate.

URBANA, ILLINOIS RECEIVED NOVEMBER 20, 1939

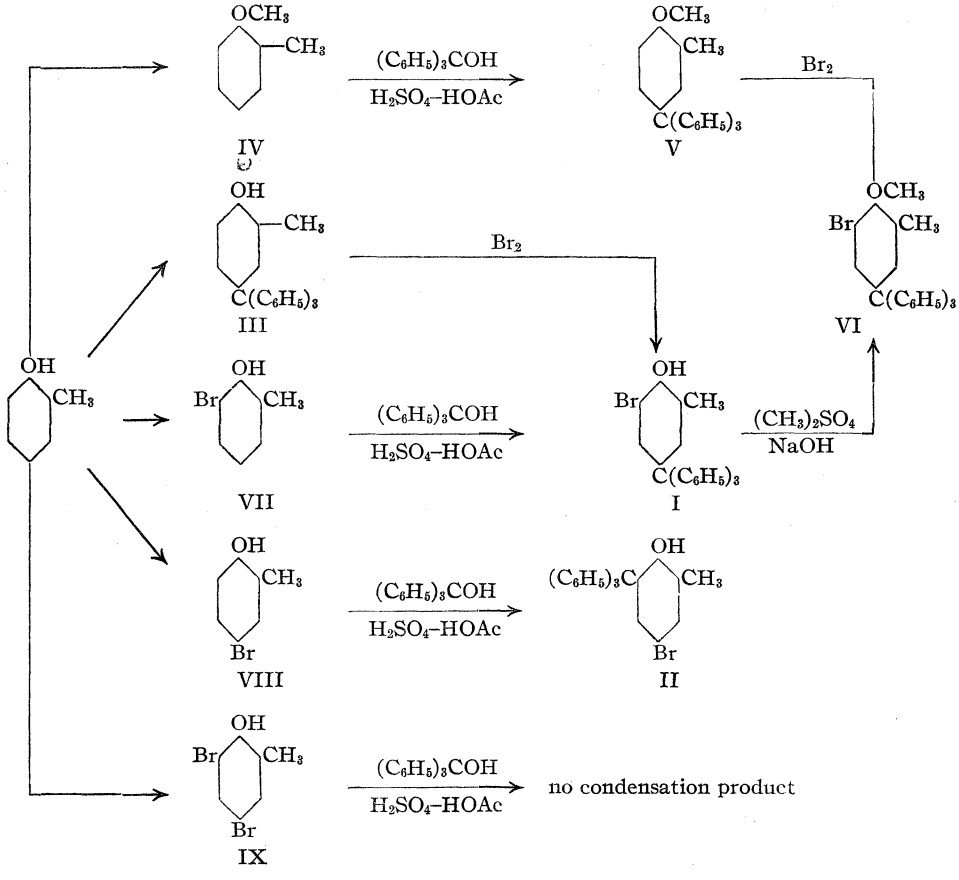
[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF NEW HAMPSHIRE]

Rearrangement of the Triphenylmethyl Ethers of Ortho Cresol and Brominated Ortho Cresols

BY H. A. IDDLES, W. H. MILLER AND W. H. POWERS

In a previous communication[1] a derivative of the postulated rearrangement product[2,3] from the triphenylmethyl ether of *o*-cresol was reported. However, the synthetic α-2-methoxyphenyl-β,β,-β-triphenylethane possessed a lower m. p. of 142–143° than the methylated cryptophenol, m. p. 165°, which supported the interpretation[4] that the triphenylmethyl group had not migrated to the side chain of *o*-cresol.

To substantiate the alternate hypothesis that migration involves a ring position, certain positions in the *o*-cresol molecule were blocked by bromine atoms, thus limiting the possible positions which a triphenylmethyl group might enter in the ensuing ether rearrangement or direct condensation reactions. The products of these reactions were then compared with the brominated product from the cryptophenol under consideration. This is shown in the accompanying schematic set of reactions.



Parallel condensations were made using triphenylcarbinol, sulfuric acid and glacial acetic acid on 6-bromo-*o*-cresol, VII, 4-bromo-*o*-cresol, VIII, and 4,6-dibromo-*o*-cresol, IX. In the case of VII, in which a para position is free, a good yield (55%) of product I was obtained, whereas using VIII in which an ortho position is open, there was a low yield of product (6.75%) and no condensation product from IX could be recovered. Further by adding an equivalent of bromine to the cryptophenol III[2] in carbon tetrachloride solution, the same monobrominated product I was obtained, which indicates the entrance

(1) Iddles, French and Mellon, THIS JOURNAL, **61**, 3192 (1939).
(2) Schorigin, *Ber.*, **59**, 2502 (1926).
(3) Van Alphen, *Rec. trav. chim.*, **46**, 287 (1927).
(4) Boyd and Hardy, *J. Chem. Soc.*, 630 (1928).

of bromine into position 6 and indirectly that position 4 must be occupied by the triphenylmethyl group prior to bromination.

Since Boyd and Hardy[4] had condensed *o*-methoxytoluene with triphenylcarbinol in an acid medium and then brominated the resulting methyl ether to give a product, m. p. 180°, to which they assign structure VI, the present structure I was methylated and found to produce a material with the same m. p., 183–184°. Thus it is shown in preparing product I by two routes and product VI by two different sets of investigators and procedures, a common product was formed in each case.

In reactions[2,5,6,7] leading to the formation of the triphenylmethyl ethers of the three brominated *o*-cresols, an ether was produced from VIII but no ether formation occurred with VII and IX, apparently due to spacial hindrance. However, from VII a good yield of rearranged product I, m. p. 152°, was produced directly, agreeing with the compound prepared by the two procedures described above.

Experimental

Preparation of Brominated Cresols.—The 6-bromo-*o*-cresol VII was prepared by the procedure of Huston and Neeley.[8] The 4-bromo-*o*-cresol VIII was prepared as described by Goldschmidt, Schulz and Bernard.[9] The 4,6-dibromo-*o*-cresol IX was prepared similarly by dissolving 27 g. of *o*-cresol in 90 ml. of carbon tetrachloride and adding 80 g. of bromine in 10 ml. of carbon tetrachloride to the cooled, stirred solution during a two-hour period. After standing for fifteen minutes, yellow needles separated. These were filtered off and the mother liquor evaporated under reduced pressure to yield several further crops. Recrystallization from alcohol yielded a colorless product, m. p. 56.5–57.5°, in a 70% yield.

Condensation of *o*-Cresol and Triphenylcarbinol.—The rearranged product resulted as described previously.[1]

Condensation of 6-Bromo-*o*-cresol VII and Triphenylcarbinol.—Twenty grams of 6-bromo-*o*-cresol, 135 g. of glacial acetic acid, and 4.5 g. of triphenyl-carbinol were mixed and 23 g. of sulfuric acid was added dropwise, producing a deep reddish-brown coloration. After standing for three weeks, the solution was poured into 1500 ml. of water, producing a deep violet solution and a slight precipitate. The solution and solid were extracted with ether, washed with 10% sodium hydroxide to remove unreacted 6-bromo-*o*-cresol, then with water and dried over anhydrous sodium sulfate. After distilling off the ether the remaining amber oil was dissolved in 500 ml. of ligroin and extracted with Claisen's solution. The extract was acidified with hydrochloric acid, producing a precipitate which was recrystallized from alcohol or ligroin giving a 55% yield, m. p. 149–151°.

Anal. Calcd. for $C_{26}H_{21}OBr$: Br, 18.61. Found: Br, 18.39, 18.29.

Condensation of 4-Bromo-*o*-cresol VIII and Triphenylcarbinol.—4-Bromo-*o*-cresol, 26 g., was mixed with 135 g. of glacial acetic acid and 4.5 g. of triphenylcarbinol and 23 g. of sulfuric acid added slowly. No solid separated after standing for several weeks. Then the solution was poured into two liters of water, producing a black oil which was extracted with ether. After washing the ether extract with 10% sodium hydroxide, 21 g. of unchanged 4-bromo-*o*-cresol was recovered by acidifying the basic washings. The ether layer was dried and evaporated to yield a brown oil which was taken up in ligroin. Treatment with Claisen's solution, followed by acidification, gave a product which was recrystallized from alcohol with a yield of 0.5 g. or 6.75%, m. p. 208–209°.

Anal. Calcd. for $C_{26}H_{21}OBr$: Br, 18.61. Found: Br, 18.81, 18.57.

Attempted Condensation of 4,6-Dibromo-*o*-cresol IX and Triphenylcarbinol.—When the dibromo-*o*-cresol was carried through the usual condensation procedure, no significant condensation product could be recovered in the various steps of recovery.

Bromination of Schorigin's Cryptophenol III.—The simple cryptophenol (m. p. 180–183°), 7 g., was dissolved in 325 ml. of carbon tetrachloride, a few tacks were added and, while cooling and stirring, one equivalent (3.2 g.) of bromine dissolved in 25 ml. of carbon tetrachloride was added slowly. As the reaction proceeded the remaining cryptophenol dissolved and hydrogen bromide was evolved. After standing six hours, the reaction mixture was washed with water, dried with anhydrous sodium sulfate and then evaporated under reduced pressure. A creamy residue resulted which was recrystallized from ligroin (70–90°) and gave 7.35 g. or 85.7% yield, m. p. 149–151°. A mixed melting point with I obtained by the condensation of 6-bromo-*o*-cresol and triphenylcarbinol, also m. p. 149–151°, gave no depression and thus they were proved to be identical.

Methylation of Compound I.—One gram of the monobrominated cryptophenol I, dissolved in 50 ml. of benzene, was refluxed with 30 g. of sodium hydroxide in 60 ml. of water while adding 2 g. of dimethyl sulfate during a period of fifteen minutes. After one-half hour, another portion of alkali was added to destroy excess of dimethyl sulfate. Following ether extraction, washing with water and drying, the solvents were partially evaporated. Upon addition of ligroin (70–90°) crystallization resulted yielding 0.8 g. of product, m. p. 183–184°. By another synthesis[4] this product was found to melt at 180°.

Preparation of Rearranged Compound from 6-Bromo-*o*-cresol VII and Triphenylchloromethane.—In an attempt to prepare the triphenylmethyl ether of 6-bromo-*o*-cresol, 19 g. of the cresol was dissolved in 50 ml. of dry ether and 2.3 g. of sodium added. After complete reaction of the sodium, 15 g. of triphenylchloromethane dissolved in 200 ml. of dry ether was added and the reaction mixture refluxed for five hours. The cooled ether layer was washed with water and carried through the usual treatments with

(5) Gomberg and Kamm, THIS JOURNAL, **39**, 2013 (1917).
(6) Baeyer and Villiger, *Ber.*, **35**, 3018 (1902).
(7) Claisen, *Ann.*, **418**, 69 (1919).
(8) Huston and Neeley, THIS JOURNAL, **57**, 2176 (1935).
(9) Goldschmidt, Schulz and Bernard, *Ann.*, **478**, 14 (1930).

10% sodium hydroxide and Claisen's extraction of a ligroin solution. Upon acidification of the two alkaline solutions, 9.5 g. (41.5%) of product, m. p. 150–152°, was obtained. This agreed by mixed melting point and analysis with the rearranged product I obtained by the direct condensation above. Further attempts to prepare the ether using potassium, potassium carbonate and acetone or a pyridine medium produced varying quantities of the same rearrangement product.

Attempted Preparation of Triphenylmethyl Ether of 4,6-Dibromo-*o*-cresol IX.—Ten grams of the 4,6-dibromo-*o*-cresol was treated with 1.5 g. of sodium in dry ether and 10 g. of triphenylchloromethane was added. After refluxing and carrying out the usual steps of recovery, no ether could be obtained but a large portion of the original brominated *o*-cresol and triphenylcarbinol was recovered.

Preparation of the Triphenylmethyl Ether of 4-Bromo-*o*-cresol VIII.—Eleven grams of 4-bromo-*o*-cresol was dissolved in 45 ml. of pyridine (dried and distilled from barium oxide) and 15 g. of triphenylchloromethane was added. After heating the mixture for ten hours, water and ether were added and the ether layer was washed with dilute hydrochloric acid, then with 10% sodium hydroxide and finally with water. After drying the ether layer and evaporation, the residue was taken up in ligroin (70–90°) and washed with Claisen's solution. No product was removed by the alkaline washing but from the ligroin layer, a product was obtained which was recrystallized from alcohol. A yield of 11.25 g. or 48.7%, m. p. 113.5–114°, was obtained.

Anal. Calcd. for $C_{26}H_{21}OBr$: Br, 18.61. Found: Br, 18.74, 18.65.

Attempted rearrangement of this ether in glacial acetic acid–sulfuric acid mixtures by dry hydrogen chloride or by zinc chloride was unsuccessful. Only small portions of triphenylcarbinol could be recovered in each case.

Conclusions

Condensation products have been obtained from the reaction in acid medium of triphenylcarbinol on 4-bromo-*o*-cresol VIII and 6-bromo-*o*-cresol VII. The latter product I agreed with the substance obtained by mono-bromination of Schorigin's cryptophenol. Methylation of product I gave a substance agreeing with the material prepared in a different series of steps by Boyd and Hardy[4] and postulated to have structure VI. Thus from these two reaction cycles the evidence places the triphenylmethyl group in the para position in the simple cryptophenol, as shown in structure III.

DURHAM, NEW HAMPSHIRE RECEIVED OCTOBER 4, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. LXXXII. Estrane Derivatives

BY RUSSELL E. MARKER AND EWALD ROHRMANN

Although the catalytic hydrogenation of estrone has been studied by a number of investigators,[1–5] the only reduction products which have been studied to any extent are the isomeric estradiols and an estranediol-3,17(α). This latter product is of considerable interest inasmuch as it is undoubtedly identical with one of the estranediols isolated from human non-pregnancy urine.[6,7] No information has been presented concerning the configurations at C-5 and at C-3 of this substance. The problem concerning the isomeric reduction products of estrone is complicated by the fact that the C-10 position becomes an asymmetric center during the course of the reduction. Thus the reduction of α-estradiol theoretically could give rise to eight isomeric estranediols. The fact that an isomeric estranediol, m. p. 242°, was isolated from human non-pregnancy urine[6,7] indicates that additional isomers exist. This particular estranediol-3,17 has not as yet been encountered in the *in vitro* reduction of estrone.

The fact that the catalytic hydrogenation of estrone in acidic medium results in the formation of mono-hydroxyestranes is of interest and in this respect it would appear to be analogous to equilenin, which readily yields a monohydroxy compound on reduction under similar conditions.[8,9,10] Dirscherl[4] has reported the isolation of two estranols from the reduction products of estrone in acidic ethanol. Butenandt[1] reported that in the hydrogenation of estrone acetate in neutral ethanol with platinum oxide catalyst the carbonyl group is reduced to a methylene group, the aromatic ring reduced and the acetate residue re-

(1) Butenandt, *Z. physiol. Chem.*, **191**, 140 (1930).
(2) Butenandt, Stormer and Westphal, *ibid.*, **208**, 149 (1932).
(3) Butenandt and Westphal, *ibid.*, **223**, 147 (1934).
(4) Dirscherl, *ibid.*, **239**, 53 (1936).
(5) Marker and Rohrmann, THIS JOURNAL, **60**, 2927 (1938).
(6) Marker, Rohrmann, Wittle and Lawson, *ibid.*, **60**, 1512 (1938).
(7) Marker, Rohrmann, Lawson and Wittle, *ibid.*, **60**, 1901 (1938).
(8) Marker, Kamm, Oakwood and Tendick, *ibid.*, **59**, 768 (1937).
(9) Ruzicka, Muller and Morgeli, *Helv. Chim. Acta*, **21**, 1394 (1938).
(10) Marker and Rohrmann, THIS JOURNAL, **61**, 3314 (1939).

moved to yield an estranol-3. This product was reported to be identical with the estranol obtained by the hydrogenation of 17-desoxyestrone in acidic ethanol[3] but unfortunately no direct comparison of the two products was reported in their experimental work.

In our experience the reduction of estrone in neutral ethanol under conditions apparently more drastic than used by Butenandt[1] gives rise to α-estradiol in over 90% yields and no evidence of the reduction of the aromatic ring was observed. The removal of the acetate residue by catalytic hydrogenation in neutral ethanol as observed by Butenandt is most probably due to the presence of a trace of alkali in the catalyst, a possibility demonstrated by the experiments of Miescher and Scholz.[11] In this Laboratory we have experienced no difficulty in hydrogenating estrone esters in ethanol solution with Adams catalyst to give the mono-esters of α-estradiol.[12]

That the predominant estranol obtained from the reduction of estrone in acidic ethanol is an estranol-17 seems most likely especially since the analogous reduction of equilenin gives high yields of estratriene-5,7,9-ol-17(α). By carrying out the reduction of the 17-mono acetate of α-estradiol with Adams catalyst in acetic acid, we have obtained an estranol apparently identical with that obtained by the catalytic hydrogenation of estrone in acidic ethanol. Inasmuch as the reduction of an acetoxy group at C-17 to a methylene group under the conditions of the hydrogenation is hardly probable, it would appear that the product is an estranol-17(α).

Further evidence that the hydroxyl group at C-3 is removed in the reduction is shown by the work of Butenandt and Westphal[3] on the catalytic hydrogenation of estriol in acidic medium. This reduction yielded two isomeric diols which upon dehydration with potassium bisulfate yielded ketonic compounds. This indicates a vicinal arrangement of the hydroxyl groups, which would be possible only in the C-17,C-16 positions.

The fact that estranediol-3,17(α) may be regarded as a *nor*-androstanediol or a *nor-etio*-cholanediol makes the substance of considerable interest because of its possible relationship to the androgenic hormones. Estranediol-3,17(α) on mild oxidation with chromic anhydride yields an estranedione-3,17 which we have now found to exist in two interconvertible polymorphic crystal forms, m. p. 146° and m. p. 180°. Estranedione readily reacts with bromine in acetic acid to yield a nicely crystalline bromo-estranedione. The removal of hydrogen bromide from this product with boiling pyridine proceeded smoothly to yield an estrenedione (*nor*-androstenedione). While the position of the ethylenic linkage in this substance is not proved, it appears probable that it is in the C-4,5 position, especially since the bromo compound behaves as a substance of coprostane configuration at C-5 in its reaction with pyridine.

An attempt to prepare crystalline *nor*-testosterone was unsuccessful. An estranol-17-one-3 was prepared by the reduction of the 17-monoacetate of α-estradiol and subsequent oxidation with chromic anhydride and hydrolysis with ethanolic alkali. The resulting ketone readily reacted with bromine to liberate hydrogen bromide but no crystalline bromide was obtained. Likewise, reaction with pyridine gave a non-crystalline product.

We wish to thank Parke, Davis and Company for their generous help and assistance in the various phases of this work.

Experimental Part

Estranediol-3,17(α), m. p. 205–206°, was prepared by the catalytic hydrogenation of estrone in acidic ethanol as described by Dirscherl.[4]

Estranedione.—This was prepared by the chromic anhydride oxidation of estranediol as described previously by us.[7] The product was crystallized from dilute acetone and dilute methanol to give a product of m. p. 176–178°.

The mother liquors remaining from the reduction of estrone after removal of part of the estranediol were evaporated and the residual sirup taken up in acetic acid and oxidized with chromic anhydride at room temperature for two hours. The crude oily oxidation product was sublimed in high vacuum. The first fraction sublimed at 80–90° and evidently consisted of mono-ketones which could not be crystallized. The higher fraction subliming at 125–140° consisted of estranedione which was crystallized from dilute acetone to give a product, m. p. 144–146°.

Anal. Calcd. for $C_{18}H_{26}O_2$: C, 78.8; H, 9.6. Found: C, 78.9; H, 9.6.

Upon another crystallization from ether–pentane white needles, m. p. 179–180°, were obtained. The mixture, with the lower melting form, melted at 160–178°. In another case the higher melting form was observed to revert to the lower form, m. p. 144–146.5°, on recrystallization from dilute acetone.

Estranol-17(α) from Estrone.—The material subliming at 80–90° obtained above was dissolved in a mixture of 300 cc. of absolute ethanol and 3 cc. of concentrated hydro-

(11) Miescher and Scholz, *Helv. Chim. Acta*, **20**, 263 (1937).
(12) Marker and Rohrmann, THIS JOURNAL, **61**, 1922 (1939).

chloric acid. The solution was shaken with Adams catalyst at two atmospheres hydrogen pressure at 25° for five hours. The reduction product was crystallized from aqueous methanol as white needles, m. p. 105–107°. This gave no depression with a sample of m. p. 106–108°, prepared by the direct catalytic hydrogenation of estrone.

Anal. Calcd. for $C_{18}H_{30}O$: C, 82.4; H, 11.5. Found: C, 82.2; H, 11.5.

An attempt to obtain a crystalline ketone on oxidation with chromic anhydride was unsuccessful.

Bromoestranedione.—To a solution of 700 mg. of estranedione in 20 cc. of acetic acid acidified with two drops of 48% hydrobromic acid was slowly added 5.3 cc. of 0.5 *M* bromine in acetic acid. Water was added and the precipitated solid collected, washed and dried. The product was crystallized from ether to give white crystals, m. p. 170–172°.

Anal. Calcd. for $C_{18}H_{25}O_2Br$: C, 61.2; H, 7.1. Found: C, 61.0; H, 7.1.

Estrenedione.—A solution of 400 mg. of bromoestranedione in 5 cc. of dry pyridine was refluxed for nine hours. The solution was diluted with water and the precipitated solid taken up in ether and freed from pyridine by washing with dilute hydrochloric acid. The ether was removed and the residue sublimed in high vacuum at 130–140°. The sublimate was crystallized from pentane as white leaflets, m. p. 146–148°.

Anal. Calcd. for $C_{18}H_{24}O_2$: C, 79.5; H, 8.9. Found: C, 79.2, 79.4; H, 8.9, 8.9.

Hydrogenation of Estrone in Neutral Medium.—Estrone (m. p. 259°) (5 g.) was shaken in absolute ethanol (300 cc.) with Adams catalyst (0.5 g.) and hydrogen at 3 atm. pressure at room temperature for eighteen hours. The reduction product was crystallized from aqueous acetone to give α-estradiol (4.6 g.), m. p. 173–175°. The mother liquors upon being subjected to sublimation in high vacuum gave no evidence of the presence of substances other than the isomeric estradiols.

17-Mono-acetate of α-Estradiol.—This was prepared in almost theoretical yields by the hydrolysis of α-estradiol diacetate with methanolic potassium carbonate at 20° as described by Miescher and Scholz[11] for the preparation of the 17-mono-*n*-butyrate of α-estradiol. The product formed white crystals, m. p. 215–217°. Miescher and Scholz[11] prepared the compound by carrying out the partial hydrolysis with Adams catalyst in ethanol in the presence of alkali and in an atmosphere of carbon dioxide. They report a m. p. of 215–217.5°.

Reduction of 17-Mono-acetate of α-Estradiol.—A mixture of 4 g. of the 17-monoacetate of α-estradiol, 250 cc. of glacial acetic acid, 70 cc. of absolute ethanol and 800 mg. of Adams catalyst was shaken with hydrogen at 10 pounds pressure at room temperature for fourteen hours. The catalyst was filtered and the filtrate diluted with water. The milky mixture was shaken with ether and the ethereal layer washed well with water and the ether removed. The residual sirup was dissolved in 100 cc. of glacial acetic acid and to this solution was added a solution of 2 g. of chromic anhydride in 25 cc. of 80% acetic acid. After standing at room temperature for two hours the mixture was diluted with water and the precipitated solid taken up in ether. The ether was removed and the residual sirup hydrolyzed with ethanolic potassium hydroxide.

The ketonic fraction was separated by means of Girard's reagent. After sublimation in high vacuum at 120–130° the product was crystallized from ether–pentane and aqueous acetone as white needles, m. p. 102–104°.

Anal. Calcd. for $C_{18}H_{28}O_2$: C, 78.2; H, 10.2. Found: C, 78.0; H, 10.1.

The product readily absorbed a mole of bromine in acetic acid solution acidified with a trace of hydrobromic acid. Hydrogen bromide was liberated. The bromination product could not be obtained crystalline. Heating with pyridine gave a non-crystalline product.

The neutral fraction (non-ketonic) from the chromic anhydride oxidation was sublimed in high vacuum and the fraction subliming at 100° was collected. This was crystalized from aqueous methanol as white needles, m. p. 106–108°. This gave no depression with a sample of estranol, m. p. 106–108°, obtained in the direct catalytic hydrogenation of estrone in acidic medium.

Anal. Calcd. for $C_{18}H_{30}O$: C, 82.4; H, 11.5. Found: C, 82.3; H, 11.4.

Summary

Estrenedione has been prepared from estranedione-3,17.

The major monohydroxyestrane resulting from the reduction of estrone in acidic medium appears to be an estranol-17(α).

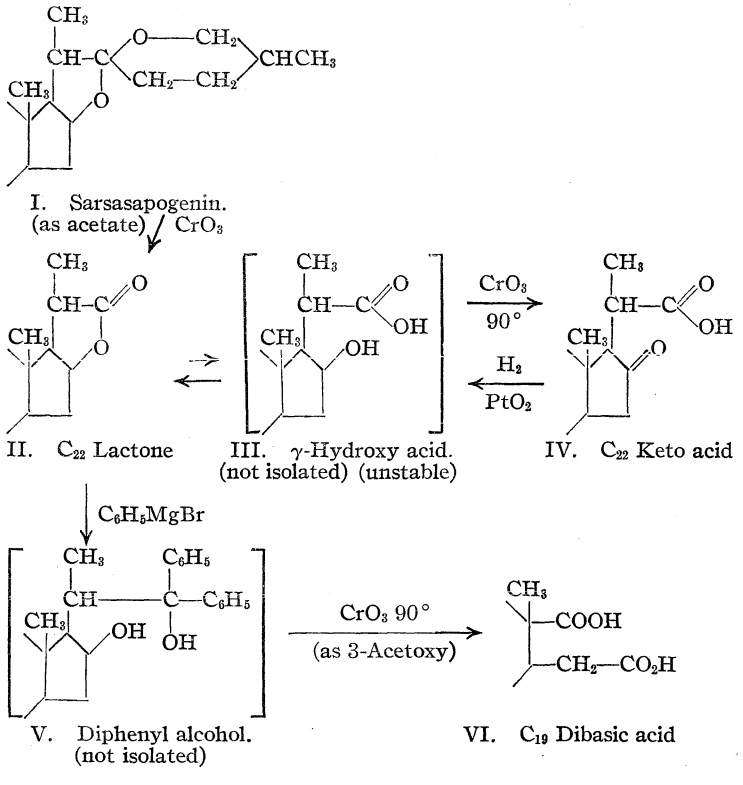
STATE COLLEGE, PENNA. RECEIVED OCTOBER 23, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. LXXXIII. Oxidation Products of Sarsasapogenin. Studies on the C_{22} Lactone

BY RUSSELL E. MARKER AND EWALD ROHRMANN

Perhaps one of the most striking characteristics common to all of the more extensively studied steroid sapogenins is the formation of lactones upon rather vigorous oxidation with chromic anhydride (after adequate protection of the nuclear hydroxyl groups).[1] Sarsasapogenin,[2] smilagenin,[3] tigogenin,[4] chlorogenin,[5] gitogenin[6] and digitogenin,[6] have thus been oxidized to C_{22} lactones.



While all these lactones undoubtedly contain the same number of carbon atoms, it should be pointed out that many of the analyses reported for the substances do not distinguish between a C_{22} and a C_{23} compound. Our analytical results on the sarsasapogenin lactone and its various derivatives are in accord with the C_{22} composition. However, it is evident, as we pointed out previously,[7] that the final proof of the structure and composition of the lactone will depend upon its *stepwise* degradation to a known sterol derivative, an achievement not yet reported.

That the lactone (II) has a very slight tendency to exist as a γ-hydroxy acid (III) is indicated by the fact that the lactone acetate upon rather vigorous oxidation with chromic anhydride gives rise to some of the C_{22} keto acid (IV) which was previously obtained from a similar oxidation of sarsasapogenin acetate.[8]

The most fruitful process of degrading the sarsasapogenin lactone to a known product has been by the method of Tschesche and Hagedorn[4] involving the oxidation of the diphenyl Grignard addition product (V) of the lactone. By this method Farmer and Kon[3] degraded the desoxy lactone to *etio*-bilianic acid. We have carried out a similar degradation of the hydroxy lactone to obtain the C_{19} dibasic acid identical with that previously obtained by the chromic anhydride oxidation of the acetates of sarsasapogenin,[9] sarsasapogenoic acid[9] and dihydrosarsasapogenin.[10] This acid is most likely 3-hydroxy-*etio*-bilianic acid. The fact that we were unable to oxidize the C_{22} keto acid with chromic anhydride after acetylation with boiling acetic anhydride is of interest. This suggests that the γ-keto acid has a tendency to exist in a lactone form which would be stabilized to oxidation by acetylation (*cf.* levulinic acid).

Simpson and Jacobs[11] observed that sarsasapogenin upon oxidation with sodium hypobromite yielded a dibasic acid which upon further oxidation with nitric acid yielded a lactone dibasic acid. We have obtained a similar acid by the oxidation

(1) Strain, "The Sterols and Related Compounds" in "Gilman's Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1938, Chap. 15, p. 1346.
(2) Askew, Farmer and Kon, *J. Chem. Soc.*, 1399 (1936).
(3) Farmer and Kon, *ibid.*, 414 (1937).
(4) Tschesche and Hagedorn, *Ber.*, **68**, 1412 (1935).
(5) McMillan and Noller, THIS JOURNAL, **61**, 1630 (1939).
(6) Marker and Rohrmann, *ibid.*, **61**, 2724 (1939).
(7) Marker and Rohrmann, *ibid.*, **61**, 846 (1939).
(8) Marker and Rohrmann, *ibid.*, **61**, 1285 (1939).
(9) Marker and Rohrmann, *ibid.*, **61**, 2722 (1939).
(10) Marker and Rohrmann, *ibid.*, **61**, 3477 (1939).
(11) Simpson and Jacobs, *J. Biol. Chem.*, **109**, 573 (1935).

TABLE I

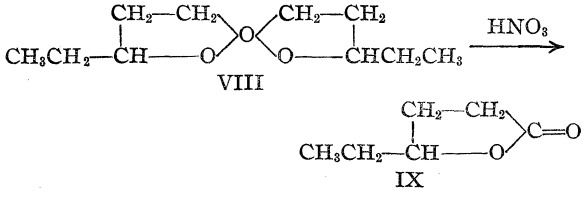
Substance	Composition	M. p., °C.	Analysis Calcd. C	Calcd. H	Found C	Found H
Lactone acetate[a]	$C_{24}H_{36}O_4$	184.5–185.5	74.15	9.37	74.26	9.30
Lactone benzoate[b]	$C_{29}H_{38}O_4$	207.5–209	77.28	8.49	77.16	8.49
Hydroxylactone	$C_{22}H_{34}O_3$	199–200	76.25	9.89	76.35	10.04
3-Keto lactone	$C_{22}H_{32}O_3$	184–185	76.69	9.37	76.55	9.37
Desoxy lactone	$C_{22}H_{34}O_2$	128–129	79.93	10.37	79.88	10.37

[a] The acetate was purified by sublimation in high vacuum at 130–140°. [b] The benzoate was prepared in pyridine solution with benzoyl chloride at room temperature and crystallized from acetone–pentane.

of sarsasapogenin lactone with chromic anhydride. The same acid was obtained by the direct oxidation of sarsasapogenone with nitric acid. While no comparison was made between our acid and that of Simpson and Jacobs the substances are very probably identical, as the melting points of the free acids and of the methyl esters are in good agreement. While this lactone dibasic acid is undoubtedly either a 2 || 3 or a 3 || 4 diacid there is insufficient evidence at present to distinguish between the two possibilities, especially in view of recent work[12] on the acids of the coprostane series resulting from the oxidation of ring A.

The question regarding the origin of the C_{22} lactones is of great interest but there is little information available on the course of the oxidation. However, it is now fairly certain that the sapogenoic acids are not intermediates in the formation of the lactone.[13,14,15]

The fact that nitric acid exerts a specific action on the side chain to yield lactones[11,15,16] is of considerable interest. In this connection it is probably significant that diethyl oxetone (VIII), a substance of the ketone spiro acetal type and consequently analogous to our proposed structure of the sapogenin side chain[7] (I), is oxidized by nitric acid to yield caproic lactone (IX) and propionic acid.[17]



In previous work concerning the hydrogenation of the C_{22} keto acid[8] a C_{22} lactone was obtained in two forms, m. p. 188° and m. p. 198°, which appeared to be polymorphic or possibly steroisomers. That the two forms are polymorphic is indicated by the fact that they yielded the same acetates and upon oxidation gave the same 3-keto-lactones.

We wish to thank Parke, Davis and Company for their generous help and assistance in the various phases of this work.

Experimental Part

Sarsasapogenin Lactone (II).—The lactone and its derivatives were prepared as described by previous workers. Our analytical data are summarized in Table I.

An attempt to reduce the hydroxylactone with phosphorus and hydriodic acid (sp. gr. 1.7) at 160° gave only non-crystalline neutral products. The products were very insoluble in methanol and distilled in high vacuum at 90°, suggesting substances of a hydrocarbon nature. The lactone showed no tendency to esterification when allowed to stand for several days with absolute ethanol and concentrated sulfuric acid.

***epi*-Lactone.**—A mixture of 500 mg. of the keto lactone, 500 mg. of Adams catalyst, and 80 cc. of 98% ethanol was shaken with hydrogen at 3 atmospheres pressure at room temperature for three hours. The mixture was filtered and the filtrate evaporated *in vacuo*. The residue was taken up in 10 cc. of hot 95% ethanol and to this solution was added a hot solution of 500 mg. of digitonin in 15 cc. of 80% ethanol. The mixture after standing at 0° was filtered. The filtrate was diluted with water and the precipitated solid taken up with ether. Evaporation of the ether gave a residue which crystallized from ether–acetone–pentane as white needles, m. p. 198–200°. This gave a 10° depression with the 3-β-hydroxylactone, m. p. 199–200°.

Anal. Calcd. for $C_{22}H_{34}O_3$: C, 76.25; H, 9.89. Found: C, 76.33; H, 9.95.

The *epi*-lactone when refluxed for twenty minutes with acetic anhydride yielded the *epi-lactone acetate* which crystallized from ether–pentane as white crystals, m. p. 159–160°.

Anal. Calcd. for $C_{24}H_{36}O_4$: C, 74.2; H, 9.35. Found: C, 73.9; H, 9.2.

Oxidation of Hydroxylactone to Lactone Dibasic Acid.—To a well-stirred solution of 2 g. of hydroxy lactone in 50 cc. of glacial acetic acid heated at 50–55° was added a solution of 3 g. of chromic anhydride in 20 cc. of 80% acetic acid over a period of three hours. The solution was stirred for an additional two hours at 55°. The mixture was then evaporated *in vacuo* to a volume of 30 cc. The residual material was diluted with water and the precipi-

(12) Marker, Plambeck, Wittle, Rohrmann, Krueger and Ulshafer, THIS JOURNAL, **61**, 3317 (1939).
(13) Fieser and Jacobsen, *ibid.*, **60**, 2753 (1938).
(14) Marker and Rohrmann, *ibid.*, **61**, 2072 (1939).
(15) Windaus and Linsert, *Z. physiol. Chem.*, **147**, 275 (1925).
(16) Jacobs and Simpson, *J. Biol. Chem.*, **105**, 501 (1934).
(17) Fittig and Dubois, *Ann.*, **256**, 141 (1889).

tated solid extracted with ether. The ethereal extract was washed well with water and the solution evaporated to a volume of 30 cc., compact white crystals separated. These were recrystallized from methanol–ether to give a product with m. p. 285–288° dec.

Anal. Calcd. for $C_{22}H_{32}O_6$: C, 67.3; H, 8.2. Found: C, 67.0; H, 8.4.

When treated with an ethereal solution of diazomethane the acid yielded a *dimethyl ester* which crystallized from ether–pentane as fine white needles, m. p. 170–171°.

Anal. Calcd. for $C_{24}H_{36}O_6$: C, 68.5; H, 8.6. Found: C, 68.2; H, 8.7.

Oxidation of Sarsasapogenone with Nitric Acid.—To a suspension of 1 g. of sarsasapogenone in 9 cc. of glacial acetic acid was added 15 cc. of nitric acid (d. 1.50). Brown fumes were liberated and the solid dissolved almost at once. The mixture was heated at 90° for one hour. The solution was diluted with water and the precipitated solid collected and washed with water. The solid was dissolved in ether and shaken with 3% sodium hydroxide solution.

The neutral fraction which would not crystallize was not investigated further. The sodium hydroxide extract was acidified with hydrochloric acid and extracted with ether. Evaporation of the ether gave compact white crystals which were recrystallized from ether–acetone, m. p. 285–289° dec. This gave no depression with the sample of dibasic lactone acid obtained previously, m. p. 285–288° dec.

Anal. Calcd. for $C_{22}H_{32}O_6$: C, 67.3; H, 8.2. Found: C, 67.0; H, 8.3.

With diazomethane the acid yielded a product which crystallized from ether–pentane as fine white needles, m. p. 170–171.5°. This gave no depression with the sample obtained above, m. p. 170–171°.

Oxidation of Lactone Acetate to C_{22}-Keto Acid.—To a solution of 800 mg. of lactone acetate, m. p. 183–184°, in 30 cc. of glacial acetic acid was added a solution of 2 g. of chromic anhydride in 40 cc. of 80% acetic acid. The resulting solution was heated on the steam-bath at 90° for three hours. The mixture was diluted with water and extracted with ether. The ethereal extract was washed well with water and then extracted with 3% sodium hydroxide solution. The sodium hydroxide extract was heated for twenty minutes on the steam-bath, cooled, acidified with hydrochloric acid and the solid acid extracted with ether. The ether upon slow evaporation deposited compact white crystals. These, after crystallization from ether–methanol, melted at 285–287° dec. and gave no depression with a sample of the C_{22} keto acid, m. p. 285–287°.

Anal. Calcd. for $C_{22}H_{34}O_4$: C, 72.9; H, 9.5. Found: C, 73.0; H, 9.6.

The neutral fraction consisted of unchanged lactone acetate.

Degradation of Hydroxylactone to C_{19}-Dibasic Acid.—To a Grignard reagent prepared from 1.25 g. of magnesium, 9 g. of phenyl bromide and 45 cc. of ether was added a solution of 2 g. of hydroxy lactone, m. p. 199–201°, over a period of ten minutes. The mixture was refluxed on the steam-bath for two hours after which the solvent was removed. The residue was dissolved in 50 cc. of dry pyridine and treated with 5 cc. of acetic anhydride at room temperature for eighteen hours. The mixture was decomposed with water and extracted with ether. After washing well with dilute hydrochloric acid the ether was evaporated to give a yellow non-crystalline sirup.

This was dissolved in 50 cc. of acetic acid and to the resulting solution heated at 90–95° was added 8 g. of chromic anhydride in 70 cc. of 80% acetic acid over a period of one hour. The mixture was heated for an additional two hours, the excess oxidizing agent was destroyed with ethanol and the mixture concentrated *in vacuo* to a volume of about 50 cc. The residual mixture was diluted with water and the precipitated solid taken up in ether. The residue remaining upon evaporation of the ether was refluxed for thirty minutes with an excess of ethanolic potassium hydroxide. The solid which separated upon dilution with water was taken up in ether and discarded. The alkaline water layer was acidified with hydrochloric acid and the acids taken up in ether. Evaporation of the ether gave a residue which crystallized from chloroform as white crystals, m. p. 218–220°; yield, 150 mg. This gave no depression in melting point with a sample of the C_{19}-dibasic acid, m. p. 220–222°.

Anal. Calcd. for $C_{19}H_{30}O_5$: C, 67.4; H, 8.9. Found: C, 67.2; H, 8.8.

Further Characterization of C_{22} Keto Acid.[8]—Treatment of the methyl ester of the keto acid with boiling acetic anhydride for thirty minutes followed by decomposition of the excess acetic anhydride with water yielded a *methyl ester acetate* which crystallized from ether–pentane as compact white crystals, m. p. 198–199.5°.

Anal. Calcd. for $C_{25}H_{38}O_5$: C, 71.7; H, 9.1. Found: C, 71.5; H, 9.1.

Treatment of the acid with hydroxylamine hydrochloride under the usual conditions gave an *oxime* which crystallized from aqueous methanol as small compact white crystals, m. p. 206–208° dec.

Anal. Calcd. for $C_{22}H_{35}O_4N$: C, 70.0; H, 9.3; N, 3.7. Found: C, 69.8; H, 9.2; N, 3.8.

Acetylation of the acid with boiling acetic anhydride gave a non-crystalline product. Oxidation of this product with chromic anhydride in acetic acid at 90–95° followed by alkaline hydrolysis of the total products yielded largely the original acid and none of the C_{19} dibasic acid was isolated.

The lactone, m. p. 186–188°, obtained by the catalytic hydrogenation of the C_{22} keto acid in ethanol–hydrochloric acid solution upon refluxing with acetic anhydride gave an acetate, m. p. 183–184°. This gave no depression with an authentic sample of the normal lactone acetate, m. p. 184.5–185.5°. Oxidation of the lactone with chromic anhydride at 25° gave the 3-ketolactone, m. p. 184–185°. This gave no depression with an authentic sample of the 3-ketolactone, m. p. 184–185°.

Summary

Oxidation of the acetate of the C_{22} lactone from sarsasapogenin with chromic anhydride yielded the C_{22} keto acid.

The C_{22} lactone has been degraded to the C_{19} dibasic acid.

STATE COLLEGE, PENNA. RECEIVED NOVEMBER 6, 1939

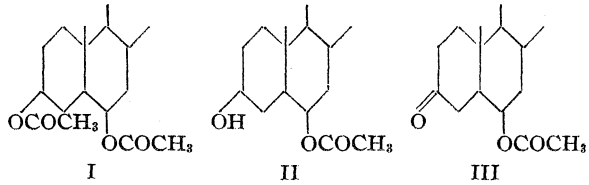
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. LXXXIV. Progesterone from Hyodesoxycholic Acid

BY RUSSELL E. MARKER AND JOHN KRUEGER

Preferential reactions in the sterol series have been widely used. Thus, Marker and co-workers acetylated the 3-position in both desoxycholic acid[1] and *allo*-pregnanediol,[2] leaving intact the 12-hydroxy group and the 20-hydroxy group, respectively. Half-hydrolysis of the diacetate of pregnanediol-(α),(α) gave pregnanol-20(α)-one-3[3] and Ellis and Petrow[4] obtained 6-acetoxycholestane-3,5-diol from 3,6-diacetoxycholestane-5-ol. Ruzicka and Wettstein[5] and Butenandt and Hanisch[6] utilized the difference in hydrolytic rate between acetoxy groups substituted in the 3- and 17-positions in the preparation of testosterone.

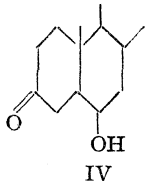
We assumed that, in analogy to the hydrolytic reactions previously cited, the main product in the partial hydrolysis of a 3,6-diacetoxy derivative would be a 3-hydroxy-6-acetoxy compound. We investigated the series of reactions I to VI using cholestanediol-3,6. Cholestanediol-3,6 of m. p. 216° has been described by Windaus[7] as the product of the sodium–alcohol reduction of 6-keto-cholestanol. We found platinum oxide in alcohol solution a more convenient reagent for the hydrogenation of 6-keto-cholestanol. Under these conditions a practically quantitative yield of a cholestanediol-3,6 of m. p. 190° was obtained. This substance VIII is stereoisomeric with the compound of m. p. 216° described by Windaus.



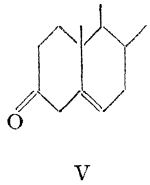
I

II

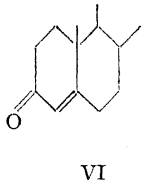
III



IV

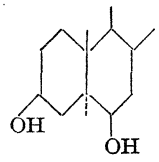


V

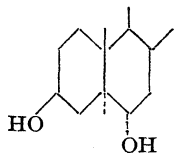


VI

(1) Marker and Lawson, THIS JOURNAL, **60**, 1334 (1938).
(2) Marker, Kamm and Jones, *ibid.*, **59**, 1595 (1937).
(3) Marker, Kamm, Wittle, Oakwood, Lawson and Laucius, *ibid.*, **59**, 2291 (1937).
(4) Ellis and Petrow, *J. Chem. Soc.*, 1081 (1939).
(5) Ruzicka, THIS JOURNAL, **57**, 2011 (1935); Ruzicka and Wettstein, *Helv. Chim. Acta*, **18**, 1264 (1935).
(6) Butenandt and Hanisch, *Ber.*, **68**, 1859 (1935).
(7) Windaus, *ibid.*, **50**, 133 (1917).



VII



VIII

The diacetate (I) of cholestanediol-3,6 was preferentially hydrolyzed at position-3 either by potassium hydroxide in methanol at 20° or by refluxing with sodium bicarbonate in methanol a short time to yield the hydroxy acetate (II) which was not isolated but oxidized to 6-acetoxycholestanone (III). Hydrolysis of the 6-acetoxycholestanone and dehydration of the resulting 6-hydroxycholestanone by distillation over fused potassium bisulfate produced cholestenone (VI) in good yield.

We have now utilized the above reactions for the preparation of progesterone from hyodesoxycholic acid. The side chain of hyodesoxycholic acid was degraded by the Barbier–Wieland method to produce a keto group at C-20. The procedure used was similar to the directions of Hoehn and Mason[8] for the degradation of desoxycholic acid and the yields obtained were comparable to theirs. The 3,6-diacetoxy-*etio*-cholanyl methyl ketone was hydrolyzed preferentially at position 3. The resulting product was oxidized to a ketone which, after hydrolysis and sublimation from potassium bisulfate, yielded progesterone.

We wish to thank Parke, Davis and Company for their generous support and assistance in the various phases of this work.

Experimental Part

Cholestanediol-3,6.—6-Ketocholestanol,[9] m. p. 143°, (25 g.), 1.0 g. of platinum oxide catalyst and 300 cc. of methanol were shaken under 3 atm. of hydrogen. Reduction was complete within forty-five minutes. The catalyst and solid diol was filtered off, and the precipitate was then dissolved in warm alcohol and was filtered from the catalyst. The combined filtrates were concentrated by evaporation. The solution on cooling deposited 20 g. of white crystals which melted at 188°. The diol crystallized from methanol as large transparent prisms of m. p. 190°.

(8) Hoehn and Mason, THIS JOURNAL, **60**, 1493 (1938).
(9) Cf. Heilbron, Jackson, Jones and Spring, *J. Chem. Soc.*, 104 (1938).

Anal. Calcd. for $C_{27}H_{48}O_2$: C, 80.1; H, 12.0. Found: C, 80.3; H, 12.0.

The diacetate was prepared by refluxing the diol for a short time in acetic anhydride. It crystallized from methanol as white flakes, m. p. 138°.

Anal. Calcd. for $C_{31}H_{50}O_4$: C, 76.5; H, 10.4. Found: C, 76.3; H, 10.5.

6 - Acetoxycholestanone.—Cholestanediol - 3,6 - diacetate, m. p. 138° (10 g.), was dissolved in 3 liters of methanol by warming, then cooled to 25° and a solution of 0.92 g. of potassium hydroxide in 177 cc. of methanol was added. The solution was allowed to stand at 20° for forty-eight hours. It was then exactly neutralized by addition of 16.9 cc. of 0.96 normal sulfuric acid. The solution was evaporated *in vacuo* and the residue was dissolved in 250 cc. of acetic acid. Chromic oxide (1.2 g.) dissolved in 50 cc. of 90% acetic acid was added to the reaction mixture. After standing at room temperature for three hours, water was added and the oily precipitate was extracted with ether. The ethereal solution was washed with water and then was evaporated. Remaining acetic acid was evaporated *in vacuo*. 6-Acetoxycholestanone crystallized from petroleum ether as thick white needles and from methanol as fine white needles of m. p. 101°.

Anal. Calcd. for $C_{29}H_{48}O_3$: C, 78.4; H, 10.9. Found: C, 78.3; H, 10.9.

6-Acetoxycholestanone also was prepared by refluxing 1.0 g. of the diacetate of cholestanediol-3,6 for one and one-half hours with 1.0 g. of sodium bicarbonate in a solution of 10 cc. of water and 250 cc. of methanol. The reaction mixture was poured into water and was extracted with ether. The residue left by evaporation of the ether was treated as described above, although in this case Girard's reagent was used to purify the product which melted at 100° and showed no depression with an analyzed sample of 6-acetoxycholestanone, m. p. 101°.

6-Hydroxycholestanone.—6-Acetoxycholestanone (3.7 g.) was refluxed for one and one-half hours with 150 cc. of 2% methanolic potassium hydroxide. Water was added and the precipitated product was allowed to stand overnight. The crystals collected by filtration weighed 3.0 g. and melted at 183–187°. Recrystallization from methanol gave white leaflets of m. p. 190°.

Anal. Calcd. for $C_{27}H_{46}O_2$: C, 80.5; H, 11.5. Found: C, 80.3; H, 11.6.

Cholestenone.—6-Hydroxycholestanone (100 mg.) and 0.5 g. of fused potassium bisulfate were pulverized together and heated for two hours at 125°, then at 185° for five hours under 4 mm. pressure. The distilled substance after crystallization from methanol melted at 80° and showed no depression in melting point when mixed with an authentic sample melting at the same temperature.

Methyl Ester of Hyodesoxycholic Acid.—The acid was refluxed for two hours with 1% methanolic hydrogen chloride. The solvent was evaporated *in vacuo*. Addition of benzene to the oily residue caused crystallization. It melted at 86°.

Anal. Calcd. for $C_{25}H_{42}O_4$: C, 73.8; H, 10.4. Found: C, 74.2; H, 10.0.

***nor*-Hyodesoxycholic Acid.**—The methyl ester from 200 g. of hyodesoxycholic acid was added in hot benzene solution to 16 moles of phenylmagnesium bromide in ether. The thick gray suspension was refluxed for two hours, then most of the solvent was distilled off. Dry benzene (or toluene) was added and the mixture was heated overnight on a steam-bath. The suspension was decomposed by pouring it on ice and hydrochloric acid. It was then extracted with ether. The ethereal extract was washed with dilute hydrochloric acid, dilute potassium hydroxide, and then finally with water. The solvents were completely evaporated and the crystalline diphenyl alcohol was refluxed for two hours with 600 cc. of acetic anhydride. This solvent was evaporated *in vacuo* and the oily residue was refluxed for six hours with acetic acid. Evaporation of the acetic acid left an oil which did not crystallize but which was oxidized by chromic oxide in acetic acid–chloroform–water mixture exactly as described by Hoehn and Mason.[8] After addition of water and reduction of the excess chromic anhydride with sulfur dioxide, the mixture was extracted with ether. The ethereal extract was well washed with water and was then extracted with 2 *N* potassium hydroxide solution. The basic solution was boiled one and one-half hours and was poured slowly on a stirred mixture of ice and hydrochloric acid. The flocculent white precipitate could be easily filtered and washed with water. It was crystallized from a large amount of ethyl acetate to give a product melting at 198°; yield 110 g. The mixed melting point with hyodesoxycholic acid was 175–180°.

Anal. Calcd. for $C_{23}H_{38}O_4$: C, 72.9; H, 10.1. Found: C, 72.6; H, 10.1.

The methyl ester was prepared by refluxing *nor*-hyodesoxycholic acid in 1% methanolic hydrogen chloride solution. The substance crystallized from benzene with benzene of crystallization. It melted at 95°. After drying in a vacuum at room temperature the analysis showed it to contain 1 mole of benzene.

Anal. Calcd. for $C_{24}H_{40}O_4 \cdot C_6H_6$: C, 76.5; H, 9.8. Found: C, 76.8; H, 9.6.

***bis-nor*-Hyodesoxycholic Acid.**—This acid was prepared in yields of 42 g. from 100 g. of *nor*-hyodesoxycholic acid by the method described for the preparation of *nor*-hyodesoxycholic acid. A crystalline diphenyl alcohol of m. p. 222° (from toluene) was obtained.

Anal. Calcd. for $C_{35}H_{45}O_3$: C, 81.3; H, 9.4. Found: C, 81.3; H, 9.4.

bis-nor-Hyodesoxycholic acid crystallized from a large volume of ethyl acetate as white crystals of m. p. 240°.

Anal. Calcd. for $C_{22}H_{36}O_4$: C, 72.5; H, 10.0. Found: C, 72.4; H, 10.0.

Methylation of this acid in methanolic hydrogen chloride yielded an unsharply melting substance. Methylation with excess diazomethane in ether alcohol solution furnished a quantitative yield of the methyl ester of *bis-nor*-hyodesoxycholic acid of m. p. 146°.

Anal. Calcd. for $C_{23}H_{38}O_4$: C, 72.9; H, 10.1. Found: C, 72.7; H, 10.1.

3,6-Diacetoxy-*etio*-cholanyl Methyl Ketone.—The methyl ester of *bis-nor*-hyodesoxycholic acid was added in benzene solution to 16 moles of phenylmagnesium bromide. The reaction was carried out as described for the

preparation of *nor*-hyodesoxycholic acid. The alcohol was acetylated with acetic anhydride and pyridine at 100° for twenty hours. The solvents were evaporated *in vacuo* and the residue was taken up in ether. The ethereal solution was washed with dilute hydrochloric acid and sodium carbonate and was then evaporated to dryness. The residue was dehydrated for six hours by refluxing it with acetic acid. The solvent was evaporated *in vacuo*. The crude ethylenic compound was ozonized in chloroform solution at 0°. The ketones were separated by Girard's reagent and crystallized from ether–pentane. 3,6-Diacetoxy-*etio*-cholanyl methyl ketone melted at 100°.

Anal. Calcd. for $C_{25}H_{38}O_5$: C, 71.7; H, 9.2. Found: C, 72.0; H, 9.0.

Progesterone.—To 0.9 g. of 3,6-diacetoxy-*etio*-cholanyl methyl ketone in 200 cc. of methanol at 20° was added 42 cc. of methanolic potassium hydroxide containing 0.8 mole of base. The solution was allowed to stand at 20° for forty-eight hours. It was then exactly neutralized by addition of 1.7 cc. of 0.96 *N* sulfuric acid. The solvent was completely evaporated *in vacuo*, and the oily residue was oxidized in one hour at room temperature in 25 cc. of acetic acid with a solution of 5 cc. of 90% acetic acid containing 0.5 g. of chromic oxide. Water was added and the precipitated material was extracted with ether. The ethereal solution was washed with water, and then concentrated. This product was refluxed with 40 cc. of 2% methanolic potassium hydroxide for seventy-five minutes. Water was added and the organic material was extracted with ether. The ethereal solution was washed with water and was then evaporated to dryness. The solid remaining was covered with 5.0 g. of fused potassium bisulfate and was heated at 4 mm. at 130° for an hour and a half. The temperature was then raised to 180° for four hours. The ethereal solution of the distillate on evaporation left a pale, mobile oil, which, when crystallized from acetone–water, yielded greasy crystals. Recrystallization from ether–pentane produced small white crystals of m. p. 120°, which gave no depression in melting point with an authentic sample of progesterone.

Anal. Calcd. for $C_{21}H_{30}O_2$: C, 80.2; H, 9.6. Found: C, 80.4; H, 9.6.

Summary

The Barbier–Wieland degradation applied to hyodesoxycholic acid produced 3,6-diacetoxy-*etio*-cholanyl methyl ketone. This compound was converted into progesterone by a method described for the conversion of 3,6-cholestanediol diacetate into cholestenone.

STATE COLLEGE, PENNA. RECEIVED NOVEMBER 7, 1939

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY, THE UNIVERSITY OF CHICAGO]

The Peroxide Effect in the Addition of Reagents to Unsaturated Compounds. XXIV. The Addition of Hydrogen Iodide to Propene, 1-Bromopropene, Allyl Chloride, and Allyl Bromide

BY M. S. KHARASCH, JAMES A. NORTON,[1] AND FRANK R. MAYO

The work here reported was undertaken in extension of the previous studies of Kharasch and Hannum,[2] and for the purpose of discovering, if possible, the reasons for the discordance between the results of those studies and that of Ingold and Ramsden.[3]

The consensus among the earlier workers has been that isopropyl iodide is the sole product of the addition of hydrogen iodide to propene.[4] The cited work of Kharasch and Hannum confirms that opinion. Ingold and Ramsden, however, report addition products comprising as much as 25% of normal propyl iodide. The highest yields of the normal iodide were obtained in the absence of solvent and in the presence of the typically non-polar solvent propane. Relatively polar solvents, such as nitrobenzene, acetic acid, and water, were said to give rise to relatively smaller yields of the normal iodide. According to Ingold and Ramsden, the "solvent effect" varies with the "mean molecular fraction of hydrogen iodide in its mixture with the solvent (if any) during the course of the reaction." Unfortunately the "mean molecular fraction" is not precisely defined, nor are complete details of the experiments given. Their method consisted in breaking a sealed tube of propene within a sealed tube of hydrogen iodide (and solvent, if any) at a temperature of 18 ± 2°, which was maintained throughout the reaction.

(1) University Fellow, 1938–1939. This paper is an abstract of a thesis submitted by James A. Norton in partial fulfilment of the requirements for the Ph.D. degree, the University of Chicago, 1939.

(2) Kharasch and Hannum, THIS JOURNAL, **56**, 712, 1782 (1934).

(3) Ingold and Ramsden, *J. Chem. Soc.*, 2746 (1931).

(4) For references see ref. 2; *cf.* also Emschwiller, *Ann. chim.*, (10) **17**, 500 (1932).

Discussion

The Addition of Hydrogen Iodide to Propene.—A series of experiments performed in accordance with our usual technique (i. e., with exclusion of air, moisture, and light), and with hydrogen iodide–propene ratios varying from 0.36/

1.0 to 3.51/1.0 (the majority at approximately 1/1), at temperatures from −80° to room temperature (the majority at 0°), and with reaction times varying from one to twenty-one hours, yielded only isopropyl iodide as the addition product. To obtain 90% or more of addition product under the conditions indicated, about three hours were required at 0° or one hour at room temperature.

In order to make sure of the stability of normal propyl iodide under these experimental conditions at room temperature, about one-third mole of normal iodide per mole of propene was added in one experiment, and about one mole in another. In both cases the normal iodide added was unchanged, and the addition product was exclusively the secondary iodide.

The homogeneity of the reaction at 0° was tested by an experiment in which 0.5 g. of powdered Pyrex glass was present during the reaction of 5 g. of propene with an equimolecular quantity of hydrogen iodide. The direction of addition was not altered, and there was no appreciable change of rate.

The admission of air to reactions otherwise similarly conducted at 0° and at 10° did not materially affect the rate of addition, and did not alter the product (100% secondary iodide). Moisture in the ratio of 0.05 mole of water to one mole of propene had no marked catalytic effect, and did not alter the direction of addition.

Since the results of these experiments gave no clue to the discrepancy in the observations of Ingold and Ramsden and of this Laboratory, an attempt was made to reproduce some of their experiments as closely as the available description would permit. Three experiments were carried out in the absence of a solvent, using 1.01 to 1.11 moles of hydrogen iodide. One of these reaction tubes contained air; the other two did not. A fourth otherwise similar reaction mixture contained 0.78 mole of propane as solvent and no air. All of these experiments gave more than 90% yield of addition products which were exclusively isopropyl iodide. Other experiments in which propane, pentane, acetic acid, and nitrobenzene[5] were employed in similar proportions as solvents, but in which the reactants were not mixed by the Ingold procedure, also gave isopropyl iodide as the exclusive addition product.

(5) Some reduction of the nitrobenzene with precipitation of crystalline hydroiodide was observed; *cf.* Baumhauer, *Ann., Supp.*, **7**, 208 (1870).

In several experiments there was a small amount of high-boiling residue, in accord with the previous observation of Michael and Leighton.[6] However, the index of refraction was lower than that of isopropyl iodide, indicating that the normal iodide could not have been present in significant amount. The quantity of high-boiling material available was too small for conclusive identification, but it is suspected to be a hexyl iodide.

Catalysis of Hydrogen Iodide Addition to Propene.—It was previously reported by Kharasch and Hannum[2] that peroxides accelerate the addition of hydrogen iodide to olefins without affecting the direction of addition. In the present study it was found that with our usual technique equimolecular quantities of hydrogen iodide and propene react completely at 0° in about two hours. Under similar conditions, in the presence of 0.005 mole of ascaridole, the addition is complete in less than one minute at −80°. Since ascaridole must react with hydrogen iodide to liberate iodine (as is further indicated by the color of ascaridole reaction solutions), a similar experiment was conducted in the presence of 0.005 mole of iodine (without ascaridole). Again the addition was complete in less than a minute at −80°. (At higher temperatures peroxide- or iodine-catalyzed reactions proceed with almost explosive violence.) It seems likely, therefore, that peroxide catalysis of hydrogen iodide additions is essentially iodine catalysis.

A possible mechanism of iodine catalysis is found in the observation of Malbot[7] that hydrogen iodide reacts with propene iodide to give iodine and isopropyl iodide

$$C_3H_6 + I_2 \longrightarrow CH_3CHICH_2I$$
$$CH_3CHICH_2I + HI \longrightarrow CH_3CHICH_3 + I_2$$

Mercuric iodide also proved to be an effective catalyst. In experiments similar to those just described, in the presence of about 0.015 mole of mercuric iodide (per mole of olefin), the reaction of equimolecular quantities of propene and hydrogen iodide was complete in less than ten minutes at 0°. An addition reaction carried out in a tube in which a mercury mirror had previously been deposited was complete in about one-half hour.

Antioxidants do not appear to inhibit or otherwise affect the reaction. Thus, the presence of 0.005 mole of diphenylamine was without effect.

(6) Michael and Leighton, *J. prakt. Chem.*, [2], **60**, 445 (1899).
(7) Malbot, *Ann. chim.*, [6] **19**, 345 (1890).

In the presence of ethyl mercaptan (0.27 mole), however, there was thioether formation, with consequent reduction in yield (59%, as compared with the usual 95–98%). In all cases investigated the sole addition product was isopropyl iodide.

Two additional experiments show that hydrogen iodide can prevent the peroxide-catalyzed addition of hydrogen bromide. Ascaridole promotes the "abnormal" addition of hydrogen bromide to propene. In the presence of ascaridole (0.4 mole %) and (11 mole %) of hydrogen iodide, 1.02 moles of hydrogen bromide added to propene to give only the "normal" addition product (isopropyl bromide). In a similar experiment conducted for a month at room temperature, vinyl chloride and hydrogen bromide gave a 38% yield of the "normal" addition product, together with unchanged reactants; no ethylene chlorobromide was formed. The logical inference is that either peroxides are immediately and completely destroyed in the presence of hydrogen iodide or that hydrogen iodide inhibits the abnormal addition of hydrogen bromide.

Addition of Hydrogen Iodide to Allyl Bromide.—The addition of hydrogen iodide to allyl bromide yielded 1-bromo-2-iodopropane as the sole addition product but this reaction was accompanied by an oxidation–reduction reaction which yielded iodine and addition products of propene. The latter consisted of isopropyl bromide and iodide and contained no normal propyl halides. To reduce the reduction reaction to a minimum, only a small excess (1–10%) of hydrogen iodide and temperatures of 0° and below were usually employed. Air, moisture, and light were generally excluded. Observations of volume changes of reaction mixtures indicated that in reaction at 0° there is an induction period of about one hour during which little or no adddition takes place but iodine is slowly liberated. As iodine accumulates, addition becomes more rapid and reaches completion in two to four hours, with a yield of 70–90% of addition product and weights of recovered allyl and isopropyl halides ranging up to 30% of the initial allyl bromide used. Both addition and reduction take place more slowly at −33°, and at −80° no reaction was observed during twenty-one hours.

That iodine catalyzes the addition reaction at 0° is shown by the fact that addition of 0.5 to 1 mole % of iodine eliminated the induction period, and caused the reaction to take place in a few minutes. At −33°, addition was also accelerated by iodine but a day was required for complete reaction. No reduction was observed under these conditions and yields as high as 96% are readily obtained. At −80°, addition took place at the rate of 30–35% a day in the presence of iodine. The iodine catalysis may be due to the easy reduction of the unknown 1-bromo-2,3-diiodopropane by hydrogen iodide.

These experiments and the fact that the addition product, 1-bromo-2-iodopropane, is fairly stable toward hydrogen iodide at 0°, suggest that it is allyl iodide, formed by halogen exchange between allyl bromide and hydrogen iodide, or its hydrogen iodide addition product, which is reduced to isopropyl iodide by hydrogen iodide.[7,8] The effect of 6 mole per cent. of water in shortening the induction period at 0° is ascribed to facilitation of the halogen interchange necessary for formation of iodine.

Ascaridole had about the same effect as iodine in eliminating the induction period and accelerating the addition. The best result at 0° was obtained with the smallest proportion of peroxide, 0.7 mole per cent., when the yield of addition product was 93% within one hour. Equally good results were obtained with a sample of allyl bromide which gave a strong peroxide test. Use of larger amounts of ascaridole resulted in tar formation and reduction, probably because of rapid reaction and overheating.

Attempts to obtain an addition product from allyl bromide other than 1-bromo-2-iodopropane were made. Thus, additions were carried out in the presence of 0.7 mole per cent. of diphenylamine at 0°, and by adding hydrogen iodide and ascaridole very slowly at room temperature (and in the presence of air) to allyl bromide mixed with 1.68 moles of pentane.

The Addition of Hydrogen Iodide to Allyl Chloride.—The addition of hydrogen iodide to allyl chloride differs from the addition to allyl bromide chiefly because of the slower halogen exchange to give allyl iodide. Since the iodine formed by the interaction of this product with hydrogen iodide is the controlling factor in the rate of addition, the reaction is slow compared to that with allyl bromide. The addition of hydrogen iodide to allyl chloride gave exclusively 1-chloro-2-iodopropane in yields of 90–100%. Fur-

(8) Simpson, *Ann.*, **129**, 127 (1864).

thermore, since this dihalide is more stable to hydrogen iodide than that formed from allyl bromide, the extent of formation and reduction of the allyl halide by hydrogen iodide could be determined conveniently by titration of the iodine formed. All the reactions with allyl chloride were carried out at 0°, using a 10 to 20% excess of hydrogen iodide.

In the absence of air, peroxides, iodine, moisture, and light, the induction period was about twelve hours. The reaction proceeded to completion in the next twenty-four hours, and 0.3 to 0.4% of iodine was formed. Six mole per cent. of water decreased the induction period so that reaction was complete in six to twelve hours, and increased the iodine formed to nearly 3%.

One-half mole per cent. of iodine eliminated the induction period so that reaction was complete in six hours or less. One mole per cent. of mercuric iodide appeared to shorten the induction period without markedly affecting the rate of the subsequent addition reaction. The addition of 19–27 mole per cent. of reduced iron[9] to one addition reaction carried out at room temperature and to another at −33° was without effect on the direction of addition.

Addition of Hydrogen Iodide to 1-Bromopropene.—Previous work in this Laboratory[10] has shown that the addition of hydrogen chloride and hydrogen bromide to 1-bromopropene gives rise to mixtures of 1,1- and 1,2-dihalides. It was concluded that such mixtures represent the "normal" addition products and that the directing influences of the bromine atom and methyl group on the ethylene bond are nearly balanced. Although this work indicated that ferric chloride catalyzes the "normal" additions of both acids without influencing the direction of addition, the necessity for the use of this catalyst in both additions (to attain practical addition rates), and the extreme sensitivity to peroxides of the hydrogen bromide addition, suggested the desirability of confirming earlier conclusions by the addition of hydrogen iodide. The latter reagent should add sufficiently rapidly without a catalyst, and the direction of addition to unsaturated compounds is not affected by peroxides.

Three experiments were carried out with hydrogen iodide and a mixture of the *cis* and *trans* isomers of 1-bromopropene, at 0°, in the absence of air, moisture, and light, and using about 1.15 moles of hydrogen iodide per mole of 1-bromopropene. In one experiment, 17.6 g. of 1-bromopropene giving a strong peroxide test was used. At the end of two days, a 76% yield of addition product was obtained along with unchanged bromopropene. The product was shown to contain 36% of 1-bromo-1-iodopropane and 64% of 1-bromo-2-iodopropane, in excellent agreement with the proportion of 1,1-dihalide found[10] in hydrogen chloride (35, 36%) and hydrogen bromide (33, 33, 41%) additions. The other two experiments (10 g. peroxide-free 1-bromopropene) gave 21 and 24% 1,1-dihalide. The rates of all of these reactions were about the same, and iodine (1.4 mole %) apparently had little effect on the rate of the reaction. In no experiment was there evidence of much reduction.

Conclusions

It has been established in this paper that only one product results from the addition of hydrogen iodide to propene, allyl bromide, and allyl chloride. A similar conclusion was drawn by Kharasch and Hannum[2] from their work on propene, 1-butene, neopentylethylene, vinyl chloride, and allyl bromide. In view of the extent of the work, these data provide strong evidence that the direction of addition of hydrogen iodide to olefins cannot be reversed. The present paper elucidates the accelerating effect of peroxides on this addition. It shows that peroxides are immediately destroyed by hydrogen iodide with the liberation of iodine, and that the latter catalyzes the normal addition reaction. It is noteworthy that the direction of addition of hydrogen iodide, hydrogen chloride, and the normal addition of hydrogen bromide to unsaturated compounds of several types, including 1-bromopropene which yields a mixture, is the same, within the experimental error, for all three halogen acids.

Experimental

Materials and Reagents.—Propene and propane of higher than 99% purity were obtained from commercial sources. The pentane was a commercial *n*-pentane–isopentane mixture. Allyl bromide[11] and allyl chloride[12] were prepared from allyl alcohol and the concentrated halogen halides in the presence of 1–2% of the corresponding cuprous halides. Before use they were agitated with

(9) Urushibara and Takabayashi, *Bull. Chem. Soc. Japan*, **11**, 692, 754 (1936); **12**, 51 (1937). They report that iron, among other metals, causes an abnormal addition of hydrogen bromide to allyl bromide.

(10) Kharasch, Engelmann, and Mayo, *J. Org. Chem.*, **2**, 288 (1937); Kharasch, Kleiger, and Mayo, *ibid.*, **4**, 428 (1939).

(11) Kharasch and Mayo, THIS JOURNAL **55**, 2468 (1933).

(12) Dewael, *Bull. soc. chim. Belg.*, **39**, 40 (1930).

acidulated ferrous sulfate solution to destroy peroxides, dried rapidly over phosphorus pentoxide, and distilled. 1-Bromopropene was prepared by treatment of propylene bromide with alcoholic sodium ethoxide.[10] The crude product was washed with dilute sulfuric acid to remove unsaturated ethers, which were inseparable by fractionation.

Hydrogen iodide was prepared by the convenient method of Houben, Boedler and Fischer.[13] The gas was collected in a large trap containing some phosphorus pentoxide and a mercury mirror (prepared by heating a drop of mercury in the empty trap). The trap was cooled by dry ice–acetone. After collection, the gas was distilled in the absence of air into the storage vessel, which was a large 30-mm. glass tube mirrored with mercury and equipped with ground joint and stopcock. The usual high-vacuum technique was employed for this purpose; air was not permitted to come in contact with the hydrogen iodide. The storage vessel was kept in dry-ice–acetone when not in use.

Experimental Procedure.—The usual apparatus employed in most of the propene addition experiments, as well as in the allyl bromide, and 1-bromopropene additions, consisted of a series of tubes attached to a vacuum line. In most cases the olefin and volatile solvent (if any) were weighed into a tube containing a little phosphorus pentoxide, which was then sealed to the vacuum line for degassing and eventual distillation of the contents into the reaction tube. When nitrobenzene and acetic acid were used as solvents, the solvent and the propylene were dried and degassed in separate tubes. When water, iodine, diphenylamine, ascaridole or other relatively non-volatile addenda were used, these were weighed into the tube that was eventually to become the reaction tube, which was then sealed to the line. Hydrogen iodide was distilled from a storage reservoir through a ground-glass joint into a tube already attached to the vacuum line. Rough estimation of quantity was made by volume calibration of one tube; exact amounts used were determined by weighings of the storage reservoir. Transfer of reactants to the reaction tube was effected by high-vacuum distillation with appropriate manipulation of stopcocks and cooling baths. Except in the experiments expressly designed to investigate the effect of air upon the addition, the reaction tube was sealed off without access of air, and was maintained at the desired temperature throughout the reaction period.

In about one-fourth of the propene, and in all of the allyl chloride experiments, hydrogen iodide and olefin were stored in the absence of air, in containers attached to the vacuum line. Hydrogen iodide and propylene were measured as gases, allyl chloride as a liquid, in calibrated bulbs, from which they were condensed in an empty tube before distillation into the reaction tubes. This procedure removed small amounts of non-condensable gases, mercury (from manometers), and mercuric iodide (from the hydrogen iodide storage vessel). High-boiling materials were placed in the bomb tube directly, as before.

About 0.1 mole of unsaturated compound usually was employed. The techniques described ordinarily gave colorless reaction mixtures, but a faint iodine color appeared in a few hours in propylene experiments, faster in others.

(13) Houben, Boedler, and Fischer, *Ber.*, **69B**, 1773 (1936).

In attempts to reproduce the experiments of Ingold and Ramsden, the following procedure was employed. Propene was condensed in a small bomb tube in the absence of air, using high vacuum technique. The end of this tube was drawn out to a long capillary, and sealed, and the tube was slipped into a larger bomb tube. The open end of the large bomb tube was drawn down (meanwhile the other end, containing the propene bomb tube, occasionally was cooled in liquid nitrogen), and was sealed onto the vacuum line. Then, after evacuation, hydrogen iodide (and solvent, if used) were distilled into the large bomb tube and the whole was sealed from the line. The bomb was allowed to warm to room temperature, and by suitable manipulation the long capillary was shattered and the contents mixed. Evacuation was omitted in one experiment.

Analysis of Reaction Products.—In most of the propene experiments the bomb contents (after completion of the reaction) were washed with aqueous sodium sulfite and aqueous potassium carbonate to remove iodine and hydrogen iodide, dried over potassium carbonate, and distilled through a Podbielniak column. A single fraction of boiling point corresponding to the "normal" addition product (isopropyl iodide) was obtained in each case. These products were later combined and refractionated. The index of refraction of the principal fraction was that of isopropyl iodide (n^{20}D 1.4988). The relatively small forerun and residue had lower indices of refraction, excluding the possibility of the presence of appreciable amounts of normal iodide (n^{20}D 1.5052). In the propene experiments involving the presence of added normal iodide, and in several others, the bomb contents were distilled at 10 mm. into a trap cooled by dry-ice–acetone. The distillate was then analyzed by index of refraction, the index being a linear function of the composition of iso–normal propyl iodide mixtures.

In some of the propene and all of the allyl bromide experiments the first procedure was modified in that the distillate was cut into several fractions of which the indices of refraction were determined separately. The addition product of allyl bromide was distilled at 20 mm. pressure. The 1-bromo-2-iodopropane was found to boil at 66.8° at this pressure and to have the refractive index n^{20}D 1.5916.

In the allyl chloride experiments free iodine was first titrated with standard thiosulfate solution, and the product was then dried and fractionated at 40 mm. pressure. The 1-chloro-2-iodopropane boiled at 66.2° at 50 mm., n^{20}D 1.5472.

Reduction Products of Allyl Bromide.—The low-boiling materials from a number of allyl bromide experiments were combined and fractionated through a Podbielniak column. They comprised about 40% allyl bromide and a like amount of iospropyl iodide together with about 10% isopropyl bromide. The last was identified by halogen analysis and preparation of isopropyl 3,5-dinitrobenzoate.

1-Bromo-1-iodopropane.—The various fractions from the 1-bromopropene experiments were combined and fractionated to obtain a sample of 1-bromo-1-iodopropane. The amount of available material was too small to permit isolation of a pure sample, but the index of refraction was estimated from those of several fractions: n^{20}D 1.5826;

b. p. 61.3° at 20 mm. Fractions having indices both above and below the estimated value were obtained, and it is believed that the error in the index of refraction is less than ±0.0010.

Structure of 1-Chloro-2-iodopropane.—The structure of the addition product of hydrogen iodide and allyl chloride was established by the action of zinc and hot alcohol on the addition product. An 87% yield of propylene (identified by its addition of hydrogen iodide to give nearly the theoretical yield of isopropyl iodide) was obtained. Had the product been a 1,3-dihalide, cyclopropane (which yields *n*-propyl iodide upon treatment with hydrogen iodide) would have been produced. A 1,1-dihalide would have given 3-hexene. It was then shown that the 1,2-dihalide was 1-chloro-2-iodopropane by adding to it an equimolecular proportion of warm alcoholic sodium ethoxide. The product was a mixture of propene with the *cis* and *trans* isomers of 1-chloropropene.[10] The latter were identified by boiling point and index of refraction.

Summary

1. In a thorough investigation of the addition of hydrogen iodide to propene, allyl bromide and allyl chloride only one (the "normal") addition product was obtained in each case.

2. The addition of hydrogen iodide to 1-bromopropene yields a mixture of approximately one-third 1,1- and two-thirds 1,2-dihalides.

3. It is shown that iodine is a catalyst for the addition of hydrogen iodide, and that peroxides accelerate this addition because they liberate iodine from hydrogen iodide.

4. 1-Chloro-2-iodopropane and 1-bromo-1-iodopropane have been prepared in the pure and nearly pure states, respectively.

CHICAGO, ILLINOIS RECEIVED SEPTEMBER 2, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA]

An Investigation of the Exchange between a Metal and Ions in Solution by Using Radioactive Indicators

BY B. V. ROLLIN

In experiments using the naturally radioactive isotope of lead, Hevesy and Biltz[1] have shown the existence of an exchange of atoms between the surface of a sheet of metallic lead and a solution of a plumbous salt in contact with it. In one hour, under the conditions of their experiment, they found that the quantity of lead which had exchanged with the solution corresponded to a depth of about a thousand atomic layers of the metal. The study of this type of exchange is interesting because it is important in understanding the mechanism of corrosion processes and so it was considered worth while to continue the investigation with other metals using, as indicators, artificially radioactive isotopes produced by bombardment in the cyclotron.

A. Inactive Metal Shaken with Active Solution

(1) Zinc.—For a preliminary experiment radioactive zinc was prepared by deuteron bombardment of zinc followed by chemical separation. The zinc was used in the form of the chloride in a solution of about 300 mg. of chloride in 30 cc. of water acidified to a *p*H of about 5. The total activity of the solution was about 10 microcuries. The metal, in the form of a powder, was first shaken for one hour with a concentrated solution of inactive zinc chloride, then filtered and washed, and about 1 g. of the powder then shaken with the active solution for one hour. The solution was filtered off and the powder very carefully washed. On testing the powder with an electroscope it was found to be quite appreciably radioactive. No quantitative results could be deduced from this experiment because the metallic zinc was slowly attacked by the solution during the period of shaking.

(2) Silver.—Silver was chosen because (in the absence of oxygen) it is only dissolved to a negligible extent by water and because it forms stable ions in solution which are not reduced to a lower valence state by contact with the metal. It would, for example, have been impossible to study the exchange between copper and cupric ions because the results would be obscured by the exchange brought about by the reaction

$$Cu^{++} + Cu \rightleftarrows 2Cu^{+}$$

Preparation of the Radioactive Silver.—The isotope used was Ag^{106} having an eight-day half-life and was obtained by bombarding palladium with 8 Mev. deuterons. The palladium was digested with fuming nitric acid and 9 *N* perchloric acid and 100 mg. of silver added as carrier. The silver was precipitated as chloride, washed and dissolved in excess of ammonium hydroxide, then precipitated with ammonium sulfide, filtered and the precipitate dissolved in hot nitric acid. The solution was evaporated to dryness and the silver nitrate residue dissolved in 30 cc. of water. The total (β-ray) activity of the solution was 10 microcuries.

(a) A sheet of silver of area 20 sq. cm. was polished with crocus cloth, washed with nitric acid and water, shaken with inactive silver nitrate solution for two hours and then shaken with the active silver nitrate solution for twenty-four hours. At the end of this time it was care-

(1) G. von Hevesy and M. Biltz, *Z. physik. Chem.*, **B3**, 271 (1929).

fully washed, then shaken with water for several hours and its activity tested. It was found to have acquired an activity corresponding to an exchange with the solution of about 150 atomic layers of the metal (assuming the actual surface of the metal is the same as the measured surface).

(b) The experiment was repeated using sheets of gold and platinum instead of silver. These were also found to have acquired an activity representing the transference of about 100 atomic layers from the solution. The activity was apparently not due to simple contamination with ions as it was not appreciably reduced by further washing with water for forty-eight hours.

(c) In this experiment the solution was shaken with a different type of surface. The surface was a silver mirror deposited on the inside of a glass flask by evaporation of silver in a vacuum from a heated tungsten strip. After evaporation of the mirror the flask was filled with nitrogen and the solution introduced. The flask was then evacuated again and shaken so that the solution was in contact with the mirror for one hour. After careful washing the solution was found to have an activity corresponding to the transference of about twenty atomic layers.

B. Active Surface Shaken with Inactive Solution.— The radioactive silver was obtained by electrolysis of the active nitrate solution. The surface was prepared by evaporation of a few milligrams of the silver in vacuum as in (c) above. Before evaporation the silver was carefully washed to free it from silver ions. After deposition of the mirror the flask was filled with nitrogen and the mirror washed several times with distilled water. The mirror was then shaken for one hour with distilled water (under vacuum), this water then discarded, a fresh quantity introduced and the shaking repeated. In this way the mirror was freed from all radioactive contamination as shown by testing the second water washing by adding silver ions (as carrier), precipitating the silver as bromide and testing the bromide with a Geiger counter. The mirror was now shaken for two hours with a solution of silver nitrate (containing 1 g. of silver nitrate in 20 cc. of water). On precipitating the silver as bromide it was found to contain an activity corresponding to the exchange of ten atomic layers.

To investigate whether the nitrate ion had any influence on the exchange, the mirror was now shaken for one hour with a solution of sodium nitrate (0.5 g. sodium nitrate in 20 cc. of water). Following the usual procedure of adding silver ion as carrier and then precipitating the silver as bromide and testing its activity, it was found that no activity had been taken up by the solution.

On washing the mirror again with silver nitrate solution for one hour and measuring the activity taken up by the silver solution, an unexpected result was found. The activity was now very high corresponding to the transference of about 150 atomic layers from the mirror. On washing the mirror with water and then shaking with silver nitrate solution again for two hours it was found that the activity in the solution was now that of only ten layers again. To verify the effect of treatment of the mirror with sodium nitrate solution, the experiment was repeated and again an exchange of about 100 atomic layers was found.

The results are summarized in Table I.

TABLE I

Soln.	Time of shaking, hours	Activity (atomic layers)
Water	2	Not measd.
Water	1	Less than 1
Water	1	Not measd.
$AgNO_3$	2	10
$NaNO_3$	1	0
$AgNO_3$	1	150
$AgNO_3$	2	10
$NaNO_3$	1	Not measd.
$AgNO_3$	1	100

Discussion

The experiments with silver in a solution of silver nitrate show that there is an actual exchange of atoms between the metal and the solution. The exchange appears to involve from ten to a hundred atomic layers and, as one can completely neglect the diffusion over these distances in the metal, the only reasonable mechanism seems to be that of local electrolysis caused by the existence of irregularities on the surface of the metal. However this hypothesis does not account for the activity obtained by the gold and platinum sheets from the silver solution unless the surfaces of the metals contained considerable impurities, which seems unlikely. It is very difficult to explain why treatment of the silver surface with sodium nitrate should increase the activity obtained by the silver surface solution from the mirror. The phenomenon is perhaps due to some kind of activation of points on the surface of the silver by sodium ions but no reason can be seen why this should take place. It seems that further experiments will be needed before the mechanism of these effects can be explained.

It is a pleasure to record the advice and coöperation in these experiments of Dr. G. T. Seaborg and also of Dr. S. Ruben, who very kindly made all the Geiger counter measurements. I am especially indebted to Professor E. O. Lawrence for enabling me to use the cyclotron to obtain the radioactive substances.

Summary

Experiments using radioactive silver have shown that exchange takes place between a solution of silver ions and a surface of metallic silver. In two hours an exchange of silver corresponding to ten atomic layers was found. The exchange was increased by a factor of ten if the surface was pretreated with sodium nitrate solution.

BERKELEY, CALIFORNIA RECEIVED NOVEMBER 2, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CARNEGIE INSTITUTE OF TECHNOLOGY]

The Heat Capacity of Nickel Oxide from 68–298°K. and the Thermodynamic Properties of the Oxide

BY HARRY SELTZ, BERNARD J. DEWITT AND HUGH J. MCDONALD

This paper describes the results of measurements of the heat capacity of nickel oxide, NiO, from 68–298.1°K., making use of the calorimeter described in a previous publication.[1] From these results the entropy has been evaluated at 298.1°K., and from published heats of formation and heat capacities at higher temperatures the complete thermodynamic properties of the oxide have been derived.

Material.—The nickel oxide used was a C. P. Baker analyzed grade containing less than 0.2% of impurities. Microscopic examination (×1000) showed the material to be made up of transparent cubic crystals of uniform size. This is the only form of the pure oxide which has been reported. The powder was dried for several days at 100°, and a sample then showed no ignition loss on heating to bright redness in a platinum crucible. The total charge of nickel oxide used in these measurements was 151.085 g. (*in vacuo*) or 2.0229 moles. Frequent checks of the calorimeter resistance against the calibrated thermocouple during the heat capacity measurements showed no significant changes in the calibration.

Experimental Results.—In Table I the experimental heat capacities for the oxide are given, and the results are plotted in Fig. 1. The overall accuracy of these measurements is estimated at ±0.2%.

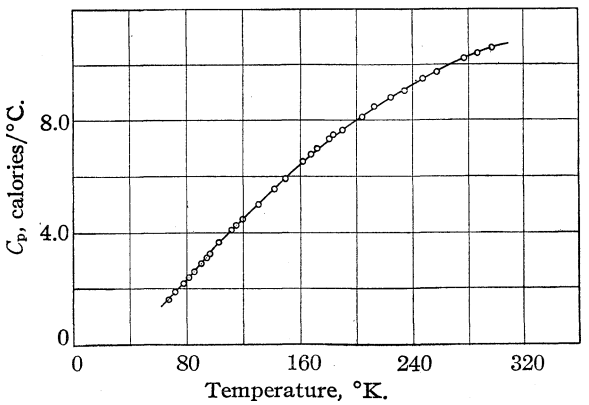


Fig. 1.—Molal heat capacity of NiO.

Calculations

The Entropy of NiO.—The method of Kelley[2] was used to extrapolate the heat capacity values from 68–0°K. It was found that

$$C_v = D\left(\frac{404}{T}\right) + E\left(\frac{620}{T}\right)$$

(1) McDonald and Seltz, THIS JOURNAL, **61**, 2405 (1939).

(2) Kelley, "Bureau of Mines Bulletin 350," 1932, p. 8.

TABLE I

Temp. °K.	C_p, cal./mole	Temp. °K.	C_p, cal./mole
68.05	1.607	151.86	6.02
71.96	1.909	162.37	6.54
78.19	2.185	168.09	6.80
82.07	2.403	172.61	7.02
85.89	2.625	181.32	7.36
86.70	2.644	183.01	7.50
91.08	2.927	190.75	7.64
94.42	3.094	204.20	8.12
96.32	3.298	213.13	8.54
103.13	3.693	225.34	8.84
111.70	4.094	235.37	9.09
115.71	4.242	247.81	9.52
120.33	4.464	257.49	9.75
131.10	5.00	277.20	10.27
141.72	5.58	286.32	10.43
150.08	5.93	296.68	10.56

fitted the experimental curve very well up to 150°K. The contribution of the Debye function to the entropy was 0.648 e. u. at 68°K., while the contribution of the Einstein function was less than the experimental error. The entropy change from 68–298.1°K. was determined graphically and this amounted to 7.716 e. u. The rounded sum of the experimental and extrapolated entropies is 8.36 e. u. at 298.1°K. Since two moles of the oxide were used in these measurements, the accuracy of this value is estimated to be better than ±0.1 e. u.

Thermodynamic Properties of Nickel Oxide.—Using accepted[3] values for the entropies of nickel and oxygen, we calculate $\Delta S_{298.1} = -18.00$ for the entropy of formation of the oxide. The heat of formation given by several investigators varies greatly, but the most acceptable value seems to be that given by Bichowsky and Rossini[4] $\Delta H_{298.1} = -58{,}400$ cal. From this value and the entropy of formation we calculate $\Delta F^\circ_{298.1} = -53{,}034$ for the free energy of formation. We thus write

$$Ni(s) + {}^1/_2O_2(g) = NiO(s);\ \Delta S_{298.1} = -18.00;\ \Delta H_{298.1} = -58{,}400;\ \Delta F^\circ_{298.1} = -53{,}034$$

Watanabe[5] and Bogatskii[6] independently have studied the equilibrium

$$NiO(s) + CO(g) = Ni(s) + CO_2(g)$$

(3) Kelley, "Bureau of Mines Bulletin 394," 1935, p. 35.

(4) Bichowsky and Rossini, "The Thermochemistry of the Chemical Substances." Reinhold Publishing Corp., New York, N. Y.

(5) M. Watanabe, *Science Repts. Tôhoku Imp. Univ.*, **22**, 436 (1933).

(6) D. P. Bogatskii, *Metallurg.*, **13**, No. 2, 18 (1938).

From his measurements Watanabe calculates the free energy of formation of NiO(s) as $\Delta F^\circ_{298.1} = -50{,}333$ cal., while Bogatskii's results lead to a value $\Delta F^\circ_{298.1} = -52{,}092$ cal. Pease and Cook[7] have studied the reduction equilibrium with hydrogen at two temperatures, 485 and 600°, and from these data calculate for the formation of the oxide, $\Delta F^\circ_{298} = -56{,}497$ cal. It will be noticed that the value obtained in this paper represents about the mean of the three previous determinations.

Kapustinskii and Novosel'tsev[8] have measured the heat capacity of NiO at temperatures from 373 to 1373°K. Their results can best be represented by the equation

$$C_p = 13.69 + 0.83 \times 10^{-3}T - 2.915 \times 10^{5}T^{-2}$$

Using Kelley's[9] equations for Ni(α) up to 626°K. and for Ni(β) above this temperature, and his equation for O_2, we obtain

$$\mathrm{Ni}(\alpha) + {}^1/_2\mathrm{O_2(g)} = \mathrm{NiO(s)}: \quad \Delta F^\circ = -60{,}387 - 5.29T \ln T + 2.85 \times 10^{-3}T^2 + 0.988 \times 10^{5}T^{-1} + 52.84T$$

$$\mathrm{Ni}(\beta) + {}^1/_2\mathrm{O_2(g)} = \mathrm{NiO(s)}: \quad \Delta F^\circ = -59{,}692 - 2.55T \ln T + 0.102 \times 10^{-3}T^2 + 0.988 \times 10^{5}T^{-1} + 35.80T$$

Summary

1. The heat capacity of nickel oxide, NiO, has been measured from 68-298°K.

2. The entropy of the oxide is found to be 8.36 e. u., with an estimated accuracy better than ±0.1 e. u.

3. The free energy of formation of the oxide has been calculated, $\Delta F^\circ_{298.1} = -53{,}034$ cal., and has been expressed as a function of the temperature.

(7) Pease and Cook, THIS JOURNAL, **48**, 1199 (1926).

(8) A. F. Kapustinskii and K. A. Novosel'tsev, *J. Phys. Chem., U. S. S. R.*, **11**, 61 (1938).

(9) Kelley, "Bureau of Mines Bulletin 371," 1932.

PITTSBURGH, PENNSYLVANIA

RECEIVED NOVEMBER 13, 1939

[CONTRIBUTION FROM THE HAYDEN MEMORIAL LABORATORIES OF NORTHEASTERN UNIVERSITY]

The Precision Conductivity Bridge Assembly

BY W. F. LUDER

I. Introduction

The papers of Jones and Josephs[1] and of Shedlovsky[2] marked the beginning of a new era in the investigation of various chemical phenomena by means of conductivity measurements. The precision which they obtained was, and still is, sufficient for most such investigations. However, the rapid development of communication engineering since the publication of their papers has now made it possible to effect several desirable improvements in the whole conductivity bridge assembly. Furthermore, by taking advantage of recent developments, the expense and difficulty of assembling a complete bridge can be greatly reduced.

At about the same time as the work of Jones and Josephs and Shedlovsky on the conductivity bridge, an increased interest in many other types of alternating current bridges was evident in the large number of papers which were published each year. According to Hague,[3] well over 250 papers on a. c. bridge methods must have appeared since 1928. There were 48 in 1932 alone. One of the most thorough of the recent papers is that of Astin.[4] Although his bridge is of the Schering type, Astin has used a Wagner ground, and certain conclusions reached by him are of value in conductivity bridge design. Following Ogawa,[5] Astin has brought a. c. bridge theory to a high degree of perfection. In surveying this large field, however, chemists will do well to keep in mind the fact that the requirements of such bridges as those of Astin and of Balsbaugh and Herzenberg[6] are considerably greater than similar requirements for a conductivity bridge. The conductivity bridge is one of the simpler alternating current bridges.

Communication engineering has more than kept pace with requirements of low frequency a. c. bridges. The application of inverse feedback to the problem of tuning an oscillator or an amplifier[7] probably will be of value in many cases. It is doubtful, however, whether much advantage is to be gained by using it with the ordinary conductivity bridge. This is especially true in

(1) Jones and Josephs, THIS JOURNAL, **50**, 1049 (1928).

(2) T. Shedlovsky, *ibid.*, **52**, 1793 (1930).

(3) B. Hague, "A. C. Bridge Methods," Pitman, N. Y. (1938).

(4) A. V. Astin, *Bur. Standards J. Research*, **21**, 425 (1938).

(5) Kazukiyo Ogawa, *Researches Electrotech. Lab. Tokyo*, No. 254 (1929); No. 277 (1930).

(6) Balsbaugh and Herzenberg, *J. Franklin Inst.*, **218**, 49 (1934).

(7) H. H. Scott, *Proc. Inst. Radio Engrs.*, **26**, 226 (1938).

view of the fact that a very simple and inexpensive, low output, low harmonic-content oscillator is now available.[8] Constant-frequency oscillators, degeneratively tuned amplifiers, cathode ray tube null indicating devices, vibration galvanometers and similar complicated and expensive instruments are increasingly necessary in communication engineering and for use with Schering and other types of bridges. It is questionable, however, whether chemists have anything to gain by using them with the conductivity bridge.

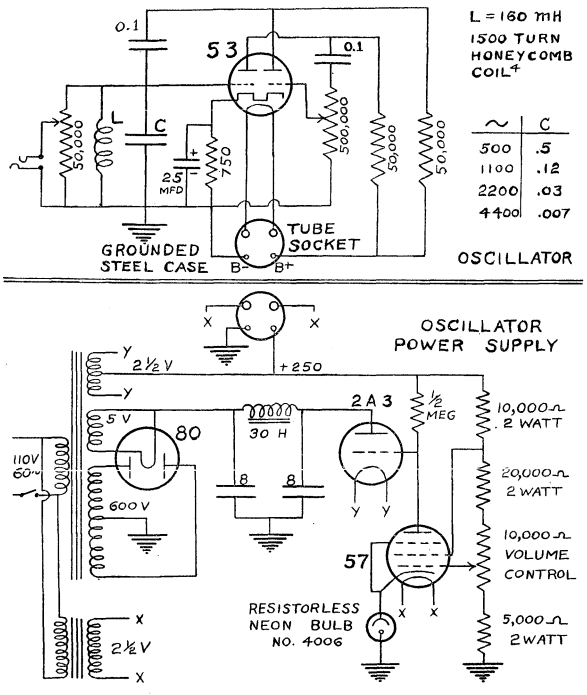


Fig. 1.

Securing the answer to this question was one of the objectives of the present investigation. Several different forms of the oscillator and its power supply, of the bridge network, and of the amplifier have been constructed and tested in this Laboratory. A preferred combination and several alternatives are suggested and discussed. Throughout the investigation the problem of easily duplicating the assembly as a unit has been kept in mind. Standard, readily-obtainable parts have been used. With the description given, any radio amateur or repair man should be able to complete the assembly in two or three days. This standardization has been secured with no loss in precision and with some gain in convenience in the operation of the bridge. Depending on the resistors chosen, it is possible to keep the cost of the whole assembly below $200.

(8) "Technical Service Bulletin TS-2," R. C. A. Manufacturing Co., Inc., p. 97.

II. The Oscillator

Headphones and a high gain amplifier make the most convenient detector in a bridge assembly where they can be used to good advantage. This is certainly true for the conductivity bridge. When bridge balance is indicated by zero amplitude of a 1000 cycle note, it is important to keep all other sounds at a minimum level. Undesired noise in the phones comes from four principal sources: (1) harmonics generated by the oscillator or introduced by transformers, (2) a. c. hum, (3) stray pickup, and (4) tube noise. The first two arise primarily in the oscillator and its power supply; the others will be discussed subsequently.

Oscillators are generally considered satisfactory for most purposes if their harmonic content is less than 2–3%. This value is too high for a precise bridge balance unless a filter is used in the detector. Such filters in the past have been rather unsatisfactory. (The question of whether or not a tuned amplifier should be used will be discussed in Part III.) The use of degenerative tuning[7] has made possible the construction of oscillators with remarkably low harmonic content.[9] Such oscillators have other good features, among which are low hum level and more easily controlled and constant frequency. They are, however, somewhat complicated and expensive, and offer no advantages, for conductivity bridge use, over the oscillator shown in Fig. 1.[10] By careful adjustment of the regeneration control of this oscillator, the harmonics can be reduced to 0.1%. This is not necessary, however. With ordinary care the percentage distortion will be approximately 0.3%. No harmonics can then be heard when the bridge is balanced using an untuned three-stage amplifier (two 6J7's and one 6C5).

An easy method of reducing a. c. hum is to make the power supply for the oscillator of the constant voltage type. The constant plate voltage probably contributes, also, to the observed stability of the regeneration control. The circuit of a simple constant voltage power unit is given

(9) For example, in one commercial model, the General Radio 608-A, the harmonic content may be kept under 0.1%.

(10) The use of this oscillator was suggested by Professor Carl F. Muckenhoupt, Chairman of the Physics Department of Northeastern University. Acknowledgment is due the R. C. A. Manufacturing Co., Inc., Harrison, N. J., for their kind permission to reproduce the diagram from page 97 of their Technical Service Bulletin TS-2.

in Fig. 1. When the bridge is balanced using the oscillator and power supply shown in Fig. 1, each in a separate steel case connected by cable and plugs, no a. c. hum can be heard in the output of a three-stage untuned amplifier.

Therefore the first two sources of unwanted noise can be eliminated easily without the use of a complicated oscillator or a tuned amplifier.

A further consideration in the design of an oscillator for conductivity bridge use is its output voltage. Most oscillators will supply too much power to a conductivity bridge. The output voltage of the oscillator described, 0.5 volt or less, is about the correct value.[11] If the noise level can be kept low enough, an oscillator voltage of 0.5 volt is sufficient to give a sensitivity in bridge reading of one or two parts per million using a two-stage amplifier consisting of one 6J7 and one 6C5.

The operating characteristics of the oscillator are given. (No alternative is suggested for the oscillator and its power supply, because there seems to be no more suitable combination for use with conductivity bridges at the present time. In addition to its having the correct operating characteristics, this oscillator is simple, inexpensive, and easy to construct and operate.)

Wave Form.—With the regeneration control properly adjusted[12] and the fundamental frequency set at approximately 1100 cycles per second, the harmonic content in the output voltage is less than 0.3%.[13]

Frequencies.—Approximately 500, 1100, 2200, 4400 c. p. s., are obtained by selecting different capacitances by means of a dial switch on the front panel.[14]

Output Voltage.—With the regeneration control properly adjusted and the oscillator connected to the bridge through a General Radio type 578-B bridge transformer, the maximum output voltage at the transformer secondary is approximately 0.5 volt.

Power Supply.—Controllable constant plate supply type. At 250 volts d. c. output the a. c. line voltage may be varied between 85 and 130 volts without causing a variation of more than one volt in the oscillator plate voltage.

(11) Jones and Bollinger, THIS JOURNAL, **51**, 2407 (1929).

(12) The adjustment is made by retarding the regeneration control until oscillation stops, then carefully advancing it until oscillation just begins again.

(13) A General Radio 736-A Wave Analyzer was used to make the distortion measurements. The author is indebted to Dr. Muckenhoupt for the use of the wave analyzer, a cathode ray oscilloscope, and a vacuum tube voltmeter.

(14) The inductance is a 1500 turn honeycomb coil (L = 160 mH) obtainable from the Radio Shack, 167 Washington St., Boston, Mass. Only rough observations were made on frequency stability, since conductivity measurements are not affected by small frequency changes.

III. The Amplifier

Since bridge balance is indicated by zero amplitude of the oscillator frequency, the useful gain of an amplifier is limited to a value not much greater than that at which the tube noise from the first tube becomes distinctly audible. This is true, of course, only if harmonics, hum, and stray pickup have been eliminated. Stray pickup will be discussed in Part IV.

The first amplifier constructed during this investigation was untuned and consisted of one 6J7 and one 6C5, supplied by batteries. Batteries were used because of the difficulties involved in preventing coupling between the oscillator and amplifier when both secure their power supply from a common a. c. source. "B" batteries are needed for a d. c. bridge with which to measure solvent conductance, at any rate. The same batteries may be used for the amplifier plate supply. The tube noise was just perceptible in this amplifier, which indicated that it had about the maximum useful gain that could be used without tuning. This gain was high enough to permit bridge balance to one or two parts per million in a quiet room. Therefore it is evident that when harmonics, hum, and stray pickup have been practically eliminated, such a two-stage untuned amplifier is sufficient for ordinary use of the bridge.

Little is to be gained by increasing the gain of the amplifier unless some means of tuning is employed. A three-stage untuned amplifier, constructed by adding another 6J7 tube to the two-stage amplifier, resulted in greatly increased volume of both the oscillator frequency and the tube noise. This may be of value if the bridge is to be used in noisy surroundings. However, in order to secure any great increase in sharpness of the bridge balance, a three-stage amplifier must be tuned. The best method seems to be degenerative tuning.[7] Inverse feedback is used to cancel all frequencies except that for which the degeneration network is balanced. Scott places the network around three direct coupled tubes in order to secure high selectivity. Direct coupling of three tubes, however, requires a very high voltage plate supply.

After some experimenting with degenerative

tuning, it seemed that the results in this case were not enough better than those obtainable by another method to justify the additional expense and difficulty of construction involved. This is particularly true with this assembly, since there is no need of suppressing harmonics from the oscillator. When noise other than tube noise has been practically eliminated from the assembly, the important requirement is a substantial reduction of tube noise with little decrease in signal strength. A simple method of tuning[15] which, although not extremely sharp, meets this requirement, is shown in the grid circuit of the 6C5 in Fig. 2.[16] Such an arrangement eliminates much of the background noise in the amplifier.

A number of such tuned circuits could be used for various frequencies by connecting them to a dial switch, but such an arrangement seems unnecessarily complicated. Most conductivity measurements are made at one frequency, usually 1000 cycles, so it seems best to include only one tuned circuit. A toggle switch is provided for

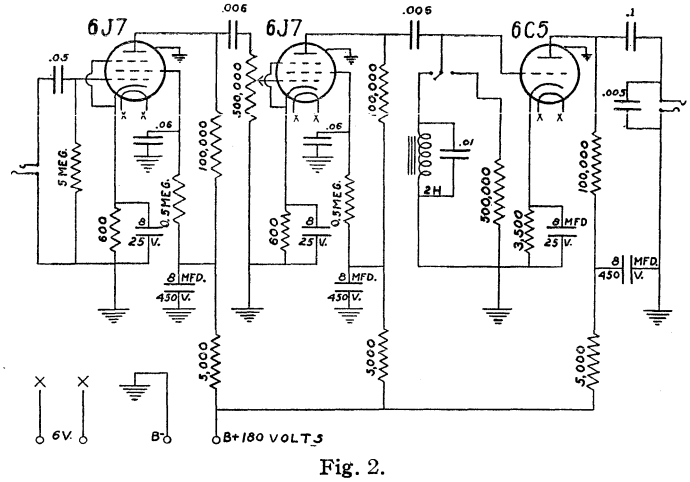


Fig. 2.

connecting a 500,000 ohm resistor in place of the tuned circuit. This permits the use of the amplifier as an untuned amplifier whenever measurements must be made at other frequencies.

An inductance of two henries is about right. This value can be obtained by increasing the separation between the I and E core pieces of a 10 henry, 50 milliampere, midget filter choke. If the frame is unclamped and seven strips of paper (cut to fit from typing paper) are inserted between the core pieces, the inductance will be about two henries. To tune this choke to 1,000 cycles a condenser of approximately 0.01 mfd. is needed. Since the inductance of the choke will not be exactly two henries, the correct value of the condenser should be chosen by experiment, starting with a value of 0.005 mfd. and adding 0.002 and 0.001 mfd. condensers in parallel until the correct value is reached. This is easily done by connecting the condensers while listening to the 1000 cycle note when the bridge is slightly off balance.

It seems that a two-stage amplifier is in many cases suitable. Where higher gain is necessary, sufficient tuning must be employed to reduce tube noise. Probably the most convenint method of tuning is the one described above.

IV. The Bridge Network

For most purposes there is no need of attempting to improve the precision obtained by Jones and Josephs.[1] There are, however, several refinements which may now be made. One of them involves a different method of connecting and balancing the Wagner ground circuit, called by Astin[4] separate balancing of the detector terminals to ground (Fig. 3). This method makes possible the elimination of the transformer usually employed between the bridge and the detector. A transformer in such a position is unsatisfactory for several reasons. Probably it is partly responsible for the fact that bridges using it show a great decrease in sensitivity as the resistance being measured is increased. At any rate, the bridge in the form now used in this Laboratory shows very little variation in balance sensitivity over its normal range of 1000 to 200,000 ohms. (Another factor in this nearly constant sensitivity will be referred to later.) A high impedance transformer is undesirable because of the effect stray fields may have upon it, thus making for a higher noise level.

If the more common form of Wagner ground described by Jones and Josephs[1] is to be retained, the elimination of the detector input transformer means that the amplifier cannot be grounded directly. Grounding a direct-coupled input amplifier makes the Wagner ground useless. An ordinary ungrounded amplifier, however, introduces

(15) This method is a common one in communication engineering. It will not attenuate adjacent harmonics sufficiently if they are present to any great extent in the oscillator output.

(16) For a two-stage amplifier, one of the 6J7's and the tuned circuit should be left out. The choke, condenser, and switch should be removed and the grid connected directly to the 500,000 ohm resistor.

an intolerable amount of stray noise. An ungrounded, doubly shielded amplifier[17] may be used, but involves unnecessary difficulties of construction. An alternative is to wire the amplifier so that the B minus line is isolated from the grounded chassis. A 0.5 mfd. condenser is connected from the midpoint of the bridge ratio arms to ground. The B minus side of the amplifier is connected to the midpoint. This arrangement functions satisfactorily[18] except that the volume is cut down considerably when the Wagner ground is being balanced. This is because the low impedance of the condenser is then directly across the amplifier input. Astin has shown that the only effect of the large admittance of the capacitance to ground is to make the bridge balance more dependent upon the Wagner ground adjustment. The requirement for non-critical adjustment is that the ground admittances from the detector terminals must be similar in ratio to the ratio between the admittances of the arms in either of the two pairs between the detector terminals. The large admittance to ground of the 0.5 mfd. condenser makes the Wagner ground adjustment nearly as critical as it is when the detector terminals are balanced separately to ground. Therefore it seems best to adopt the separate terminal balance since a conventional grounded amplifier can then be used.

Separate balancing of the detector terminals to ground requires that the Wagner ground balance be adjusted as carefully as the bridge proper. This is easily done by using verniers R_2 and C_2 as shown in the bridge network arranged for separate terminal balance (Fig. 3). The bridge is balanced roughly with S_1 upward. Then with S_1 downward the Wagner ground adjustment is made, first roughly with C_1 and R_1, then exactly with C_2 and R_2. Finally with S_1 upward again, the bridge is balanced exactly.[19] It is rarely necessary to repeat the procedure. (S_2, once set, is left untouched unless the oscillator leads are reversed.)

Jones and Josephs[1] and Shedlovsky[2] used 1,000-ohm resistors in the ratio arms and in the Wagner ground circuit of their bridges. It has

(17) Dye and Jones, *J. Inst. Elec. Engrs. London*, **72**, 169 (1933).

(18) No difference as great as 0.001% in measuring a resistance in the place of the cell can be detected when the frequency is changed from 500 to 4400 cycles.

(19) Those unfamiliar with separate terminal balance will be well repaid by a study of Astin's paper (ref. 4). (One of the Referees for this paper states that separate terminal balance was first proposed by Behr and Williams, *Proc. Inst. Radio Engrs.*, **20**, Fig. 13a, 985 (1932).)

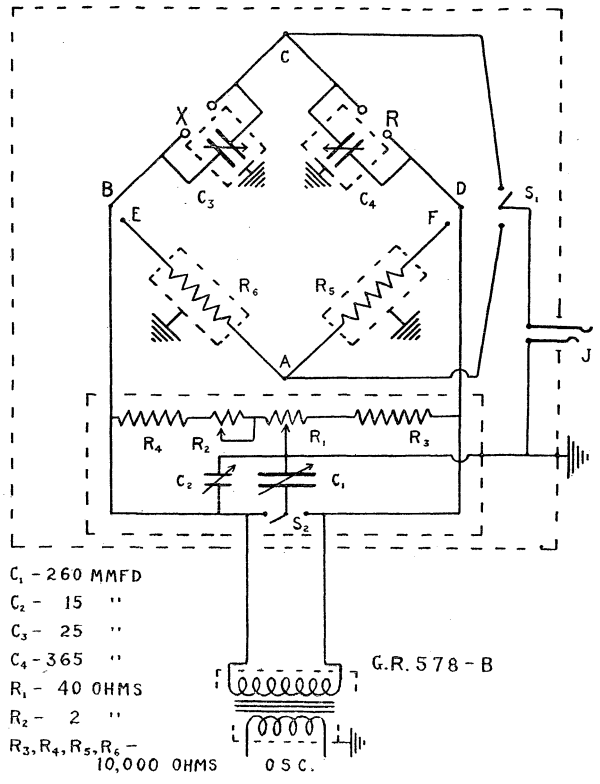


Fig. 3.

long been known[20] that one of the conditions for maximum balance sensitivity is to have the impedances of the four arms as nearly equal as possible. Therefore it seems desirable, for a bridge designed to cover the range of 1,000 to 200,000 ohms, to make the ratio arms and large Wagner ground resistances each equal to 10,000 ohms instead of 1000 ohms. When this combination is used with the readily available General Radio type 578-B bridge transformer step-up from oscillator to bridge, the oscillator–bridge impedance relationships are such as to give maximum energy transfer within the resistance range of the bridge.[21] This assists indirectly in making the bridge sensitivity comparatively constant. If the turns ratio of the transformer is such as to give maximum energy transfer from the oscillator to some impedance outside, or near one end of, the range represented by the bridge at the transformer secondary, considerable variation in apparent bridge sensitivity may be observed.

The chief source of stray pickup seems to be in the leads from the amplifier to the bridge and in the parts of the bridge connected directly to

(20) Reference 3, page 83.

(21) Different turns ratios of the transformer were tried, using a tapped telephone transformer.

these leads. For this reason, the shields around the ratio arms should be grounded directly instead of connected to the midpoint. Switch S_1 should be a toggle switch, the frame of which is connected to ground. The connections to the amplifier should be made by shielded plugs and cable.

From the above considerations it seems preferable: (1) that the Wagner ground be of the separate terminal balance type, (2) that 10,000 ohm resistances be used in the ratio arms and Wagner ground circuit, (3) that thorough shielding be employed. A description of the bridge control panel constructed by the author utilizing these features follows.

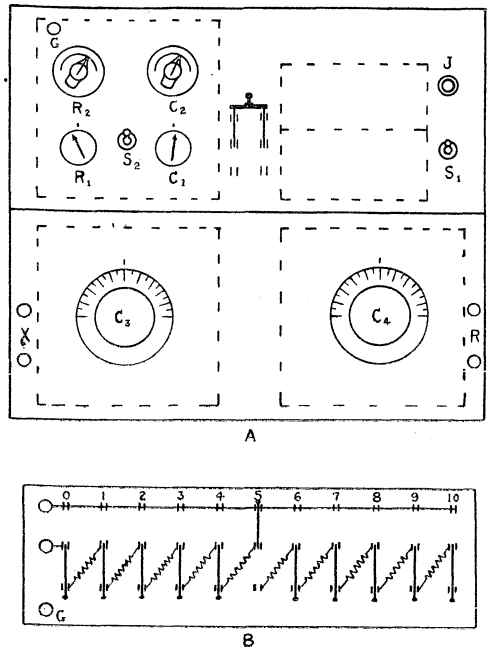


Fig. 4.

The panel itself consists of two $7'' \times 18'' \times 3/16''$ (18 × 45 × 0.5 cm.) hard rubber radio panels bolted together by means of a hardwood frame under the two panels (Fig. 4). The Wagner ground assembly is contained in one standard $6'' \times 6'' \times 6''$ (15 × 15 × 15 cm.) radio shield bolted to the panel underneath the farther left-hand corner. S_2 is a toggle switch. R_1 and R_2 are ordinary radio potentiometers. Each balancing condenser is contained by itself in a $6'' \times 6'' \times 6''$ shield. The farther right-hand section of the panel is shielded by copper sheet under the panel. It carries the ratio-arm shield, the jack for the amplifier plug and the toggle switch S_1. The ratio-arm shield is constructed of sheet copper just enough smaller than the other three shields to leave room for the switch and jack. The shield is divided into two compartments by a sheet of copper. Each compartment contains one of ratio arms. The reversing switch for the ratio arms[2] is a double-pole-double-throw knife switch mounted above the panel near the center. It is so connected as to reverse the connections E and F (Fig. 3) to B and D. The 10,000 ohm resistors are General Radio type 500-J without their cases. The two employed as ratio-arms should be so chosen (from the group to be used in constructing resistance boxes) as to have as nearly identical resistances as possible.

The walnut case which contains the control panel assembly is lined with thin sheet copper connected to the common ground. Shielded cable is used for the oscillator leads. The bridge transformer is connected step-up to the bridge from the oscillator. Its primary shield is grounded, its secondary shield is left floating. The transformer is placed about midway between oscillator and bridge. With this assembly it has not been found necessary to keep the bridge more than ten feet (3 meters) from the oscillator. The oscillator power supply is about five feet (1.5 meters) from the oscillator.

Suitable resistors are now produced by two companies: Leeds and Northrup and General Radio. General Radio resistors were used in this investigation. According to the General Radio catalog, their resistors have a higher temperature coefficient than Leeds and Northrup resistors, but are less expensive.[22] The temperature coefficient is not so high that thermostating is necessary, unless extreme precision is desired. Humidity changes sometimes cause greater changes in resistance than do temperature changes. In observations of the resistance of a sealed 10,000 ohm resistor measured against a combination of unsealed decade resistors no definite humidity effect could be noted. An extra precaution would be to dip the higher resistors in paraffin.[23]

A standard 602-F decade box is suitable for the three lowest decades (0.1, 1, 10 ohm steps). For the 100 ohm and 1000 ohm step decades, 510-D and 510-E decades were modified as follows. Each decade was removed from its close-fitting shield and mounted in a $6'' \times 6'' \times 6''$ radio shield. In the 1000 ohm step decade, in order to move them farther apart, alternate resistors were unsoldered and replaced projecting outward. The shields were then bolted together to make one two-dial decade box. Two 100,000 ohm resistance boxes were constructed using ten 10,000 ohm resistors in each.[24] The resistors were connected to small knife switches as suggested by Jones and Josephs[1] and shown in Fig. 4-B. Throwing only one switch gives the desired resistance without leaving any dead-end resistances. The wooden boxes are lined with grounded copper sheeting, but fortunately it is unnecessary to attempt to shield panel and switches. Unshielded leads are used between the resistance boxes.

(22) The temperature coefficient for Leeds and Northrup resistors is given as 0.0001% (Dike, *Rev. Sci. Instruments*, **2**, 393 (1931)). For General Radio resistors, the value is given as "less than 0.002%." Dike states that the Leeds and Northrup resistances are wound with manganin wire. In the specifications for their decade units, the General Radio catalog states that the lower resistors are wound with manganin wire and the 10,000 ohm cards with a combination of Nichrome and Ohmax to give "nearly zero" temperature coefficient. Therefore, in view of the fact that the General Radio Company is usually conservative in its performance claims, it seems probable that the temperature coefficients are considerably less than the value 0.002% given.

(23) Reference 3, p. 103.

(24) General Radio type 500-J resistances may be obtained without cases. Their a. c.-d. c. resistance difference is less than 0.1% at 50 kilocycles. Therefore, at one kilocycle it should be less than 0.001%.

Shielding of the network from stray pickup together with the absence of harmonics and hum from the oscillator have made it possible to balance the bridge to one or two parts per million using only the two-stage untuned amplifier described. When the bridge is at balance using this amplifier, no sound other than the barely perceptible hiss of the tube noise can be heard in the phones, even though the amplifier is untuned.

V. Summary

1. The conductivity bridge assembly has been investigated to determine to what extent it is advantageous for chemists to employ recent complicated and expensive developments in communication engineering in such a simple type of alternating current bridge.

2. Several different forms of the oscillator and its power supply, of the bridge network, and of the amplifier, incorporating recent developments in a. c. bridge methods and communication engineering, have been constructed and tested.

3. An adaptation of a new and simple low-distortion oscillator to conductivity bridge use is described. The oscillator plate supply is of the constant voltage type to reduce a. c. hum and stabilize the regeneration control.

4. Separate detector terminal balance to ground is suggested for conductivity bridges, and its adaptation and use described. The use of 10,000 ohm instead of 1,000 ohm resistors for the ratio-arms and Wagner ground circuit is proposed. Shielding to reduce stray pickup to a minimum is described.

5. A two-stage untuned amplifier with gain sufficient to permit balancing the bridge to one or two parts per million when oscillator harmonics, a. c. hum, and stray pickup have been practically eliminated is suggested for ordinary use of the bridge. A description of a three-stage tuned amplifier is also given.

6. Simplification, ease of construction, and lowered cost have been attained with no loss in precision and with some gain in convenience in the operation of the bridge.

BOSTON, MASS. RECEIVED JUNE 17, 1939

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF NEW HAMPSHIRE]

The Magnetic Rotation of Praseodymium, Samarium, and Europium Chlorides in Aqueous Solution at 25°

BY CHARLES M. MASON, JOSEPH W. HICKEY AND WILFRED K. WILSON

Recently[1] this Laboratory has presented the results of an investigation of the magnetic rotation of lanthanum and neodymium chlorides in aqueous solution. In the present work this method of investigation has been extended to the aqueous solutions of praseodymium, samarium, and europium chlorides. The Verdet constants have been obtained for these solutions over a concentration range from zero (pure water) to 3.5 molal. The dispersion has been studied from 4811 to 6438 Å.

Experimental Details

The rotations were measured with a Franz Schmidt and Haensch model 55 Landolt–Lippich triple-shadow polarimeter with non-magnetic frame. The instrument could be read to one-hundredth degree of arc. The light sources used were a mercury Lab-Arc, sodium Lab-Arc, and a Zeiss electrical spectral lamp fitted with Osram zinc and cadmium-filled bulbs. Monochromatic light was obtained by means of a Winkel–Zeiss monochromator inserted in the optical path between the spectral source and the polarimeter. By this means it was possible to isolate the principal lines of the various spectra with enough intensity left to properly operate the polarimeter.

The solution, the rotation of which was to be measured, was placed in a water-jacketed cell of Pyrex brand glass equipped with optical windows of the same material fused to the ends of the cell. This cell, as placed in the magnet, is shown in Fig. 1. The magnet consisted of 17 layers of approximately 162 turns each of No. 16 B. and S. gage, silk-covered copper wire wound on a bakelite tube 3.5 cm. inside diameter and 24 cm. long. The total number of turns was 2753 and the length of the coil was 23.1 cm. The length of the light path through the solution was 20.08 cm. measured by calibrating the tube with carefully purified sucrose. These data enabled the computation of the field strength, H, of the coil at any point along the axis. The product of the effective field strength times the length of the light path in the cell was determined by integration between limits based on the diameter of the first and last layers of turns to be 11,089.4 gauss. Integration for each layer of turns and summation gave a value of 11,084.6 gauss, a check well within the experimental error of the methods used to measure the angle of rotation. This field strength, when used to compute the Verdet constant of water, gave a value of 13.11×10^{-3} for that constant at 25° and wave length 5893 Å. This com-

(1) C. M. Mason, R. D. Gray and G. L. Ernst, THIS JOURNAL, **58**, 1600 (1936).

pares very favorably with the value of 13.07×10^{-3} given for water under the same conditions by Rodger and Watson[2] when it is considered that an error of 0.01° in rotation is equivalent to 0.05×10^{-3} in the Verdet constant. The rotation of the end plates was corrected by the determination of their rotation when the cell was empty.

A current of 4.0 ± 0.001 amperes was used, supplied by storage batteries. Current regulation was obtained with a potential divider which was a modification of that described by MacInnes and Longsworth.[3] A potential drop of 0.4 volt was maintained across a standard tenth ohm resistor by controlling the potential divider in the circuit with the magnet so that the galvanometer in the potentiometer circuit showed no deflection during the course of a measurement.

All refractive indices were measured at 25° with a standard Pulfrich refractometer. Care was taken to eliminate or correct for any error due to evaporation during the measurement. The temperature was controlled with the same equipment described below for the electromagnet. The refractometer was checked with carefully prepared distilled water using the tables of Tilton and Taylor[4] as a source of standard values.

The temperature in the polarimeter cell was kept constant by circulating water from a thermostat through the jacket of the tube. The temperature of the thermostat was kept so that the temperature in the water jacket of the cell was 25.00 ± 0.03°. A mercury thermoregulator connected through a relay to an electric heater maintained the thermostat at a constant temperature. The actual temperature in the cell was taken as the average of the two thermometers at the ends of the cell, as shown in Fig. 1. All thermometers used were checked against a standard thermometer which had been calibrated by the United States Bureau of Standards.

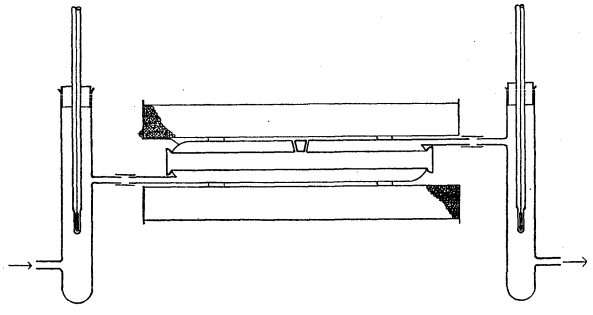


Fig. 1.—Cell, showing position in magnet.

The rare earth salts had been carefully prepared by repeated recrystallization. The samarium material had been obtained from the Maywood Chemical Co. and the praseodymium material from the estate of the late Charles James. The europium material was very kindly loaned to the department by Dr. Herbert N. McCoy. We wish at this time to thank Dr. McCoy for his generosity in loaning us this material. Its purification and purity is described elsewhere.[5] Since our sample of europium was from the same source, we used the atomic weight, 151.96, recently determined by Baxter and Tuemmler.[6] The chlorides were used as concentrated solutions prepared from the hydrates and analyzed for chloride ion and rare earth ion in the usual way.

The hydrated chlorides were prepared by the following procedure. The oxalate was ignited to the oxide in a muffle furnace at as low a temperature as possible and then dissolved in redistilled arsenic-free hydrochloric acid. It was found best to ignite the oxalate in small batches because it had a tendency to "boil" on decomposition and spatter out of the dish. The oxide was then cooled and added in small portions to the arsenic-free hydrochloric acid in a large beaker. Since some of the oxalate decomposed only to the carbonate, care was taken to prevent the solution from foaming over at this point. It was necessary in some cases to heat the solution for a time on a steam-bath to dissolve the last of the oxide. If, as often was the case, there was carbon remaining from the ignition, it was filtered out at this point. Igniting at high temperatures to remove all of the carbon often makes the oxide difficultly soluble and was to be avoided if possible.

After filtering, the solution was evaporated to a sirup on the steam plate or bath and the chloride shaken out at 0° with hydrogen chloride gas. This hydrated salt was then dried in a current of warm air in a hot-air drier until all of the hydrogen chloride seemed to be removed. The dried salt was then dissolved in a minimum amount of water, one or two drops of concentrated hydrochloric acid added to prevent hydrolysis, and evaporated to a thick sirup. This may be done either over a steam-bath or over a burner. In either case one must be careful to evaporate until just before the sirup begins to crystallize. Not enough evaporation will reduce the yield and too much will cause the whole to set to one solid mass which is of no value and must be dissolved in water and reworked. The sirup was quickly chilled to 0° while stirring very rapidly with a glass stirrer propelled by a motor. This action produced a mass of fine crystals of the hydrate which were easily filtered onto a fritted-glass plate and sucked free of mother liquor. The crystals were then washed with absolute ethanol and dried in a hot-air drier. A good test for the removal of hydrogen chloride was found to be as follows. The hydrate was placed in a glass-stoppered bottle for several days and then examined to see if any odor of the gas had collected in the top of the bottle. Its sharp penetrating odor was very easy to detect.

All of the water used was distilled in an ordinary electrically-heated laboratory still. Only about one-third of the vapor was condensed and collected, the rest being allowed to escape as steam. By employing this procedure, and protecting the water during cooling from the air, it was found that the water so obtained was free of carbon dioxide and other gases. The conductance of the water so obtained was of the order of 10^{-6} reciprocal ohms at 25°.

(2) J. W. Rodger and W. Watson, *Z. physik. Chem.*, **19**, 356 (1896).

(3) C. M. Mason and R. D. Gray, *Rev. Sci. Instruments*, **7**, 289 (1936); D. A. MacInnes and L. C. Longsworth, *Chem. Rev.*, **11**, 189 (1932).

(4) L. W. Tilton and J. K. Taylor, *J. Research Natl. Bur. Standards*, **20**, 419 (1938).

(5) H. N. McCoy, THIS JOURNAL, **57**, 1756 (1935); **58**, 1577, 2278 (1936); **59**, 1131 (1937).

(6) G. P. Baxter and F. D. Tuemmler, *ibid.*, **60**, 602 (1938).

Results

The relationship of the magneto-optical rotation to the field strength and length of the light path is expressed by Verdet's law[7]

$$r = VHl \cos \alpha \qquad (1)$$

where r is the rotation in minutes, V is the Verdet constant, H is the field strength, l is the length of the light path in cm., and α is the angle between the path of light and the axis of the magnetic field. For the Faraday effect where the axis of the magnet and the rays of light are parallel, this law reduces to

$$r = VHl \qquad (2)$$

When an electromagnet of less than infinite length is used, this becomes

$$r = V \int H \, dl \qquad (3)$$

where $H\ dl$ is the average field strength over the light path used. If we choose to calibrate our cell with some pure liquid whose Verdet constant is known, such as water,[2] we find that

$$V = rV_s/r_s \qquad (4)$$

where r_s and V_s are the rotation and Verdet constants of the standard liquid used and r and V are those for the solution being measured. The Verdet constants of the rare earth solutions were obtained by measuring the magnetic rotation of the various solutions and then computed by means of equation (4). The results obtained are given in Table I.

It was also found necessary to determine the densities of the solutions used where they could not be found in the literature. These were determined in a 25-g. Regnault specific gravity bottle in duplicate and are given in Table III as a part of the calculation of the molecular and specific rotation. The refractive indices which were obtained have been expressed in terms of linear equations of the type $\eta = \eta_0 + am + bm^2$ where η is the refractive index, η_0 the refractive index of water, a and b are constants and m is the molality. The values of the constants of these equations are given in Table II, and the refractive indices reproduced by these equations are to within the experimental error, namely, ± 0.0002.

TABLE I

THE VERDET CONSTANTS OF THE RARE EARTHS IN AQUEOUS SOLUTION IN MIN./GAUSS/CM.

Praseodymium Chloride, $PrCl_3$ (mol. wt. 247.29)

Molality[a]	$V \times 10^3$ 5086 Å.	5461 Å.	6362 Å.	6438 Å.
3.2173	−32.73	−26.68	−19.23	−18.75
3.00	−29.28	−23.78	−17.52	−16.66
2.50	−21.53	−17.41	−12.53	−12.13
2.00	−13.71	−10.77	− 7.66	− 7.50
1.50	− 5.84	− 4.39	− 2.95	− 2.89
1.00	2.25	2.20	1.66	1.71
0.50	10.17	8.92	6.43	6.32
.25	14.03	12.32	8.90	8.52
.00	18.00	15.50	11.19	10.81

Samarium Chloride, $SmCl_3$ (mol. wt. 256.80)

Molality	$V \times 10^3$ 5086 Å.	5461 Å.	5893 Å.	6438 Å.
3.2644	28.02	23.78	20.19	16.82
3.00	27.69	23.52	19.88	16.55
2.50	26.24	22.55	18.90	15.96
2.00	24.96	21.37	18.10	15.00
1.50	23.46	20.17	16.96	14.08
1.003	21.69	18.64	15.75	13.34
0.50	20.25	17.25	14.44	12.43
.25	18.88	16.29	13.82	11.50
.10	18.37	15.86	13.50	11.20
.00	18.00	15.50	13.07	10.82

Europium Chloride, $EuCl_3$ (mol. wt. 258.33)

Molality	$V \times 10^3$ 4811 Å.	5086 Å.	5461 Å.	5893 Å.	6362 Å.	6438 Å.
2.847	27.16	23.94	20.71	17.73	15.47	15.06
2.50	26.84	23.73	20.41	17.47	15.32	14.92
2.00	26.20	22.98	19.77	16.98	14.89	14.35
1.50	25.06	21.99	18.85	16.07	14.15	13.71
1.00	23.94	20.73	17.94	15.21	13.45	12.85
0.50	22.23	19.44	16.82	14.23	12.32	11.62
.25	21.37	18.73	16.12	13.66	11.78	11.47
.00	20.57	18.00	15.50	13.07	11.19	10.81

[a] Moles of anhydrous salt per 1000 g. of water.

(7) E. Verdet, *Ann. chim. phys.*, **41**, 370 (1854); *ibid.*, **43**, 37 (1854); *ibid.*, **52**, 129 (1858); *ibid.*, **69**, 415 (1863).

TABLE II

CONSTANTS FOR THE EQUATIONS FOR THE REFRACTIVE INDICES OF RARE EARTH SOLUTIONS

$\eta = \eta_0 + am + bm^2$

Wave length, Å.	η_0	a	b
	Praseodymium Chloride		
5086	1.33545	0.04658	−0.00261
5461	1.33386	.04704	− .00289
6362	1.33112	.04638	− .00285
6438	1.33071	.04644	− .00287
	Samarium Chloride		
5086	1.33545	0.04628	−0.00266
5461	1.33386	.04614	− .00269
5893	1.33238	.04578	− .00267
6438	1.33071	.04572	− .00276
	Europium Chloride		
4811	1.33678	0.04661	−0.00276
5086	1.33545	.04642	− .00278
5461	1.33386	.04586	− .00269
5893	1.33238	.04516	− .00259
6362	1.33112	.04527	− .00268
6438	1.33071	.04538	− .00272

Discussion

Okazaki[8] has published a series of papers on the

(8) A. Okazaki, *Mem. Ryojun Coll. Eng.*, **6**, 181 (1933); *ibid., Inouye Commemoration Volume*, 209 (1934); **9**, 13, 101 (1936); **10**, 89, 115 (1937); **12**, 33, 45 (1939).

Faraday effect in solutions of electrolytes. He has used the following modification of the Schönrock mixture rule

$$(w) = t_1(w_1) + t_2(w_2) \quad (5)$$

where w, w_1 and w_2 are the specific rotations of the solution, solvent, and solute, respectively, and t_1 and t_2 are the weight percentages of the solvent and the solute. The molecular rotation, $M(w)$, may be obtained easily by multiplying the specific rotation by the molecular weight. We have used this formula to compute the molecular rotation of the solute, $M(w_2)$. The values so computed are included in Table III. We have also included the molecular rotation of aluminum, lanthanum, and neodymium chlorides calculated from data obtained previously.[1,9]

TABLE III

THE MOLECULAR ROTATION OF RARE EARTH CHLORIDES IN SOLUTION

Aluminum Chloride ($AlCl_3$)			Neodymium Chloride ($NdCl_3$)	
	$M(w_2)$			$M(w_2)$
Molality	5461 Å.	5893 Å.	Molality	5461 Å.
2.78	3.97	3.08	0.50	−7.14
2.00	3.67	3.14	.40	−7.11
1.50	3.64	3.20	.30	−6.71
1.00	3.65	3.25	.20	−6.82
0.50	3.83	3.48	.10	−7.17
0.10	..	3.45	Av.	−6.99
Av.	3.75	3.27		

Lanthanum Chloride ($LaCl_3$)					
	$M(w_2)$			$M(w_2)$	
Molality	5461 Å.	5893 Å.	Molality	5461 Å.	5893 Å.
3.40	3.93	3.31	1.7509	4.18	3.53
3.10	3.97	3.34	1.40	4.17	3.50
2.80	3.98	3.36	0.9967	4.19	3.48
2.50	4.00	3.42	.80	3.97	3.53
2.20	4.02	3.43	.40	4.05	3.61
			Av.	4.05	3.45

Samarium Chloride ($SmCl_3$)					
			$M(w_2)$		
Molality	Density	5086 Å.	5461 Å.	5893 Å.	6438 Å.
3.2644	1.6558	4.00	3.33	2.85	2.40
3.00	1.6115	4.12	3.43	2.91	2.44
2.50	1.5231	4.09	3.51	2.91	2.54
2.00	1.4291	4.19	3.54	3.03	2.52
1.50	1.3298	4.26	3.64	3.04	2.54
1.003	1.2250	4.21	3.58	3.05	2.84
0.50	1.1138	4.92	3.86	3.04	3.48
0.25	1.0563	3.87	3.46	3.26	2.94
Av.		3.96	3.54	3.01	2.60

Europium Chloride ($EuCl_3$)							
				$M(w_2)$			
Molality	Density	4811 Å.	5086 Å.	5461 Å.	5893 Å.	6362 Å.	6438 Å.
2.847	1.5880	3.18	2.85	2.49	2.20	2.00	1.97
2.50	1.5244	3.34	3.03	2.60	2.30	2.13	2.11
2.00	1.4298	3.58	3.16	2.71	2.45	2.29	2.19
1.50	1.3298	3.68	3.26	2.75	2.44	2.42	2.31
1.00	1.2247	3.97	3.25	2.89	2.52	2.59	2.36
0.50	1.1140	3.81	3.30	3.01	2.63	2.53	1.87
0.25	1.0562	3.64	3.30	2.81	2.64	2.60	2.88
Av.		3.60	3.16	2.75	2.45	2.37	2.24

Praseodymium Chloride ($PrCl_3$)				
		$M(w_2)$		
Molality	5086 Å.	5461 Å.	6362 Å.	6438 Å.
3.2173	−16.9	−14.1	−10.1	−9.9
3.00	−16.8	−13.9	−10.2	−9.7
2.50	−16.6	−13.8	− 9.9	−9.6
2.00	−16.3	−13.5	− 9.7	−9.4
1.50	−16.1	−13.4	− 9.5	−9.2
1.00	−15.7	−13.3	− 9.5	−9.1
0.50	−15.5	−13.0	− 9.4	−8.9
0.25	−15.7	−12.5	− 9.0	−9.0
Av.	−16.20	−13.44	− 9.66	−9.35

An examination of Table III shows that the mixture rule (equation 5) when applied to the data in Table I holds within limits of experimental error at concentrations below about 3 molal, which represents about 40% anhydrous salt in the solutions. There are some discrepancies in the more dilute solutions but in this region where the rotation is small the errors of measurement are magnified in the computation of the Verdet constant and further magnified in the computations of the molecular rotation. These results in general confirm and are consistent with the results obtained by Okazaki[8] for many other electrolytes.

Roberts, Wallace and Pierce[10] have calculated for cerium sulfate solutions a quantity Δ/W which they call the "specific rotation." This is defined in the equation

$$\Delta = \frac{nV}{(n^2+2)^2 d} - \frac{n_w V_w}{(n_w^2+2)^2 d_w}(1 - W/100) \quad (6)$$

where n is the refractive index of the solution, n_w that for water, and W is the number of grams of salt per 100 g. of solution. V is the Verdet constant for the solution and V_w is that for water. From the theory from which this equation is developed, the quantity Δ/W should be independent of the concentration for any given wave length. This constant is independent of the concentration for cerium nitrate[10] and an examination of the data given in Table IV will show if this be true for the salts studied in this investigation.

A study of the data in Table IV shows that the values of Δ/W obtained for solutions of praseodymium are constant within limits of error but that in the case of samarium and europium chlorides there seems to be a definite trend to decrease in the more concentrated solutions. It may also be noted that all specific rotations decrease with increasing wave length.

(9) C. M. Mason, THIS JOURNAL, **60**, 1644 (1938).

(10) R. W. Roberts, L. A. Wallace and I. T. Pierce, *Phil. Mag.*, (7) **17**, 934 (1934).

TABLE IV

"SPECIFIC ROTATIONS," Δ/W, OF THE RARE EARTH SOLUTIONS

Praseodymium Chloride ($PrCl_3$)			
	$\Delta/W \times 10^5$		
Molality	5086 Å.	5461 Å.	6438 Å.
3.00	−6.02	−5.01	−3.51
2.50	−6.01	−5.01	−3.50
2.00	−6.00	−4.89	−3.48
1.50	−6.01	−5.02	−3.47
1.00	−5.96	−5.04	−3.46
0.50	−5.95	−5.02	−3.44
0.25	−6.09	−4.89	−3.53
Av.	−6.00	−4.98	−3.48

Samarium Chloride ($SmCl_3$)				
	$\Delta/W \times 10^5$			
Molality	5086 Å.	5461 Å.	5893 Å.	6438 Å.
3.2644	1.17	0.97	0.84	0.72
3.0	1.21	1.01	.86	.74
2.50	1.22	1.04	.87	.78
2.0	1.26	1.07	.92	.78
1.50	1.30	1.11	.93	.80
1.003	1.30	1.19	.94	.92
0.50	1.57	1.22	.95	..
0.25	0.80	1.21	..	..
Av.	1.29	1.10	.90	.79

Europium Chloride ($EuCl_3$)					
	$\Delta/W \times 10^5$				
Molality	4811 Å.	5086 Å.	5461 Å.	5893 Å.	6438 Å.
2.847	0.86	0.78	0.69	0.60	0.56
2.50	.91	.85	.73	.65	.61
2.00	1.00	.90	.78	.71	.65
1.50	1.03	.94	.80	.72	.69
1.0	1.14	.95	.85	.75	.72
0.5	1.05	.98	.90	.80	.54
0.25	0.92	.99	.84	.81	..
Av.	.99	.91	.80	.72	.62

An interesting anomaly appears in the case of the results for europium chloride. Samarium is definitely less paramagnetic than cerium or praseodymium, as shown by the fact that the Bohr magneton number is about 3.6 for praseodymium and 2.5 for cerium, whereas for samarium it is only about 1.5,[11] and the decidedly less magnetic optical rotatory power of samarium might be explained on this basis. In the case of europium, however, the magneton number given by Van Vleck[11] and since recalculated by Schmidt[12] is about 3.4. Therefore, one might expect that europium would have magnetic optical rotatory powers of the order of those of cerium and praseodymium rather than of the order of magnitude of samarium which it does have. We are not able to offer an explanation of this apparent anomaly.

Summary

The magnetic rotations of the aqueous solutions of praseodymium, samarium, and europium chlorides have been measured at 25° for the wave lengths λ4810.5, λ5085.8, λ5460.7, λ5893, λ6362.4, and λ6438.47 Å. except in those cases where absorption interfered.

The refractive index of these aqueous solutions has been reported at 25°.

The Verdet constants have been calculated, those for samarium and europium solutions being positive and those for praseodymium solutions being negative when referred to water.

The specific and molecular rotations have been calculated and the variation of these properties with concentration noted and discussed.

An interesting anomaly has been observed in the comparison of the Verdet constants with the known magnetic moments of these ions.

(11) These data have been taken from Van Vleck, "The Theory of Electric and Magnetic Susceptibilities," Oxford University Press, Oxford, 1932, p. 243.

(12) Th. Schmidt, *Z. Physik*, **108**, 408 (1938).

DURHAM, NEW HAMPSHIRE RECEIVED JULY 19, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Photochemistry of Diiodoacetylene and Tetraiodoethylene

BY JOHN W. TAMBLYN AND GEORGE S. FORBES

The present research represents a further attempt to correlate the mechanisms of photoiodination on either side of the convergence limit of iodine, 499 mμ. Brown[1] states that a continuum in the red, corresponding to production of normal atoms, is not visible below 50°. Bonhoeffer and Harteck[2] hold that this mode of dissociation is of minor importance photochemically. The data of Rabinowitch and Wood,[3] however, might lead to a contrary conclusion. Dickinson and Nies[4] re-evaluated the data of Schumacher and Steiger[5] in terms of the influence of absorbed light intensity. They found the relative efficiencies of quanta corresponding to λλ 578, 546 and 436 mμ to be 0.75, 0.87 and 1.00, respectively. The temperatures were 76.6 and 99°. On the other hand,

(1) Brown, *Phys. Rev.*, **38**, 1187 (1931).

(2) Bonhoeffer and Harteck, "Grundlagen der Photochemie," Steinkopff, Dresden, 1933, p. 94.

(3) Rabinowitch and Wood, *Trans. Faraday Soc.*, **32**, 547 (1936).

(4) Dickinson and Nies, THIS JOURNAL, **57**, 2382 (1935).

(5) Schumacher and Steiger, *Z. physik. Chem.*, **B12**, 348 (1931).

Forbes and Nelson[6] found that light of λ 644 mμ was much less efficient than light of λ 436 mμ in promoting iodination of *cis*-butene in chloroform. Quanta corresponding to λ 644 mμ are still substantially greater than the minimum requisite for production of normal atoms. Rollefson[7] has ably discussed the issues involved in this situation.

Diiodoacetylene represents a type of compound not yet investigated with the above stated problem in mind. The thermal addition of iodine takes place slowly in carbon disulfide[8] and rapidly in boiling toluene.[9] We found that the photochemical reaction proceeds smoothly in visible light, at 0°, without important thermal reaction. We varied light intensity, and concentrations, measured quantum yields and temperature coefficients, and set up rate equations valid for the different spectral regions.

Materials.—Diiodoacetylene was prepared according to Dehn[10] with the additional precaution that the acetylene was washed with lead acetate to remove hydrogen sulfide.[11] The product was twice recrystallized from petroleum ether. After storage at 0° in the dark for a period of nine months, no change in appearance or in melting point could be detected.

Tetraiodoethylene was prepared following the directions of Datta and Prosad,[12] also by boiling diiodoacetylene in toluene with purified iodine. The product was in each case recrystallized twice in toluene distilled from sodium.

Hexane, from Eastman Kodak Co., was shaken with portions of concentrated sulfuric acid until one remained colorless for several hours. Three or four treatments with fuming acid followed over a period of one to two days. A final washing with alkaline permanganate preceded distillation. Our criterion of purity was 99% transmission of light of λ254 mμ in a 5-mm. layer. The product, which boiled over the range 64 to 69°, was evidently a mixture of hydrocarbons, but it did not react thermally with iodine, nor photochemically even in light of λ254 mμ.

Apparatus and Method.—The quartz reaction cell previously used by Forbes and Nelson[6] had plane parallel faces 5 × 2 cm. in area and 1 cm. apart. It was surmounted by a quartz cylinder with a ground-in hollow Pyrex stopper through which passed sealed-in tubes for ingress and egress of nitrogen. For removal of oxygen, which retards many halogenation reactions, the best method found was to bubble nitrogen (said to be 99.93% pure) through the reaction mixture at dry-ice temperature, for an hour at the rate of two bubbles per second. After this, the solution was warmed to 0° and shaken to redissolve precipitated iodine. The following relative reaction rates were observed at 0° and in constant red light after an hour's treatment with the following mixtures of nitrogen and oxygen, respectively:

p_{O_2} (atm.)	0.0000[b]	0.0007[a]	0.028	0.21	0.995[c]
Rate, R	9.3	9.5	1.92	1.55	0.78

[a] Tank nitrogen. [b] Nitrogen treated with hot copper. [c] Tank oxygen.

In addition, R was found to be 3.9 in a solution prepared in air, frozen at liquid air temperature, pumped out, melted, again frozen, and so on, three times in all. Willard and Daniels[13] repeated such a cycle six or seven times before their reaction rates reached maximum values. Unless otherwise specified, all solutions mentioned below were freed from oxygen by tank nitrogen as described above.

The reaction cell[6] was lowered into an air thermostat[6] with a double quartz window to avoid condensation of moisture. Temperature was held at 0 ± 1° by a regulated current of chilled air. Whenever a prism monochromator was not employed, a light-filter cell one inch thick was in contact with the thermostat window. The solution was shaken as often as seemed desirable.

Since the quantum yields varied with incident light flux, the divergent beam from the exit slit of a monochromator, having a wide range of intensity over its cross section, would have been unsuitable in certain experiments. A tungsten lamp was employed with its U-shaped filament parallel to the cell window. Thanks to an efficient voltage regulator, the readings of an ammeter in series were constant within 3%. Known relative light intensities were realized by use of the inverse square law, valid within 1% except perhaps at the highest point of Graph II, Fig. 1.

Analytical.—Immediately after photolysis the solution was analyzed in dim light. Grease was carefully removed from the mouth of the cell, and the mixture was transferred to a flask containing 1 g. of potassium iodide in 5 cc. of water. The cell was rinsed into the flask with a little more potassium iodide solution, after which the iodine was titrated, while shaking, with 0.01 N thiosulfate. The thermal reaction, never more than 3% of the whole, was subtracted. The speed of this reaction was not measurably altered by packing the cell with quartz fragments, glass beads or glass wool.

Influence of Light Intensity.—To minimize undesirable thermal reactions, experiments were conducted at 0°. In Series I a 200-watt bulb was used. A ferric thiocyanate filter transmitted light, λ ≧ 600 mμ, according to visual observations with a Hilger wave-length spectrometer. No change in the absorption limit could be detected after exposure. In Series II, a 500-watt bulb was used behind a Corning filter H R Signal Red, λ ≧ 610 mμ. In Series III, blue light, λ ≦ 480 mμ, was transmitted by a cuprammonium sulfate filter. Exposure times varied from a few minutes to an hour. In Fig. 1, $\log_{10} R$ (reaction

(6) Forbes and Nelson, THIS JOURNAL, **59**, 693 (1937).

(7) Rollefson, "The Photochemistry of the Halogens," Hermann et Cie., Paris, 1938, esp. pp. 5–9 and 48–49.

(8) Maguenne and Taine, *Z. allgem. österr. Apoth.-Ver.*, **31**, 810 (1893).

(9) Biltz, *Ber.*, **30**, 1202 (1897).

(10) Dehn, THIS JOURNAL, **33**, 1598 (1911).

(11) Biltz and Küppers, *Ber.*, **37**, 4415 (1904).

(12) Datta and Prosad, THIS JOURNAL, **39**, 451 (1917).

(13) Willard and Daniels, *ibid.*, **57**, 2240 (1935).

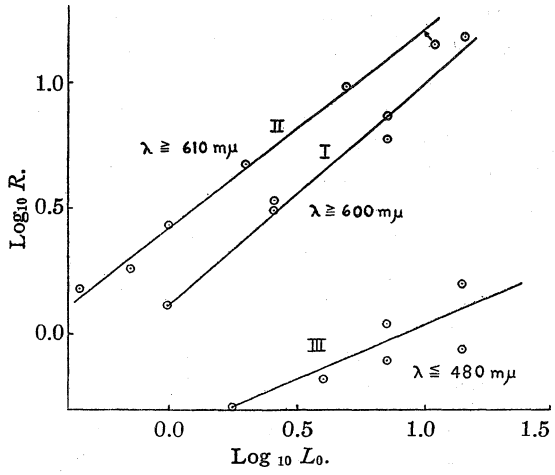


Fig. 1.—Influence of light intensity L_0 on reaction rate, R. The values of R on line II were multiplied by ten before plotting.

rate) is plotted against log L_0 (incident light flux), both in arbitrary units. As filter II had a relatively low transmission, and lamp distances were greater, all values of R_{II} were multiplied by ten before plotting. Drawing the best straight lines, $\Delta \log R_I = 0.90\ \Delta \log L_0$; $\Delta \log R_{II} = 0.78\ \Delta \log L_0$; and $\Delta \log R_{III} = 0.40 \log L_0$. Giving Series II slightly more weight than Series I, we wrote $R_{red} = k_{red} L_0^{0.8}$ and $R_{blue} = k_{blue} L^{0.4}$. An additional series, IV, was carried out with a dichromate filter, $\lambda \geqq 530$ mμ. Although the results are open to objection because air was not removed, it appears reasonable that $R_{yellow} = k_{yellow} L^{0.65}$; that is, the exponent lies between 0.8 and 0.4.

Influence of Diiodoacetylene Concentration.—This was varied from 8×10^{-4} to 8×10^{-2} M, and no visible light was absorbed. Lamp I with filters I and III was employed. Figure 2 gives the experimental data in comparison with curves plotted from the equations

$$R_{red} = \frac{[C_2I_2]}{0.038 + 4.0[C_2I_2]} \text{ and } R_{blue} = \frac{[C_2I_2]}{0.108 + 28[C_2I_2]}$$

which suffice to predict these data within experimental error.

Iodine concentration could not be varied widely, because saturation was reached at 10^{-2} M, and light transmission became excessive below 1.5×10^{-3} M. The solutions were made up determinate at 25° and a correction applied for the contraction to 0°. A mercury lamp[14] operated under atmospheric pressure, and the radiations λλ 578, 546 and 436 mμ were isolated by a monochromator having a large prism of extra dense

(14) Forbes and Heidt, THIS JOURNAL, **53**, 4349 (1931).

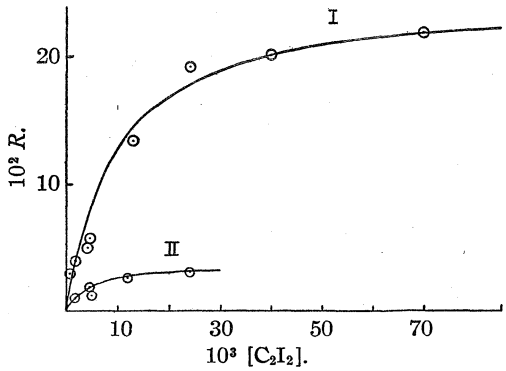


Fig. 2.—Influence of diiodoacetylene concentration on reaction rate, R. On Curve I, $\lambda \geqq 600$ mμ, and on Curve II, $\lambda \leqq 480$ mμ.

flint glass. Red light was similarly isolated from a constant spark[15] between cadmium bars. L_0 was measured radiometrically by the method of integration.[16] The extinction coefficients of iodine in hexane at 0° were obtained by interpolation of data by Groh and Papp[17] which we also checked at several points. Absorbed light energy was referred to average iodine concentration and average absorption in every case. The quantum yield ϕ is the ratio of m the number of iodine molecules reacting photochemically to q the number of quanta absorbed by iodine per second. Figure 3 summarizes these experiments. The temperature was

TABLE I

IODINE CONCENTRATIONS AND QUANTUM YIELDS

λ, mμ	Time, sec.	$q \times 10^{-15}$	$m \times 10^{-18}$	ϕ	$[I_2] \times 10^3$	$\phi/[I_2]$
644	870	2.9	2.3	0.9	4.6	0.20
578	1230	3.5	1.5	.35	1.32	.27
578	900	4.2	2.7	.71	2.67	.27
578	750	4.6	4.9	1.4	4.41	.32
578	600	5.0	3.7	1.2	4.55	.26
578	660	5.0	3.6	1.1	4.57	.24
578	750	3.7	4.7	1.7	9.40	.18
						.25
546	1500	4.0	7.8	1.3	4.98	.26
546	900	3.7	4.6	1.4	4.98	.28
						.27
436	1200	0.46	0.65	1.2	1.42	.85
436	900	.95	1.80	2.1	2.77	.76
436	1420	.99	6.4	4.6	4.23	1.1
436	810	1.03	6.5	6.2	4.24	1.5
436	740	1.27	3.7	4.0	4.54	0.88
436	810	1.15	3.7	4.0	4.55	.88
436	540	1.33	3.3	4.6	4.59	1.0
436	750	1.28	4.3	4.5	9.44	0.48
						0.92

(15) Brackett and Forbes, *ibid.*, **53**, 3973 (1931).
(16) W. G. Leighton and Forbes, *ibid.*, **52**, 3139 (1930).
(17) Groh and Papp, *Z. physik. Chem.*, **149**, 153 (1930).

0°, and initial $[C_2I_2]$ was uniformly 0.005. Although measurements at λ 436 mμ were unexpectedly discordant, no trend in $\phi/[I_2]$ is anywhere apparent.

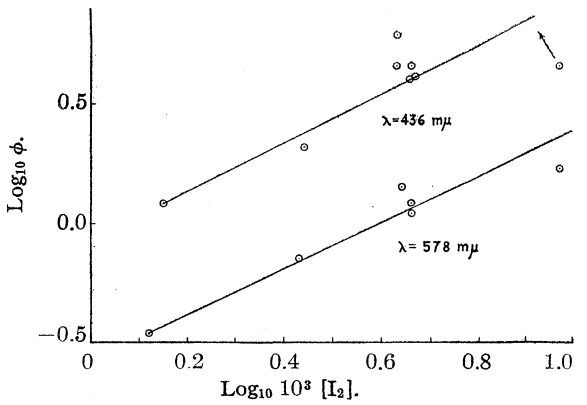


Fig. 3.—Influence of iodine concentration on quantum yield, ϕ.

Evidently $\phi/[I_2]$ increases slowly with decreasing wave length as the convergence limit is approached, and becomes considerably greater after this has been passed.

The ten-degree temperature coefficient Z of the photochemical reaction was found from eleven measurements at −32, 0 and 25°, behind the ferric thiocyanate and cuprammonium sulfate filters. The relative fractions of L_0 absorbed at each temperature were estimated by interpolation of data by Groh and Papp[17] on iodine at −53° and at room temperature. In red light Z = 1.11 between −32 and 0°, Z = 1.22 between 0 and 25°. In blue light both the corresponding values of Z were 1.18. Within experimental error all these values of Z can be considered identical.

To exclude the possibility of side reactions, a solution of average composition, free from oxygen, was exposed to red light until 5.23×10^{19} molecules of iodine had reacted. The hexane, together with the unchanged diiodoacetylene, was evaporated off. The residue, at constant weight, was 0.0450 g., *i. e.*, the weight of 5.16×10^{19} molecules of tetraiodoethylene. The melting point was 188° both before and after addition of a known sample of tetraiodoethylene. Apparently, therefore, the only important over-all reaction is $C_2I_2 + I_2 = C_2I_4$.

Experiments without removal of oxygen were performed at 0° and at 25° in purified hexane and in absolute ethanol. Both initial concentrations were 0.005 *M*. The only reaction product detected was tetraiodoethylene. In Table II, *d* is the extreme variation in ϕ_{air} within the group of experiments considered. In the last column, ϕ refers to experiments in solutions with the same initial concentrations but with oxygen removed. The second and third of these were performed at 0° but have been referred to 25° through multiplication by $(1.18)^{2.5}$.

TABLE II

QUANTUM YIELDS, OXYGEN NOT REMOVED

λ, mμ	Solvent	*t*	Expts.	*d*	ϕ_{air}	ϕ
644	C_6H_{14}	0°	2	0.02	0.16	0.9
546	C_6H_{14}	25°	8	.07	.25	1.95
436	C_6H_{14}	25°	5	.22	.62	6.8
436	C_2H_5OH	25°	2	.01	**.15**	
366	C_2H_5OH	25°	2	.04	**.17**	

The retarding effect of oxygen, in hexane solutions at least, seems to increase with decreasing wave length. The solvation of iodine in ethanol may well be responsible for the lower quantum yields there. Berthoud and Mosset,[18] likewise, found triiodide ions only one-fifth as effective as iodine molecules for iodination of allyl alcohol.

Photolysis of tetraiodoethylene was studied in hexane using an argon-filled mercury resonance lamp. About 83% of the total radiation was of wave length 254 mμ according to measurements by Leighton and Leighton.[19] Radiant flux was measured by actinometry with uranyl oxalate; the transmission of which for other wave lengths was much like that of tetraiodoethylene. Absorption of light by the iodine and diiodoacetylene formed by photolysis was shown to be negligible.

In absence of oxygen, two distinct reactions were observed: first a rapid liberation of 85% of the iodine corresponding to the equation $C_2I_4 = C_2I_2 + I_2$, then a (much slower) photolysis of diiodoacetylene, during which a characteristic odor different from that of diiodoacetylene was noticeable. In one experiment not carried to the second stage, liberated iodine was titrated; hexane and diiodoacetylene were evaporated off. The original weight of tetraiodoacetylene minus the weight of the residue corresponded within one milligram to the weight of iodine found by titration. Two other experiments (oxygen removed) gave ϕ = molecules of I_2 produced/quanta absorbed by C_2I_4 = 0.77 and 0.79. Parallel experiments without removal of oxygen gave ϕ = 0.81, 0.80 and 1.00 in hexane, also ϕ = 0.50, 0.57 and 0.58 in ethanol.

(18) Berthoud and Mosset, *J. chim. phys.*, **33**, 287 (1936).
(19) Leighton and Leighton, *J. Chem. Education*, **12**, 139 (1935).

Photolysis of Diiodoacetylene in Hexane.—In absence of oxygen (λ = 254 mμ), two reaction stages were observed. At the start iodine appeared very slowly and the solution became somewhat milky. Later, but before the diiodoacetylene had been largely decomposed, iodine was released more rapidly. The milkiness tended to disappear, and a brownish deposit formed upon the cell window. Only about 55% of the original combined iodine could be liberated as such by light. The brown deposit evolved iodine when dried and heated, or when treated with alcohol or with potassium iodide solution. When the exposed solution was evaporated after extraction of iodine, a pale yellow oil remained having the odor already noted in the second stage of the photolysis of tetraiodoethylene. This oil turned brown upon exposure to air. If the photolysis was conducted in hexane or ethyl alcohol without exclusion of air, the liberation of iodine began at once. No milkiness or brown deposit was observed at any time, but carbon dioxide was detected when oxygen was bubbled first through the irradiated solution and then through barium hydroxide.

Attempts at photoiodination of tetraiodoethylene were unsuccessful in benzene, carbon disulfide, hexane and ethanol. Red, orange and white light was employed in succession, and temperatures ranged from −40 to 25°.

Reaction Mechanism in Blue Light.—A complete rate expression for addition of iodine to diiodoacetylene in blue light follows from the experiments described above, in which L_0, $[I_2]$, and $[C_2I_2]$ were varied one at a time. A suitable correction for incomplete absorption of incident light was made in each separate experiment.

$$-\left[\frac{d[I_2]}{dt}\right]_{\text{over-all}} = k_{\text{blue}} L_0^{0.4} [I_2]^{1.0} \frac{[C_2I_2]}{a_{\text{blue}} + b_{\text{blue}}[C_2I_2]}$$

Schumacher and Wiig,[15] for the iodine-sensitized decomposition of ethylene iodide, found a ten-degree temperature coefficient Z of 1.57, corresponding to an activation energy E of 11.8 kcal. per mole which they assigned to a reaction analogous to the reverse of equation (3) above. Since ΔH for this step should be nearly zero,[20] E should be nearly the same in both directions. We found for the iodination of diiodoacetylene Z = 1.18, corresponding to E = 2.5 kcal./mole. Then unless the formation of tetraiodoacetylene at λ 436 mμ proceeds mainly by way of the less probable step (5), E_3 must be much smaller than that of the analogous reaction for ethylene iodide. For the over-all dark reaction we found Z = 3, approximately, representing E = 20 cal./mole. By an argument similar to that of Polissar,[21] this should be equal to half the heat of dissociation of iodine (18 kcal./mole) plus E_3, which predicts E_3 = 2 kcal./mole in agreement with the over-all activation for the photochemical reaction calculated above.

Reaction Mechanism in Red Light.—The exponent of L_0 in red light is 0.8, in orange light between 0.7 and 0.6, and in blue light 0.4. This progression indicates either a continuous change in one particular mechanism or in the relative efficiencies of two mechanisms, as the convergence limit is passed. Several imaginable explanations are all open to well-recognized objections.

Direct addition to diiodoacetylene, of an excited iodine molecule is improbable in view of the observed dependence of ϕ upon $[I_2]$. Ogg[20] has argued against the addition, in a single act, of any halogen to an ethylenic linkage. Moreover, a chain mechanism initiated by molecules excited by red light cannot be seriously proposed, since about a thousand collisions with solvent molecules will on the average precede one with diiodoacetylene. As an exercise, we worked out a reaction scheme in harmony with our experimental results and plausible except for this fundamental objection. The same objection would impair any scheme assuming that the excited iodine atoms formed in blue light are more effective in starting chains than normal iodine atoms formed, exclusively, in red light.

Primary formation of halogen atoms need not in itself preclude linear dependence of reaction rate upon L_0. Booher and Rollefson[22] showed this for the photobromination of acetylene by omitting from their reaction scheme all steps involving reaction between two radicals. By analogous treatment of our reaction scheme proposed above for blue light, the results in red light could be made to appear reasonable, but those in blue light would then in turn become anomalous.

A remaining possibility, that atoms produced by a quantum of red light, less energetic at first than those produced by one of blue light, might recombine more rapidly in presence of third bodies, and thus lead to lower quantum yields, cannot be tested by the data of the present paper.

(20) Ogg, THIS JOURNAL, **58**, 607 (1936).

(21) Polissar, *ibid.*, **52**, 956 (1930).

(22) Booher and Rollefson, *ibid.*, **56**, 2288 (1934).

The Measure of Spectral Efficiencies.—Allmand,[23] also Dickinson and Nies,[4] have pointed out that when R is not proportional to $L_0^{1.0}$, ϕ_λ is no longer, in any simple sense, a measure of spectral efficiency, unless the variation of extinction coefficient is negligible over the spectral range considered. Usually there is considerable variation, and then a less simple but still practicable measure of efficiencies is found[4] in the specific rate constant k^* provided that a uniform rate expression is valid throughout the spectral region in question. The constant k^* may be obtained by an integration from front to back of the reaction mixture, of the rate expression taken as valid at any point in the light path. But when, as in the iodination of diiodoacetylene, the rate expression varies with wave length, the situation becomes more complex than that encountered by Dickinson and Nies. Consider a solution in which iodine is the only absorbent. In any layer of thickness dl perpendicular to the monochromatic light beam and l cm. behind the cell window, let L_l be the quanta per sec. absorbed per cc. Let L_0 represent quanta per second passing the cell window, as usual, and k_{I_2} the extinction coefficient of iodine for λ, the wave length employed.

$$L_l = -\frac{dL}{dl} = -\frac{d(L_0 10^{-k_{I_2}[I_2]l})}{dl}$$
$$= L_0 10^{-k_{I_2}[I_2]l} \ln 10\, k_{I_2}[I_2]$$

The reaction rate in such a layer is given by the equation

$$-\frac{d[I_2]}{dt} = k_\lambda^* L_l^x [I_2] \frac{[C_2I_2]}{a_\lambda + b_\lambda [C_2I_2]}$$

The relation between k_λ^* and ϕ_λ for negligible changes in $[I_2]$, is obtained by evaluating

$$\int_0^d -\frac{d[I_2]}{dt}\, dl$$

whereby we finally obtain

$$k_\lambda^* = \phi \left\{ x \frac{k_{I_2}^{1-x} L_0^{1-x}}{[I_2]^x} \frac{1-T}{1-T_x} \frac{a_\lambda + b_\lambda [C_2I_2]}{[C_2I_2]} \right\}$$

in which each variable, x included, has the value appropriate to λ, and

$$T = 10^{-k_{I_2}[I_2]d}$$

(23) Allmand, *J. Chem. Soc.*, 1557 (1929).

the transmitted fraction of incident light energy at depth d in the layer.

In this equation

$$\phi = -\left[\frac{d[I_2]}{dt}\right]_{\text{over-all}} \frac{V}{A[L_0(1-T)]}$$

where V = volume of reaction mixture in cm.^{3} and A = cross section of the light beam in cm.^{2}. It thus appears that relative efficiencies are not expressible in terms of any concept more simple than the equation for k_λ^*.

Summary

The photoiodination rate of diiodoacetylene in hexane, with careful exclusion of oxygen, was studied quantitatively in red and in blue light. A chain reaction is found to occur. Tetraiodoethylene is shown to be formed quantitatively.

The equation

$$-\frac{d[I_2]}{dt} = k^\lambda L_0^{x_\lambda} [I_2] \frac{[C_2I_2]}{a_\lambda + b_\lambda [C_2I_2]}$$

generalizes the data obtained. k_λ, x_λ, a_λ and b_λ must be evaluated separately for each spectral interval considered.

The mechanism of the reaction appears to vary with the wave length of light employed. In blue light the exponent of L_0 is 0.4, in orange light between 0.6 and 0.7, and in red light 0.8. It appears that the expedients hitherto employed for treatment of photochemical data here lead to difficulties.

A specific rate constant was obtained by integration which is valid at any given wave length provided that proper values for four constants dependent upon wave length are supplied.

Tetraiodoethylene in hexane was photolyzed in ultraviolet light, λ = 254 mμ (oxygen removed). At first one molecule of free iodine appears for each molecule of tetraiodoethylene which disappears, and the quantum yield is 0.8. In the late stages of the photolysis an unidentified product was observed.

The photolysis of diiodoacetylene in hexane was studied qualitatively. Apparently it is complicated by formation of polymeric substances.

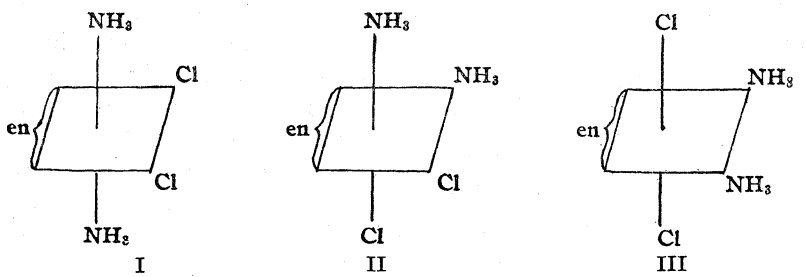
CAMBRIDGE, MASSACHUSETTS RECEIVED AUGUST 8, 1939

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

The Stereochemistry of Complex Inorganic Compounds. VI. A Study of the Stereoisomers of the Dichloro-diammino-ethylenediamine Cobaltic Ion

BY JOHN C. BAILAR, JR., AND DONALD F. PEPPARD[1]

The dichloro-diammino-ethylenediamine cobaltic ion can exist in three stereoisomeric forms



stable. The assignment of configurations is based upon the fact that ion II is asymmetric, while ion I is not. Attempts to resolve ion II itself were unsuccessful, but the carbonato salt derived from it was shown to be resolvable.

In attempting to prepare salts of these stereoisomeric ions, we first followed the directions given by Chaussy

$$NH_4[Co(NH_3)_2(NO_2)_4] \xrightarrow{NH_4OH} [Co(NH_3)_3(NO_2)_3] \xrightarrow{en} [Co\,en(NH_3)(NO_2)_3] \xrightarrow{HCl} [Co\,en(NH_3)(H_2O)Cl_2]Cl \xrightarrow{NH_4OH}$$

$$\xrightarrow{HCl} [Co\,en(NH_3)_2Cl_2]Cl\ (green) \xrightarrow{K_2CO_3} [Co\,en(NH_3)_2CO_3]Cl\ (red) \xrightarrow{HCl,\ NH_4Br} [Co\,en(NH_3)_2Cl_2]Br\ (violet)$$

Salts of two of these were prepared by Chaussy,[1a] who designated them as "*cis*" and "*trans*" (referring to the relative positions of the chloride groups) or simply as "blue" and "green." Chaussy made no mention of the fact that two *cis* series are possible. This is discussed, however, in a later account of Chaussy's work.[2]

cis-Dichloro-*trans*-diammino-ethylenediamine cobaltic ion (I) and *cis*-dichloro-*cis*-diammino-ethylenediamine cobaltic ion (II) would be expected to be violet, like *cis*-dichloro-tetrammino cobaltic ion and *cis*-dichloro-diethylenediamine cobaltic ion. The *trans*-dichloro-*cis*-diammino-ethylenediamine cobaltic ion (III) should be green, like its analogs in the ammino and ethylenediamine series. The colors of these ions determine the relative positions of the chloride groups with certainty but do not distinguish between the two *cis*-dichloro configurations.

This paper reports the preparation and a brief study of the properties of all three of the isomeric ions. It is shown that Chaussy's "blue" compounds are probably salts of the *cis*-dichloro-*cis*-diammino ion (II). This has almost exactly the same color as the *cis*-dichloro-*trans*-diammino ion (I), but its salts are much more soluble and less

The second step was very troublesome, always giving a product containing from 2–5% too much carbon. Trinitrotriammine cobalt prepared according to the directions of Riesenfeld and Klement,[3] however, gave a satisfactory product in good yield. This material, when treated with hydrochloric acid according to Chaussy's directions, did not yield a product exhibiting the properties of the dichloro-aquo-ammino-ethylenediamine cobalt described by him. There is no certainty, of course, that the trinitro-triammine cobalt used in the present study was the same stereoisomer as that used by Chaussy, as it was prepared by a different method. The problem is further complicated by the possibility of four stereoisomers of dichloro-aquo-ammino-ethylenediamine cobaltic chloride.

Chaussy's method finally was abandoned, and an entirely new approach was sought. The desired salts were prepared finally according to the following scheme:

$$\underset{cis\text{-disulfito}}{NH_4[Co(NH_3)_4(SO_3)_2]} \xrightarrow{en} \underset{cis\text{-disulfito-}trans\text{-diammino}}{NH_4[Co\,en(NH_3)_2(SO_3)_2]} \xrightarrow{HCl} [Co\,en(NH_3)_2Cl_2]Cl$$

Configurations were first assigned to $NH_4[Co(NH_3)_4(SO_3)_2]$ and $NH_4[Co\,en(NH_3)_2(SO_3)_2]$ by Klement,[4] on the basis of the fact that ethylenediamine replaces two of the ammonia molecules much more readily than the other two. If the

(1) From a portion of the doctorate thesis of Donald F. Peppard, University of Illinois, 1939.

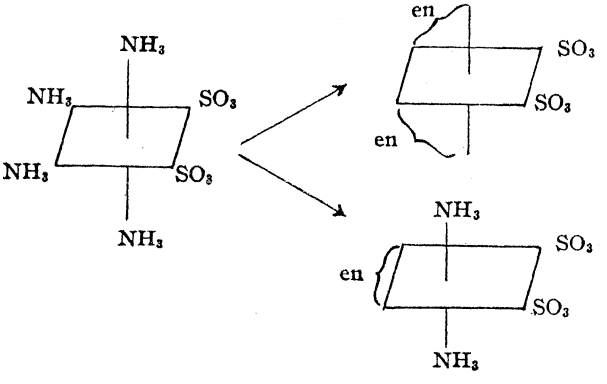
(1a) Chaussy, Dissertation, Zürich, 1909.

(2) Werner and Chaussy, *Ann.*, **386**, 254–264 (1912).

(3) Riesenfeld and Klement, *Z. anorg. allgem. Chem.*, **124**, 1–21 (1922).

(4) Klement, *Z. anorg. allgem. Chem.*, **150**, 117–125 (1925).

sulfito groups are *trans* to each other, the four ammonia molecules are equivalent, and all of them would be replaced by ethylenediamine with equal ease. If the sulfito groups are *cis* to each other, however, the introduction of ethylenediamine may follow either of two paths; one of these allows the replacement of only two ammonia molecules:



Since only two ammonia molecules are replaced under the conditions used, Klement believed the product to be ammonium *cis*-disulfito-*trans*-diammino-ethylenediamine cobaltiate. The evidence to be presented in this paper confirms this view.

Treatment of ammonium *cis*-disulfito-*trans*-diammino-ethylenediamine cobaltiate with hydrochloric acid must produce *cis*-dichloro-*trans*-diammino-ethylenediamine cobaltic chloride, unless rearrangement takes place. That the experiment actually yields the green *trans* salt is not at all surprising, however, for the analogous *cis*-dichloro-diethylenediamine cobaltic chloride rapidly rearranges to the *trans* form in aqueous hydrochloric acid. Treatment of the disulfito salt with hydrogen chloride dissolved in absolute alcohol (in which these cobalt compounds are not soluble) yields a nearly pure violet dichloro salt, which can be purified by conversion to the slightly soluble *dextro*-α-bromocamphor-π-sulfonate and reconversion to the chloride by cold concentrated hydrochloric acid. This *cis* dichloro-salt could not be resolved by means of ammonium *dextro*-α-bromo-camphor-π-sulfonate, although it readily forms a nicely crystalline precipitate when treated with this reagent. This ion will later be shown to be the unresolvable *cis*-dichloro-*trans*-diammino form (I).

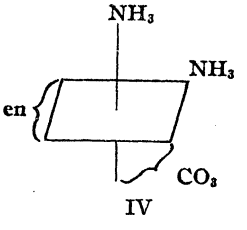
The *cis*-dichloro-*cis*-diammino isomer is most readily obtained through the following reactions:

$$[Co\,en(NH_3)_2Cl_2]Cl \xrightarrow{Ag_2CO_3} [Co\,en(NH_3)_2CO_3]_2CO_3 \xrightarrow{\text{alc. HCl}} [Co\,en(NH_3)_2Cl_2]Cl$$

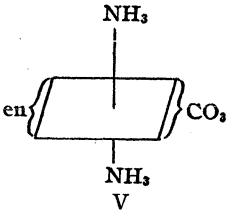
trans-dichloro-*cis*-diammino (III) — carbonato-*cis*-diammino

The product formed in the second of these reactions is a mixture of the *trans*-dichloro salt (III) and the *cis*-dichloro-*cis*-diammino salt (II). It seems impossible to prevent some rearrangement of this *cis*-dichloro form to the *trans* form.

The configurations of the two *cis*-dichloro forms were assigned through a study of the corresponding carbonato complexes. The carbonato salt prepared by treating *trans*-dichloro-*cis*-diammino-ethylenediamine cobaltic chloride with silver carbonate can be resolved partially by shaking a solution of it with optically active quartz[5] and yields, on treatment with alcoholic hydrogen chloride, a *cis*-dichloro isomer with some admixed *trans*-dichloro isomer. This *cis*-dichloro salt, when treated with silver carbonate, is again transformed into the carbonato complex which can be resolved partially by the use of active quartz. This carbonato complex must have configuration IV, and the related dichloro complex is



IV



V

almost certainly II. Since Chaussy prepared his "blue" dichloro salt from the carbonato chloride formed from the *trans*-dichloro chloride, it seems probable that his *cis*-isomer has the *cis*-dichloro-*cis*-diammino configuration.

On the other hand, the dichloro salt obtained by treating ammonium *cis*-disulfito-*trans*-diammino-ethylenediamine cobaltiate with alcoholic hydrogen chloride, when treated with silver carbonate, gives a carbonato complex which shows no resolution when shaken with active quartz (V). The original *cis*-dichloro salt, with no contamination of *trans*-dichloro-isomer, is obtained when this carbonato salt is treated with alcoholic hydrogen chloride.

It will be noted that the conversion of IV to the *trans*-dichloro salt requires the shift of one nitrogen–cobalt link, but the same conversion, in the case of V, requires the shift of two. The

(5) Tsuchida, Kobayashi and Nakamura, *Bull. Chem. Soc. Japan*, 11, 38-40 (1936).

fact that only one of the carbonato salts yields any *trans*-dichloro salt thus gives further evidence for the configurations assigned. By the same reasoning, it may be deduced that the *trans*-dichloro salt should form the carbonato complex IV.

Several reactions serving to distinguish the two *cis*-dichloro ions are summarized in Table I. In each case, the solid reagent was added to a nearly saturated solution of the dichloro-chloride and stirred vigorously.

TABLE I

Reagent	*cis*-Dichloro-*trans*-diammino (I)	*cis*-Dichloro-*cis*-diammino (II)
Ammonium dextro-α-bromocamphor-π-sulfonate	Purple crystals	No precipitate
Ammonium iodide	Dark purple crystals	Immediate precipitate of a brown and green gelatinous mixture
Sodium thiocyanate	Purple crystals	Slow deposition of a green powder

An attempt to prepare a *cis*-dibromo-diammino-ethylenediamine cobaltic salt by treating ammonium *cis*-disulfito-*trans*-diammino-ethylenediamine cobaltiate with alcoholic hydrogen bromide was unsuccessful. The *trans*-dibromo isomer was obtained under all conditions. This is not surprising, since it is difficult to prepare the *cis*-dibromo salt in the diethylenediamine series[6] and evidently impossible in the tetrammino series.

The *cis*-dichloro-*cis*-diammino-ethylenediamine cobaltic ion is asymmetric. If it were resolved it should afford some interesting studies on the Walden inversion, especially since the only cases of such inversion in inorganic complexes involve the cobalt atom with two ethylenediamine molecules attached.[7]

It may be that two such chelate groups are necessary to prevent complete loss of optical activity during substitution. On the other hand, inversion might occur more readily with only one ethylenediamine molecule in the complex, since the ammonia–cobalt link is probably ruptured more easily than the ethylenediamine–cobalt link.

Thus far, all attempts to resolve the *cis*-dichloro-*cis*-diammino-ethylenediamine cobaltic ion have failed, although the corresponding carbonato ion has been partially resolved by adsorption on active quartz.

Since the racemic dichloro complex could not be resolved directly, an attempt was made to isolate one of its optical antipodes indirectly. During a study of the active forms of chloro-aquo-diethylenediamine cobaltic ion (not yet published) it was found that if racemic *cis*-dichloro-diethylenediamine cobaltic chloride is allowed to stand in water solution until the requisite aquation has occurred and the solution then treated with a suitable resolving agent, active chloro-aquo-diethylenediamine cobaltic chloride can be obtained. The active salt also can be prepared by heating *trans*-dichloro-diethylenediamine cobaltic chloride in water solution, allowing the solution to stand for a few days, and adding a suitable resolving agent. This active chloro-aquo complex, when suspended in thionyl chloride, is transformed into active dichloro-diethylenediamine cobaltic chloride.

All attempts to isolate an active dichloro-diammino-ethylenediamine cobaltic ion in this way failed.

Experimental

Ammonium *cis*-disulfito-tetrammino cobaltiate is readily prepared by a modification of the method of Werner and Gruger.[8] Solutions of 160 g. of cobalt chloride hexahydrate in 240 cc. of water and 400 g. of ammonium carbonate in 2000 cc. of water are mixed with 1000 cc. of 28% ammonium hydroxide. Air which is first drawn through 14% ammonium hydroxide in three flasks connected in series is rapidly drawn through the solution for eight hours. Three hundred and ten grams of solid sodium bisulfite is added to the solution in the flask, and air is drawn through the solution for three or four minutes. The solution is poured into a large evaporating dish and allowed to stand open to the air for fifteen hours. It is then cooled in ice and salt for four hours, leaving the beakers open to the air and stirring occasionally. The brown salt forms in small crystals. These are filtered with suction, washed with a little cold water, absolute alcohol, and ether, and dried in air. The yield is 150 to 160 g. (62–66%). The salt is sufficiently pure without recrystallization.

Anal. Calcd. for $NH_4[Co(NH_3)_4(SO_3)_2]\cdot 3H_2O$: S, 17.83; N, 19.50; H, 6.13. Found: S, 17.74; N, 19.25; H, 6.14.

Ammonium - *cis* - disulfito - *trans* - diammino - ethylenediamine Cobaltiate.—The following method was found to give a much better yield than that of Klement.[4] Fifty grams of ammonium-*cis*-disulfito-tetramminocobaltiate and 50 or 60 glass beads are covered, in a round-bottomed flask, with a solution of 12 cc. of 60% ethylenediamine in 200 cc. of absolute ethanol. The flask is stoppered with a cork carrying a calcium oxide drying tube bent downward. The mixture is shaken continuously for one hundred and sixty hours. The suspension is drawn through a Büchner funnel without filter paper to free it from the glass beads; the powder is filtered from the liquid,

(6) Werner, Gerb, Lorie and Rapiport, *Ann.*, **386**, 110–125 (1912).

(7) Bailar and Auten, THIS JOURNAL, **56**, 774–776 (1934); Bailar, Haslam and Jones, *ibid.*, **58**, 2224–2226 (1936); Bailar, Jonelis and Huffman, *ibid.*, **58**, 2226–2227 (1936).

(8) Werner and Gruger, *Z. anorg. allgem. Chem.*, **16**, 398–423 (1898).

and washed with ethanol. The material from four such runs is combined and recrystallized by extracting at about 90° for eight or ten minutes with 400 cc. of water. After filtering, the residue is similarly extracted with 300 cc. of water. The filtrates from these extractions are cooled in ice. The precipitates are combined, washed with a little water, ethanol and ether, and dried in air. The yield of pure product is about 120 g. (56%). For analysis, the salt was dried over potassium hydroxide.

Anal. Calcd. for $NH_4[Co\ en(NH_3)_2(SO_3)_2]\cdot 2H_2O$: C, 6.54; H, 5.99; S, 17.44. Found: C, 6.48; H, 6.10; S, 17.26, 17.31.

Klement reported that the air-dried material contains three molecules of water.

***trans*-Dichloro-*cis*-diammino-ethylenediamine Cobaltic Chloride.**—Twenty-two grams of ammonium *cis*-disulfito-*trans*-diammino-ethylenediamine cobaltiate is covered with 27 cc. of concentrated hydrochloric acid. The mixture is kept at 70° until the solid dissolves and the solution becomes purple. Sixteen cubic centimeters of water is added and the solution warmed at 70° for one minute. After three days the green crystals are removed by filtration and purified by suspension in a little water. They are finally washed with 50% ethanol, absolute ethanol, and then ether. The yield is about 5 g. (32%) at best. The compound can be purified by recrystallization from concentrated hydrochloric acid, but the solution must not be heated to a temperature higher than 70°.

Anal. Calcd. for $[Co\ en(NH_3)_2Cl_2]Cl\cdot{}^1/_2H_2O$: C, 8.96; H, 5.60; N, 20.90; Cl, 39.40. Found: C, 8.95; H, 5.88; N, 20.87; Cl, 39.01, 39.12.

***trans*-Dichloro-*cis*-diammino-ethylenediamine cobaltic bromide, iodide, and thiocyanate** were prepared according to Chaussy's directions and conform to his descriptions.

***cis*-Dichloro-*trans*-diammino-ethylenediamine Cobaltic Chloride.**—Six grams of finely powdered ammonium *cis*-disulfito-*trans*-diamminoethylenediamine cobaltiate is covered with 90 cc. of absolute alcoholic hydrogen chloride (saturated at room temperature) and allowed to stand for twenty-four hours with occasional shaking. A blue salt contaminated with ammonium chloride is obtained. None of the *trans*-isomer is formed. The filtered salt is washed with absolute ethanol and ether to remove all of the hydrogen chloride. After being dried in air to remove most of the ether it is suspended three times in 3 cc. of water at room temperature, and filtered. The salt is washed with alcohol and ether.

Anal. Calcd. for $[Co\ en(NH_3)_2Cl_2]Cl\cdot H_2O$: C, 8.66; H, 5.78; N, 20.22; Cl, 38.27. Found: C, 8.76; H, 5.96; N, 19.98; Cl, 38.47, 38.59.

The salt can be purified more easily by conversion to the much less soluble *dextro*-α-bromocamphor-π-sulfonate. Two grams of the salt is stirred with 60 cc. of water at about 15° for two minutes. Five grams of ammonium *dextro*-α-bromocamphor-π-sulfonate is added to the filtered solution and the mixture stirred for thirty minutes at about 15°. The blue-purple salt is washed with absolute ethanol and ether and dried in air. It is then covered with 7 cc. of concentrated hydrochloric acid in an ice-cooled mortar and ground for a few seconds. Fourteen cubic centimeters of a mixture of equal volumes of absolute ethanol and ether are added and the grinding continued for several minutes. The blue salt is washed with absolute ethanol and ether.

The product is not optically active at the D line of sodium.

Several derivatives of the *cis*-dichloro-*trans*-diammino-ethylenediamine cobaltic ion were prepared to further characterize it. The bromide, $[Co\ en(NH_3)_2Cl_2]Br$, was obtained as follows. Slightly more than an equivalent amount of solid ammonium bromide is added with stirring to a filtered concentrated solution of *cis*-dichloro-*trans*-diamminoethylenediamine cobaltic chloride. After stirring and scraping the walls of the beaker, the blue-purple salt precipitates. It is purified by two or three suspensions in water and finally washed with alcohol and ether.

A product more easily purified is obtained by using slightly less than the calculated amount of ammonium bromide, but the yield is poorer.

Anal. Calcd. for $[Co\ en(NH_3)_2Cl_2]Br\cdot 2H_2O$: C, 7.06; H, 5.29; N, 16.47. Found: C, 6.98; H, 5.59; N, 16.95.

The iodide, prepared in similar manner, precipitates in good yield as beautiful purple crystals. In contrast to the iodide of the *cis*-dichloro-*cis*-diammino isomer, this salt is stable.

Anal. Calcd. for $[Co\ en(NH_3)_2Cl_2]I$: C, 6.84; H, 3.99; N, 15.95. Found: C, 7.17; H, 4.15; N, 16.11.

The purple thiocyanate, prepared in a similar way by the use of sodium thiocyanate, precipitates readily in good yield.

Anal. Calcd. for $[Co\ en(NH_3)_2Cl_2]SCN\cdot NaSCN$: C, 13.19; N, 23.14; S, 17.63. Found: C, 13.23; N, 23.13; S, 17.39, 17.51.

The formation of this double compound is reminiscent of the crystallization of *trans* $[Co\ en_2Cl_2]Cl\cdot HCl$ from hydrochloric acid.

***cis*-Dichloro-*cis*-diammino-ethylenediamine Cobaltic Chloride.**—Two grams of carbonato-*cis*-diammino-ethylenediamine cobaltic carbonate prepared from *trans*-dibromo-*cis*-diammino-ethylenediamine cobaltic bromide is covered with 40 cc. of alcoholic hydrogen chloride and a few glass beads added. The flask is fitted with a mercury seal allowing gases to escape but maintaining a pressure exceeding atmospheric. The apparatus is shaken for twenty-four hours, at the end of which time the light blue precipitate is filtered. It is suspended in a little water, filtered quickly from the green contamination, and 15 or 20 volumes of ethanol are added to the filtrate. A purple oil precipitates. The alcohol is decanted and the oil kept *in vacuo* over potassium hydroxide for twenty-four hours. The salt is then powdered and the drying continued.

Anal. Calcd. for $[Co\ en(NH_3)_2Cl_2]Cl$: C, 9.27; H, 5.45; N, 21.62; Cl, 40.93. Found: C, 9.47; H, 5.49; N, 21.36; Cl, 40.60, 40.71.

The bromide of the *cis*-dichloro-*cis*-diammino series is prepared by treatment of a concentrated solution of the chloride with the equivalent amount of solid ammonium bromide.

Anal. Calcd. for $[Co\ en(NH_3)_2Cl_2]Br$: C, 7.90; H, 4.64; N, 18.47. Found: C, 7.97; H, 4.71; N, 18.32.

***trans*-Dibromo-*cis*-diammino-ethylenediamine cobaltic bromide** was used in some of the preparations of the

carbonato-*cis*-diammino carbonate, as it is easier to purify than the dichloro salt. It is prepared as follows. Thirty-five cubic centimeters of 40% aqueous hydrobromic acid is heated to approximately 80° in a small beaker, and 5 g. of ammonium-*cis*-disulfito-*trans*-diammino-ethylenediamine cobaltiate is added with stirring. The heating and stirring are continued at approximately 80° until a dark green solution is formed. If the heating is continued longer than three minutes some decomposition takes place. The solution is allowed to stand at room temperature for three hours, then cooled in ice. The green crystals are filtered and purified once or twice by suspension in a little water. They are washed with absolute ethanol and ether. The yield from five such runs is 8 g. of pure product.

Anal. Calcd. for $[Co\ en(NH_3)_2Br_2]Br$: C, 6.11; H, 3.56; N, 14.25; Br, 61.07. Found: C, 6.29; H, 3.64; N, 14.01; Br, 60.73, 60.89.

The thiocyanate of the dibromo series was prepared as a pale green salt, in the same manner as the thiocyanate of the *cis*-dichloro-*trans*-diammino series.

Anal. Calcd. for $[Co\ en(NH_3)_2Br_2]SCN$: C, 9.70; N, 18.87; S, 8.63. Found: C, 9.63; N, 19.12; S, 8.76, 8.83.

Carbonato-*cis*-diammino-ethylenediamine Cobaltic Carbonate.—Eight grams of *trans*-dibromo-*cis*-diammino-ethylenediamine cobaltic bromide or 5.3 g. of the dichloro chloride, is ground with 8.4 g. of dry silver carbonate. The mortar is cooled in ice, 5 cc. of water is added and the grinding continued for half an hour. The solid is filtered and washed with a small amount of water. The combined filtrate and washings are evaporated *in vacuo*.

Anal. Calcd. for $[Co\ en(NH_3)_2CO_3]_2CO_3$: C, 17.26; H, 5.76; N, 23.05; C/N, 1.333. Found: C, 17.20; H, 6.15; N, 22.68; C/N, 1.319.

This salt was partially resolved by shaking it, in dilute solution, with optically active quartz, ground to 100-mesh. In each case, 80 cc. of the solution was shaken with 4 g. of quartz. At intervals, portions of the solutions were withdrawn, diluted, and the rotation at the sodium D line observed. The partially resolved salt is completely racemized in three minutes at 90°, or in three days at room temperature.

TABLE II

Concn. of soln., %	Time of shaking, minutes	Dilution H_2O:soln.	Rotation (*D* quartz)	Rotation (*L* quartz)
0.5	25	6/1	−0.03	+0.02
.5	120	6/1	− .03	+ .02
.5	980	6/1	− .03	+ .02
.2	60	1/1	− .04	+ .03
.2	120	1/1	− .04	+ .03
.2	300	1/1	− .04	+ .03

Aqueous hydrochloric acid converts the carbonato carbonate to *trans*-dichloro-*cis*-diammino-ethylenediamine cobaltic chloride.

Carbonato-*trans*-diammino-ethylenediamine cobaltic carbonate is prepared in the same way, using 4 g. of *cis*-dichloro-*trans*-diammino-ethylenediamine cobaltic chloride and 6.2 g. of silver carbonate. It is difficult to dry this salt completely.

Anal. Calcd. for $[Co\ en(NH_3)_2CO_3]_2CO_3 \cdot 3H_2O$: C, 15.56; N, 20.75; H, 6.30. Found: C, 15.67; N, 19.32; H, 6.02.

Its solutions, on being shaken with active quartz, show no sign of activity. Treatment of this salt with alcoholic hydrogen chloride converts it to the original *cis*-dichloro salt, while aqueous hydrogen chloride gives the green *trans*-dichloro salt.

Attempts to Prepare Chloro-aquo-diammino-ethylenediamine Cobaltic Chloride.—Two grams of *trans*-dichloro-*cis*-diammino-ethylenediamine cobaltic chloride, heated at 80–90° for sixteen hours to remove any traces of acid, was heated with 12 cc. of water in a test-tube at 85° for forty-five minutes. The solution became red a few minutes after the heating was begun. After twenty-four hours 3 g. of ammonium *dextro*-α-bromocamphor-π-sulfonate was added and the solution cooled to −5° for twelve hours. There was no precipitate. The use of ammonium *dextro*-camphor-π-sulfonate also gave only negative results.

One-half gram of *cis*-dichloro-*trans*-diammino-ethylenediamine cobaltic chloride was dissolved in 2 cc. of water at room temperature. At the end of forty-eight hours 0.6 g. of ammonium *dextro*-α-bromocamphor-π-sulfonate was added. After twenty minutes in an ice-bath the dark pink salt was filtered. It was ground with 0.5 cc. of cold concentrated hydrochloric acid, and 5 cc. of cold alcohol–ether mixture (1:1) was added. The pink-purple salt was filtered, keeping liquid on the solid at all times while washing with absolute ethanol and ether. As soon as the last of the ether was removed, the salt became sticky and assumed a deeper color. A solution of this substance exhibited no optical activity at the D line of sodium.

Summary

The three isomeric forms of the dichloro-diammino-ethylenediamine cobaltic ion have been prepared and some of their properties are described.

Improved methods of preparing several other compounds, which were obtained as intermediates, have been worked out.

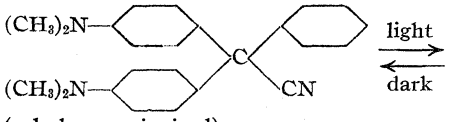
URBANA, ILLINOIS RECEIVED OCTOBER 6, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF COLORADO]

Studies on the Reactions of the Leucocyanides of the Triphenylmethane Dyes. I. The Mechanism of the Dark Reaction Following the Photolysis of Malachite Green Leucocyanide

BY FRANK E. E. GERMANN AND CHARLES LEROY GIBSON

An alcoholic solution of malachite green leucocyanide has been shown to become deeply colored when exposed to ultraviolet light. This solution again becomes colorless when placed in the dark. Two mechanisms have been proposed for this "dark reaction." Lifschitz and his co-workers[1] proposed the following equation for the photolysis and dark reaction of malachite green leucocyanide in absolute alcohol



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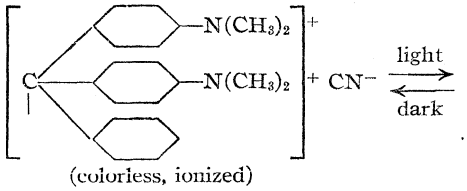

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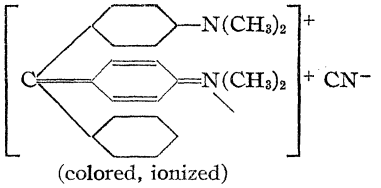


(colored, ionized)

The final product of the dark reaction was assumed to be the original leucocyanide.

Harris, Kaminsky and Simard[2] found that photolyzed and subsequently partially faded solutions of malachite green leucocyanide in alcohol containing some water recovered their color when treated with dilute hydrochloric acid. Leucocyanide solutions which had not been irradiated did not become colored when treated with the acid. They therefore suggested that the final product of the dark reaction may be the corresponding leucocarbinol, the hydroxyl ion being obtained from the water. This carbinol could be transformed into colored malachite green chloride when treated with hydrochloric acid. If exposed to ultraviolet light, this leucocarbinol would produce the colored ion of malachite green just as does the leucocyanide.

Villiger and Kopetschni[3] had at an earlier time reported that the acid always present in ordinary ethyl alcohol can quantitatively cause the removal of the ammonia from malachite green leucoamine upon warming. The end-product suggested for this reaction was $Ar_3C{\cdot}OC_2H_5$. Neutralization of the alcohol with sodium hydroxide prevented the reaction.

The purpose of the present investigation was to check these proposals of Harris, Kaminsky and Simard and of Villiger and Kopetschni by means of absorption studies of the photolyzed and then faded alcoholic solutions of malachite green leucocyanide which had been neutralized before irradiation. If the leucocarbinol were the end-product of the dark reaction, the absorption curve should shift from that of the pure leucocyanide to that of the leucocarbinol, in going from the photolyzed to the faded solutions, the amount of shift depending upon the time of irradiation.[4] Such results were not obtained.

Experimental

Preparation of Materials.—The malachite green leucocyanide was prepared from the oxalate by the Hantzsch[5] method and was purified as suggested by Harris, Kaminsky and Simard.[2] However, only five week-long extractions with ethyl alcohol were performed. The melting point of the purified crystals was found to be 174.6–175.8°. The measurements were made with a thermometer calibrated against a Bureau of Standards standard thermometer. In contrast to this Harris, *et al.*, state that they carried on extractions for ten weeks and obtained a melting point of 173.7–174.5°.

The "95%" ethyl alcohol used was the standard laboratory grade of grain alcohol. Density measurements showed the actual percentage of alcohol in the solution to be 92.6 to 92.8%. This alcohol was found to be definitely acidic. It was determined that 1 ml. of sodium hydroxide solution in "95%" alcohol of approximately 0.004 molarity was required to neutralize 50 ml. of the stock alcohol to the neutral tint of brom thymol blue. All the alcohol used in this experiment was neutralized in this manner except the absolute alcohol and the alcohol used in the purification of the leucocyanide.

(1) Lifschitz, *Ber.*, **52**, 1919 (1919); **58**, 2434 (1925); **61**, 1463 (1928); *Z. physik. Chem.*, **97**, 426 (1921).

(2) Harris, Kaminsky and Simard, THIS JOURNAL, **57**, 1151 (1935).

(3) Villiger and Kopetschni, *Ber.*, **45**, 2910 (1912).

(4) Darmois, *Compt. rend.*, **197**, 1120 (1933).

(5) Hantzsch and Osswald, *Ber.*, **33**, 307 (1900).

Procedure.—A Hilger E-3 quartz spectrograph with rotating sector was used for all spectrographic measurements. The light source was an under-water arc with tungsten electrodes. Wratten and Wainright Panchromatic plates were used for the photographs. A spectrum extending to a wave length of 2500 Å. was obtained with accurate comparisons possible to about 2700 Å. Absorption tubes one centimeter long were used throughout the experiment. The solution in the absorption tube was never allowed to be exposed to the light of the arc for more than twenty seconds, in order to avoid absorption due to the photocompound.

Fresh solutions of the leucocyanide in the neutralized 92.7% alcohol of 5×10^{-4}, 1×10^{-4}, 5×10^{-5} and 1×10^{-5} molarity were prepared in the dark and absorption spectra obtained. The absorption curve checked closely with that given by Harris, Kaminsky and Simard, which for comparison purposes has been reproduced in Fig. 1.

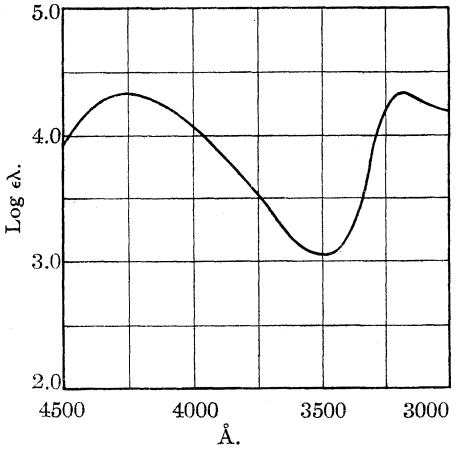


Fig. 1.—Section of curve of Harris, Kaminsky and Simard for photo-compound and chloride.

For the studies of the absorption spectra of the photocompound, the following solutions were used: (A) 5×10^{-5} *M* leucocyanide in 92.7% neutralized ethyl alcohol; (B) 5×10^{-5} *M* leucocyanide in 99.2% unneutralized ethyl alcohol; (C) 5×10^{-5} *M* leucocyanide in 84.6% ethyl alcohol (prepared by addition of water to 92.7% neutralized ethyl alcohol).

Different portions of these three solutions were illuminated for fifteen hours, ten hours, five hours and one hour in quartz flasks. The source of light was a "Bruleur Gallois" mercury vapor lamp (Type HG). After irradiation, the solutions were allowed to fade in the dark room for at least a week. At the end of that time all portions of solutions A and B were absolutely colorless. However, solutions C, even after only one hour of exposure to ultraviolet light, retained some green color after a month in the dark room. Absorption studies of solutions C were therefore not attempted.

Unfortunately, absorption bands for the faded photolyzed solutions were obtained only at low extinction (sector reading) and hence are not as accurate as they might have been. However, the appearance of a new absorption band in the region of 3400 Å. to 3700 Å. was quite evident for

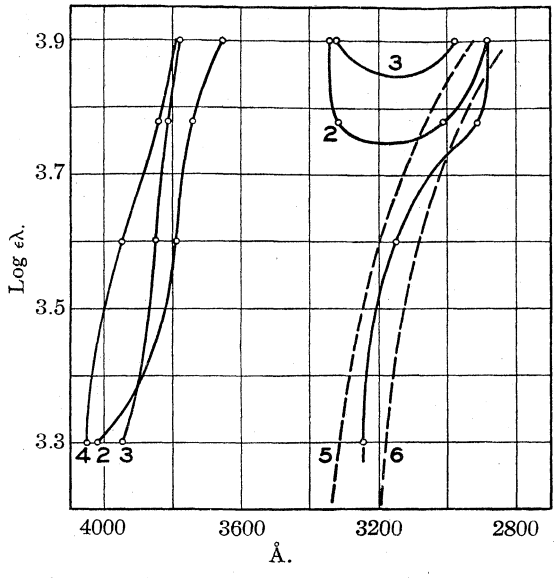


Fig. 2.—Absorption spectra of 0.00005 *M* malachite green leucocyanide in 92.7% ethyl alcohol completely faded after irradiation: curve 1, illuminated for one hour; curve 2, for five hours; curve 3, for ten hours; curve 4, for fifteen hours; curve 5, unilluminated cyanide; curve 6, unilluminated carbinol. Curves 5 and 6 are taken from the work of Harris, Kaminsky and Simard.

the solutions studied. The absorption curves obtained from the faded photolyzed solutions are shown in Figs. 2 and 3. In Fig. 2, we have inserted in curves 5 and 6 the absorption data for the leucocyanide and carbinol as taken from Harris, Kaminsky and Simard. These

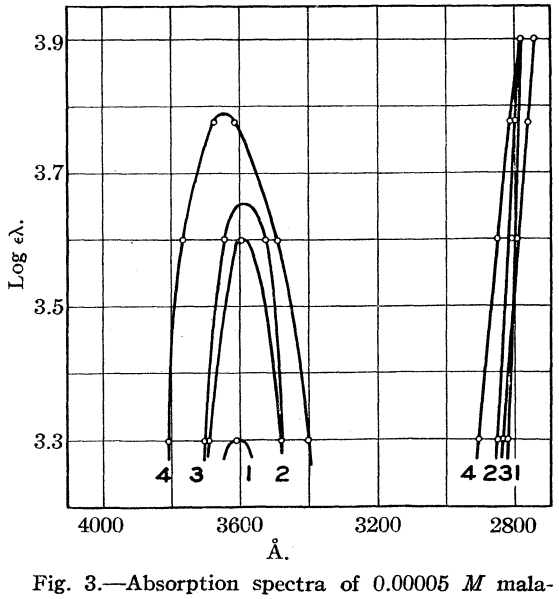


Fig. 3.—Absorption spectra of 0.00005 *M* malachite green leucocyanide in 99.25% ethyl alcohol completely faded after irradiation: curve 1, illuminated for one hour; curve 2, for five hours; curve 3, for ten hours; curve 4, for fifteen hours.

authors made no absorption measurements on the faded solutions, but refer to the colored solution as the photo compound. It will be observed that the maximum log ϵ of the faded solution between 3400 and 3700 Å. as given in Fig. 3 is about 3.8, whereas for the colored product (the photo compound of Harris, Kaminsky and Simard) at 3700 Å. in Fig. 1 it is only 3.5. This discrepancy is probably real and can hardly be accounted for by the lack of accuracy for the faded solutions at low extinction values since in this neighborhood the values are close together, the curves crossing almost at right angles. The inaccuracy of readings at low extinction would be in the horizontal direction (wave length) and not in the vertical direction (log ϵ). A comparison of curves 1 and 5 of Fig. 2 shows that our curve for the 5×10^{-5} M leucocyanide agrees with that of Harris, Kaminsky and Simard to within 50 Å. in all but point log ϵ 3.778 and wave length 2990, even at low extinction values.

When the faded solutions of A were treated with dilute hydrochloric acid they became uniformly dark green. No difference in intensity of color was apparent to the eye. The four solutions of B with similar treatment showed differences in intensities ranging from a very light green for the solution irradiated for one hour to a moderately deep green for the solution irradiated for fifteen hours. The depth of color was in the same order as the time of radiation. The darkest solution was not as heavily colored as the acidified portions of A. The solutions of C became uniformly dark green when acidified.

Discussion

The treatment of the irradiated and faded solutions with hydrochloric acid would seem to indicate that the neutralization of the alcohol used as a solvent had not changed the results previously reported in unneutralized alcohol,[2] except possibly in 84.6% alcohol.

The trend of the absorption curves as well as the results obtained with hydrochloric acid make it seem likely that the proposal of Lifschitz for the dark reaction would still be valid in 100% ethyl alcohol. In the presence of water, however, the end-product could not be the leucocyanide, the leucocarbinol, nor the photo-compound, since all of them show minima in their absorption curves at 3500 Å.

The experiment indicates that the end-product of the dark reaction of the photolysis of malachite green leucocyanide in ethyl alcohol containing some water has the following properties: (a) It is colorless, but has a peak in its absorption curve in the neighborhood of 3600 Å. (b) It is formed more easily as the amount of water in the solution increases, but it is unstable in as much as 15% water. (c) It is not as stable as the leucocyanide, being decomposed by dilute hydrochloric acid or excess water to produce the colored ion of malachite green. (d) When irradiated with ultraviolet light, it produces the colored ion of malachite green. (e) Although derived from the malachite green ion and easily reproducing this same ion, its absorption curve shows it to have a structure essentially different from the leucocyanide and leucocarbinol.

These properties would indicate that the end-product of the dark reaction must be the result of some reaction between the solvent and the malachite green ion. In analogy with the mechanism proposed by Villiger and Kopetschni,[3] this end-product might be the ether form: $Ar_3C{\cdot}OC_2H_5$. However, such a compound would be expected to be more stable than the substance produced here. Further investigation is necessary before the true identity of this end-product is established.

Summary

Absorption studies of photolyzed and subsequently faded solutions of malachite green leucocyanide in alcohol containing some water have shown that the dark reaction does not regenerate the leucocyanide as an end-product. The end-product is also shown not to be the leucocarbinol. The final product of the dark reaction is a colorless, light-sensitive substance with a peak in its absorption curve in the nieghborhood of 3500 Å. This end-product is decomposed by dilute hydrochloric acid to form a green solution similar to that of malachite green salts.

BOULDER, COLORADO RECEIVED AUGUST 17, 1939

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY, UNIVERSITY OF CHICAGO]

Hydrogen Exchange Reactions of Esters in Relation to Reactivity in Condensation Reactions

BY WELDON G. BROWN AND KENNETH EBERLY[1]

A study has been made of the base catalyzed hydrogen exchange reactions of representative esters of various types with deuteroalcohol in order to evaluate the effect on acidity[2] of structural variations and their consequent effect on reactivity in condensation reactions. Pertinent to the behavior of esters of monocarboxylic acids in the Claisen condensation, the effect of various alkyl groups has been investigated in some detail, and similarly, but less extensively, the effect of substitution has been traced in the phenylacetic and malonic ester series and correlated with the relative reactivities in alkylation reactions.

Preliminary experiments by W. R. Sprowls[3] indicated that the simple aliphatic esters do not undergo hydrogen exchange with deuteroalcohol in the presence of small amounts of sodium hydroxide either at room temperature or at 100° for long periods of time. Likewise no exchange was observed on addition of only a small quantity of metallic sodium (sufficient to form a 0.05 *M* sodium ethylate solution), evidently because of water present. We observed hydrogen exchange at a measurable rate even at room temperature, and without appreciable β-keto ester formation, on increasing the amount of sodium used to about 0.02 g. atom per mole of alcohol. A much weaker base, sodium salicylate, was required in the experiments on malonic ester and its derivatives.

Experimental Part

While the extent of hydrogen exchange has formerly been determined at this Laboratory[4,5] through density measurements on the water obtained by combustion of the alcohol recovered from reactions by distillation methods, the use of volatile esters in the present work precluded separations of the alcohol. Accordingly, in such cases, the reaction products were washed with saturated salt solution to remove the alcohol, samples (2 g.) of the separated esters were then burned and the water of combustion was collected in a cooled trap. The water, purified by heating with potassium permanagate and sodium carbonate at 180° for one hour and distilled twice *in vacuo*, was finally collected in a small tube (attached to the distilling apparatus through a ground joint) in which the density was determined with a quartz float and the deuterium content was then estimated by suitable interpolations.

Deuteroalcohol, with the C_2H_5OD content in the range 15–23 mole per cent. was prepared according to our previously described method.[4] The esters were obtained from commercial sources and purified, or were prepared according to directions in the literature.

TABLE I

HYDROGEN EXCHANGE REACTIONS OF ESTERS WITH DEUTERO-ALCOHOL[a]

Ethyl ester	M.-moles ester	Initial % D_2O[b]	Final % D_2O[c]	H at. exch.[d]	% completion
At 25°, four hours, with 38 ± 2 mg. sodium					
Acetic	51.1	3.13	1.70E	1.30	56
Propionic	43.6	3.13	0.28E	0.24	14
Butyric	37.8	3.13	0.18E	.11	6.4
Lauric	37.0	2.60	2.48	.11	6.3
Stearic	37.0	2.60	2.50	.09	5.2
Isobutyric	37.5	3.13	0.03E	.02	1.9
Isovaleric	37.0	2.60	0.06E	.05	2.9
Cyclohexylacetic	37.0	2.60	2.50	.09	5.4
α-Methoxypropionic	37.0	2.60	0.04E	.03	3.5
Crotonic	37.0	2.73	0.81E	.63	
Sorbic	37.0	2.73	2.50	.20	
ββ-Dimethylacrylic	36.0	2.60	0.39E	.35	
Citraconic	37.0	2.73	2.02	.78	
Mesaconic	37.0	2.73	2.64	.07	
At 110°, 12 hours, with 40 mg. of sodium					
o-Toluic (16 hr.)	31.5	2.60	2.56	.04	
p-Toluic	31.2	2.60	2.36	.28	
2,4,6-Trimethylbenzoic	15.2	2.73	2.68	.09	
At 0°, five minutes, with 40 mg. of sodium					
Phenylacetic	10.0	3.03	2.73	.91	48
Diphenylacetic	10.0	3.03	2.94	.25	24
α-Methoxyphenylacetic	10.0	3.03	2.97	.17	17
α-Phenylpropionic	20.8	3.03	2.94	.13	13
At 25°, four hours, with 5 mg. of sodium salicylate					
Malonic	23.0	2.60	1.78	1.71	85
Methylmalonic	23.0	2.60	2.44	0.25	25
Phenylmalonic	23.0	2.60	2.39	0.33	30

[a] The quantity of alcohol used in each experiment was 5 cc. (85.3 millimoles). [b] Data refer to deuterium content of water of combustion from stock deutero-alcohol. [c] Data refer to deuterium content of water of combustion from recovered alcohol or, where designated by "E," from the recovered ester. [d] Calculated on the assumption of statistical distribution of deuterium.

(1) Taken in part from the thesis of Kenneth Eberly submitted in partial fulfilment of the requirements for the Ph.D. degree at the University of Chicago, December, 1938.

(2) The term acidity is used throughout in the generalized sense. Since, in the condensation reactions to be considered, the anion concentration is maintained at the equilibrium value, the acid strength, not merely the rate of formation of anions as given by the rate of hydrogen exchange, is of importance. Brönsted and coworkers [see Brönsted, *Chem. Rev.*, **5**, 231 (1928)] have shown empirically, and Horiuti and Polanyi theoretically [*Acta Physicochimica, U. R. S. S.*, **2**, 505 (1935)], that the rate of proton transfer and the acid strength, in comparisons of acids of the same structural type, are directly and simply, though not linearly, related and undoubtedly the relative reactivities of similar esters in hydrogen exchange reactions will indicate correctly the order of acidity.

(3) W. R. Sprowls, Ph.D. Thesis, University of Chicago, 1938.

(4) Kharasch, Brown and McNab, *J. Org. Chem.*, **2**, 36 (1937).

(5) Brown, Kharasch and Sprowls, *ibid.*, **4**, 442 (1939).

Experiments in which the exchange reactions were substantially complete yielded values for the number of exchanging hydrogen atoms, assuming simple statistical distribution, of which the following are typical: ethyl acetate 2.25, propionate 1.74, butyrate 1.73, isobutyrate 0.91, β-dimethylacrylate 5.45, N-dimethylaminoacetate 1.98, phenylacetate 1.92, diphenylacetate 1.07, phenylmalonate 1.08. These limiting values, or estimated values in the absence of specific data, were then used in estimating the degree of completion of the exchange reaction in a series of experiments in which the reactions were interrupted before equilibrium was attained so as to obtain a quantitative comparison of the reactivities of the various esters. Typical results are given in Table I.

Discussion

The order of acidity in esters of the type RCH_2COOEt according to our results is as follows: $C_6H_5 > H > CH_3 > C_2H_5 > n\text{-}C_3H_7 > C_{10}H_{21}$, $C_{16}H_{33} >$ cyclo-$C_6H_{11} > i\text{-}C_3H_7$. Alkyl groups, relative to hydrogen, thus exert a de-activating effect which depends more upon whether the group is primary or secondary than upon the length of the chain. A second alkyl group (one example: ethyl isobutyrate) causes a further decrease in acidity, even after allowing for statistical effects. The phenyl group in phenylacetic ester appears strongly activating but a second phenyl group, as in diphenylacetic ester, fails to enhance the effect, and again, as a substituent in malonic ester, it has nearly the same (de-activating) effect as a methyl group.[6]

Vinylogic effects[7] in unsaturated esters diminish with increasing length of the conjugated bond system (*cf.* series, ethyl acetate, crotonate, sorbate) and are highly dependent upon geometrical configuration (*cf.* ethyl citraconate, mesaconate), the *trans* relationship between carbethoxy and β-methyl groups being more favorable.

The results for the esters of monocarboxylic acids are to be correlated with reactivity in the Claisen condensation, which, according to current theory,[8,9,10] involves anion formation by proton transfer as the first step, followed by reaction of the anion with another molecule of ester, etc., each step being reversible. The acid strength appears as a factor both in the rate and in the over-all equilibrium, and the failure of certain esters (notably ethyl isobutyrate and ethyl isovalerate) to undergo self-condensation under the usual conditions is ascribed to low acid strength, a conclusion supported by the observations[9,11] that condensation will occur if sufficiently powerful bases are used. Our results confirm this deduction regarding the acid strengths of ethyl isobutyrate and ethyl isovalerate, and the available data, chiefly of Roberts and McElvain[12] and Briese and McElvain,[13] on the rates and yields in condensations indicate close agreement throughout with the reactivity in hydrogen exchange. Quantitatively the correlation is less convincing, as we find, for example, the acid strength of ethyl laurate to be twice that of ethyl isovalerate, while in the acetoacetic ester condensation the former yielded 79%[13] and from the latter, under comparable conditions, "no trace of keto ester could be found."[12] The over-all equilibrium in the latter case is clearly much more unfavorable than by a factor of two, and we conclude that the variations in acidity, while similar in trend, are not wholly responsible for the variations in reactivity.[14]

In the malonic ester series we have but one example, methylmalonic ester, showing the effect of an alkyl group in decreasing the acidity but the effects of other alkyl groups are doubtless as characteristic as in the previous series, and the relative reactivity in alkylation reactions parallels that observed in the Claisen condensations of monocarboxylic esters. An outstanding example is the failure of isopropylmalonic ester to undergo further alkylation under the usual conditions, previously attributed to steric hindrance,[15]

(6) This apparently anomalous behavior of phenyl groups finds a ready explanation in the theory of damped resonance [Birtles and Hampson, *J. Chem. Soc.*, 10 (1937); Ingham and Hampson, *J. Chem. Soc.*, 981 (1939)]. The hydrogen lability of esters is due primarily to resonance stabilization of the anion and an α-phenyl group would normally reinforce this resonance by providing additional resonance forms, in which it appears doubly bonded to the α carbon, and which are therefore most effective if the benzene ring and the carbethoxy group can become coplanar. With two phenyl groups and one carbethoxy group (or one phenyl group and two carbethoxy groups) attached to the α carbon, the condition of coplanarity could not be fulfilled for steric reasons.

(7) Fuson, "The Principle of Vinylology," *Chem. Rev.*, **16**, 1 (1935).

(8) Arndt and Eistert, *Ber.*, **69**, 2381 (1936).

(9) Hauser and Renfrow, THIS JOURNAL, **59**, 1823 (1937).

(10) Renfrow and Hauser, *ibid.*, **60**, 463 (1938).

(11) Spielman and Schmidt, *ibid.*, **59**, 2009 (1937).

(12) Roberts and McElvain, *ibid.*, **59**, 2007 (1937).

(13) Briese and McElvain, *ibid.*, **55**, 1697 (1933).

(14) Spielman and Schmidt (*loc. cit.*) attributed the failure of ethyl isovalerate and isobutyrate to undergo self-condensation (with sodium ethylate) to the low acidity, indicated by negative ferric chloride tests, of the β-keto esters derived from them, and, in our opinion, this should be admitted as a contributing factor. We considered the second step of the Claisen condensation (reaction of anion with another molecule of ester) as similar in form to the alkoxy group interchange reactions of esters, and we observed in such a reaction ($RCOOAm + OEt^- \longrightarrow RCOOEt + OAm^-$, Am = optically active amyl) that ethyl isobutyrate reacted only one-fifth as rapidly than ethyl *n*-butyrate. We believe, therefore, that the influence of structure on reactivity in the Claisen condensation is threefold, exerting itself, not only on the extent of the initial anion formation, but also on the rate at which the anion reacts with the ester, and the extent to which the equilibrium is shifted by salt formation of the β-keto ester.

(15) Fischer and Dilthey, *Ann.*, **335**, 337 (1904).

but which could now be interpreted, in view of the analogous behavior of isovaleric ester in the Claisen condensation, as due in part, at least, to low acidity.[16]

(16) The tacit assumption is made that decreased acid strength hinders the alkylation reaction through its effect in lowering the equilibrium anion concentration, and while this assumption appears to be valid in the malonic ester series, this will not be the dominant effect where the acidity is of such a high order that dissociation, under the conditions of alkylation, is practically complete. The introduction of alkyl groups in barbituric acid is known from ordinary acidometric measurements, to depress the acid strength, the isopropyl group being particularly effective [Preiswerk, *Helv. Chim. Acta*, **6**, 192 (1923)], but at the same time the ease of alkylation increases and the isopropyl derivative reacts with great ease. Less extreme illustrations are to be seen in the acetoacetic and cyanoacetic ester series, in which the isopropyl derivatives undergo alkylation readily [Fischer, Rohde and Brauns, *Ann.*, **402**, 364 (1913)] and which differ also from malonic ester in that a second alkyl group is introduced somewhat more readily than the first. In these instances the role of acidity is subordinate to the reactivity of the anions (or salts) toward alkyl halides which, as Conrad and Brückner pointed out [*Z. physik. Chem.*, **7**, 283 (1891)], varies inversely with the acid strength.

We take pleasure in acknowledging the active interest of M. S. Kharasch throughout this work.

Summary

Sodium ethylate catalyzed hydrogen exchange reactions of various types of esters with deutero-alcohol are reported, and the influence of structure on acidity, as determined by the exchange reaction, is correlated with reactivity in condensation reactions.

CHICAGO, ILLINOIS RECEIVED JULY 5, 1939

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY, UNIVERSITY OF CHICAGO]

Mechanism of the Acid-catalyzed Dimerization of Anethole

BY WELDON G. BROWN AND ALEX H. WIDIGER

In connection with the possibility of obtaining evidence regarding the mechanism of the acid-catalyzed polymerization of olefins with the aid of deuterium, a study has been made of the dimerization of anethole catalyzed by deuterium chloride in methyl alcohol solution. This case was considered favorable for a test of the Whitmore[1] theory of acid catalyzed polymerizations because (1) the experimental conditions can be adjusted so as to yield almost exclusively the dimer, (2) the structure of the dimer is known and is in conformity with the Whitmore hypothesis, (3) the structure of the dimer is such that it contains no hydrogen atoms likely to be readily exchangeable under the influence of acids. It was recognized that the monomer contains at least one such hydrogen atom, namely, that attached to the β carbon atom, and that the exchange of this hydrogen with the deuterium of the medium, if fast in comparison with the polymerization process, would obscure the phenomenon we wished to observe.

The formation of isoanethole,[2] according to the mechanism of Whitmore, is shown in the equations

$$R{-}CH{=}CH{-}CH_3 + H^+ \longrightarrow R{-}CH^+{-}CH_2{-}CH_3 \quad (R = \text{anisyl}) \quad (1)$$

$$R{-}CH^+{-}CH_2{-}CH_3 + R{-}CH{=}CH{-}CH_3 \longrightarrow R{-}CH(C_2H_5){-}CH(CH_3){-}CH^+{-}R \quad (2)$$

$$R{-}CH(C_2H_5){-}CH(CH_3){-}CH^+{-}R \longrightarrow R{-}CH(C_2H_5){-}C(CH_3){=}CH{-}R + H^+ \quad (3)$$

It will be noted that the proton added becomes incorporated in the ethyl side-chain of the dimer and that the proton eliminated is derived from the second molecule of anethole. A polymerization carried out with a deutero acid should therefore yield, if no exchange reactions occur, a product containing one atom of deuterium per molecule of dimer. In the more likely event that a hydrogen exchange reaction of the monomer accompanies the polymerization reaction, but is not too rapid in comparison, it is still possible to predict that the proportion of deuterium in the dimer formed in any small interval of time during the polymerization should be greater than that present in the monomer.

Experimental Part

The polymerization of anethole (Eastman Kodak Co. product, redistilled, b. p. 225° (750 mm.)) was carried out by refluxing with 5 *N* hydrochloric acid in methyl alcohol, according to the procedure of Goodall and Haworth, except that the methyl alcohol and the hydrochloric acid were partly deuterated. The deuteration was accomplished by treating methyl alcohol with pure heavy water, thus permitting an exchange of the hydroxyl hydrogen of the alcohol with the deuterium of the water, then removing water by repeated treatment with calcium oxide. Dry hydrogen chloride was passed into the anhydrous alcohol to yield a 5 *N* solution. Analysis for deuterium was carried out by combustion, after having first removed halogen by treatment with dry silver oxide, the water of combustion

(1) Whitmore, *Ind. Eng. Chem.*, **26**, 94 (1934).

(2) The structure indicated for isoanethole is that established by Goodall and Haworth, *J. Chem. Soc.*, 2484 (1930).

being collected, purified, and analyzed for deuterium by the temperature-float method.

The dimer is of limited solubility in alcohol, and separates together with some unchanged anethole, making it possible to obtain samples by cooling and draining off the lower layer. The samples were taken up in ether, washed with aqueous alkali, then with water, and, after drying, the ether was allowed to evaporate. Fractional distillation at reduced pressure furnished samples of anethole and isoanethole which were analyzed for deuterium by combustion and density measurements on the water of combustion. The anethole fractions contained some chloride, evidently as a result of addition of hydrogen chloride but the extent of this addition was for our purposes negligible. During the period of heating a considerable part of the hydrogen chloride disappears by reacting with methyl alcohol.

In a typical experiment, a solution of 71 g. of anethole in 355 ml. (331 g.) of 5.30 *N* hydrogen chloride (HCl + DCl) in methyl alcohol was heated on a water-bath and samples were removed at intervals as described above. The deuterium present amounted to 8.90 mole per cent. of the total available hydrogen (hydroxyl hydrogen plus hydrogen chloride). The analytical results are given in Table I. The results are given in terms of mole per cent. of deuterium found in the water of combustion and in terms of the so-called exchange number.[3] In the present connection the exchange number may be considered simply as the number of deuterium atoms per anethole unit which would have been found had the available hydrogen of the medium been composed entirely of deuterium.

TABLE I

POLYMERIZATION OF ANETHOLE IN DEUTERO METHYL ALCOHOL–HYDROGEN CHLORIDE SOLUTION

Sample	Period[a] of heating, min.	Compn. of sample, g.	% D_2O in water of combustion	Exchange no.[b]
1	3	15 anethole	0.155	0.21
		7 isoanethole	.135	.18
2	6	7 anethole	.33	.45
		2 isoanethole	.18	.24
3	20	4 anethole	.61	.83
		7 isoanethole	.36	.48
4	120	4 isoanethole	.77	1.05

[a] Data in this column refer to time intervals. Thus the first sample was withdrawn three minutes after the start of the reaction, the second sample was withdrawn after a further period of six minutes, etc. [b] Atoms of deuterium per anethole unit.

(3) For the definition of the exchange number, and the method of calculation, see Brown, Kharasch and Sprowls, *J. Org. Chem.*, **4**, 442 (1939); Brown, Widiger and Letang, THIS JOURNAL, **61**, 2597 (1939).

Some information with regard to the position occupied by the deuterium in the dimer was obtained by oxidizing with alkaline permanganate, following the procedure of Goodall and Haworth, and analyzing the products for deuterium. The deuterium content of the isoanethole, expressed in terms of mole per cent. D_2O in the water of combustion (ordinary water being taken as zero), was 0.71%. The anisic acid contained 0.02%, and the ketone (3-anisylpentanone-2) contained 0.50%. Of the deuterium originally present 95% was found in the ketone. In view of the finding that deuterium is present only as a result of an exchange reaction of the monomer prior to polymerization, the conclusion was reached that virtually all of the deuterium present in the isoanethole is confined to the CH_2 group of the ethyl side chain.

Discussion

It is difficult to find any support in our results for the Whitmore mechanism of polymerization, or indeed for any mechanism involving an intermediate carbonium ion (or addition compound) in which the equivalence of the newly acquired hydrogen atom with hydrogen atoms previously present on the same carbon atom is to be assumed. The condition that there should not be a rapid interchange of hydrogen between the monomer and the medium is fulfilled, yet the predicted enrichment of the dimer with respect to deuterium is not observed. On the contrary, it is found that the dimer contains no more deuterium than can be accounted for as the result of a slow hydrogen exchange prior to its formation.

Summary

The dimerization of anethole in a partly deuterated medium of methyl alcohol and hydrogen chloride is accompanied by a slow hydrogen exchange reaction of the monomer and the dimer is found to contain no more deuterium than can be accounted for as a result of this exchange. The significance of this result for the mechanism of polymerization is pointed out.

CHICAGO, ILLINOIS RECEIVED NOVEMBER 6, 1939

[CONTRIBUTION FROM THE WALKER LABORATORY OF THE RENSSELAER POLYTECHNIC INSTITUTE AND THE KENT AND JONES LABORATORIES OF THE UNIVERSITY OF CHICAGO]

The Rates of Reaction of Cyclopropyl Ketimines with Water[1]

BY JOHN B. CLOKE[2]

Ketimines react normally with water to give the corresponding ketone and ammonia as follows

$$R—C(=NH)R' + H_2O = RCOR' + NH_3$$

a reaction which ordinarily is accelerated greatly by the addition of one equivalent of acid. Our original interest in the behavior of the cyclopropyl ketimines with water was aroused by two strikingly different reports: first, that ethyl cyclopropyl ketimmonium chloride

$$\underset{\text{CH}_2\text{CH}_2\text{CH}}{\text{CH}_2\text{CH}_2\text{CH}}—C(=NH_2Cl)C_2H_5 \qquad (I)$$

appeared to be unaltered by hot water[3]; and, second, that the phenyl cyclopropyl analog,[4] $C_3H_5C(=NH_2Cl)C_6H_5$ (II), is instantly decomposed. The first of these reports became clear when the writer proved that de Booseré's stable compound is in reality the isomeric α-ethylpyrrolinium salt.[1] The present work shows, as was anticipated, that the real cyclopropyl compound (I) is even more readily saponified by water than (II).

Experimental

Phenyl Cyclopropyl Ketimmonium Chloride.—The salt was first prepared in the form of its chloroform compound as already described.[1] This crystalline compound, which was collected on a filter in a special moisture-proof housing, was therefore exposed in a desiccator over phosphorus pentoxide at 50° and under diminished pressure until weighings showed that all chloroform had been removed. Since the compound decomposed very readily, many recrystallizations and several repetitions of the initial preparation were necessary in order to maintain a supply of reasonably pure material.

Ethyl Cyclopropyl Ketimmonium Chloride.—Ethylmagnesium bromide was first prepared in the usual manner from 42.3 g. of ethyl bromide, 9.0 g. of magnesium and 150 cc. of anhydrous ether according to the procedure of Moureu and Mignonac.[5] To this ethereal solution 10.35 g. of cyclopropyl cyanide[6] in three times its volume of ether was added slowly from a dropping funnel. The material was then boiled gently for about twelve hours, when it was transferred to a separatory funnel from which it was added slowly to about 300 cc. of liquid ammonia[7] in a 500-cc. Dewar flask, which was then connected with a five-foot (1.5-meter) lime tower. From time to time during a twenty-hour period the mixture was agitated gently in order to disintegrate lumps. At this point about 200 cc. of dry ether was added carefully to the mixture, and about half an hour thereafter the solution was filtered through a Büchner in a moisture-proof apparatus. The residue on the filter was well washed with dry ether, and the combined filtrates were refiltered into a suction flask. In order to remove ammonia, a current of very dry air was aspirated through the ketimine solution, which was then diluted somewhat with ether and treated with dry hydrogen chloride.

The hydrogen chloride gave a white crystalline precipitate of the ethyl cyclopropyl ketimmonium chloride and a sticky material,[8] which collected on the walls of the flask. The entire precipitate was then dissolved in 50–60 cc. of a cold mixture of 100 cc. of glacial acetic acid[9] and 10 cc. of acetic anhydride, from which it was reprecipitated by the addition of 500 cc. of dry ether. At first a dusky, oily layer was obtained, but eventually this crystallized completely after the flask wall was scratched with a glass rod. Finally, the salt was collected on a suction filter in the absence of moisture, when it was exposed in a vacuum desiccator over sodium hydroxide and calcium chloride for a day, giving 10 g. or a 48.5% yield.

The substance appeared to shrink from 70–80°, but it did not melt until 95–97°, and then it gave a somewhat turbid liquid. Other cyclopropyl ketimmonium salts have behaved similarly, possibly because they pyrolyze to give pyrrolinium salts.

Anal. (micro) Calcd. for $C_6H_{12}NCl$: N, 10.49; Cl, 26.55. Found: N, 10.59, 10.47; Cl, 26.93.

When the salt was redissolved in dry chloroform containing a little acetic anhydride and reprecipitated by ether, neither properties nor composition were changed significantly. However, in a melting point determination begun at 87°, the compound melted at 98.5–100.5°.

Reaction Rate Measurements.—The rates with which the ketimmonium salts react with water were ascertained

(1) The data reported herein have been taken from the second part of a dissertation presented by J. B. Cloke to the University of Chicago in partial fulfilment of the requirements for the degree of Doctor of Philosophy. The first part was published in 1929, THIS JOURNAL, **51**, 1174 (1929).

(2) The problem discussed herein was suggested by Dr. Julius Stieglitz, whose inspiration, confidence and fatherly advice will always be treasured by the writer. For various reasons, Mrs. Stieglitz has suggested that her husband's name should be withheld from this second paper, which was his own wish in the case of the first.

(3) de Booseré, *Bull. soc. chim. Belg.*, **32**, 26 (1923).

(4) Bary, *ibid.*, **31**, 404 (1922).

(5) Moureu and Mignonac, *Compt. rend.*, **156**, 1801 (1913); *Ann. chim.*, [9], **14**, 322 (1920).

(6) Cloke, Anderson, Lachmann and Smith, THIS JOURNAL, **53**, 2791 (1931).

(7) The use of liquid ammonia for the decomposition of the bromomagnesium derivatives of ketimines was developed independently by Cornell, *ibid.*, **50**, 3314 (1928), and by Cloke and Van Wyck, *Thesis*, Rensselaer Polytechnic Institute, 1927. As a rule, the Grignard solution runs quite easily into the ammonia through a tube of precipitate formed at the tip of the funnel. Plugs may be removed with a wire.

(8) The formation of this viscous material, which has often been observed in connection with the precipitation of ketimine hydrochlorides, appears to be the result, in part at least, of the use of an excess of hydrogen chloride.

(9) Later work indicated that chloroform is better than the acetic acid.

by modifications of the method of Stieglitz and Derby[10] for the imido ester hydrochlorides. The method is based upon the fact that a ketimine can be liberated from its salt by the action of sodium hydroxide and that the free base, unlike ammonia, may be extracted from its aqueous solution by carbon tetrachloride. The reaction velocity constant, k, was calculated arithmetically and graphically from the equation for a monomolecular reaction

$$k = \frac{2.303}{t_2 - t_1} \log \frac{v_1}{v_2}$$

where v_1 and v_2 represent the relative concentrations of the ketimmonium salt at times t_1 and t_2.

Phenyl Salt.—In the work on the phenyl cyclopropyl ketimmonium chloride, special care was taken in order to prepare the aqueous solution rapidly at 0° and to maintain it at this temperature. Furthermore, the transfer pipet used for the removal of the samples was kept cold, when not in use, by allowing it to stand in a long tube, which was clamped in the well-stirred bath of water and cracked ice. Each sample was transferred at a noted time to a Squibb funnel containing a known volume of standard alkali and 30 cc. of purified carbon tetrachloride. At once the mixture was well shaken, the tetrachloride layer was drawn off and the extraction repeated three times with 25, 20 and 15 cc. portions of the immiscible solvent. Finally, the aqueous solution in the funnel was washed into a flask and titrated with standard acid with methyl orange as the indicator. Table I represents a typical run, wherein t is the time in minutes from the moment of preparation of 100 cc. of 0.05 M solution and v_b and v_a designate the volumes used of the 0.1 N sodium hydroxide and hydrochloric acid, respectively; samples of 17.6 cc. were taken.

TABLE I

t	$v_b - v_a$	k, min.$^{-1}$
2	8.06	.....
14	5.85	0.02669
33	3.75	.02469
44	2.87	.02460
55	2.13	.02510
70	(1.51)	.02463
	Average k	0.02514

The graphical computation of the data in Table I gives a value for k of 0.0246. Table II presents a summary of the constants, computed graphically, for several successive runs on the phenyl salt at 0° in 0.05 M and 0.1 M solutions. The grand averages for the average constants

TABLE II

k, min.$^{-1}$ for 0.05 M soln.	k, min.$^{-1}$ for 0.1 M soln.
0.0246	0.0242
.0249	.0234
.0249	.0232
.0257	.0217
.0243	
.0250	
Grand av. .0249	.0231

computed arithmetically are 0.0252 and 0.0243 respectively, results for which the first points are generally responsible.

(10) Derby, *Am. Chem. J.*, **39**, 439 (1908).

Ethyl Salt.—Ethyl cyclopropyl ketimine differs from the phenyl analog in that it is decidedly more soluble in water and more reactive by far with water. In addition, it differs from all other ketimines thus far studied in that the base is more sensitive to saponification than the hydrochloride salt. These characteristics made it necessary to adopt the following modification of the analytical method used for the phenyl salt, and, even with the changes indicated, the results are not as accurate as might be desired.

A 100-cc. portion of purified carbon tetrachloride and a suitable volume of 0.5 N sodium hydroxide solution from a microburet were added in order to each of five Squibb funnels, which were suspended in the ice-bath. The ketimmonium salt solution was then prepared in a wide-necked, weighted Erlenmeyer flask, which stood in the bath, by the dropping of the proper weight of compound into the flask, which contained the proper volume of water measured at 0°. At once a definite volume of the well-mixed reacting solution together with a 5-g. portion of finely powdered sodium nitrate were transferred to one of the waiting funnels. The mixture was then shaken vigorously for a few moments, the lower layer was removed and at once the extraction was repeated with a 30-cc. and a 20-cc. portion of ice-cold tetrachloride, when the analysis was finished as in the case of the phenyl salt.

In the foregoing work, the very rapid extraction procedure, which was demanded by the great reactivity of the liberated base, undoubtedly removed some alkali mechanically. However, this error would be offset to some extent, especially in the first analyses, by the rapid decomposition of the base together with its significant solubility in water. The graphical computation of the results of three runs gave the following values of k: 0.0366, 0.0360, (0.0316).

Saponification of Ethyl Cyclopropyl Ketimine Base.—Since several unsuccessful attempts to prepare pure ethyl cyclopropyl ketimine indicated that this could only be accomplished with much effort, a general idea of its stability to saponification was obtained as follows. In short, the base was liberated from its hydrochloride salt at the moment when it was required by the dropping of the equivalent weight of the salt into a definite volume of 0.05 N sodium hydroxide solution at 0°. Without delay a 10-cc. portion of this solution was pipetted into a Squibb funnel containing 100 cc. of ice-cold tetrachloride and 5 g. of sodium nitrate, when the run was completed as above. The results of two runs, computed graphically, follow: k, min.$^{-1}$ = 0.46, 0.53.

The foregoing data, which indicate a half time value of about a minute and a half for the ketimine in water at 0°, are only of relative significance: first, on account of the haste necessary in the analytical work[11]; and, second, because a slight excess of sodium hydroxide, giving a high pH, might greatly accelerate the reaction. The last question may be ascertained in time.

Saponification of Phenyl Cyclopropyl Ketimine Base.—In view of the striking rate with which ethyl cyclopropyl ketimine base reacts with water in comparison with the rate for the salt, the work was extended to the phenyl analog. The procedure followed was analogous to that used for the ethyl compound with the exception that the

(11) In this connection the writer appreciates the aid of Dr. E. C. Knowles, Mr. R. J. Anderson and the Mrs. Sarah and Mary Cloke.

reaction was carried out in a special vessel provided with an efficient stirrer. The results of two runs are given in Table III. It is important to note that the reaction

TABLE III

Successive Values of $k \times 10^3$, min.$^{-1}$ at 0°

10.1	9.6	9.4	8.6	8.3	7.8	7.3
11.3	10.3	9.7	8.9	8.4	8.0	6.4

mixture was not strictly homogeneous and that the values obtained are therefore not truly comparable with other data in the paper. The drift in the values of k was probably the result chiefly of the reversing action of the ammonia, as in the saponification of diphenyl ketimine.[12]

The Retardation of Ketimmonium Salt Saponification by Acid.—The idea that the presence of an excess of acid would decrease the rate of reaction of ethyl cyclopropyl ketimmonium chloride with water, which was suggested by the foregoing data, has been confirmed for all ketimmonium salts thus far studied. Data on the two cyclopropyl compounds are given in Table IV. A study of these data shows that the rate with which these two

TABLE IV

Cyclopropyl ketimmonium chloride	HCl, N	Av. k, min.$^{-1}$ at 0°
Ethyl	0.05	0.00284
Ethyl	.20	.00118
Phenyl	.01	.00747
Phenyl	.05	.00435
Phenyl	.20	.00189

ketimmonium salts react with water decreases remarkably as the hydrogen-ion concentration increases. The imido ester salts are much less sensitive to changes in pH, as shown by the work of Stieglitz and Derby.[10]

Discussion

By analogy with ethyl phenyl ketimmonium chloride, $C_2H_5C(=NH_2Cl)C_6H_5$,[13] and the diphenyl compound, $C_6H_5C(=NH_2Cl)C_6H_5$,[12,14] the ethyl cyclopropyl ketimmonium chloride (I) is less reactive with water than would be expected. This deduction is also supported by the great reactivity of the ethyl cyclopropyl ketimine base with water, for ketimine bases are normally less reactive with water than their salts.[5] The foregoing considerations are in harmony with the supposition that the salt (I) exists in aqueous solution largely in the form of its enammonium tautomer, presumably $\underset{\llcorner\!\!\lrcorner}{CH_2CH_2CH}—C(—NH_3Cl)=CHCH_3$.

The reason for suggesting that the tautomerism,[15] if it exists, concerns the ethyl rather than the cyclopropyl group will be considered in a later communication.

Summary

Ketimines are saponified by water to give a ketone and ammonia; similarly, ketimmonium salts give a ketone and an ammonium salt. The measurement of the reaction velocity constants for the saponification of ethyl cyclopropyl ketimmonium chloride and for the phenyl cyclopropyl analog shows, contrary to a previous report, that the former compound is more reactive with water than the latter. More notable is the fact that the free ethyl cyclopropyl ketimine base is still more reactive with water than is its hydrochloride, an anomalous behavior which suggests that the dissolved salt may exist largely in the form of an enammonium tautomer. The work has also shown that the reaction velocity for the decomposition of a ketimmonium salt by water decreases as the hydrogen-ion concentration rises.

Subsequent papers will consider various aspects of ketimine stability.

TROY, NEW YORK RECEIVED SEPTEMBER 18, 1939

(12) E. M. Davis, *Thesis* Rensselaer Polytechnic Institute, 1934.

(13) N. B. Tweed, *Thesis*, Rensselaer Polytechnic Institute, 1932.

(14) Culbertson, *et al.*, *Proc. Iowa Acad. Sci.*, **39**, 177 (1932); *ibid.*, **41**, 170, 172 (1934).

(15) In order to get additional evidence for the idea, much effort was expended in the measurement of the hydrolysis constants of the bases corresponding to the salts (I) and (II), and also of the free ethyl cyclopropyl ketimine base. Since these measurements were made a number of years ago by a somewhat involved quinhydrone electrode method, which was subject to several unavoidable errors, the data will not be given until they can be checked by more straightforward methods now available. Nevertheless, the data, as collected, indicated that the base corresponding to the more stable phenyl salt (II) is stronger than that of the less stable ethyl analog (I). The same relationship was found by Stieglitz and his associates in the case of the imido esters.

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, No. 206]

Condensations by Sodium. XV. Reactions of Disodium Compounds with Ethylidene and Methylene Chlorides*

BY AVERY A. MORTON AND JOHN T. MASSENGALE

Amylidenedisodium has failed[1] to give branched chain hydrocarbons with monohalogen alkyls. However, reaction with ethylidene chloride is now shown to take place smoothly with formation of the expected heptene-2 (equation 1) in a yield of

$$C_4H_8CHNa_2 + Cl_2CHCH_3 \longrightarrow C_4H_9CH{=}CHCH_3 + 2NaCl \quad (1)$$

13%, or 80% of the maximum possible (17%) estimated from the butylmalonic acid usually obtained by carbonation. This compound is the first Wurtz product from disodium compounds reported in this work. Its isolation in the quantity noted is in agreement with the view that amylidenedisodium is present as an intermediate[2] from which butylmalonic acid is derived by carbonation.

Efforts to use this reaction for showing the existence of some benzylidenedisodium along with benzylsodium as a product of the exchange reaction between phenylsodium and toluene were qualitatively successful. Styrene from methylene chloride and methylstyrene from ethylidene chloride were both formed though the yield (not over 4%) did not exceed a quarter of that expected. It will be recalled[2] that a secondary reaction made estimation of this disodium intermediate by carbonation unreliable. Accordingly, an indirect method was used. Benzylsodium was first determined by measuring the amount of ethylbenzene produced with methyl iodide and with methyl sulfate. These values are in approximate agreement (46 and 43%, respectively) with each other and are considered a fair index of the quantity of benzylsodium since reactions of this organosodium compound have so far been among the most quantitative[3] with respect to the Wurtz product observed in this series. The difference between the total organosodium intermediates found by carbonation and the mono product approximated by the above method amounts to around 15%. Low yields of styrene may be due to difficulties in isolating the product as well as to poor reaction. Efforts to increase the styrene yield by heating benzylsodium with excess phenylsodium led to inactivation of the latter.

On the supposition that styrene might come by splitting out of hydrochloric acid from another likely intermediate (equation 2), beta-phenylethyl chloride, addition of the latter instead of methylene chloride was tried. No trace of styrene could be observed.

$$CH_2Cl_2 \xrightarrow{C_6H_5CH_2Na} \quad (2)$$

$$C_6H_5CH_2CH_2Cl \begin{cases} \xrightarrow{-HCl} C_6H_5CH{=}CH_2 \\ \xrightarrow[RNa]{} C_6H_5CH_2CH_2CH_2C_6H_5 \end{cases}$$

Chlorobenzene instead of amyl chloride was used as a source of phenylsodium in most of this work. The yield was as high as that which has been obtained with amyl chloride and benzene (78%)[4] but the resulting phenylsodium was less reactive with toluene so that the quantities of phenylacetic and phenylmalonic acids were below those produced by the former method. This result is probably due to the higher temperature (85 instead of 55°) necessary for exchange. Indeed, when the time at 85° was extended or the temperature raised to 110° the yield dropped appreciably. Indicative also of lower activity of this phenylsodium was the failure of methyl iodide to give ethylbenzene unless the exchange mixture were heated to 85° though this reagent uncovered evidence of metallation at room temperature in the case of the reactive phenylsodium from amyl chloride, benzene, and sodium.[2] The physical appearance of the two phenylsodiums was also different, that from chlorobenzene being a black powder which settled quickly when stirring was stopped so that an almost clear solution resulted. The green phenylsodium from amyl chloride, on the other hand, remained suspended for some time.

Attempts to use benzyl chloride and benzal chloride as sources of mono- and di-sodium compounds, respectively, were unsuccessful, either because the sodium compound formed was too reactive for isolation in the presence of incoming

(*) Original manuscript received April 17, 1939.

(1) Morton and Fallwell, Jr., THIS JOURNAL, **59**, 2387 (1937).

(2) Morton, Fallwell, Jr., and Palmer, *ibid.*, **60**, 1426 (1928).

(3) Morton and Fallwell, Jr., *ibid.*, **60**, 1429 (1938).

(4) Morton and Hechenbleikner, *ibid.*, **58**, 2599 (1936).

benzyl chloride or because little or no reaction occurred with the metal. Behavior of the disodium compounds with other di-halogen compounds such as pentamethylene dibromide and benzal chloride also was tried but no evidence of the expected reaction was found.

Experimental

Heptene-2.—Amylidenedisodium was made in the usual manner[1] from 63.9 g. (0.6 mole) of amyl chloride and 37 g. (1.6 atoms) of sodium at 20–25° in a special cut of petroleum ether which boiled below 45°. It reacted vigorously when 23 g. (0.24 mole) of ethylidene chloride was added. Fractionation of the product yielded 2 g. of material boiling at 50–95° and 3.8 g. at 95–97°. The latter was strongly unsaturated when tested with bromine water and corresponded in boiling point with that recorded[5] for heptene-2 (97.8°); boiling point of dibromide 95–96° at 12 mm.; refractive index 1.4997. Recorded values were 96.2° at 12 mm. and 1.5000, respectively. The yield was 13% calculated on an amyl chloride basis. A higher boiling fraction, 110–115° at 120 mm. amounting to 5.2 g., was examined in hope that it might prove to be 6-ethylundecane but was found to have a molecular weight (Rast) of 226, and to be unsaturated to bromine.

Under similar conditions methylene chloride was added to amylidenedisodium which had been prepared in solvent ligroin carefully fractionated to remove material boiling below 85°. After decomposing in the usual manner a fraction unsaturated to bromine and boiling 61–66° corresponding to hexene-1 was obtained.

Phenylsodium from Chlorobenzene and Its Exchange with Toluene.—Chlorobenzene, 68 g. (0.6 mole), was added with stirring to 37 g. (1.6 atoms) of fine sodium sand which had been activated by addition of 5 ml. of *n*-amyl alcohol while suspended in petroleum ether. Reaction was very sluggish below 30° whereas amyl chloride reacts smoothly below 0°. After two and one-half hours required for addition of chlorobenzene, the mixture was stirred one hour longer before adding 135 g. of toluene and refluxing at 52° for two hours. Carbonation showed that this phenylsodium was relatively inactive, no exchange having occurred. The yield of benzoic acid was 53.5 g. (79%). Diphenyl, 2.7 g. (8%), also was recovered. Addition of methyl iodide in place of carbon dioxide likewise failed to show occurrence of any exchange, 35 ml. or 55% excess toluene being recovered.

When the above experiment was repeated, enough petroleum ether was distilled from the reaction mixture after addition of toluene to make the boiling temperature 85°. The mixture was maintained with stirring at this temperature for two hours before carbonation: yield of phenylacetic acid 21.6 g. (26%); of phenylmalonic acid 19.1 g. (35%). A similar experiment in which more petroleum ether was distilled from the mixture so that the exchange temperature with toluene was 106° produced 14.2 g. (17%) of phenylacetic and 21.2 g. (39%) of phenylmalonic acid. Separation of acids from this and a number of other experiments in which the exchange temperature was 106 to 115° was complicated by presence of an oily impurity which was removed only after repeated precipitations and extractions. In all cases yields were progressively lower with increasing temperatures of metallation.

Exchange of phenylsodium with toluene gave low yields when the organosodium compound was heated for some time before adding all of the toluene. Thus, phenylsodium prepared from 0.6 mole of chlorobenzene in 250 ml. of benzene was treated successively with 30-g. and 200-g. portions of toluene, each addition being followed by heating at 85° for one and one-half hours. Exchange was not complete, for on carbonation 2.6 g. (3.6%) of benzoic acid was found with 13.1 g. (16%) of phenylacetic acid and 13.8 g. (26%) of phenylmalonic acid. Addition of 215 ml. of toluene to a similar preparation of phenylsodium followed by heating at 85° for two hours yielded 2.2 g. (3%) of benzoic acid, 12.4 g. (22%) of phenylacetic acid, and 16.9 g. (31%) of phenylmalonic acid. It was necessary, however, to heat for some time to effect an exchange at 85°, for holding the temperature at 85° for five minutes (the experiment was identical in other respects with the one using petroleum ether as a solvent) yielded benzoic acid, 28 g. (38%), phenylacetic acid, 2.5 g. (3%) and phenylmalonic acid, 11.4 g. (20%).

Styrene.—Preparation of organosodium intermediates from toluene and phenylsodium was made at 85° as first described. A vigorous reaction ensued as methylene chloride, 16.9 g. (0.2 mole), was added as quickly as possible over a thirty- to forty-minute interval, the reaction temperature being kept at 35° while the kerosene bath temperature was maintained at −10° by addition of dry-ice. The mixture was stirred at 30° for one-half hour longer and then carbonated to ensure that all possible products had been obtained. After decomposing excess sodium by adding water (care must be taken that the first few portions of water have had time to react before more is added) directly to the reaction flask under an atmosphere of carbon dioxide, the organic layer was separated, washed twice with water, once with dilute acid, and three times again with water before distilling through a fifteen-plate column. By careful fractionation at a 15 to 1 reflux ratio over a period of two and one-half days, a fraction beginning at 78° and 160 mm., containing some amyl alcohol, and ending at 104° and 6 mm. (when diphenyl began to crystallize in the condenser), was obtained which gave, upon reaction with bromine in carbon tetrachlorde, 2.7 g. (3.3%) of styrene dibromide, m. p. 69–71°. The pure material is reported[6] melting at 73°.

Anal. Calcd.: Br, 60.6. Found: Br, 60.3. No acids were recovered by acidifying the water layer.

In an experiment with a larger quantity, 112.5 g. (1 mole) of chlorobenzene and 61 g. (2.6 atoms) of sodium sand there was obtained 5 ml. of the fraction which contained styrene at 90–92° and 27 mm., 6.4 g. (8%) of diphenyl at 129–132° at 11 mm., and 19 ml. of a fraction boiling 145–149° at 8 mm. corresponding to diphenylpropane.

To discover some of the factors affecting the yield of styrene, *i. e.*, of benzylidenedisodium, a series of runs was made. For each set of conditions, reactions with carbon dioxide, methyl iodide, and methylene chloride were successively tried. Results are listed in Table I with the theoretical amount of benzylidenedisodium possible cal-

(5) Soday and Boord, THIS JOURNAL, **55**, 3293 (1933).

(6) Von Miller, *Ber.*, **11**, 1450 (1878).

culated as the difference between total acids and ethylbenzene. Where toluene was formed from unreacted phenylsodium and methyl iodide the amount was added to that of ethylbenzene in estimating the quantity of styrene possible. No diphenylethane was found among products of the reaction with methyl iodide.

TABLE I

ESTIMATION OF MONO- AND DI-SODIUM INTERMEDIATES PRESENT FROM REACTION OF PHENYLSODIUM WITH TOLUENE UNDER VARYING CONDITIONS

Products	Percentage yields obtained for condition a	b	c
Benzoic acid		19	24
Phenylacetic acid	26	14	7
Phenylmalonic acid	35	18	23
Total acids	61	51	54
Ethylbenzene	46	35	22
Toluene	..	13	15
Total monosodium, acid	46	48	37
Styrene { Theoretical	15	3	17
Styrene { Observed	3.3	1.4	2

[a] Phenylsodium prepared from chlorobenzene in petroleum ether and exchange carried out at 85° as described earlier in this paper. [b] Phenylsodium prepared from 0.6 mole of chlorobenzene in 250 ml. of benzene followed by addition of 30 g. of toluene and heating for two hours at 84°. [c] Same as in (*b*) except that 15 g. of toluene was added, the mixture heated for one and one-half hours at 82°, 15 g. additional toluene then added, and the mixture again heated for two hours at 83°. The purpose of conditions (*b*) and (*c*) was to test if a deficiency of toluene favored formation of benzylidenedisodium; the result actually revealed that phenylsodium had been inactivated by heat.

Methylstyrene.—Benzylidenedisodium was prepared from phenylsodium (chlorobenzene source) at 85° and treated with 23 g. of ethylidene chloride added gradually at 35° over a period of one hour. The product was then carbonated and decomposed with water. Acidifying the water layer gave no acids recoverable by ether extraction. On careful fractionation of the hydrocarbon layer a portion boiling from 85 to 95° at 70 mm. and amounting to 12 g. was found to be unsaturated to bromine water. The dibromide isolated amounted to 2.7 g. (3%), m. p. 63–64°; recorded[7] value 66.5°. Analysis for bromine in this sample showed a value high enough (56.7%, theory 57.5) to distinguish it from any other possible product.

Benzylsodium and Dimethyl Sulfate.—The organosodium intermediates were prepared from 112.5 g. (1 mole) of chlorobenzene and other reactants in proportion. After heating for two hours at 85° in order to metallate toluene, the mixture was cooled to 35° and treated with 70 g. (0.55 mole) of undiluted dimethyl sulfate over a two and a half hour period. Addition was discontinued as soon as heat ceased to be evolved. After decomposition the hydrocarbon layer was washed with sodium carbonate several times and then twice with water but on distillation some decomposition with evolution of sulfur dioxide began. Distillation was therefore halted until the mixture had been steam distilled. The distillate was then fractionated under a 10 to 1 reflux ratio through the fifteen-plate column whereupon 46 g. (43%) of ethylbenzene, b. p. 134–134.8°, was obtained. No fraction corresponding to isopropylbenzene was found. Above 200° sulfur dioxide fumes were evolved.

Reaction with Phenylethyl Chloride.—Benzylidenedisodium, with the accompanying benzylsodium, was made in the same manner employed for the styrene experiment except that 30.3 g. of chlorobenzene with a proportionately smaller amount of sodium was used. β-Phenylethyl chloride, 25 g. (0.18 mole), Eastman Kodak Co. grade, was added in place of methylene chloride. After decomposing and fractionating no dibromide could be isolated nor could even a test for unsaturation be detected in the fraction which should have contained styrene. Diphenylpropane was the only product obtained from this experiment.

Reaction with Benzal Chloride.—The mixture of benzyl sodium and benzylidenedisodium was treated dropwise with 29 g. (0.18 mole) of benzal chloride which had been distilled just before use. Fractionation of the hydrocarbon layer obtained after decomposing excess sodium gave at 6 mm. and a reflux ratio of 10 to 1: at 104–106°, 4.1 g. of diphenyl; at 106–129°, 1 g. of a liquid; and at 129–132°, 6.2 g. of a liquid which crystallized upon chilling and scratching, m. p. 46–48°. Several crystallizations from petroleum ether did not raise its melting point above 51–51.5°. No depression was observed with an authentic sample of diphenylethane.

Reactions of Benzyl and Benzal Chlorides with Sodium.—Benzyl chloride, 76 g. (0.6 mole), was added at 25° to 37 g. (1.6 atoms) of sodium sand which had been activated by addition of 5 ml. of amyl alcohol. Petroleum ether, 300 ml., was used as the solvent. There was an immediate reaction and the mixture became blue-black in color. No heat was evolved on carbonation and the product after decomposing in the usual manner had a strong odor of unreacted benzyl chloride. After distilling up to 200° at atmospheric pressure, the residue crystallized, giving 29.1 g. of diphenylethane. The yield was 51%, no allowance being made for unreacted benzyl chloride. The reaction was repeated using petroleum ether, 300 ml., and toluene, 50 ml., as the solvent in the hope that benzylsodium would be stable in this mixed solvent as it had once before[4] proved to be when amyl chloride had been used. Again no acids were found after carbonation. Some unreacted benzyl chloride was present, and the yield of dibenzyl was 20 g. (45%).

Benzal chloride, 48.3 g., was added to 37 g. of sodium sand in the same manner first tried with benzyl chloride above. No acids were found after carbonation. A considerable quantity of unreacted benzal chloride was present but the products in general were difficult to separate. A small amount of stilbene, m. p. 118–120°, was isolated.

Pentamethylene Dibromide with Benzylidene- and Amylidenedisodium.—Benzene, 300 ml., was added to phenylsodium from 0.6 mole of chlorobenzene and 1.6 atoms of sodium in 250 ml. of petroleum ether. After distilling until the temperature of the mixture reached 78°, 60 ml. of toluene was added, the mixture refluxed at 86° for two hours, cooled to 25°, and treated dropwise with 36 g. (0.16 mole) of pentamethylene bromide[8] over a one

(7) Rügheimer, *Ann.*, **172**, 131 (1874).

(8) Von Braun, "Org. Syntheses," Coll. Vol. I, 1932, p. 419.

and a half hour period. Carbonation yielded no acids. The hydrocarbon layer was washed and fractionated at atmospheric pressure until nothing more would come over with the jacket temperature of the column at 186°. At 10 mm. pressure 11 ml. of material boiling from 98 to 112° and obviously containing some diphenyl, along with the hoped for cyclohexylbenzene, was obtained. This fraction was nitrated according to the procedure of Kursanoff,[9] in an attempt to obtain the 4-nitrocyclohexylbenzene, m. p. 57.5–58.5°. The only products obtained were apparently higher melting nitro derivatives of diphenyl for the crude material melted 71–95°, and after crystallization from dilute acetic acid at 90–98°. Sublimation did not change the value appreciably.

Unsatisfactory results were likewise obtained in the reaction of this dibromide with amylidenedisodium, the latter being made from 63.9 g. of amyl chloride with 37 g. of sodium in 300 ml. of petroleum ether in the usual manner. The dibromide, 36 g., was added dropwise. Carbonation produced no acids. Upon fractionation 9 ml. boiling 161–172° at atmospheric pressure was collected. It contained some decane as well as some of the expected *n*-butylcyclohexane. Hydrogen sulfide was evolved when the fraction was heated with sulfur but no evidence of *n*-butylbenzene could be obtained on applying Ipatieff's[10] procedure for making the diacetamino derivative.

(9) Kursanoff, *Ann.*, **318**, 321 (1901).

(10) Ipatieff and Schmerling, THIS JOURNAL, **59**, 1056 (1937).

Summary

Ethylidene chloride reacts with amylidenedisodium to form heptene-2. The yield is the same within the experimental error as that of butylmalonic acid obtained by carbonation.

Methylene chloride and ethylidene chloride react with benzylidenedisodium, yielding styrene and methylstyrene, respectively.

Styrene is not obtained from the reaction of β-phenylethyl chloride with benzylsodium.

Phenylsodium prepared from chlorobenzene is not as active in exchanges with toluene as is phenylsodium prepared from amylsodium.

Methyl iodide and dimethyl sulfate give approximately the same yields of ethylbenzene when added to the mixture of benzylsodium and benzylidenedisodium. In neither case is the branched chain hydrocarbon, isopropylbenzene, found among the products.

CAMBRIDGE, MASS. RECEIVED NOVEMBER 7, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, No. 207]

Condensations by Sodium. XVI. The Formation of Decane in the Wurtz Reaction

BY AVERY A. MORTON AND GRAHAM M. RICHARDSON

It is the purpose of this work to show that no Wurtz product, decane, is formed until after formation of organosodium compounds. In brief, free radicals, if formed prior to organosodium intermediates by reaction of amyl chloride and sodium, do not dimerize to yield decane. The method employed was the simple one of increasing the quantity of sodium and noting whether the yield of organosodium compounds approached 100% as that of decane fell to zero. Such an examination of the early stages of addition of amyl chloride to sodium showed (Fig. 1) that yields were essentially quantitative, as high as 95% total organosodium compounds (amylsodium and amylidenedisodium) being revealed by carbonation. This Wurtz reaction is therefore sharply divisible into two phases: first, the formation of organosodium compounds and, second, their reaction with alkyl chloride. Decane was exclusively a product of the second stage. Under certain conditions the yield of decane was as high as 90% with respect to the monosodium compound.

At one time or another presence of free radicals has been proposed for nearly every stage of the Wurtz reaction. One argument for their existence is the finding of products of disproportionation, in this instance, pentane and pentene. Because of the prevalence of the free radical view and the failure of alternative mechanisms to prove satisfactory, presence of amylidenedisodium (butylmalonic acid) was attributed[1] to occurrence of this active intermediate. Such a mechanism is in full accord with present notions of free radicals in solution and their behavior. Yet critical questions can be asked. Why, for example, should disproportionation occur when the free energies of the products unquestionably favor dimerization? Thus, in the case of ethyl reacting with itself to form ethylene and ethane or butane

(1) Morton and Hechenbleikner, THIS JOURNAL, **58**, 2599 (1936); Morton, Fallwell, and Palmer, *ibid.*, **60**, 1426 (1938).

the free energies[2] are +12,300, −10,700, and −6200, respectively. Data for trimethylethylene (+13,700), pentane (−8600), and decane (−2900) suggest that the same relations exist for the products in the reaction of amyl chloride and sodium. If heats of formation of bonds are considered, a greater amount of heat would be evolved for dimerization than for disproportionation. By applying Rice's[3] method of calculating the probable proportion of products, the amount of disproportionation should be trifling. It is indeed an interesting fact that alkyl disproportionation, universally considered as evidence for free radicals, should not occur according to this single aspect of thermodynamics.

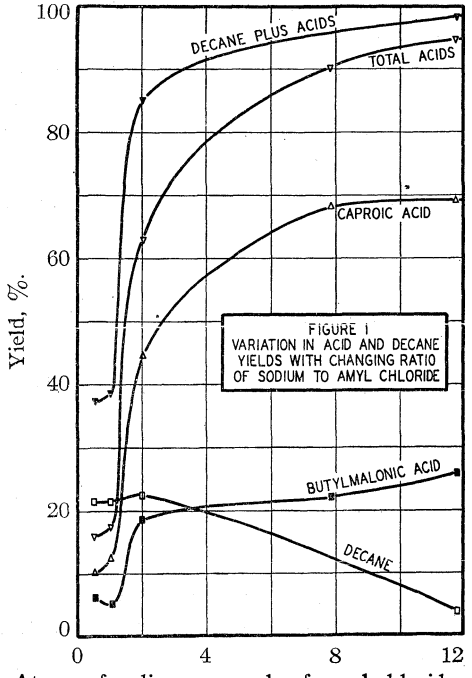


FIGURE 1
VARIATION IN ACID AND DECANE YIELDS WITH CHANGING RATIO OF SODIUM TO AMYL CHLORIDE

Fig. 1.—Variation in acid and decane yields with changing ratio of sodium to amyl chloride.

Furthermore, if free radicals are present in the first phase of reaction between amyl chloride and sodium and they react with sodium to form amylsodium or disproportionate to an -idene radical which in turn adds two atoms of sodium, one must concede that metallic sodium has acted as a nearly perfect trap for this radical or its disproportionated product. Yet how free can a free radical be which never escapes the influence of the surface of a metal on which it is formed and how can such a radical be distinguished from a radical in a complex, evidences of which are not entirely lacking in these reactions? Far more serious is the question of why disproportionation should be the sole product of reaction of a free radical with itself on the metal surface when free energies so overwhelmingly favor decane formation.

Our present opinion of the Wurtz reaction can be stated briefly. The Wurtz product, *i. e.*, the dimer, is reached by way of an intermediate organometallic compound. There is no need for any other special mechanism, although it is possible to superimpose on this view an ionic (organosodium compounds are salts) or a free radical mechanism. Owing to the vigor of the reactants and of the organosodium reagent, simultaneous side reactions and decompositions may occur to subordinate the Wurtz synthesis. Assumption of an intermediate free radical provides at present a convenient explanation for some of these products. This suggestion, while in general accord with current notions, requires further clarification before it can be unqualifiedly accepted. Certainly, at present, the evidence for such an intermediate is no better than that for a radical within a complex.

Experiments

General Conditions.—The general method described in previous papers was employed but owing to the purpose of the work special attention was paid to a number of factors having to do with increased yields. Sodium sand was made in pound lots in a special 1-liter flask[4] in which stirring was more effective. The particles were about one-fourth the size of those formerly obtained. The reactions themselves were carried out in similar flasks which before alteration had a capacity of 500 ml. The quantity of amyl alcohol needed to activate 30 g. of sodium metal was found to be 2 ml. by the following series of experiments. Amyl chloride, 20 ml., in 40 ml. of benzene was dropped onto 30 g. of sodium in a mixed solvent of 80 ml. of benzene and 25 ml. of petroleum ether under an atmosphere of nitrogen at 0 to −4° over a period of one hour. The mixture was then stirred for two hours at room temperature, more of the solvent mixture being added if necessary, before carbonation at 22–28°. Yields of total acids were 82, 88, 84, 76, and 73% when the amounts of alcohol used to activate the metal were 0, 2, 4, 6, and 8 ml., respectively. At room temperature amylsodium was converted to phenylsodium but amylidenedisodium was largely unaffected so that yields of different acids in this series were, respectively: for benzoic acid, 72, 83, 62, 71, and 64%

(2) Parks and Huffman, "The Free Energies of Some Organic Compounds," The Johns Hopkins Press, Baltimore, Md., 1935.

(3) Rice and Rice, "The Aliphatic Free Radicals," The Johns Hopkins Press, Baltimore, Md., 1935.

(4) Morton, *Ind. Eng. Chem., Anal. Ed.*, **11**, 170 (1939).

(14.6, 15.4, 12.7, 14.2 and 13 g.); for butylmalonic acid, 9.5, 5.0, 22.5, 5.0, and 8% (1.3, 0.7, 3, 0.7, and 1.0 g.). Total yields of all acids showed a definite drop when large quantities of alcohol were used but the respective amounts of benzoic and butylmalonic acid varied once (with 4 ml.) in an unpredictable manner. In general loss of monosodium compound was greater.

Purifying nitrogen by passing it over heated copper, through sulfuric acid, and then finally through a preliminary reaction mixture to ensure thorough scrubbing showed little, if any, difference from results obtained with no gas purification. Thus under conditions identical with those described in the preceding paragraph except that 4 ml. of amyl alcohol was used to activate the sodium, yields of 16.3 g. (81%) of benzoic acid and 0.8 g. (6%) of butylmalonic acid were obtained. The total yield of 87% was only slightly higher than the corresponding value of 84% reported above. The purified and dried nitrogen had been allowed to bubble slowly through the prereaction scrubber which contained double the quantity of amylsodium for a total time of twenty hours. After carbonating and decomposing the contents of this scrubber in the usual manner there was found 29.5 g. (73%) of benzoic acid and 1.2 g. (5%) of butylmalonic acid (total 78%). No nitrogen-containing compound could be observed among the products. In all other experiments reported in this paper no attempt was made to purify the commercial nitrogen being used as the inert atmosphere.

Effect of Varying the Quantity of Sodium.—Amyl chloride, 20 ml. (0.17 mole), dissolved in 40 ml. of petroleum ether was dropped onto varying amounts of sodium sand suspended in 120 ml. of petroleum ether. The amyl alcohol used to activate the sodium was in the proportion of 2 ml. of alcohol to 30 g. of metal. The temperature was maintained at −15 to −20° throughout the one hour needed for addition, the thirty minutes required for agitation, and the time for carbonation. Usually it was unnecessary to add more solvent to facilitate stirring. At this low temperature elimination of side reactions such as decomposition of amylsodium, or metallation of sodium caproate during carbonation was expected. With 2, 4, 7.6, 30 and 45 g. (0.5, 1, 2, 7.9 and 11.8 ratio of atoms of sodium to moles of amyl chloride) of sodium the yields of total acids were 16, 17, 63, 90 and 95%, respectively, distributed between caproic 10, 12, 44, 68, and 69% (1.1, 2.4, 8.5, 13.1, and 13.2 g.) and butylmalonic acid 6, 5, 19, 22, and 26% (0.4, 0.7, 2.4, 2.9, and 3.4 g.). Decane was determined by fractionation, 40 ml. of Nujol being added in order to have a high boiling residue in the flask. In a test run, 10 ml. out of 10 ml. of decane was recovered in this manner. Corresponding yields of decane in the above series were 21, 21, 22, —, 3.8% (1.4, 2.51, 2.62, —, 0.44 g.). The blank space represents failure to estimate decane accurately because the Nujol method had not been developed at that time. The remainder of the product was a little high boiling residue but largely pentane and pentene, determined by difference. Results are shown graphically in Fig. 1. Attention is called to the stability of amylsodium under these conditions which even in the presence of excess amyl chloride (experiments with 0.5 atom of sodium to a mole equivalent of amyl chloride) failed to react completely. From this experiment 45% (7.9 g.) of unreacted amyl chloride was recovered. From all other experiments no such halide fraction was found. Another interesting fact is that the ratio of percentage yields of butylmalonic to caproic acid did not vary greatly in this series, being 0.6, 0.4, 0.4, 0.3, 0.4, respectively. These data are in accord with the view that the disodium compound is not a secondary product of amylsodium.

Effect of Benzene and Petroleum Ether Mixtures.—This series of experiments was made in expectation that yields of organosodium compounds might be higher if the alkyl- were converted to the relatively inactive phenylsodium. The series showed, however, that amylsodium did not react with benzene below 0° and that the use of a mixed solvent had little effect on the yields of organometallic reagents. Results from typical experiments are shown in Table I.

TABLE I

EXPERIMENTS IN MIXTURES OF PETROLEUM ETHER AND BENZENE AS SOLVENTS

Constant factors: sodium 30 g. in a mixture of benzene and petroleum ether, amyl alcohol 4 ml., amyl chloride 20 ml. in 40 ml. of benzene; addition temp. −0 to −4°, addition time one and one-half hours, stirring temperature 27°, stirring time two hours, carbonation at room temp.

Benzene–petroleum ether mixture		Carbonation products				
		Benzoic		Butylmalonic		Total,
Benzene, ml.	Petroleum ether, ml.	G.	%	G.	%	%
80	50	11.5	57	3	23	79
80	25	12.7	62	3	22	84
80	10	12.4	61	3	22	83
80	5	10.0	49[a]	1.5	11	60
80	25	10.5	54[b]	3	24	78

[a] Owing to the small amount of petroleum ether present, the benzene crystallized from the solution and prevented uniform stirring. [b] Caproic rather than benzoic acid because the temperature of stirring and carbonation was 0 to −4°. Amyl alcohol, 2 ml., used for activation.

Attention is called to (a) the lower yields in this series as compared with the one (90%) just previous, possibly because of the higher temperature at which these runs were made, (b) the constancy of the values for butylmalonic acid which were approximately the same as that in petroleum ether alone (22%) at −15 to −20° and which remained practically unchanged in the last experiment when carbonation was carried out at 0 to −4°, (c) the comparative inactivity of amylidenedisodium which did not react with benzene under these conditions, although amylsodium was entirely changed.

Decane.—The following experiments were made in order to see whether the yield of decane could be made approximately quantitative with respect to the amylsodium. Amylsodium was prepared from 20 ml. of amyl chloride and 2 atom equivalents (8 g.) of sodium sand according to the method used in studying the effect of varying the quantity of sodium. After the customary half hour of stirring at −15° the mixture was warmed to 30° and an additional lot of 20 ml. of amyl chloride added over a period of thirty minutes. The mixture was stirred for a half hour longer, carbonated and decomposed.

Caproic acid, 0.24 g. (0.6%), and butylmalonic acid, 0.17 g., were obtained. On fractionation 6.2 g. of amyl chloride and 7.6 g. of decane were recovered. The decane amounted to 40% of the amyl chloride actually consumed. The yield when the same experiment was carried out at −15° amounted to only 21%.

In the same apparatus with the same quantities of material but with the sodium being added to a solution of amyl chloride at 30° rather than amyl chloride to sodium, the yield of decane was 10 g. (41%). This last experiment was prompted by the idea that excess amyl chloride might act as a trap for amylsodium and thereby show whether the initial phase of the reaction were yielding a larger amount of amylsodium than was being obtained by the usual method. The decane formed, however, did not exceed the amount of amylsodium (44%) revealed by carbonation experiments.

High-boiling Compounds.—In order to see whether part of the amylsodium had been consumed during carbonation to form triamylcarbinol or other oxygen-containing substances, the non-acid products from eleven runs in petroleum ether as a solvent were combined and fractionated. The quantity represented was a total of 285 g. of amyl chloride, 430 g. of sodium activated by 41 g. of amyl alcohol from which 143 g. (46%) of caproic acid, 57 g. (27%) of butylmalonic acid, had been recovered. After removing 1 ml. of low-boiling material, 8.7 ml. of *n*-amyl alcohol and 24 ml. of decane, the residue consisting of 17 g. (only 7% of the total amyl chloride) was fractionated at 2 ml. pressure through an 8-plate column of the Podbielniak type. Six cuts were made from 44 to 114° but carbon (85%) and hydrogen (15%) determinations showed that no oxygen was present. A final residue of 2.5 g. was fractionated at 1 mm. in the apparatus of Peakes[5] yielding 1 g. at 110–130°, 0.5 g. at 130–170° and 0.6 g. at 170–230°. This last fraction contained 3% of oxygen and was the only one found not to be entirely a hydrocarbon. All fractions showed a positive test for unsaturation with permanganate.

(5) Peakes, Jr., *Mikrochemie*, **18**, 100 (1935).

In the case of experiments in benzene, however, there was evidence of considerable oxygen-containing material. From thirteen separate experiments made in mixtures of petroleum ether and benzene involving a total of 280 ml. of amyl chloride, 420 g. of sodium and 58 ml. of amyl alcohol for activation, there was obtained a grand total of 164 g. (58%) of benzoic acid, 21 g. (6%) of butylmalonic acid and 11 g. (4%) of caproic acid, this last material coming from one run listed in Table I in which the temperature of carbonation was kept at 0 to −4°. The non-acidic portions from these experiments were combined and the benzene and petroleum ether removed by distillation. Triphenylcarbinol, 4.4 g. (0.7%), crystallized from the residue and was identified by its melting point and mixed melting point with an authentic sample. The remaining 35 g. of residue was stripped of about 12 g. of amyl alcohol and decane and then fractionated at reduced pressures. The oxygen content of this high-boiling material changed from an initial zero value to 3.9% for the last fraction. This oxygen was apparently not due to triphenylcarbinol since no further quantity could be separated from these portions.

Summary

No decane is formed prior to formation of amylsodium in the reaction between amyl chloride and sodium.

This Wurtz synthesis is divided into two distinct phases, that concerned with formation of the organometallic compound and that related to reaction of this intermediate with addition of alkyl chloride.

If free radicals are present in the early phase, their activity is limited to addition with sodium or to disproportionation and combination of the -idene product with two atoms of sodium to form another organometallic compound.

CAMBRIDGE, MASS. RECEIVED MAY 8, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, No. 208]

Condensations by Sodium. XVII. Comments on the Formation of Triphenylene

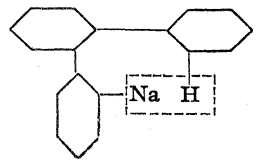
BY AVERY A. MORTON, JOHN T. MASSENGALE AND GRAHAM M. RICHARDSON

In an excellent paper by Bachmann and Clarke,[1] presence of around 2.0% of triphenylene among the products of the reaction of chlorobenzene and sodium was noted. Lately, Blum-Bergmann[2] has reported small quantities of the same compound from the reaction of phenylsodium and bromobenzene thus showing that this substance can arise from the second stage of a Wurtz synthesis. The importance of this material is that its formation is one of the major arguments for a free radical mechanism in Wurtz reactions, Bachmann and Clarke regarding its presence "among the reaction products as decisive in favor of the free radical explanation." In this paper we shall record the inadequacy of two other possible mechanisms not considered by the original investigators.

The first alternative is that *o*-phenylbiphenyl

(1) Bachmann and Clarke, THIS JOURNAL, **49**, 2089 (1927).
(2) Blum-Bergmann, *ibid.*, **60**, 1999 (1938).

could be metallated in the ortho position giving *o*-phenylbiphenylsodium, which then would split



out sodium hydride after the general method suggested for ethylsodium by Carothers[3] to form triphenylene. Under the conditions for isolating intermediate organometallic compounds employed in our work, triphenylene was shown to occur to a small extent from the reaction of chlorobenzene with sodium. Yet no evidence of metallation of *o*-phenylbiphenyl or of biphenyl itself by phenylsodium could be obtained. It is true that both of these hydrocarbons were metallated by amylsodium but no indication was observed that sodium hydride split from such a substance and formed triphenylene. Neither did the carrying out of a reaction between chlorobenzene and sodium in the presence of *o*-phenylbiphenyl produce any measurable conversion of that material into triphenylene.

The second proposition is that chlorobenzene could be metallated by phenylsodium giving chlorophenylsodium which could then condense with two similar molecules to give triphenylene. Substance is given to this idea by the work of Goldschmidt and Schön[4] suggesting that sodium and iodine might be present together in the cresol molecule, and by the work of Wittig[5] and of Gilman[6] in which lithium and bromine were likewise substituents together in methoxy containing compounds such as dimethoxybenzene and anisole. In the latter work indeed reference was made to a private communication from Wright that chlorobenzoic acid was obtained by carbonating the product of the reaction of chlorobenzene with sodium. Under conditions employed in our work, however, there is no evidence that a similar reaction occurred here. We have tested the action of both phenyl- and amylsodium on chlorobenzene under conditions which favor isolating such an intermediate product and find after carbonating no trace of chlorobenzoic acid.

Although the free radical mechanism is a convenient vehicle for expressing the manner in which triphenylene is formed, it does not necessarily follow that a similar mechanism has been demonstrated for occurrence of biphenyl, for the presence of such a small amount of triphenylene is equally explicable on the basis of its being the result of a side reaction wholly unrelated to the main one. In this connection it is worth noting that the free radical, phenyl, obtained by decomposition of phenylazotriphenylmethane by Wieland[7] showed no tendency to form biphenyl. The general comments relative to radicals (free or in a complex) and the role of organometallic compounds in Wurtz syntheses as mentioned in the paper just previous are worthy of consideration in this case also.

Experiments

Triphenylene and other Phenylated Polymers. (J. T. M.).—Formation of triphenylene under conditions employed in our work for isolating intermediate organometallic compounds was demonstrated by combining the high-boiling residues from nine separate experiments, in which chlorobenzene[8] (total of 550 g., 5.8 moles) had been added to sodium at room temperature to obtain a yield of approximately 75% of phenylsodium which was later used to metallate toluene. These high-boiling ends were distilled carefully through a fifteen-plate column. Out of 14.1 g. collected in three fractions from 135 to 155° at 2 mm., a total of 4.6 g. *o*-phenylbiphenyl, m. p. 52–53° (recorded[1] value 57°) was collected. A mixed melting point with an authentic sample (m. p. 55°) gave a value of 53–54°. The uncrystallizable oil from this fraction was adsorbed from a petroleum ether solution on 40–60 mesh activated alumina, giving several short indistinct bands at the top of the tube and one long band with deep blue fluorescence under the ultraviolet light. This last band was extracted with benzene yielding 0.9 g. of additional *o*-phenylbiphenyl, making a total of 1.5%.

From the fraction boiling from 155 to 165° there was isolated 0.3 g. of material melting at 144 to 146° which was not identified. The residue from the above distillation was distilled in a molecular still and the 4.8 g. of distillate was chromatographically adsorbed as described above. Several indistinct bands of a yellowish tint were in the top of the tube and one long band with a very bright blue fluorescence under the ultraviolet light in the lower portion. This material was also removed by benzene from which on evaporation fine needle-like crystals separated out of a viscous mother liquid. These were identified by their melting point of 192–194° (recorded[1] 199°, cor.) and by a mixed melting point (193–195°) with an authentic sample. The residual yellow liquid was dissolved in a mixture of petroleum ether and benzene and allowed to evaporate over a period of several days whereupon a mass of fine needle-like crystals and ten large diamond-shaped

(3) Carothers and Coffman, THIS JOURNAL, **51**, 588 (1929).
(4) Goldschmidt and Schön, *Ber.*, **59**, 948 (1926).
(5) Wittig, Pockels and Dröge, *Ber.*, **71**, 1903 (1938).
(6) Gilman, Langham and Jacoby, THIS JOURNAL, **61**, 106 (1939).
(7) Wieland, Popper and Seefried, *Ber.*, **55**, 1816 (1922); Wieland, *Rec. trav. chim.*, **41**, 576 (1922); see also Hey and Waters, *Chem. Rev.*, **21**, 169 (1937).
(8) Morton and Massengale, THIS JOURNAL, **62**, 123 (1940).

crystals were deposited. The residual oil was sucked off by vacuum filtration and the crystals were washed quickly with a mixture of benzene and petroleum ether. The ten large crystals were then picked out with a pair of tweezers and brushed clean from the needles. Their weight was 0.1 g., melting point 115–117° (recorded[1] value for *o,o'*-diphenylbiphenyl is 118°) and mixed melting point with an authentic sample 117°.

Metallation of *o*-Phenylbiphenyl. (J. T. M.).—Phenylsodium was prepared from 64 g. (0.6 mole) of amyl chloride, 37 g. (2.7 atom equivalents) of sodium sand activated by 5 ml. of *n*-amyl alcohol in 600 ml. of benzene. Phenylbiphenyl, 10 g., was added and the solution stirred and refluxed at 73° for nineteen hours before cooling and carbonating. On distillation 81% of the phenylbiphenyl was recovered intact, together with smaller amounts contaminated with adjacent fractions. No trace of triphenylene could be detected in the final residue. The acid recovered proved to be entirely benzoic and amounted to 33 g. (46%).

The experiment was repeated and methyl iodide, 60 g. (0.42 mole) instead of carbon dioxide added to the supposedly metallated *o*-phenylbiphenyl since methyl iodide once before[9] proved to be a more sensitive reagent for testing occurrence of an exchange reaction. Toluene was the chief product and 91% of the 7.5 g. of *o*-phenylbiphenyl originally added was recovered pure. The remainder was present as contamination in adjacent fractions. No trace of triphenylene could be noted.

Amylsodium was prepared from 8 g. of amyl chloride and 2.7 equivalent atoms of sodium sand in 100 ml. of petroleum ether. *o*-Phenylbiphenyl, 11.3 g., was added, the mixture warmed for thirty minutes at 40° and then carbonated. A mixture of acids with a neutralization equivalent of 189 between that for a mono- (284) and a dicarboxylic acid (164) of the phenylbiphenyl compound was obtained after separating the benzoic acid. The unchanged hydrocarbon amounted to 80% and no trace of triphenylene was noted.

Phenylsodium was prepared from 30 g. of chlorobenzene and 6 g. of sodium sand in the presence of 7.5 g. of *o*-phenylbiphenyl in order to see whether the reaction in the presence of this hydrocarbon would provoke ring closure or if the hydrocarbon would be metallated. After four hours of stirring at 40° and carbonating the products, 30% of benzoic acid and 20% of diphenyl was obtained. Of the original hydrocarbon, 90% was recovered unchanged in one fraction. No triphenylene corresponding to the missing 10% could be noted.

Metallation of Diphenyl. (G. M. R.).—When amylsodium from 150 ml. of amyl chloride and 75 g. of sodium in petroleum ether were stirred for eighty-eight hours with 12 g. of biphenyl at room temperature, the mixture after carbonation showed definite evidence of the expected metallation. Caproic acid, 4.7 g. (3%) and ether soluble acids (13%) were recovered. From the brown gummy residue, after ether evaporation, a white crystalline acid, 0.7 g., with neutralization equivalent of 188 and melting point of 205° in the crude state was obtained. It appeared to be *p*-phenylbenzoic acid (224°). On purifying and converting to the methyl ester a melting point of 116–117° (recorded[10] value 117–118°) was obtained. More of this same material (0.7 g.) precipitated from a petroleum ether wash of the residue and 0.4 g. of still more impure material of similar properties was obtained on further extraction with petroleum ether. The residue consisting of 1.9 g. was extracted with ether, acetic acid and benzene and appeared to be a mixture of di- and tri-substituted acids but no definite product was isolated. The non-acid portion contained no biphenyl but after evaporation left 2.7 g. of a thick amber colored liquid which was distilled in a molecular still at temperatures ranging from 114 to 230°. From the three fractions thus collected no crystalline derivative such as might be expected from splitting out of sodium hydride from two molecules could be obtained.

Metallation of biphenyl by phenylsodium failed when a mixture of 8.8 g. of biphenyl in 100 ml. of benzene was added to amylsodium prepared from 38 g. of amyl chloride and 35 g. of sodium (activated by 2.5 ml. of amyl alcohol) in benzene at room temperature. After stirring at 27° for two hours and at 75° for one and one-half hours, the mixture was carbonated. No trace of acids of biphenyl could be noted, although 9.7 g. (26%) of benzoic acid was obtained. Curiously enough, 5.5 g. (22% or the usual amount) of butylmalonic acid was found, presence of biphenyl apparently being sufficient to prevent the exchange of amylidenedisodium with benzene even at 75°.

Attempted Metallation of Chlorobenzene. (J. T. M.).—The Beilstein[11] test was found to be unreliable as a test for halogen in benzoic acid since the purest samples could be made to give a green color. In order to test for very small traces of chlorobenzoic acid, 30 g. of pure benzoic acid and 0.1 g. of chlorobenzoic acid were treated with ethyl alcohol, benzene, and sulfuric acid as a catalyst, the water removed to effect complete esterification by means of a ternary mixture under a fractionating column of fifteen plates, the mineral acid separated by washing, and the ester then distilled. Chlorine could be detected readily in the last 1 ml. of distillate, either by the Beilstein test or by sodium fusion and subsequent testing with silver nitrate. In parallel experiments with benzoic acid, no chlorine could be observed. This method was applied to the combined benzoic acid residues from a number of preparations of phenylsodium from chlorobenzene and sodium but no evidence of chlorobenzoic acid could be found. Furthermore, a mixture of 11 g. of amyl chloride and 12 g. of chlorobenzene (0.1 mole of each) was dropped onto 0.5 atom of sodium in 200 ml. of petroleum ether. Addition and stirring time were one-half hour each. The temperature during these periods and during carbonation did not exceed 3° in order to make the conditions as favorable as possible for isolating chlorophenylsodium. The yield of benzoic acid was 1.9% based on the combined reactants and contained no detectable trace of chlorobenzoic acid when tested in the above manner. The hydrocarbon layers likewise gave no halogen tests in the fraction which boiled above the boiling point of chlorobenzene.

Phenylsodium was prepared from 43 g. of amyl chloride and 24 g. of sodium in benzene in the usual manner and treated dropwise with 68 g. of chlorobenzene over a period

(9) Morton and Fallwell, THIS JOURNAL, **60**, 1426 (1938).

(10) Meyer and Hofmann, *Monatsh.*, **38**, 353 (1917).

(11) Similarly the Beilstein test for chlorine was found (G. M. R.) to be worthless in the case of caproic acid.

of one hour and a half before carbonation. The mixture of acids obtained from this experiment gave no halogen test. Similarly amylsodium was prepared in petroleum ether and the mixture stirred for four hours at room temperature before carbonation. Tests for halogen in the acid and hydrocarbon fractions were negative.

Summary

o-Phenylbiphenyl and biphenyl are not metallated by phenylsodium but are by amylsodium.

Under the conditions in which organometallic compounds are isolated in this work no evidence of metallation of chlorobenzene could be detected.

Triphenylene is not formed under the conditions of this work either as a result of metallation of *o*-phenylbiphenyl or of chlorobenzene.

CAMBRIDGE, MASS. RECEIVED NOVEMBER 7, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, No. 209]

Condensations by Sodium. XVIII. A Study of the Possible Conversion of Amylsodium to Amylidenedisodium

BY AVERY A. MORTON AND GRAHAM M. RICHARDSON

In an earlier paper[1] primarily connected with formation of phthalic acid, curves related to exchange of amylsodium with benzene showed that with small amounts (5 ml.) of benzene a drop in yield of caproic acid appeared with an increase of butylmalonic acid. These results suggested conversion of amylsodium into amylidenedisodium at 42° and necessitated reëxamination of the subject. As a result of an extensive investigation we find: (a) that higher yields of butylmalonic acid are more apt to be obtained if the mixture of organosodium compounds is heated at 42° or stirred for a long time at room temperature but the results are very erratic and if such a change occurs it does not exceed 10%; (b) that at −15° where the experiments proved quite reproducible no hint of such a change has been observed even on long stirring; (c) that when benzene is used as a trap at room temperature amylidenedisodium is still formed. These results, together with the earlier work on this subject, confirm the original opinion[2] that the chief source of amylidenedisodium is not by way of amylsodium. Subject to the restriction on the nature of free radicals in these solutions as discussed in two papers just previous in this series, the view of a radical origin for this material appears the most reasonable.

Irrespective of whether conversion actually occurs, warming at 42° is reasonably successful as a general method of increasing the yield of butylmalonic acid. Higher temperatures (70–80°) have earlier[3] been shown to lead to decomposition. The erratic results (see Tables I and II) at 42° are probably due to thickening of the reaction mixture when warmed, a difficulty absent at −15°.

In hope that a nickel catalyst would labilize the hydrogen atom and promote the hoped for change, experiments were made in the presence of this metal. The results were unexpected in that no increase in butylmalonic acid was observed and that portion of the amylsodium which formerly had been converted to the disodium intermediate, was decomposed. Apparently a small amount only of the amylsodium is active, possibly because of particle size or because of a complex salt structure.

It might be argued from these facts that the original amylidenedisodium present before heating at 42° owed its origin also to a certain proportion of very active amylsodium. Against this notion some experiments in benzene can be cited. Amylsodium reacts readily with benzene at room temperature, thereby making it possible to use it as a trap. Amylidenedisodium reacts more slowly so that it is possible to find butylmalonic acid among the products of carbonation when addition of amyl chloride to sodium is made in benzene at room temperature. Indeed, when biphenyl was present (preceding paper) the disodium compound apparently was protected and the quantity of butylmalonic acid was essentially the same as when petroleum ether was the solvent. An especially active amylsodium, however, would be expected to be more active also toward benzene so that little or no disproportionation should occur. The same argument applies also to the

(1) Morton and Fallwell, Jr., THIS JOURNAL, **60**, 1924 (1938).
(2) Morton and Hechenbleikner, *ibid.*, **58**, 2599 (1936).
(3) Morton and Hechenbleikner, *ibid.*, **58**, 1697 (1936).

experiments under pressure of carbon dioxide reported[4] early in this series.

In the curve referred to at the beginning of this paper a second minimum (total acids) in addition to the first already discussed, was noted when a larger amount of benzene was added. This second point is now shown to be due in all probability to physical factors such as stirring. The reaction mixture becomes very thick during this exchange reaction and erratic results are therefore possible. As a result of a considerable number of experiments under greatly improved stirring, we find that it is possible to eliminate this second minimum entirely. Erratic results are still secured but under proper agitation the number is reduced materially. The reconstructed curve (Fig. 1) suggests that amyl- may be more closely related to phenyl-sodium and amylidenedisodium to phenylenedisodium than was at first suspected.

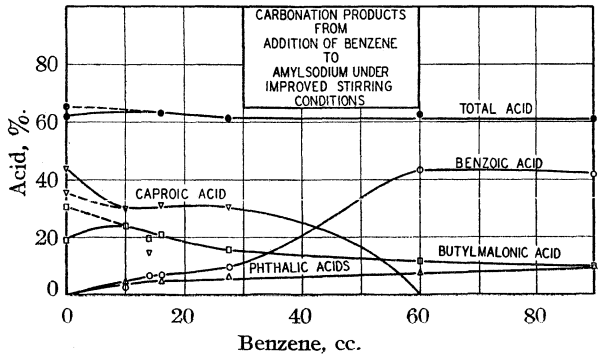


Fig. 1.—Carbonation products from addition of benzene to amylsodium under improved stirring conditions.

Much effort has been spent in order to effect 100% metallation of benzene by excess amylsodium in hope that the procedure would be useful in identification or analysis of benzene in certain petroleum fractions. The best results, however, did not reveal more than 50% of benzene converted to phenylsodium. In contrast to these results biphenyl is completely removed by amylsodium as shown in the paper just previous. This greater susceptibility toward metallation by amylsodium of biphenyl over benzene is particularly interesting since phenyl appears to have a greater affinity for sodium than the biphenyl radical.

Experiments

Effect of Warming Amylsodium.—The general conditions described in the two previous papers were applied to this work. Amyl chloride[5] was distilled before use and a fraction boiling at 107–108° was used. The quantities employed and the results obtained are listed in Tables I and II.

TABLE I

AMYLSODIUM PREPARED AT 18 TO 22°

Constant factors: amyl chloride 37.5 ml. diluted with 25 ml. of petroleum ether; sodium 17.5 g. activated with 2 ml. of *n*-amyl alcohol; petroleum ether 150 ml. at start of the reaction, more being added as the mixture thickened on heating; addition time one and one-half hours; carbonation at 22 to 28°.

No.	Hrs. stirring time at 27°	Hrs. stirring time at 42°	Yields of acids: Caproic G.	Caproic %	Butylmalonic G.	Butylmalonic %	Total, %
1	1	0	15.8	43	4.7	19	62
2	3	0	13.0	36	4.5	18	54
3	4	0	10.9	30	7.4	30	60
4	6	0	13.0	36	4.5	18	54
5	1	2	12.5	35	7.6	31	66
6	1	2	14.5	40	4.5	18	58
7	4	2	14.8	41	5.9	24	65

Attention is called to the first four experiments in which the time of stirring was gradually lengthened. In the four-hour period a yield of 30% of butylmalonic acid with a decreased yield of caproic acid was obtained. The inconsistency of this result is shown in experiment 4, in which such a change could not be effected even in six hours. Experiment 5 likewise gives a high yield of the dicarboxylic acid which was not duplicated in 6. Experiment 7 was intended to be a combination of the two best conditions noted before. Although the yield of the malonic acid in this case was disappointingly low, it nevertheless was the third highest in the whole series.

TABLE II

ADDITION OF AMYL CHLORIDE AT 0 TO −4°

Constant factors: amyl chloride 20 ml. diluted with 40 ml. of petroleum ether; sodium 30 g. activated by 2 ml. of *n*-amyl alcohol; petroleum ether 150 ml. at start of the reaction; addition time one hour; carbonated at 0 to −4°.

No.	Hrs. stirring time at 0–4°	Hrs. stirring time at 42°	Yields of acids: Caproic G.	Caproic %	Butylmalonic G.	Butylmalonic %	Total %
8	3.5	0	11.0	58	2.9	22	80
9[a]	0.5	0	10.8	56	2.5	20	76
10	.5	0	11.5	60	3.0	23	83
11	.5	1	11.5	60	3.4	26	86
12	.5	2	13.1	68	3.1	21	89
13	.5	2	10.9	57	2.4	18	75
14	.5	3	10.1	53	4.0	31	84
15	.5	8	9.8	51	3.6	27	78

[a] Special attention is called to the changes which occur in experiments 9 to 15, in which the time of heating at 42° gradually was extended to eight hours.

In one experiment only could the yield of butylmalonic acid be raised to 31% although the second highest yield was one in which long heating had been applied. The only suggestion of consistency in these results is that the two experiments which were heated for the longest time

(4) Morton and Hechenbleikner, THIS JOURNAL, **58**, 754 (1936).

(5) Amyl chloride was furnished by the courtesy of the Sharples Solvent Corporation.

had the highest yields of butylmalonic acid and the lowest yields of caproic acid.

In another experiment, using the same quantity of reagents given in Table II but carrying out the addition at −15 to −20°, the stirring time at that same temperature was varied from one-half hour to four hours. Carbonation at the same low temperature resulted in the same yields in both cases for butylmalonic acid, 2.9 g. or 22% but the yield of caproic acid fell during that period from 13 to 11 g. (68 to 59%).

Experiments with a Nickel Catalyst.—The conditions were the same as those employed in Table II except that nickel catalyst prepared from 4 g. of Raney nickel was employed under the conditions specified.

TABLE III

No.	Hrs. stirring time at 0 to −4°	Hrs. stirring time at 42°	Yields of acids: Caproic G.	Caproic %	Butylmalonic G.	Butylmalonic %	Total %
16	3.5[a]	0	11.5	60	3.0	23	83
17	0.5[a]	3	10.1	53	2.4	18	71
18	.5[b]	3	10.0	52	3.0	23	75

[a] Catalyst present during addition of amyl chloride. [b] Catalyst added after addition of amyl chloride.

Experiment 16 was almost an exact duplicate of experiment 8 in Table II and shows that nickel was without appreciable effect as long as the mixture was not heated. Experiment 17 is a duplicate of number 14 and shows that while caproic acid decreased the butylmalonic acid was not increased. Experiment 18 likewise shows the effect of nickel on amylsodium. Yields of caproic acid in 17 and 18 are as low as the two lowest in Table II.

Experiments in Benzene.—The results listed in Table IV show the formation of amylidenedisodium (butylmalonic acid) from amyl chloride and sodium in presence of solvent used as a trap for amylsodium. Addition temperature in all cases was at 18–22°. Carbonation temperature was at 22 to 28°. All results and special conditions are listed in the accompanying table with explanatory notes.

TABLE IV

No.	Yields of acids: Benzoic G.	Benzoic %	Butylmalonic G.	Butylmalonic %	Total %
19[a]	14.4	38	2.5	10	48
20[b]	30.0	40	3.3	7	47
21	27.9	37	4.9	10	47
22	9.7	26	5.5	22	48

[a] Experiment 19: amyl chloride 37.5 ml., sodium 53 g. activated by 7.5 ml. of amyl alcohol, 500 ml. creased flask as a reaction vessel. Addition time three hours, stirring at 27° for one hour. [b] Experiment 20: amyl chloride 75 ml., sodium 35 g., 1-l. three-necked flask as a reaction vessel, addition time two and one-half hours. Stirring time four hours at 27°. From among the products phthalic acid (iso- and tere- mixture) 3.2 g. or 6% was isolated also. In experiment 21, conditions were the same as in 20 except that a 1-l. creased flask was used as the reaction vessel. Experiment 22 is the one which contained biphenyl and is described in the paper immediately preceding. A trace of the phthalic acid was formed.

Exchange Reaction of Amylsodium with Benzene.—In these experiments a 500-ml. creased flask was used to effect better agitation. Amyl chloride, 37.5 ml., mixed with an equal quantity of petroleum ether was added dropwise over a one and one-half hour period to 35 g. of sodium sand activated with 5 ml. of alcohol, and suspended in 250 ml. of petroleum ether; addition temperature was 18 to 22°. After addition was complete the mixture was stirred at 25 to 30° for one hour. Benzene was then usually added and the mixture with or without benzene heated at 42° for two hours. Carbonation was at 22 to 28°. Quantities of benzene added in separate experiments were 10, 14, 16, 27.5, 60 and 90 ml. Corresponding yields of acids are caproic: 10.7, 5.4, 11.2, 11.0, 0 and 0.9 (30, 15, 31, 0, 0.7%); butylmalonic acid 5.9, 4.9, 5.1, 3.9, 2.9 and 2.5 g. (24, 20, 21, 16, 12 and 10%); benzoic acid, 1.1, 2.5, 2.5, 3.5, 16.4 and 15.8 g. (3, 7, 7, 9, 43 and 41%); phthalic acid 1.1, 0.7, 1.2, 1.6, 2.0 and 2.5 g. (4, 3, 5, 6, 8 and 10%). In the graph the values for zero benzene are from two separate observations in one of which (dotted line) the conversion did not occur.

Attempted Quantitative Metallation of Benzene.—In addition to the foregoing experiments, 5 ml. of benzene was put in the solvent before addition of amyl chloride and treated in the usual manner. Not more than 28% of this benzene was converted to benzoic and phthalic acids. In another case, 5 ml. of benzene was added after addition of amyl chloride was completed and the mixture then stirred at room temperature for seventy-two hours. In this way 50% of the benzene was converted to acids.

Summary

Amylidenedisodium frequently is obtained in somewhat higher yields if the mixture is warmed at 42° or is stirred for a very long time. Simultaneously lower yields of caproic acid are usually found. These results suggest that amylsodium is capable of being converted into amylidenedisodium but the change is an uncertain one and does not exceed 10% at the most.

Active nickel appears to decompose a portion of the amylsodium at 42°.

Under appropriate conditions butylmalonic acid is one of the carbonation products of the reaction of amyl chloride on sodium in benzene solution although amylsodium is completely removed by the solvent at room temperature.

Small quantities of benzene are not quantitatively metallated by amylsodium.

CAMBRIDGE, MASS. RECEIVED NOVEMBER 7, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF HARVARD UNIVERSITY AND TRINITY COLLEGE]

Further Evidence on the Mills–Nixon Effect

BY WARREN C. LOTHROP

In view of much recent evidence[1] indicating that in the case of hydrindene no quantitative stabilization of one Kekulé form exists as had been proposed,[2] it seemed well to describe some further confirmatory observations of our own. The successful diazo coupling of 5-hydroxy-6-methylhydrindene[3] gave evidence in agreement with the above, and Table I contains the results of these coupling tests on 0.1-g. samples with excess diazotized *p*-nitroaniline.

TABLE I

Case	Soln., cc.	*N* NaOH	Crude product, g.	% yield
1	10.5	0.119	0.072	35.9
2	11.0	.226	.046	23.0
3	12.0	.415	.029	14.5
4	14.0	.679	.017	8.5
5	16.0	.932	.009	4.5
6	20.0	1.24	.002	1.0
7	15.0	2.49	.001	0.5

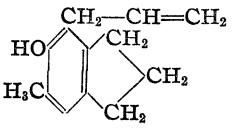
The apparent importance of the alkaline concentration to the coupling was investigated in further tests using buffered solutions and the theoretical quantities of a freshly prepared solution of *p*-nitrobenzenediazonium sulfate with the results given in Table II as the percentage yield of alkaline insoluble material. This seemed justifiable since the coupling products are the chief substances present which are insoluble in alkali and have all been reported and prepared by the same method. These figures indicate that the derivatives of hydrindene and tetralin are all inferior to β-naphthol in coupling ability and are more comparable with 2,4-dimethylphenol.

TABLE II

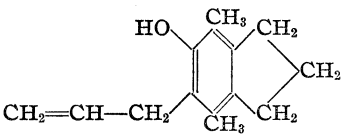
PER CENT. YIELD OF CRUDE COUPLING PRODUCT

Compound	*p*H 7.5	*p*H 11.3	10% NaOH
β-Naphthol	95.0	96.0	4.0
2,4-Dimethylphenol	71.5	52.5	5.8
5-Hydroxy-6-methylhydrindene (I)	69.0	68.7	0.5
5-Hydroxy-4,7-dimethylhydrindene (II)		69.5	5.7
6-Hydroxy-5,8-dimethyltetralin		55.5	7.0
1-Benzyl-2-hydroxynaphthalene	Alkali-soluble tars		
1,5-Diallyl-2,6-dihydroxynaphthalene	Alkali-soluble tars		

While this evidence seemed sufficient to classify hydrindene among the benzenoid compounds, samples of both I and II were converted into their allyl ethers and subjected to pyrolysis in sealed tubes, when both the ethers underwent the Claisen rearrangement to yield the corresponding substituted phenols (III) and (IV)



III



IV

These results are in complete agreement with all the evidence cited and with the similar case of fluorene.[4]

In conclusion the author wishes to express his appreciation to Professor L. F. Fieser for many helpful suggestions.

Experimental Part

The **preliminary coupling tests** (Table I) require no special description, but for the **buffered coupling tests** (Table II) the procedure was varied from the usual in that dioxane (5 to 10 cc.) was added to each 10-cc. portion of the buffer (containing 0.000675 mole of the substance to be tested) in order to achieve complete solution. The buffers were standard sodium and potassium phosphate mixtures, and the standardized diazonium solution was prepared[5] and standardized[6] as described in the literature.

5-Alloxy-6-methylhydrindene (allyl ether of I).—A mixture of 2.0 g. of 5-hydroxy-6-methylhydrindene (I), 2.2 g. of powdered anhydrous potassium carbonate and 1.8 g. of allyl bromide in 50 cc. of methyl ethyl ketone was refluxed for sixty-four hours and poured into water. The light brown oil which separated was warmed with 5% potassium hydroxide for one hour, recovered by ether extraction and distilled *in vacuo*, being thus obtained as a colorless oil (b. p. 95–97° at 3 mm.). The yield was 2.5 g. or 98%.

Anal. Calcd. for $C_{13}H_{16}O$: C, 82.92; H, 8.55. Found: C, 82.90; H, 8.88.

4-Allyl-5-hydroxy-6-methylhydrindene (III).—A mixture of 0.97 g. of the above allyl ether and 2.75 g. of dimethylaniline was heated in a sealed tube at 245° for

(1) Arnold, THIS JOURNAL, **61**, 1405 (1939); Clapp, *ibid.*, **61**, 2733 (1939); Sandin and Evans, *ibid.*, **61**, 2916 (1939); Lindner, *et al.*, *Monatsh.*, **72**, 330, 335, 354, 361 (1939).

(2) Mills and Nixon, *J. Chem. Soc.*, 2510 (1930); Fieser and Lothrop, THIS JOURNAL, **58**, 2050 (1936).

(3) Fieser and Lothrop, *ibid.*, **59**, 945 (1937).

(4) Lothrop, *ibid.*, **61**, 2115 (1939).

(5) Hantzsch and Jochem, *Ber.*, **34**, 3337 (1901); Schoutissen, *Rec. trav. chim.*, **40**, 763 (1921).

(6) Hantzsch, *Ber.*, **33**, 2517 (1900).

one hour. The pale brown solution was then poured into cold dilute hydrochloric acid. On standing the product solidified in faintly purple needles. It weighed 0.83 g. (86%) and was soluble in alkali. The material had a phenolic odor and showed a characteristic tendency to sublime, filling the tube in which it was stored with a dense mass of fine needles (m. p. 43–45°).

Anal. Calcd. for $C_{13}H_{16}O$: C, 82.92; H, 8.55. Found: C, 82.86; H, 8.74.

5-Alloxy-4,7-dimethylhydrindene (allyl ether of II).—A mixture of 2.2 g. of 5-hydroxy-4,7-dimethylhydrindene (II) 2.2 g. of finely powdered anhydrous potassium carbonate and 1.8 g. of allyl bromide in 35 cc. of methyl ethyl ketone was refluxed for twenty-four hours. The product was a colorless oil distilling at 107–108° at 2 mm. The yield was nearly quantitative.

Anal. Calcd. for $C_{14}H_{18}O$: C, 83.14; H, 8.95. Found: 3, 83.20; H, 8.70.

5 - Hydroxy - 6 - allyl - 4,7 - dimethylhydrindene (IV).—When a mixture of 1.34 g. of the above allyl ether and 3.00 g. of dimethylaniline was heated to 280° in a sealed tube and the amine was removed by dilute hydrochloric acid, the product was obtained in 75% yield as a pink solid. The color was removed by two crystallizations from petroleum ether but always returned on standing in contact with air. A sample stored in the ordinary way turned a bright violet in the course of two months while one kept in a sealed tube showed no color change. The melting point remained unaffected, however, at 66–67°.

Anal. Calcd. for $C_{14}H_{18}O$: C, 83.14; H, 8.95. Found: C, 83.38; H, 8.94.

Summary

The diazo coupling of and the rearrangement of the allyl ethers of 5-hydroxy-6-methylhydrindene and 5-hydroxy-4,7-dimethylhydrindene have been investigated with results which concur with much other evidence that the Mills–Nixon effect is at the most qualitative in the case of hydrindene.

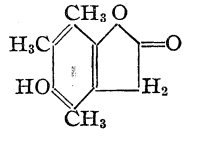
HARTFORD, CONNECTICUT RECEIVED OCTOBER 13, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

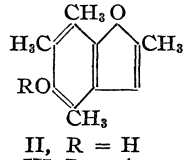
The Reaction between Quinones and Metallic Enolates. X. Trimethylquinone and the Enolates of β-Diketones[1]

BY LEE IRVIN SMITH AND E. W. KAISER[2]

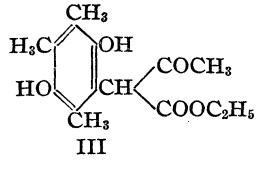
A few years ago, Smith and MacMullen[3] added the enolates of malonic ester and acetoacetic ester to trimethylquinone. From the malonic ester addition, one product, the isocoumaranone I, was obtained, while the addition of acetoacetic ester led to two substances, the isocoumaranone I, and the coumaron II. The formation of these products



I



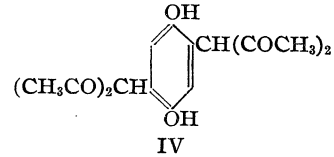
II, R = H
IX, R = Ac



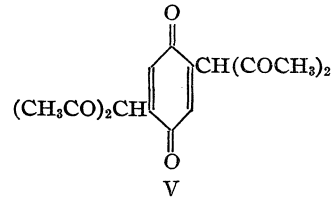
III

was interpreted as a primary 1,4-addition of the enolate to the quinone conjugated system which carried no substituent in the β-position, to give III (from acetoacetic ester), followed by the usual cleavages and ring closure.

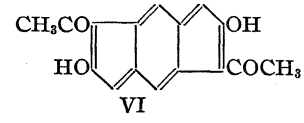
Ionescu[4] studied the reaction between acetylacetone and *p*-benzoquinone. The reaction was interpreted as an initial 1,4-addition of the β-diketone (two molecules), leading first to IV (not isolated) which was then oxidized by excess quinone or by air to V (also not isolated). The latter



IV



V



VI

(1) Paper IX, *J. Org. Chem.*, **4**, 342 (1939).

(2) Abstracted from a thesis by E. W. Kaiser, presented to the Graduate Faculty of the University of Minnesota, in partial fulfilment of the requirements for the Ph.D. degree, August, 1939.

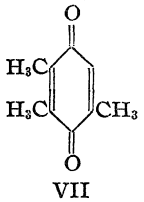
(3) THIS JOURNAL, **58**, 629 (1936).

(4) Ionescu, *Bull. soc. chim.*, **37**, 913 (1925); **41**, 1094 (1927); **51**, 171 (1932).

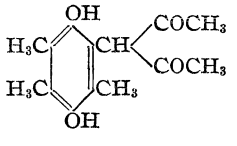
substance then underwent ring closure by elimination of water between the quinone oxygen atoms and a methyl group in each of the side chains, to give the final product, which was represented as VI. This substance VI is essentially a methylenequinone, and its formation from IV or V by ring closure involving a break in the carbon–oxygen bond of the quinone V or hydroquinone IV represents a rather unusual type of reaction.

In order to study this reaction, as well as to extend the general study of the addition of enolates to quinones, we have investigated the addition of the enolates of two β-diketones (acetylacetone and acetylisobutyrylmethane) to trimethylquinone VII. This quinone was chosen because it has but one open position, and previous work[3] had indicated that only one molecule of enolate would add to a quinone substituted in this manner. Moreover, since the first reaction products would be substances of the type of III, it seemed possible that this reaction might serve as a useful method for preparation of a variety of 5-hydroxycoumarons, which would be useful as sources of model compounds for use in investigations of certain phases of the chemistry of vitamin E.

When a dilute alcoholic solution of the quinone VII was added slowly to the enolate of acetylacetone, the product, formed in 72% yield, was the phenylacetyl acetone VIII. This substance reacted with phenylhydrazine, and was readily converted into the known coumarone II by action of hot concentrated hydrochloric acid.

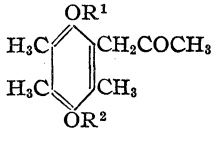


VII



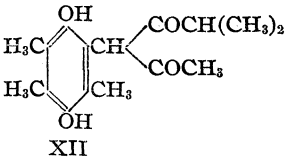
VIII

X, $R^1 = R^2 = Ac$
XI, monoxime of X
XIV, $R^1 = (CH_3)_2CHCO$; $R^2 = Ac$
XV, monoxime of XIV
XVII, $R^1 = Ac$; $R^2 = (CH_3)_2CHCO$
XVIII, $R^1 = Ac$; $R^2 = CH_2ClCO$

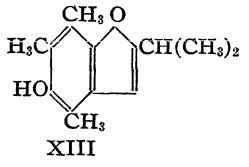


The action of acetic anhydride containing a trace of sulfuric acid upon the diketone VIII resulted in acetylation of both hydroxyl groups and the simultaneous loss of one of the acetyl groups from the β-diketone residue. The product X formed a monoxime XI, gave a negative phenol test (Folin), and was transformed by hot concentrated hydrochloric acid into the coumaron II. Attempts were made to hydrolyze the acetate X to the dihydroxy compound, using dilute sodium hydroxide, but this reagent also transformed X into the coumaron II, even at room temperature. Dilute hydrochloric acid under varying conditions either did not attack the acetate X, or else transformed it into the coumaron. From these results, and analogy with previous work,[3] there appears to be little doubt concerning structure VIII for the primary product of the reaction.

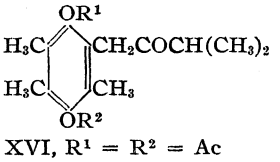
When the enolate of acetylisobutyrylmethane was added to the quinone VII, the product, formed in 81% yield, was the phenylated diketone XII. This substance reacted with phenyl-



XII



XIII



XVI, $R^1 = R^2 = Ac$

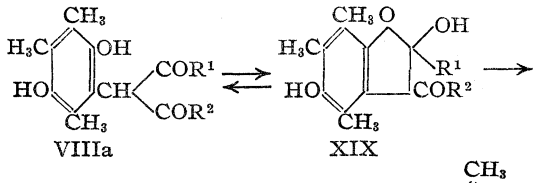
hydrazine, and was converted by action of hydrochloric acid into a mixture of coumarons, II and XIII, although the pure compounds were not separated from this mixture. Acetylation of XII with acetic anhydride containing a trace of sulfuric acid produced a mixture, from which a substance having the composition $C_{18}H_{24}O_5$ was isolated. This substance formed a monoxime XV, and in analogy with the acetylation of VIII, it was at first thought that the substance was the diacetoxybenzyl isopropyl ketone, XVI. However, when it was discovered that the action of hot hydrochloric acid upon $C_{18}H_{24}O_5$ produced the coumaron II, it became obvious that this compound could not possess the side chain of XVI, but must contain the acetone side chain of X, since XVI, on cyclization, would produce the coumaron XIII. Since $C_{18}H_{24}O_5$ gave a negative phenol test, and since it was isomeric with XVI, only two formulas for it were possible: XIV and XVII.

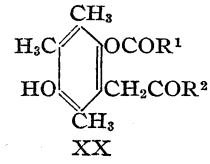
The choice between XIV and XVII was made as follows: the diketone VIII from acetylacetone was acylated with isobutyric anhydride. The product, XVII, formed in 56% yield, was a new substance also having the composition $C_{18}H_{24}O_5$. This substance also gave a negative phenol test. When VIII was acylated with chloroacetic anhy-

dride a product XVIII resulted which contained only one chloroacetyl group. It followed, therefore, that when substances of the type of VIII and XII were acetylated, the reaction involved a migration of one of the acyl groups from the diketone side chain to the *ortho* oxygen atom, and simultaneous acylation of the other hydroxyl group by the acylating agent used. On this basis, the first substance was assigned structure XIV, while its isomer, obtained from isobutyric anhydride and VIII, was assigned structure XVII. It followed also that the chloroacetyl derivative XVIII had an analogous structure; that is, an acetyl group of VIII migrated from the side chain to the *ortho*-oxygen atom, and simultaneously the other hydroxyl group was chloroacetylated.

That the reaction is a true intramolecular rearrangement is indicated by the yields of the products obtained in these acylations. If the reaction involved a complete rupture of an acyl group from the molecule, this acyl group would then be present in the reaction mixture as an acid, a simple anhydride, or a mixed anhydride, together with a large excess of the acylating agent used. Under these circumstances, *acetylation* of XII could give rise to no less than seven different compounds. Unless the isobutyryl group had a *much* greater acylating power than any of the other possible acyl groups, it could not have left the molecule entirely and then reëntered at some other position to give over 30% of XIV in the presence of a large excess of acetic anhydride. The fact that cleavage of the mixed β-diketone XII could occur in more than one way renders the probability of isolating XIV in good yield even less likely, assuming a mechanism which involved cleavage. Moreover, chloroacetic anhydride is much more reactive toward the hydroxyl group than is acetic anhydride, while isobutyric anhydride is the least reactive of the three in this respect.[5] Therefore, if in the acylation of VIII with either chloroacetic anhydride or isobutyric anhydride, the cleavage of an acetyl group had occurred to give acetic anhydride, competing reactions would have resulted in the formation of acylation products containing two chloroacetoxy groups in one case and two acetoxy groups in the other. Actually, however, the acylating agent used supplies only one acyl group; the other acetoxy group is derived from one of the acyl groups in the β-diketone side chain.

These results can be explained by assuming a primary ring closure between one carbonyl group of the β-diketone VIIIa and the *ortho* hydroxyl group to give a hemiacetal, XIX. This intermediate, being a potential β-diketone, can be cleaved to give the final product, a phenolic ester XX





This cleavage is analogous to the well-known decarboxylation of certain β-hydroxy acids which occurs on dehydration, and also to the cleavage of the addition products of certain β-diketones and Grignard reagents, observed by Kohler and Erickson.[6]

In these rearrangements, there is involved the shift of an acyl group from carbon to oxygen. Such rearrangements are very unusual, the reverse shift, from oxygen to carbon, being the common type. Nevertheless, a few examples of this sort have been recorded. Thus Kohler and Erickson[6] found that addition of one mole of phenylmagnesium bromide to diphenyl triketone XXI produced not the expected phenyldibenzoylcarbinol XXII but the benzoate of benzoin XXIII. Likewise, Blatt and Hawkins[7] reported that dibenzoylcarbinol XXIV, when vacuum distilled, rearranged to the benzoate of benzoylcarbinol XXV.

$C_6H_5COCOCOC_6H_5$ XXI

$(C_6H_5CO)_2C(OH)C_6H_5$ XXII

$C_6H_5COCH(C_6H_5)OCOC_6H_5$ XXIII

$C_6H_5COCHOHCOC_6H_5$ XXIV

$C_6H_5COCH_2OCOC_6H_5$ XXV

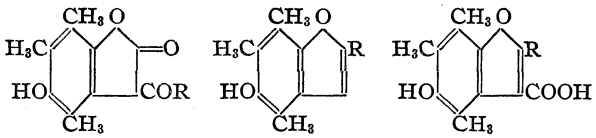
Attempts were made to add *n*-butyrylacetylmethane, benzoylacetone, and dibenzoylmethane to trimethylquinone, without success. Addition of the first of these diketones led to an oil, which could not be crystallized; addition of benzoylacetone produced only a very small amount of tan solid; while the only product obtained when dibenzoylmethane was used was unchanged diketone.

(5) Wilson and Sidgwick, *J. Chem. Soc.*, **103**, 1959 (1913).

(6) Kohler and Erickson, THIS JOURNAL, **53**, 2305 (1931).

(7) Blatt and Hawkins, *ibid.*, **58**, 81 (1936).

The method of Smith and MacMullen has been used by Bergel, Jacob, Todd and Work[8] for the preparation of coumaron and coumaran derivatives; from the product of addition of acetoacetic esters to trimethylquinone, these authors isolated three substances, the acyl isocoumaranone XXVI (main product), the coumaron XXVII, and the coumaron carboxylic acid XXVIII (R = $C_{15}H_{31}$ and $C_{17}H_{35}$).



XXVI XXVII XXVIII

Karrer, Escher and Rentschler[9] have also used the method; by addition of propionylacetic ester to the quinone they obtained the coumaron XXVIII (R = C_2H_5).

Repetition of the experiment of Smith and MacMullen[3] under slightly different conditions, has led to a good yield of the isocoumaranone XXVI (R = CH_3). This substance is a solid which melts at 126.5–128°; when steam distilled, it is transformed into the two products obtained by Smith and MacMullen, *viz.*, the isocoumaranone I and the coumaron II. Neither the intermediate III nor the coumaron acid (XXVIII, R = CH_3) was obtained, although these substances may have been formed in small amounts and lost in the purification of the main product, which required several crystallizations.

Experimental Part[10]

Acetylacetone and acetylisobutyrylmethane were prepared by the method of Sprague, Beckham and Adkins.[11] **Acetylacetone** was distilled several times through a Widmer column and the fraction boiling at 135–136°, obtained in 27% yield, was used. **Acetylisobutyrylmethane**, purified in a similar manner, boiled at 159–161° and was obtained in 20% yield.

Trimethylquinone (VII) was prepared by the method of Smith, Opie, Prichard and Wawzonek.[12]

(3,6 - Dihydroxy - 2,4,5 - trimethylphenyl) - acetylacetone, VIII.—Acetylacetone (3.8 g., 0.038 mole) was added to alcoholic sodium ethoxide (prepared from sodium, 0.75 g., 0.0326 mole, and dry ethanol, 12 cc.). The solution was cooled (0°) and stirred, and to it was added slowly (twelve hours) a solution of trimethylquinone (2.25 g., 0.015 mole) in dry ethanol (30 cc.). The resulting deep purple solution was stirred for an hour at room temperature, and then, with cooling (0°) and stirring, concd. hydrochloric acid was added dropwise until the color changed to light yellow. The acidified mixture was poured over cracked ice (300 g.) and the solid (2.7 g.) was removed and crystallized from benzene–petroleum ether (b. p. 90–100°). The product was white and melted at 129–130°.

Anal. Calcd. for $C_{14}H_{18}O_4$: C, 67.16; H, 7.21. Found: C, 67.47; H, 7.28.

Reaction with Phenylhydrazine.—The diketone VIII (0.32 g.) was dissolved in ethanol and water was added until the first trace of turbidity resulted. Phenylhydrazine (0.5 cc.) and acetic acid (1 drop) were added. A solid precipitated almost immediately. After standing overnight, this was removed and crystallized from ethanol. It weighed 0.43 g., and melted at 205–206° with decomposition. The structure was not investigated.

Anal. Found: C, 69.41; H, 6.94.

2,4,6,7-Tetramethyl-5-hydroxycoumaron (II).—The diketone VIII (0.5 g.) was refluxed with concd. hydrochloric acid (30 cc.) and ethanol (1 cc.) for three and one-half hours. Water (70 cc.) was added and the mixture was steam distilled. The product (0.3 g.) was isolated from the distillate and crystallized from dilute ethanol. It melted at 138–139°, alone or when mixed with an authentic specimen.[3]

2,4,6,7-Tetramethyl-5-acetoxycoumaron IX.—The coumaron II (0.5 g.) was acetylated in the usual way with acetic anhydride (2.1 cc.) and a drop of sulfuric acid. The product (0.46 g.) after crystallization from dilute ethanol, melted at 91–92°.

Anal. Calcd. for $C_{14}H_{16}O_3$: C, 72.39; H, 6.92. Found: C, 72.13; H, 7.12.

(3,6-Diacetoxy-2,4,5-trimethylphenyl)-acetone X.—The diketone VIII (1.04 g.) was acetylated with acetic anhydride (6.2 cc.) and a drop of sulfuric acid. The reaction was slightly exothermic and the diketone slowly dissolved. After standing at room temperature for an hour, the mixture was poured over ice (75 g.). The product (0.99 g., 81%) melted at 130–132°; after crystallization three times from petroleum ether (b. p. 90–100°), it melted at 135.5–136.0°. The material gave a negative Folin test and was insoluble in cold 10% sodium hydroxide. Attempts to remove the acetyl groups from this ketone invariably gave either unchanged material or the coumaron II. Dilute (0.12 *N*) hydrochloric acid was without action during eight hours at 65°; the action of more concentrated acid (1 *N*) at 100° for seven hours led to a mixture of starting material and II; while concentrated acid (12 *N*) gave only the coumaron. Likewise dilute sodium hydroxide gave only the coumaron.

Anal. Calcd. for $C_{16}H_{20}O_5$: C, 65.71; H, 6.91. Found: C, 65.91; H, 7.42.

Oxime XI.—The oxime (0.12 g.) was prepared from the ketone X (0.16 g.) in the usual way. The crude product melted at 160–162°; after several crystallizations from dilute ethanol, the monoxime melted at 172–175° with decomposition. The oxime dissolves immediately in 10% sodium hydroxide, giving a yellow solution.

(8) Bergel, Jacob, Todd and Work, *J. Chem. Soc.*, 1375 (1938).
(9) Karrer, Escher and Rentschler, *Helv. Chim. Acta.* **22**, 1287 (1939).
(10) Microanalyses by J. W. Opie, H. H. Hoehn and C. O. Guss.
(11) Sprague, Beckham and Adkins, THIS JOURNAL, **56**, 2665 (1934).
(12) Smith, Opie, Prichard and Wawzonek, *J. Org. Chem.*, **4**, 318 (1939).

Anal. Calcd. for $C_{16}H_{21}O_5N$: C, 62.48; H, 6.90; N, 4.56. Found: C, 63.02; H, 7.18; N, 4.55.

(3 - Isobutyroxy - 6 - acetoxy - 2,4,5 - trimethylphenyl)-acetone, XVII.—The diketone VIII (0.53 g., 0.0021 mole) was dropped into isobutyric anhydride (5.3 cc.) and sulfuric acid (2 drops) at room temperature. After two hours, all of the solid dissolved. After seven hours, the mixture was poured over ice (75 g.) and concd. ammonium hydroxide (8 cc.) was added. The solid was removed and washed thoroughly with water. It weighed 0.38 g. (56%) and melted at 117.5–123°. After crystallization from petroleum ether, the white solid melted at 127.5–128°. It gave a negative Folin phenol test.

Anal. Calcd. for $C_{18}H_{24}O_5$ (XVII): C, 67.46; H, 7.57; mol. wt., 320. Calcd. for $C_{22}H_{30}O_6$ (diisobutyrate of VIII): C, 67.66; H, 7.75; mol. wt., 390. Found: C, 67.55; H, 7.43; mol. wt. (Rast), 336, 302.

(3 - Chloroacetoxy - 6 - acetoxy - 2,4,5 - trimethylphenyl)-acetone, XVIII.—The diketone VIII (0.53 g., 0.0021 mole) was warmed (45–50°) with chloroacetic anhydride (6 g., 0.0033 mole) for an hour and fifteen minutes. The mixture was poured onto ice (75 g.) and allowed to stand for fifteen minutes. The oily solid was removed and washed several times with small portions of petroleum ether (b. p. 28–38°). It melted at 47–53° and was contaminated with much chloroacetic anhydride. The aqueous filtrate, on standing overnight, deposited 0.1 g. (17.5%) of a white solid (XVIII), which after several crystallizations from benzene–petroleum ether (b. p. 90–100°) melted at 162–163°. Although the yield of pure solid was poor, the actual yield of product was undoubtedly much higher. This substance gave a strongly positive Folin test, which, however, was of little consequence since chloroacetic anhydride itself gave a positive test.

Anal. Calcd. for $C_{16}H_{19}O_5Cl$: C, 58.79; H, 5.85. Found: C, 59.02; H, 6.29.

(3,6 - Dihydroxy - 2,4,5 - trimethylphenyl) - acetylisobutyrylmethane XII.—Acetylisobutyrylmethane (10 g., 0.078 mole) was added to alcoholic sodium ethoxide (prepared from sodium, 1.51 g., 0.066 mole, and dry ethanol, 14 cc.). The solution was cooled (0°) and stirred, and to it was added slowly (two hours) a solution of trimethylquinone (4.95 g., 0.033 mole) in dry ethanol (20 cc.). Stirring was continued for half an hour at room temperature after the addition, and then, with cooling (0°) and stirring, concd. hydrochloric acid was added dropwise until the deep violet color changed to yellow. The acidified mixture was poured onto ice (250 g.), the solid was removed and washed three times with petroleum ether (25 cc. each time, b. p. 40–70°) and once with water (25 cc.). The product XII weighed 7.43 g. (81%). After crystallization from dilute ethanol or benzene–petroleum ether (b. p. 90–100°) the substance formed colorless needles which melted at 131.5–132.5°.

Anal. Calcd. for $C_{16}H_{22}O_4$ (XII): C, 69.02; H, 7.97. Calcd. for $C_{12}H_{16}O_3$ (X, $R^1=R^2=H$): C, 69.30; H, 7.67. Found: C, 69.36; H, 7.98.

Reaction with Phenylhydrazine.—The diketone XII (0.32 g.) reacted with phenylhydrazine (0.5 cc.) and acetic acid (3 drops) in dilute alcohol, to give a product (0.3 g.) which melted at 167° with decomposition. The structure of this compound was not investigated.

(3 - Acetoxy - 6 - isobutyroxy - 2,4,5 - trimethylphenyl)-acetone XIV.—The diketone XII (1.64 g., 0.0059 mole) was dropped into acetic anhydride (12 cc.) containing a drop of sulfuric acid. The mixture became warm, and the solid dissolved. After standing for an hour, the solution was poured onto ice (75 g.). The solid was removed, washed with water, and dried. It weighed 1.44 g. After crystallization from petroleum ether (b. p. 90–100°), the solid weighed 0.52 g. and melted at 114–115.5°.

Anal. Calcd. for $C_{18}H_{24}O_5$: C, 67.46; H, 7.57. Found: C, 67.19; H, 7.27.

The filtrate on evaporation, left a mixture which melted at 100–115°.

When the ketone XIV (0.25 g.) was refluxed with concd. hydrochloric acid (17 cc.) for two and one-half hours, the product (0.13 g.) was the coumaron II, m. p. and mixed m. p., 137–138°.

Anal. Calcd. for $C_{12}H_{14}O_2$ (II): C, 75.75; H, 7.42. Calcd. for $C_{14}H_{18}O_2$ (XIII): C, 76.99; H, 8.33. Found: C, 75.57, 75.42; H, 7.81, 7.60.

Oxime XV.—The ketone XIV (0.24 g.) was converted to the oxime (0.1 g.) in the usual way. After crystallization from dilute ethanol, the product melted at 165–170° with decomposition. When mixed with the oxime XI, the substance melted at 150–160°.

Anal. Calcd. for $C_{18}H_{25}O_5N$: C, 64.41; H, 7.56; N, 4.18. Found: C, 64.50; H, 7.47; N, 4.51.

Cyclization of XII.—The diketone (0.53 g., 0.0019 mole) was refluxed for two and a half hours with concd. hydrochloric acid (25 cc.) and ethanol (1 cc.). The reaction mixture, after dilution with water, was steam distilled. The white solid (0.36 g.) which was removed from the distillate melted at 100–125°. This mixture probably consisted of the coumarons II and XIII, but the amount of material available was too small for fractional crystallization.

Addition of Other Diketones.—(a) Trimethylquinone (0.65 g.) was added to the sodium enolate of *n*-butyrylacetylmethane (from 1.3 cc. of diketone) in dry ethanol as described for the addition of acetylacetone. The only product was an oil which could not be crystallized. (b) The quinone (1.65 g.) in dry ethanol (10 cc.) was added to a suspension of sodium benzoylacetone (sodium, 0.58 g., diketone, 4.1 g., ethanol, 10 cc.) in the same manner. Only a few milligrams of a tan solid, m. p. 110–120°, was obtained. (c) The quinone (0.75 g.) in ethanol (10 cc.) was added to a suspension of the enolate of dibenzoylmethane (sodium, 0.21 g., diketone, 2.20 g., ethanol, 30 cc.) as described. The only product was dibenzoylmethane, m. p. and mixed m. p. 74–76°.

3 - Acetyl - 4,6,7 - trimethyl - 5 - hydroxyisocoumaranone (XXVI, R = CH_3).—Acetoacetic ester (5.7 g.) was added to a solution of sodium ethoxide prepared from sodium (0.97 g.) and dry ethanol (20 cc.). The quinone (3.1 g.) in ethanol (2 cc.) was gradually added and the deep purple solution was allowed to stand at room temperature for three and one-half hours. The reaction mixture was poured into ice (200 g.) and hydrochloric acid (20 cc.). The product appeared as an oil which soon crys-

tallized to a tan solid (4.5 g.) melting at 100–121°. Repeated crystallization from benzene–petroleum ether (b. p. 90–100°) gave white needles (2.58 g.) which melted at 126.5–128°.

Anal. Calcd. for $C_{13}H_{14}O_4$: C, 66.64; H, 6.03. Found: C, 66.48, 67.00; H, 5.88, 6.19.

The substance is relatively stable toward heat and inert solvents, but is unstable toward polar solvents. It is insoluble in sodium carbonate and in sodium bicarbonate solutions. No ether was formed using either methyl sulfate or diazomethane, nor could an oxime be obtained.

When the acetylisocoumaranone (0.4 g.) was steam distilled, coumaron II (0.07 g.), m. p. and mixed m. p. 137–138°, was isolated from the distillate and the isocoumaranone I (0.26 g.), m. p. 200.5–202.5°,[13] remained in the flask.

Summary

1. The sodium enolates of acetylacetone and isobutyrylacetylmethane react with trimethylquinone to give (3,6-dihydroxy-2,4,5-trimethylphenyl)-acetylacetone (VIII) and -acetylisobutyrylmethane (XII), respectively. No pure substances could be isolated from the product of the reaction between the quinone and the enolates of *n*-butyrylacetylmethane or benzoylacetone, and only unchanged diketone was isolated when the enolate of dibenzoylmethane was used.

2. Acylation of the diketones VIII and XII involves a rearrangement of one of the side chain acyl groups from carbon to the *ortho*-oxygen atom; simultaneously, the other hydroxyl group is acylated by the reagent used. A mechanism is suggested for this rearrangement.

3. An intermediate has been isolated from the reaction between trimethylquinone and sodium acetoacetic ester. This intermediate, when steam distilled, gives the final products obtained previously in a study of this reaction.

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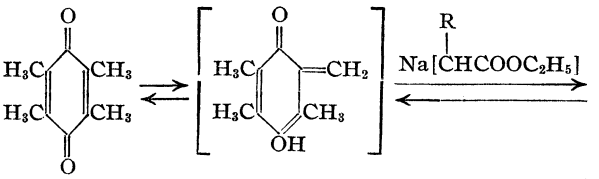
(13) The m. p. previously reported was 197–198°.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

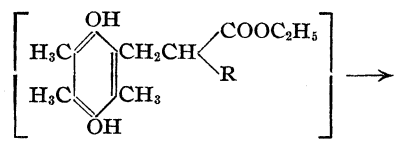
The Reaction between Quinones and Metallic Enolates. XI. Duroquinone and the Enolates of Cyanoacetic Ester and of β-Diketones[1]

BY LEE IRVIN SMITH AND E. W. KAISER[2]

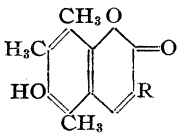
The reaction between duroquinone and sodium malonic ester,[3] was extended to other tetrasubstituted quinones by Webster,[4] who used 2,3-dimethyl-1,4-naphthoquinone, and by Johnson,[5] who used trimethylbromoquinone. Tenenbaum[6] varied the enolate by using sodium acetoacetic ester, but in all these cases the reaction led to a substituted coumarin (III, IV), and evidence was supplied by Horner[7] that the quinone was first converted into a "pentad-enolate" (I) which then underwent a Michael reaction with the other enolate. The first product (II) was cyclized and oxidized, leading to the coumarin as the final product. In every case so far studied, the enolate used contained an ester group so that the ring closure, by elimination of an alcohol, took place easily, and it has been thought that this easy ring closure was in large part responsible for driving



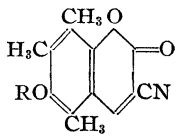
I



II



III, R = $COOC_2H_5$
IV, R = $COCH_3$
V, R = H
VI, R = Ac



VII, R = $CONH_2$
VIII, R = COOH
IX, Diacetate of VII

the series of reactions to completion, since the first step presumably, and the second step certainly, are reversible. In order to explore still further the limits of this reaction, the enolates of cyanoacetic ester and of two β-diketones (acetylacetone

(1) Paper X, THIS JOURNAL, **62**, 133 (1940).

(2) Abstracted from a Thesis by E. W. Kaiser, presented to the Graduate Faculty of the University of Minnesota, in partial fulfilment of the requirements for the Ph.D. degree, August, 1939.

(3) Smith and Dobrovolny, THIS JOURNAL, **48**, 1693 (1926).

(4) Smith and Webster, *ibid.*, **59**, 662 (1937).

(5) Smith and Johnson, *ibid.*, **59**, 673 (1937).

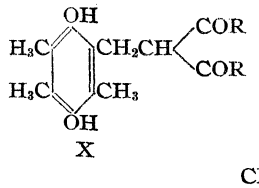
(6) Smith and Tenenbaum, *ibid.*, **59**, 667 (1937).

(7) Smith and Horner, *ibid.*, **60**, 676 (1938).

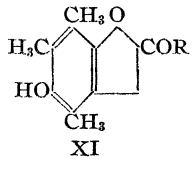
and dibenzoylmethane) have been studied with regard to their behavior toward duroquinone.

Sodium methyl cyanoacetate and duroquinone reacted in benzene to give the yellow cyanocoumarin V. In common with coumarins of the type of III and IV, this yellow coumarin V gave a colorless monoacetate, VI. The presence of the cyano group in the coumarin was shown by hydrolysis to the amide (VII). Although the cyano compound survived the action of hydrogen peroxide,[8] it was hydrolyzed to the amide in fair yield by warming with 80% sulfuric acid. This amide was resistant to further hydrolysis by sulfuric acid or phosphoric acid, consequently it was not possible to convert it to the acid VIII, a known substance. However, the acid VIII was readily converted into the amide VII via the acid chloride, and the two specimens of VII thus prepared were identical. Both specimens also gave the same acetate IX. Although this acetate IX was not a simple acetate and was probably a diacetate, the identity of the amides prepared by the two methods and the identity of the acetates prepared from these amides, serve amply to fix the structure of the coumarin V. This coumarin is therefore 3-cyano-5,7,8-trimethyl-6-hydroxycoumarin, and its formation from duroquinone and sodium cyanoacetic ester shows that this enolate, in common with all of the enolates containing a carbalkoxyl group, enters into a reaction with the quinone which involves the loss of the elements of alcohol as one of the steps.

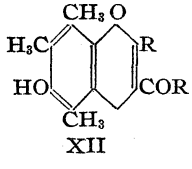
Turning to the β-diketones, it is obvious that the reaction between the enolates of these substances and duroquinone, involving as an intermediate an analog X of II, cannot be completed by elimination of the elements of an alcohol. Elimination of the elements of an aldehyde RCHO to give the 2-acylcoumaran XI would not be very probable, but elimination of water from the enolate of X to give the 2-alkyl-3-acyl-Δ^2-chromene XII would be a possibility. Attempts were made to add the enolates of acetylacetone and dibenzoylmethane to duroquinone, under varying conditions, without success. No products were obtained under any of the experimental conditions tried and in most cases considerable unchanged duroquinone was recovered. The failure of the β-diketones to add to duroquinone is of significance in connection with the mechanism of the addition of enolates to this quinone, and lends support to the hypothesis that an easy ring closure is necessary in order that the sequence from I to III may be completed. This sequence involves a Michael reaction which is reversible[9]; if, therefore, in the intermediate X ring closure is difficult, reversal of the Michael reaction will result in the recovery of the starting materials, or products resulting from the action of alkali upon them. It therefore may be concluded from these results that elimination of the elements of water (or NaOH) from the enol of the diketone X is inherently more difficult than the elimination of the elements of alcohol (or RONa) from such a substance as II. Definite statements, however, must await the synthesis of substances such as X and a study of the action of alkali upon them; such experiments are under way.



X



XI



XII

Experimental Part[10]

3-Cyano-5,7,8-trimethyl-6-hydroxycoumarin, V.—Methyl cyanoacetate (5.0 g., 0.05 mole) was converted into the enolate by refluxing it for an hour with powdered sodium (1.1 g., 0.05 mole) in dry benzene (50 cc., thiophene-free). A solution of duroquinone (6 g., 0.037 mole) in benzene (40 cc.) was added and the mixture was refluxed for seven days. The deep red solid was filtered off and washed thoroughly with benzene until the washings showed no yellow color. The solid was suspended in alcohol and iced hydrochloric acid (15 cc. acid, 15 g. ice) was added. The product weighed 2.38 g. and melted at 210–225°. After several crystallizations from acetic acid (with Norit the first time) the substance was obtained as a yellow solid which melted at 261.5–263°.

Anal. Calcd. for $C_{13}H_{11}O_3N$: C, 68.13; H, 4.80. Found: C, 68.17; H, 4.79.

3-Cyano-5,7,8-trimethyl-6-acetoxycoumarin, VI.—The coumarin (0.102 g.) was suspended in acetic anhydride (2 cc.) and a drop of sulfuric acid was added. The solid gradually dissolved and after standing for ten minutes at room temperature, the product began to crystallize out. More acetic anhydride (1 cc.) was added and the mixture was allowed to stand at room temperature for two hours. The suspension was poured onto a mixture of ice and am-

(8) (a) Murray and Cloke, THIS JOURNAL, **56**, 2749 (1934); (b) McMaster and Noller, *J. Indian Chem. Soc.*, **12**, 652 (1935).

(9) (a) Connor and Andrews, THIS JOURNAL, **56**, 2713 (1934); (b) Kroeker and McElvain, *ibid.*, **56**, 1171 (1934).

(10) Microanalyses by J. W. Opie, C. O. Guss and H. H. Hoehn.

monium hydroxide (8 cc.) and the solid was removed. It weighed 0.11 g. and melted at 213–219°. After successive recrystallization from dry ethanol, acetic acid and dilute acetic acid, it was white and melted at 227–228°.

Anal. Calcd. for $C_{15}H_{13}O_4N$: C, 66.40; H, 4.84. Found: C, 66.46; H, 5.15.

3-Carbamido-5,7,8-trimethyl-6-hydroxycoumarin, VII. The cyanocoumarin V (0.2 g.) was heated on the steam-bath with sulfuric acid (13 cc., 81%) for three and one-half hours. The reddish-yellow solution was poured over cracked ice (75 g.) and the solid was removed and crystallized from acetic acid. The product weighed 0.129 g. (60%) and melted at 290–293° (metal block) with decomposition. Repeated crystallization from acetic acid gave a product which melted at 302° (block) with decomposition; the melting point of this sample, determined in a capillary in the usual manner, was 288–290° with decomposition.

Anal. Calcd. for $C_{13}H_{13}O_4N$: C, 63.15; H, 5.55. Found: C, 62.74; H, 5.50.

Acetyl Derivative, IX.—The amide VII (0.14 g.) was refluxed for forty-five minutes in acetic anhydride (4.5 cc.) containing a drop of sulfuric acid. The cooled solution was poured over cracked ice (50 cc.) and concd. ammonium hydroxide was added until the mixture was basic to litmus. The solid (0.15 g.) was removed and crystallized from acetic acid; it then melted at 243–244.5°.

Anal. Calcd. for $C_{15}H_{15}O_5N$ (monoacetyl): C, 62.28; H, 5.19. Calcd. for $C_{17}H_{17}O_6N$ (diacetyl): C, 61.63; H, 5.13. Found: C, 60.84, 61.17; H, 5.07, 5.53.

3-Carboxy-5,7,8-trimethyl-6-hydroxycoumarin, VIII.—The acid was prepared by hydrolysis of the ester III (0.36 g.)[3] with hydrochloric acid (6 *N*, 40 cc.) in acetone (20 cc.).[11] The crude product (0.29 g.), which melted at 255–256°, was used directly for conversion to the acid chloride.

Acid Chloride of VIII, and Amide, VII.—The acid VIII (0.15 g.) was refluxed for fifteen minutes with thionyl chloride (2 cc.). Excess thionyl chloride was removed under reduced pressure and the acid chloride (not purified) was converted to the amide by addition of ammonium hydroxide (2 cc.). The amide (0.14 g.) was removed and crystallized from acetic acid, when it melted at 288–290° with decomposition (capillary tube and liquid bath) alone or when mixed with a specimen prepared from duroquinone and cyanoacetic ester.

Acetyl Derivative, IX.—The above amide VII was acetylated as already described. The product weighed 0.14 g., and after crystallization first from acetic acid and then from dilute acetic acid, it melted at 241–242.5°, alone or when mixed with the acetyl amide derived from duroquinone and cyanoacetic ester.

Anal. Calcd. given above. Found: C, 60.87; H, 5.57.

Duroquinone and Acetylacetone.—Several attempts, using different conditions, were made to carry out this condensation, but all failed.

A. In Dry Benzene with Metallic Sodium.—Acetylacetone (7 g., 0.07 mole) was added to a suspension of powdered sodium (1.60 g., 0.07 mole) in dry benzene (50 cc., thiophene free). Duroquinone (5 g., 0.031 mole) dissolved in a few cc. of benzene was then added and the mixture was refluxed for four days. The initial very dark color changed to deep blue-green during this time. The solid (8.4 g.) was filtered off and thoroughly washed with benzene. Decomposition of this material with hydrochloric acid (2 *N*, 15 cc.) gave 2.7 g. of a reddish solid, which after crystallization from alcohol melted at 112–113° alone or when mixed with duroquinone. Extraction of the acid filtrate with benzene gave 1.6 g. of acetylacetone boiling at 135–140°. No other products could be isolated.

B. In Ethanol with Magnesium Ethoxide.[5]—Acetylacetone (2.0 g.) was added to a suspension of magnesium ethoxide (1.17 g.) in dry ethanol (15 cc.). Duroquinone (1 g.) was then added and the mixture was refluxed for forty-eight hours. Most of the alcohol was removed by distillation, and replaced by ether. The light tan solid which separated was removed and decomposed with dilute hydrochloric acid. An oil resulted which soon resinified to a very dark brown mass. No definite products could be isolated from this resinous material.

C. In Ethanol with Ammonia.—A solution of duroquinone (1 g.) and acetylacetone (2 g.) in dry ethanol (40 cc.) was saturated with dry ammonia. After standing overnight at room temperature, the clear red solution was acidified with hydrochloric acid and diluted with water. The only product obtained was duroquinone, m. p. and mixed m. p. 112–114°.

D. In Ethanol with Sodium Ethoxide.—To a solution of sodium ethoxide in dry ethanol (0.42 g. sodium, 15 cc. ethanol) acetylacetone (2.0 g.) was added. Duroquinone (1 g.) in dry ethanol (25 cc.) was added to the enolate solution and the mixture was refluxed for twenty-four hours. A deep red color developed as soon as the quinone was added, but decomposition of the reaction mixture with iced hydrochloric acid gave only a brick-red solid which melted at 115–150°. This solid was very soluble in alcohol, ether, acetic acid and other organic solvents and all attempts to obtain pure material from it failed. It was probably a mixture of duroquinone (m. p. 111–112°) and diduroquinone (m. p. 207°).

Summary

1. The enolate of methyl cyanoacetate condenses with duroquinone to give 3-cyano-5,7,8-trimethyl-6-hydroxycoumarin (V), the reaction taking the same course as that of other enolates containing a carbalkoxyl group.

2. The structure of the cyanocoumarin was proved by converting it to the amide and synthesizing the latter from the known 3-carboxy-5,7,8-trimethyl-6-hydroxycoumarin.

3. The cyanocoumarin could not be hydrolyzed to the acid; all attempts failed to carry the hydrolysis beyond the amide stage.

4. The enolates of acetylacetone could not be condensed with duroquinone. The possible bearing of this fact upon the mechanism of duroquinone–enolate reactions is discussed.

MINNEAPOLIS, MINNESOTA

RECEIVED NOVEMBER 10, 1939

(11) Smith and Denyes, THIS JOURNAL, **58**, 306 (1936).

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

The Chemistry of Vitamin E. XX.[1] The Preparation of *o*-Xylohydroquinone

BY OLIVER H. EMERSON[2] AND LEE IRVIN SMITH

o-Xylenol is not available in quantity and is difficult to prepare. The preparation of *o*-xyloquinone and hydroquinone from it by the generally useful method previously described[3] is, therefore, impracticable. The present paper reports improvements in the previously described[4,5,6] synthesis of this quinone from *o*-xylene via the *o*-nitro compound and the amine. The yields obtained in the three steps are, respectively, 85, 75 and 33%, or an over-all yield of 21% of quinone from hydrocarbon. The corresponding over-all yield previously reported by this method is 12%.[4,5,6]

Procedure

3-Nitro-*o*-xylene.—*o*-Xylene (50 g.) is nitrated at −10 to 0° by stirring it vigorously and dropping into it slowly a mixture of sulfuric acid (100 g.) and nitric acid (50 g., d. 1.4). During the addition, the tip of the dropping funnel is shielded from spray by keeping it well up in the neck of the flask, out of the path of the droplets thrown by the stirrer. This prevents any contact of xylene with an excess of the nitrating mixture and thus avoids the formation of any dinitro compound.[5] The product is poured into water and washed with dilute sodium hydroxide. Any polynitro-*o*-xylene can be removed from the mono compound by steam distillation but is more efficiently eliminated by distillation in a vacuum from a Claisen flask, the fraction boiling at 115–130° at 15 mm. pressure being refractionated through a Fenske 1-meter column and the final fraction (61 g., 85.6%) boiling at 127–130° at 18 mm. pressure being taken as the pure 3-nitro compound. The residues, especially the first, should not be heated too strongly as they may decompose quite vigorously.[7]

3-Amino-*o*-xylene (II).—For the reduction of the nitro compound, the directions of Yokoyama[6] were followed, except that the amine finally was isolated as the sulfate, which is of advantage both for removal of small amounts of 4-amino-*o*-xylene whose sulfate is much more soluble, and in giving the amine in a good physical state for the subsequent oxidation. From 75 g. of the nitro compound there resulted about 60 g. of the amine. This was vigorously stirred into water (500 cc.) and sulfuric acid (30 g.) and the solution cooled overnight in a refrigerator. The amine sulfate weighed 62 g. (74%).[8]

***o*-Xyloquinone** (III).—The oxidation was based on the procedure of Yokoyama[6] but it is preferable to use the dry, powdered amine sulfate and dilute sulfuric acid rather than the free amine which forms coarse lumps when added to the strong sulfuric acid as recommended by Yokoyama. Dry, well powdered 3-amino-*o*-xylene sulfate (31 g.) was added to a solution of sulfuric acid (95 cc., 175 g.) in water (680 cc.) and the solution was placed in a refrigerator (5–10°) until cold. A solution of sodium dichromate dihydrate (22.5 g.) in water (60 cc.) was also cooled to 5–10°. During the course of an afternoon the dichromate was added to the amine solution in 4 or 5 portions, with vigorous shaking. The solutions were returned to the refrigerator between the additions, and the final solution was kept at 5–10° overnight. During the next day, more dichromate (50 g.) in water (150 cc.) was added in portions as before, and then the reaction mixture was kept in the refrigerator for thirty-six hours longer. The reaction mixture was filtered using a *large* Buchner funnel, and the filtrate was thoroughly extracted with ether (three times, 250 cc. of ether each time). The precipitate was thoroughly triturated with methanol (about 75 cc.),[9] filtered, and washed two or three times with small amounts of methanol. Ether (500 cc.) was added to the methanol filtrate; any precipitate was removed and washed with a little ether. All of the ethereal solutions and extractions were combined and shaken with water (400 cc.). Any precipitate at this point was removed, washed with ether and the ether washing was combined with the main solution. The aqueous layer was separated, and thoroughly extracted with ether. The united ether solutions and extracts were washed with small amounts of water, and the ether was distilled off. Since *o*-xyloquinone is thermolabile, care must be taken to keep a fair amount of ether in the distilling flask. Finally water was added, and the removal of the ether was completed by heating to 40–45°.

Ordinary steam distillation of the quinone is accompanied by great loss, but steam distillation under 100 mm. pressure proceeds quite well. A 500-cc. Kjeldahl flask with a side arm (12 mm. dia.) attached high up formed a very satisfactory still, and an Allihn condenser provided adequate cooling. The distillate was extracted with ether, the ether was evaporated carefully and the residue crystallized from petroleum ether (b. p. 30–60°). The quinone is quite soluble in this solvent, even in the cold, necessitating concentration of the mother liquors for second and third crops; yield 8.3 g. (33%); m. p. 56–57°.[6,10]

(1) Paper XIX, THIS JOURNAL, **61**, 3079 (1939).

(2) Honorary Fellow of the Graduate School, University of Minnesota, Spring Quarter, 1938–1939.

(3) Paper VII on Vitamin E, *J. Org. Chem.*, **4**, 318 (1939).

(4) Noelting and Forel, *Ber.*, **18**, 2670 (1885).

(5) Crossley and Renouf, *J. Chem. Soc.*, **95**, 207 (1909).

(6) Yokoyama, *Helv. Chim. Acta*, **12**, 771 (1929).

(7) The presence of small amounts of the 4-nitro isomer is of little consequence since the corresponding amine sulfate is much more soluble than the 3-amine sulfate (6 *vs.* 1.4% at 0°), Noelting and Pick, *Ber.*, **21**, 3153 (1888).

(8) Hydrochloric acid and tin or tin chloride should not be used for reduction of the nitro compound, because the product prepared in this way invariably contains considerable amounts of chloroxylidines which are very difficult to remove.

(9) A silver spatula or glass rod should be used at this point. Stainless steel appeared to catalyze the decomposition of the quinone to a red oil, while silver or glass had much less effect upon the quinone.

(10) Yokoyama, Ref. 6, reported 20% yield, m.p. 55°.

o-Xylohydroquinone.—The quinone (8.3 g.) was dissolved in acetic acid (50 cc.), water (25 cc.) was added, and the solution was refluxed with zinc (8.3 g., 20-mesh). The reduction proceeds rapidly and the solution is practically colorless in twenty minutes. Boiling water (50 cc.) is added to the hot solution, which is then immediately decanted from the zinc. The zinc is boiled with water (50 cc.) which is decanted into the main solution. On cooling, the solution deposits 7.90 g. (95%) of the hydroquinone, which melts at about 220° with complete decomposition.

Summary

1. This paper reports an improved preparation of *o*-xyloquinone and hydroquinone from *o*-xylene.

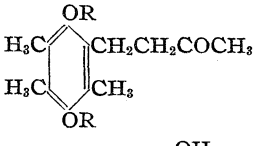
MINNEAPOLIS, MINN. RECEIVED NOVEMBER 10, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

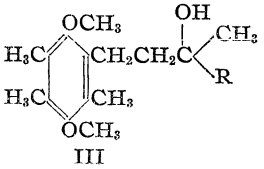
The Chemistry of Vitamin E. XXI.[1] Dealkylation of Hydroquinone Ethers Related to the Tocopherols

BY LEE IRVIN SMITH, HERBERT E. UNGNADE* AND WILLA B. IRWIN

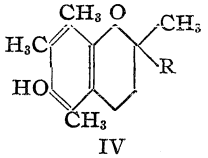
In a previous paper[2] a report has been made of the syntheses of certain compounds related to the tocopherols, using as starting materials 1-[3,6-dimethoxy-2,4,5-trimethylphenyl]-butanone-3 (I) and the closely related diacetate, II.



I, R = CH_3
II, R = Ac
IIa, R = H



III



IV
X R = CH_3

The substance I can be prepared readily from the dimethyl ether of pseudocumohydroquinone, via the chloromethyl derivative, which is used to alkylate acetoacetic ester. Hydrolysis of the substituted β-keto ester gives I, and the over-all yield in the synthesis is very good. The ketone I reacts well with Grignard reagents to give the carbinols III so that, by proper choice of Grignard reagent, a wide variety of these carbinols may be synthesized.

It was planned to convert the carbinols into the related chromans (IV) by demethylation followed by cyclization, but in the earlier work[2] no method could be found for cleaving the methoxyl groups without at the same time involving deep seated changes elsewhere in the molecule. While the acetate II underwent chloromethylation well, the chloromethyl derivative was difficult to handle and alkylation of acetoacetic ester with it gave only fair yields of the β-keto ester, from which, in turn, only a complicated mixture of products was obtained on hydrolysis. Thus, starting with either I or II, the synthesis of chromans IV appeared to involve such difficulties as to render the method of doubtful value.

While this work was in progress, a paper by John and Günther[3] appeared, in which was described the synthesis of ketone I starting with 3,4,6 - trimethyl - 2,5 - dimethoxybenzaldehyde.[4] The aldehyde was condensed with acetone to give 80% of the benzalacetone, which was then reduced to I. John and Günther found that I, when subjected to the action of hydrobromic acid, was simultaneously demethylated and reduced, giving the chroman IV (R = H). Addition of methylmagnesium iodide to I gave about 40% of III (R = CH_3), which was converted, by action of hydrobromic acid, into X. Addition of a dodecyl Grignard reagent was also carried out, although the results were not as satisfactory as those obtained using methylmagnesium iodide. Subsequently, John and Schmeil[5] by oxidation of the chroman IV (R = H) obtained the ketone IIa, and by addition of Grignard reagents to this ketone, the chromans IV, R = CH_3 and $C_{12}H_{25}$, were obtained.

It has now been found that the carbinol ether III (R = CH_3) can be cleaved by heating it at an elevated temperature with excess Grignard reagent.[6] Although the reaction does not pro-

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(1) Paper XX, THIS JOURNAL, **62**, 141 (1940).

(2) Paper VIII, *J. Org. Chem.*, **4**, 323 (1939).

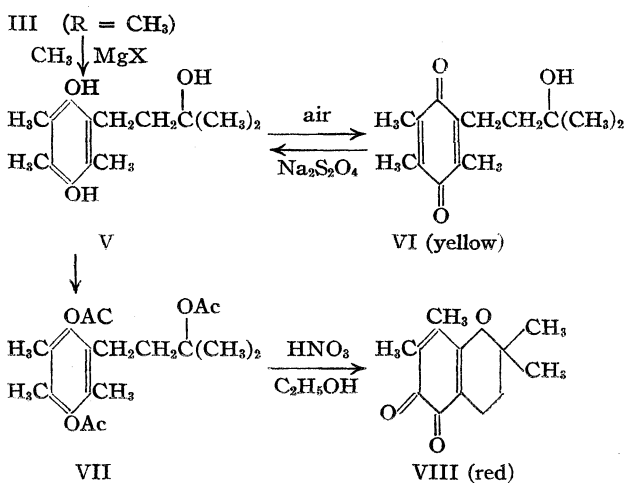
(3) John and Günther, *Ber.*, **72**, 1649 (1939).

(4) Smith, THIS JOURNAL, **56**, 472 (1934).

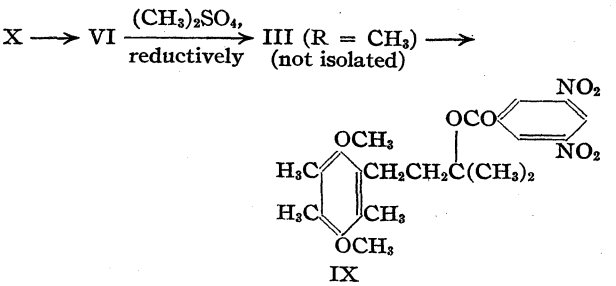
(5) John and Schmeil, *Ber.*, **72**, 1653 (1939).

(6) For other examples of ether cleavage by Grignard reagents see (a) Wessely and Prillinger, *Ber.*, **72**, 633 (1939); (b) Lüttringhaus and co-workers, *ibid.*, **71**, 1673 (1938); (c) Späth, *Monatsh.*, **35**, 319 (1914).

ceed to completion, it nevertheless affords another method of cleaving the methoxyl groups without affecting the rest of the molecule. Because of the incomplete reaction, it was not possible to isolate the products in a pure state, but sufficient evidence was available to follow the course of the reaction fairly accurately. The demethylation product appears to be the corresponding hydroquinone, V, since the ethereal solution, when shaken in air, turns to the yellow color of the quinone VI, and this color change can be reversed by shaking with sodium hydrosulfite. Neither of these substances could be isolated, since the presence of unchanged III in the reaction product prevents them from crystallizing. The reaction product was reductively acetylated, in the hope that the triacetate VII could be separated, but this likewise could not be crystallized. The product was therefore treated with nitric acid in ethanol[7]; the red color of the ortho quinone VIII[8] at once appeared. Since the carbinol ether III does not give the Furter and Meyer reaction, production of the very characteristic red color by nitric acid–ethanol after the carbinol III had been heated with the Grignard reagent indicated quite clearly that considerable demethylation had occurred.



The structure of the carbinol ether III (R = CH_3) was proved by converting it to a 3,5-dinitrobenzoate (IX), m. p. 147–148°. The same dinitrobenzoate was obtained from 2,2,5,7,8-tetramethyl-6-hydroxychroman (X) by oxidation, followed by reductive methylation of the quinone VI to the carbinol ether III (R = CH_3) and treatment of the latter with 3,5-dinitrobenzoyl chloride.



The identity of the dinitrobenzoates prepared by these two methods constitutes an additional proof of the structure of the chroman X, and it is also important as a model research for a direct structure proof of α-tocopherol, since the corresponding dimethoxy-3,5-dinitrobenzoate from α-tocopherol has already been prepared.[9]

Chromans such as IV and X have been prepared by the action of Grignard reagents upon hydrocoumarins, first by Robertson and his associates[10] and shortly thereafter in other laboratories.[11,12] Some doubt has been expressed, however, that the products of such reactions actually were chromans,[13] but the present results, together with those of John and his associates,[3,5] leave no doubt as to the course of these reactions; the products are certainly 2,2-dialkyl chromans.

Experimental Part

1 - (3,6 - Dimethoxy - 2,4,5 - trimethylphenyl) - 3-methylbutanol-3 (III, R = CH_3).—A solution of the ketone I (0.85 g.) in ether (25 cc.) was added to a solution of methylmagnesium iodide prepared from methyl iodide (1.419 g.), magnesium (0.243 g.) and ether (25 cc.). After stirring for an hour, the mixture was poured onto ice and sulfuric acid (30%) and extracted with ether. The ether extracts were washed with bicarbonate (10%), then with water, and dried over sodium sulfate. Evaporation of the solvent left 800 mg. of III, a colorless oil. It was not analyzed.

3,5-Dinitrobenzoate (IX).—The carbinol III (800 mg.) and 3,5-dinitrobenzoyl chloride (900 mg.) were allowed to stand in pure pyridine (15 cc.) for twenty-four hours. The solution was poured into iced sulfuric acid (30%) and extracted with ether. The extract was washed with bicarbonate (10%), and then with water. The residue obtained on evaporation of the solvent was crystallized from alcohol. It then melted at 147–148°; after several crystallizations it formed light yellow crystals which melted at 148–148.5°.

(7) Furter and Meyer, *Helv. Chim. Acta*, **22**, 240 (1939).
(8) Paper XVII in this series, THIS JOURNAL, **61**, 2424 (1939).
(9) John, Dietzel and Emte, *Z. physiol. Chem.*, **257**, 173 (1939).
(10) Bridge, Crocker, Cubin and Robertson, *J. Chem. Soc.*, 1533 (1937).
(11) Smith, Ungnade and Prichard, *J. Org. Chem.*, **4**, 358 (1939).
(12) John, Günther and Schmeil, *Ber.*, **71**, 2617 (1938).
(13) Private communication from Professor Robertson.

Anal. Calcd. for $C_{23}H_{28}O_8N_2$: C, 59.98; H, 6.10. Found: C, 59.78; H, 5.75.

Oxidation of 2,2,5,7,8-Pentamethyl-6-hydroxychroman (X).—A solution of the chroman (750 mg.) in methanol (30 cc.) was refluxed for an hour with silver acetate. The suspension was cooled and the sludge was removed and washed with a small amount of methanol. The combined filtrate and washings were diluted with water (100 cc.) and extracted with ether. The ether solution was washed with water and dried over calcium chloride. Evaporation of the solvent left the **quinone VI** (740 mg.) as a yellow oil. John, Dietzel and Emte[9] report that VI is a solid which melts at 62° but many preparations of VI in this Laboratory have given the substance only as an oil. This oil, when reductively acetylated, gave the known triacetate, m. p. 114–115°[9,14]; however, cleavage of the pure triacetate by methylmagnesium iodide according to the method of Doisy[15] followed by action of silver oxide upon the product also gave VI as an oil which could not be crystallized.

Carbinol III.—Reductive methylation of the quinone VI must be carried out with great care to avoid the destructive action of excess alkali upon the quinone. The general procedure of John, Dietzel and Emte[9] was used, modified so that there was never more than a momentary darkening of the reaction mixture due to free alkali. The above quinone (749 mg.) was taken up in methanol (15 cc.) and sodium hydrosulfite (700 mg.) was added. To this suspension sodium hydroxide (20%, 4 drops) was added, followed immediately by methyl sulfate (2 cc.). During the next forty-five minutes, base (12 cc.) and methyl sulfate (8 cc.) were added alternately and with intermittent refluxing, in such proportions that the solution never darkened. The final colorless solution was diluted with sodium hydroxide (3%, 100 cc.) and extracted with ether several times. The combined extracts were washed with dilute base, then with water, and dried over sodium sulfate. Removal of the solvent left a pale yellow oil (570 mg.).

3,5-Dinitrobenzoate, IX. A.—The crude carbinol III (210 mg.) was added to approximately an equivalent amount of standardized methylmagnesium iodide in ether (50 cc.). The volume of methane collected indicated roughly 0.67 mole of active hydrogen per mole of carbinol, and showed that reductive methylation of VI had not involved the aliphatic hydroxyl group too greatly. To the resulting suspension of the bromomagnesium derivative of III there was added 3,5-dinitrobenzoyl chloride (520 mg.) and the mixture was allowed to stand at room temperature for two days. It was poured into cold sulfuric acid (30%, 150 g.) and extracted with ether. The ether extracts were washed with water, saturated bicarbonate, and again with water. Evaporation of the solvent left an oily residue (360 mg.) which was taken up in a little ether and cooled. The light yellow solid was removed and washed twice with small amounts of cold ethanol. It weighed 50 mg. After crystallization from ethanol, the substance melted at 145–146°. When mixed with a specimen of IX (m. p. 147.5–148°) prepared from the dimethoxy ketone I, the substance melted at 145–147°.

B. The crude carbinol III (290 mg.) was dissolved in dry pyridine (5 cc.) and 3,5-dinitrobenzoyl chloride (550 mg.) was added. After standing at room temperature for four days, a small amount of white solid (m. p. 165–167°) was removed and the filtrate poured into cold sulfuric acid (30%, 150 g.). The product (300 mg.) was isolated and purified as described above. The solid weighed 100 mg. and melted at 143–144.5°. When mixed with the pure 3,5-dinitrobenzoate (m. p., 147.5–148°) the substance melted at 144–145.5°.

Cleavage of the Ether Carbinol, III (R = CH_3).—The ketone I (1.43 g.) in ether (30 cc.) was added to a Grignard solution prepared from methyl iodide (4.06 g.), magnesium (0.69 g.) and ether (50 cc.). After refluxing for an hour, the ether was distilled off and the residue was heated at 180° for forty-five minutes. After cooling, ice and sulfuric acid (30%) were added and the mixture was extracted with ether. A few cc. of the ethereal solution (practically colorless), when shaken in air, turned bright yellow (quinone VI). The whole of the ethereal solution was shaken with aqueous sodium hydrosulfite, and the *colorless* ethereal solution which resulted (hydroquinone V) was evaporated. The residue, a yellow oil, could not be crystallized. It was acetylated by refluxing it for thirty minutes with acetic anhydride (12 cc.), zinc (1 g.) and fused sodium acetate (3 g.). The mixture was poured into water and extracted with ether. The ether solution was washed with water, then with dilute sodium hydroxide, followed by water again. The solution was dried and the solvent was evaporated. This residue, a viscous oil (acetate VII), likewise could not be crystallized.

The acetate was dissolved in absolute ethanol (500 cc.) and nitric acid (100 cc.) and the solution was warmed on the steam-bath for thirty minutes. The deep red color characteristic of the Furter and Meyer reaction appeared at once (quinone VIII). The red quinone was removed by ether extraction, but evaporation of the solvent left a deep red oil which also could not be made to crystallize.

Summary

1. Carbinols such as III derived from 1-(3,6-dimethoxy-2,4,5-trimethylphenyl)-butanone-3 (I) by action of Grignard reagents, have been demethylated by heating with excess reagent.

2. The structure of the carbinol III (R = CH_3) has been proved by converting it to the same 3,5-dinitrobenzoate as that obtained from 2,2,5,7,8-pentamethyl-6-hydroxychroman (X) by a series of reactions involving oxidation to a quinone, reductive methylation of the quinone and conversion of the dimethoxy compound to the 3,5-dinitrobenzoate.

3. These reactions also prove the structure of the chroman X and show definitely that when Grignard reagents react with dihydrocoumarins, the products are 2,2-dialkylchromans.

MINNEAPOLIS, MINN. RECEIVED NOVEMBER 15, 1939

(14) In ref. 9, the m. p. is reported as 113°.

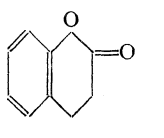
(15) Binkley, MacCorquodale, Cheney, Thayer, McKee and Doisy, THIS JOURNAL, **61**, 1295 (1939); see also Fieser, Campbell and Fry, *ibid.*, **61**, 2209 (1939).

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

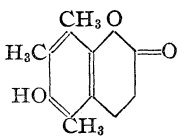
The Chemistry of Vitamin E. XXII. The Reaction between Grignard Reagents and Coumarins and Hydrocoumarins[1]

BY LEE IRVIN SMITH AND P. M. RUOFF[2]

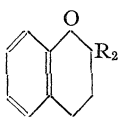
In paper XII of this series[3] a preliminary report has been given of the results obtained when certain Grignard reagents reacted with the dihydrocoumarins I and II. The products of these reactions were 2,2-dialkylchromans, III, and it was assumed that in all cases the intermediates were the ketones IVa (or IVb) and related carbinols V.



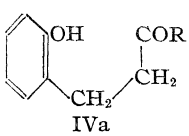
I



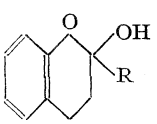
II



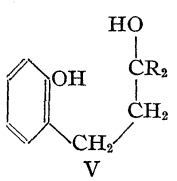
III



IVa



IVb

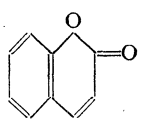


V

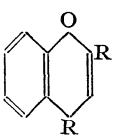
In one case, that in which R was ethyl, the carbinol V was isolated as a solid which melted at 71–72°; but in the other case studied (R = *n*-propyl) the carbinol appeared as an oil which was not characterized except by conversion to the chroman III (R = *n*-propyl).[4]

The reaction between hydrocoumarin (I) and Grignard reagents has now been extended and the series at present includes the products obtained from ethyl-, *n*-propyl- and *n*-butyl- Grignard reagents. In addition Claisen[5] prepared the carbinol V, R = CH_3, from methylmagnesium iodide and ethyl β-phenyl-propionate; he cyclized the carbinol to the chroman (III, R = CH_3) which he synthesized independently by condensation of phenol with isoprene.[6] Thus the series now includes all four of the chromans III (R = CH_3, C_2H_5, *n*-C_3H_7 and *n*-C_4H_9) as well as three of the carbinols V (R = CH_3, C_2H_5, *n*-C_4H_9). In view of this work, and the results reported in the previous paper,[1] it appears definitely established that the products obtained by action of Grignard reagents upon dihydrocoumarins consist of the carbinols V and the 2,2-dialkylchromans III derived from them. No ketones such as IVa or IVb have been isolated from these products although one such ketone recently has been synthesized in another way by John and Schmeil.[7] It is interesting that this ketone, 2,5-dihydroxy-3,4,6-trimethylbenzylacetone, shows properties which indicate that its structure may be analogous to IVb rather than to IVa.

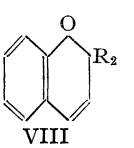
On the other hand, the action of Grignard reagents upon coumarins VI is much more complicated because of the presence of the conjugated double bond, and a variety of products, including



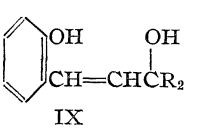
VI



VII



VIII



IX

pyrylium salts,[8] Δ²- and Δ³-chromenes (VII and VIII),[4,9] chromanols[10] as well as the unsaturated carbinols IX[9a,9b] have been reported. The evidence concerning the carbonols IX is conflicting, however, and from the work of Löwenbein[9b] it appears that Houben[9a] was in error in assigning structure IX to the product he obtained from coumarin and phenylmagnesium bromide. Nevertheless, formation of all the products so far reported can be accounted for on the basis of 1,2- or 1,4-addition of the reagent, or a combination of

(1) Vitamin E. XXI, THIS JOURNAL, **61**, 142 (1939).

(2) Present address: Department of Chemistry, Syracuse University, Syracuse, N. Y.

(3) Smith, Ungnade and Prichard, *J. Org. Chem.*, **4**, 358 (1939).

(4) In writing the previous report (Ref. 2) a paper by Bridge, Crocker, Cubin and Robertson, *J. Chem. Soc.*, 1530 (1937), was overlooked. We desire to acknowedge here the priority of Robertson and his associates; they, apparently, are the first to carry out the reaction between a dihydrocoumarin and a Grignard reagent, leading to a 2,2-dialkylchroman.

(5) *Ber.*, **54**, 200 (1921).

(6) See also Smith, Ungnade, Hoehn and Wawzonek, *J. Org. Chem.*, **4**, 311 (1939).

(7) *Ber.*, **72**, 1653 (1939); see also John, Gunther and Schmeil, *ibid.*, **71**, 2617 (1938).

(8) Decker and Fellenberg, (a) *ibid.*, **40**, 3816 (1907); (b) *Ann.*, **356**, 300 (1907); (c) Willstätter and Schmidt, *ibid.*, **57**, 1945 (1924); (d) Heilbron, Hill and Wells, *J. Chem. Soc.*, 1701 (1931).

(9) (a) Houben, *Ber.*, **37**, 489 (1904); (b) Löwenbein, *ibid.*, **57**, 1517 (1924); (c) Bergel, Jacob, Todd and Work, *J. Chem. Soc.*, 1375 (1938).

(10) (a) Löwenbein and Rosenbaum, *Ann.*, **448**, 223 (1926); (b) Heilbron and Hill, *J. Chem. Soc.*, 2005 (1927).

1,4- and 1,2-addition, with cyclization possible at almost any point in the sequence of reactions.

It has now been found that the carbinols IX (R = CH_3 and C_2H_5) are readily obtained by addition of coumarin to aliphatic Grignard reagents under carefully controlled conditions. These unsaturated carbinols IX are readily reduced to the saturated carbinols V, identical with the products obtained from Grignard reagents and dihydrocoumarin. Thus the same product, V, results regardless of whether addition of the Grignard reagent precedes or follows reduction and this could be true only when the action of the reagent is confined to the carbonyl group. From these facts, it follows that these carbinols must be derived from coumarin and dihydrocoumarin by 1,2-addition of the reagent to the carbonyl group, and that the conjugated system in coumarin is not involved in the reaction when the procedure described below is used.

The unsaturated carbinols IX were cyclized by acids to chromenes, which, from the structure of the carbinols, must have the double bond in the 3,4-position (VIII). Elimination of water from the carbinols occurred quite readily; even distillation of the crude carbinol gave a product which separated into two layers, one of them aqueous. Cyclization, however, was not the only reaction which occurred when the carbinols were dehydrated for by-products, consisting of viscous, brown oils were always formed in considerable amounts. These by-products were probably formed by dehydration of the carbinols to dienes and polymerization of the latter. Steam distillation of the carbinols from a slightly acid suspension yielded colorless oils in the distillate, but this process was too slow to serve as a practical method for obtaining the chromenes. Cyclization of the carbinols IX by acids was always accompanied by the appearance of highly colored solutions; similar colors were developed when the magnesium complexes from the Grignard reaction were hydrolyzed. These colors indicated the presence of benzopyrylium salts, but no attempt was made to isolate them.[10a]

(10a) Since this manscript was submitted for publication, a paper by Shriner and Sharp, *J. Org. Chem.*, **4**, 575 (1939), appeared on the same subject. While Shriner and Sharp did not isolate the intermediate ketones, our results in general agree with theirs, and their reaction mechanism, which we regard as essentially correct, readily can be modified to provide for the formation of the ketones. Thus their compound XII could coördinate at the heterocyclic oxygen atom with a second molecule of the Grignard reagent and the resulting complex could rearrange to give either the chromene or the magnesium derivative of the ketone.

Experimental Part[11]

Diethyl-*o*-hydroxystyrylcarbinol IX (R = C_2H_5).—Coumarin (25 g., 0.17 mole) in ether (500 cc.) was added slowly (two hours) at room temperature to a Grignard solution prepared from ethyl bromide (40 g., 0.37 mole) and magnesium (8 g., 0.33 mole) in ether (250 cc.). Each drop of the coumarin solution produced in the reaction mixture a yellow precipitate which quickly dissolved; after about half of the coumarin was added, this transitory precipitate was white. The mixture was refluxed for an hour and the clear brownish-green and slightly fluorescent solution was allowed to stand overnight. It was then decomposed by slowly stirring it into sulfuric acid (10%, 200 cc.) and ice. After standing for an hour, the ether layer was removed and the aqueous layer was extracted (with ether) until it was colorless. The combined ether solutions were washed with water and dried over anhydrous sodium carbonate. Removal of the solvent left a yellow oil (32 g.) which partially solidified. The oily solid was spread on a porous plate and after the oil was absorbed, the solid was removed and crystallized twice from a mixture of equal parts of petroleum ether b. p. 30–60° and b. p. 60–68° using Norite the second time. Approximately 20 g. of white needles, melting at 67–68°, was obtained. The carbinol gave a deep red color with concd. sulfuric acid and an olive-green color with ferric chloride. It rapidly decolorized a dilute solution of bromine in carbon tetrachloride, and gave no reaction with phenylhydrazine. It was soluble in 10% sodium hydroxide.

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.69; H, 8.78. Found: C, 75.64; H, 8.89.

1-[*o*-Hydroxyphenyl]-3-ethyl-3-pentanol V (R = C_2H_5).—The above carbinol 2.0 g. in ethanol (50 cc.) was subjected at room temperature to the action of hydrogen under slight pressure in the presence of a platinum oxide catalyst (0.01 g.). Practically the theoretical volume of hydrogen was absorbed in two hours. After removal of the catalyst, the solvent was evaporated and the residue was crystallized from petroleum ether. The product (1.5 g.) was white and melted at 74–75° alone or when mixed with a specimen prepared from dihydrocoumarin and ethylmagnesium bromide.[3] When mixed with the unsaturated carbinol (m. p. 67–68°) the substance melted at 50–54°.

2,2-Diethyl-Δ^3-chromene, VIII (R = C_2H_5).—The unsaturated carbinol (4 g.) was refluxed in acetic acid (20 cc.) for an hour and the mixture was allowed to stand overnight. The solution was diluted with water and extracted with ether. The ether solution was extracted with sodium hydroxide (10%), then washed with water and dried over calcium chloride. Removal of the solvent left a clear amber oil (3.5 g.). Distilled from a small Claisen flask, this gave 2.5 g. of a clear colorless liquid boiling at 129–132° under 19 mm.; the residue (1 g.) in the flask was dark viscous non-volatile oil. Redistillation of the crude chromene gave a turbid distillate (2.0 g.) and to complete the cyclization this distillate was again refluxed in acetic acid and the product was isolated and purified as described above. Somewhat less than 1 g. of a colorless liquid, b. p. 125–126° under 14 mm., was obtained. The remainder

(11) Microanalyses by J. W. Opie and E. E. Renfrew.

of the product was a dark viscous oil. The chromene gave a bright red color with concd. sulfuric acid.

Anal. Calcd. for $C_{13}H_{16}O$: C, 82.98; H, 8.51. Found: C, 83.07; H, 8.65.

Dimethyl-*o*-hydroxystyrylcarbinol, IX (R = CH_3).—Coumarin was added to methylmagnesium iodide in the same molar quantities and by the same procedure as that described for preparation of the diethylcarbinol above. About a third of the reaction product was collected on a porous plate as a yellowish solid (10 g.). After crystallization from petroleum ether (as above) and decolorization with Norite, the substance was obtained as a white solid which melted at 53–55°. It gave the same color reaction with sulfuric acid and ferric chloride as those given by the ethyl compound; likewise it was soluble in 10% sodium hydroxide. Due to an accident, the analytical sample was destroyed.

2,2-Dimethyl-Δ^3-chromene, VIII (R = CH_3).—The porous plate used for absorbing the oil accompanying the above dimethylcarbinol was extracted with ether. The ether was removed and the residue was distilled under 19 mm. pressure. The chromene (2 g.) boiling at 102–103° resulted as a clear, colorless liquid.[12]

Cyclization of the solid carbinol (from above) as described for the ethyl compound gave only about 1 g. of the chromene. Consequently, the Grignard reaction was repeated, and the crude product (solid and oil) was distilled under 15 mm. At 90° an oil and water appeared in the distillate; as soon as water ceased to appear, the temperature gradually rose to 142°. Only a small amount of residue remained in the flask. The distillate solidified partially, showing unchanged carbinol. The entire distillate was dissolved in acetic acid (50 cc.), a drop of sulfuric acid was added and the mixture was refluxed for half an hour. The product was isolated and purified as described for the ethyl compound above. There resulted 6 g. of the pure chromene boiling at 96–97° under 15 mm. About half the material remained in the flask as a dark viscous oil. The methyl chromene, like the ethyl compound, gave a red color with sulfuric acid.

Anal. Calcd. for $C_{11}H_{12}O$: C, 82.50; H, 7.50. Found: C, 82.19; H, 7.86.

2,2-Di-*n*-butyl-Δ^3-chromene, VIII (R = *n*-C_4H_9).—Coumarin (22 g., 0.15 mole) in ether (450 cc.) was added to *n*-butylmagnesium bromide (7.3 g., 0.30 mole of magnesium, 45.2 g., 0.33 mole of butyl bromide) in ether (225 cc.). No attempt was made to isolate the small amount of solid (carbinol) which appeared in the product; instead, the crude product was distilled directly. The distillate (23 g., b. p. 161–163° under 15 mm.) contained some water, indicating dehydration of the carbinol. The ethereal solution of the distillate was extracted several times with sodium hydroxide (10%), then washed with water and dried over calcium chloride. The solvent was removed and the residue was distilled under 15 mm. The chromene (17–18 g.), a clear oil with a faint yellow cast, boiled at 164–165° and had $n^{27}D$ 1.5220. It gave a red color with sulfuric acid.

Anal. Calcd. for $C_{17}H_{24}O$: C, 83.53; H, 9.91. Found: C, 83.10; H, 9.76.

(12) See Ref. (9a); Houben gives the b. p. as 92–93° under 11 mm.

1-[*o*-Hydroxyphenyl]-3-*n*-butyl-3-heptanol V (R = *n*-C_4H_9).—Dihydrocoumarin (14.8 g., 0.1 mole) in ether (125 cc.) was slowly (1.5 hours) added to *n*-butylmagnesium bromide (butyl bromide, 28 g., 0.2 mole; magnesium, 4.8 g., 0.2 mole) in ether (200 cc.). The reaction mixture was allowed to stand at room temperature overnight and was then decomposed by pouring it into ice (300 g.) and sulfuric acid (20 cc.). The ether layer was removed, washed with dilute carbonate solution, then with water and was dried over anhydrous sodium carbonate. Removal of the solvent left an oil (25 g.) which soon solidified. After two crystallizations from petroleum ether (b. p. 30–68°) the substance was white and melted at 67–68.5°. It gave a strongly positive phenol test (Folin).

Anal. Calcd. for $C_{17}H_{28}O_2$: C, 77.27; H, 10.60. Found: C, 76.5; H, 10.0.

2,2-Di-*n*-butylchroman, III (R = *n*-C_4H_9).—The above carbinol (16.1 g.) was dissolved in acetic acid (100 cc.). Sulfuric acid (15 cc., 50%) was added. The solution turned red and an oil separated at the top. More acetic acid (50 cc.) was added to dissolve the oil, and the mixture was refluxed for an hour. The solution was diluted with water, and extracted with ether several times. The combined ether solutions were washed with dilute carbonate, then with water, and dried over anhydrous potassium carbonate. The solvent was removed and the residue (9 g.) was distilled. The distillate (5 g., b. p. 172–173° under 16 mm.) was slightly yellow and had a faint odor of butyl acetate. Considerable brown viscous oil remained in the flask. Much better results were obtained by refluxing the crude carbinol from a duplicate preparation with 25% sulfuric acid. Steam distillation of the mixture gave a colorless oil in the distillate but the process was very slow. The oil in the flask was taken up in ether, washed free of acid and dried. After the solvent was removed, the chroman was distilled from a Claisen flask. The distillate (12 g.) was a faintly yellow liquid which boiled at 165–168° under 8 mm., and it had $n^{27}D$ 1.5097.

Anal. Calcd. for $C_{17}H_{26}O$: C, 82.92; H, 10.57. Found: C, 82.70, 82.33; H, 10.10, 10.72.

Summary

1. *o*-Hydroxystyryldialkylcarbinols have been obtained by reaction between coumarin and Grignard reagents.

2. The structures of these carbinols have been proved by reducing the diethyl compound to the saturated carbinol and preparing the same substance from dihydrocoumarin and ethylmagnesium bromide.

3. The unsaturated carbinols have been cyclized to 2,2-dialkyl-Δ^3-chromenes, VIII but the chromenes are accompanied by large amounts of dark viscous oils, probably polymeric substances.

4. Previous work on the preparation of 2,2-dialkylchromans by action of Grignard reagents on dihydrocoumarins has been extended. At present the series of chromans III is complete

from R = CH_3 to R = n-C_4H_9; the series of saturated carbonols V includes those in which R = CH_3, C_2H_5 and n-C_4H_9; the series of unsaturated carbinols IX includes those in which R = CH_3 and C_2H_5; the series of chromenes VIII includes those in which R = CH_3, C_2H_5 and n-C_4H_9.

MINNEAPOLIS, MINNESOTA
RECEIVED NOVEMBER 15, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

The Ultraviolet Absorption Spectra of Some Derivatives of 1,2-Benzanthracene

BY R. NORMAN JONES[1]

The ultraviolet absorption spectrum of 1,2-benzanthracene has been measured by Capper and Marsh,[2] by Clar[3] and by Mayneord and Roe.[4] Because of the carcinogenic activity of some of its simple alkyl and ace-derivatives, a large number of such compounds have been synthesized and their chemical and biological behavior investigated in several laboratories.[5,6,7] Since eleven such derivatives complementary to those previously studied were available in this Laboratory it seemed desirable to make a careful study of their absorption spectra.

Experimental Procedure

In this study a Bausch and Lomb Medium Quartz Spectrograph was used in conjunction with a Hilger Spekker Photometer and a hydrogen discharge tube designed by Dr. Hugh H. Darby.[8] Some difficulty was initially found in lining up the spectrograph with a photometer of different manufacture. This was overcome by mounting the photometer on a Hilger "Short Bar," the base support of which was replaced by a specially designed casting underslung from the projecting front platform of the spectrograph and accurately machined to fit the Short Bar. By means of set screws and lock nuts in the casting a lateral variation of about 10° on either side of the optical axis was possible to assist the correct alignment of the photometer and spectrograph. To obtain a sharp image it was found necessary to remove the quartz window from in front of the slit and bring the photometer to within 1 mm. of the slit cover.

The use of a hydrogen discharge tube as a source of continuous ultraviolet light is exceedingly convenient and much to be preferred to the tungsten steel spark. The Darby tube has the advantage over other designs of operating at 15 kilovolts, making it possible to interchange with the tungsten steel spark without alteration of the electrical supply circuit. It also requires no water cooling system. The Spekker photometer needs a point source of light and as the discharge in the hydrogen tube occurs along a 10 cm. capillary tube, the correct alignment of the tube with the photometer is difficult and it is necessary to mount the tube in a precision micrometer stand. Incorrect alignment is indicated by a difference in the intensities of the two spectra with no cells in the light path and the photometer drum set at zero. Once correctly aligned the tube has needed no further attention over a period of six months.

Eastman Process plates were used and developed for four minutes at 20–22° in Eastman high contrast developer (Formula D. 19). They were analyzed by visual spotting of the match points directly on the plate against a suitable uniformly illuminated background and the reading was facilitated by projection onto a ground glass screen.[9] The wave length scale was photographed onto the top and bottom of each plate and was calibrated against the spectrum of a copper spark.

All measurements were made in quartz cells of 1-cm. length with fused ends (Hilger Type H. 292). Absolute alcohol was used as solvent and solutions were prepared by progressive dilution of an initial sample weighed out on a microbalance. Measurements were made with a slit width of 0.12 mm. at 20–25°. The results are calculated in terms of $\log_{10} E_{molar}$ where $E_{molar} = \log_{10} I_0/I \cdot 1/cl$.

c = concentration of solute in moles per liter
l = cell length in cm.
$\log_{10} I_0/I$ = extinction coefficient read directly from the photometer drum

By suitable adjustment of the concentration it was possible to take the whole spectrum on four or five plates with thirty-one exposures on each, at the same time making certain that regions where fine structure was present were photographed under conditions of maximum sensitivity ($\log I_0/I > 1$).

Results

1,2-Benzanthracene.—Measurements on 1,2-benzanthracene itself were first made in order to compare the results obtained using this equipment with those of prior investigators. The first measurements of the absorption spectrum of 1,2-benzanthracene were made by Capper and Marsh,[2] whose curve agrees qualitatively in shape with that of the more recent investigators. The intensity

(1) Commonwealth Fund Fellow.
(2) Capper and Marsh, *J. Chem. Soc.*, 724 (1926).
(3) Clar, *Ber.*, **65**, 503 (1932).
(4) Mayneord and Roe, *Proc. Roy. Soc.* (London), **A152**, 299 (1935); **A158**, 634 (1937).
(5) Fieser, *Am. J. Cancer*, **34**, 37 (1938).
(6) Shear, *ibid.*, **33**, 499 (1938).
(7) Cook, *Ergebnisse der Vitamin- und Hormonforschung*, **2**, 213 (1939).
(8) Private communication.
(9) Rosebury, *Science*, **83**, 86 (1936).

measurements in terms of log E are numerically about one log unit too great but the units in which E is calculated are not stated. Clar[3] obtained substantially the same curve with intensity measurements of the correct order of magnitude. In Table I are given the wave lengths and intensities of the maxima I obtained together with the values interpolated from the graph of Mayneord and Roe[4] and those of Capper and Marsh (the latter converted from oscillation frequencies to wave lengths).

TABLE I

POSITIONS AND INTENSITIES OF THE MAXIMA OF THE ULTRAVIOLET ABSORPTION SPECTRUM OF 1,2-BENZANTHRACENE

Band[a]	R. N. J.		Mayneord and Roe		Capper and Marsh
A	2540 Å.	(4.56)	2540 Å.	(4.62)	..
B	2655	(4.60)	2660	(4.65)	..
C	2765	(4.85)	2760	(5.00)	..
D	2870	(4.97)	2880	(5.10)	2875
E	2995	(3.99)	3000	(3.92)	2994
F	3125	(3.63)	3150	(3.65)	..
G	3275	(3.80)	3270	(3.82)	3275
H	3410	(3.87)	3400	(3.85)	3413
I	3580	(3.69)	3575	(3.70)	3593
I′	3655	(3.41)	...	..	3650
J	3755	(2.73)	3730	(2.70)	3745
K	3845	(3.07)	3840	(2.95)	3840

[a] See Fig. 1.

It will be observed that agreement in both wave lengths and intensities of the maxima is very satisfactory except for the intensities of the two most strongly absorbing bands C and D for which the intensity measurements of Mayneord and Roe are appreciably high.

Monomethyl and Dimethyl Derivatives of 1,2-Benzanthracene.—The spectra and intensities measured for ten of the derivatives are given in Table II. All these give curves of the same general shape. The bands A, B, C, D and H are of approximately constant intensity throughout the series. Noticeable variations occur in the bands E, J, and K, E and J are missing entirely in the 9-methyl, 5,8-dimethyl and 9,10-dimethyl derivatives. The band K is missing also in the 10-methyl compound and is ill-defined in the 9-methyl compound. Variations are also to be observed in the degree of resolution of bands I and I′. Resolution into two separate bands is well-defined in the 1′-, 4-, 5-, 8- and 10-monomethyl compounds and in the 5,8-derivative but is absent in the others. It can just be resolved in the parent hydrocarbon. It does not seem possible to asso-

TABLE II

POSITION OF THE MAXIMA AND CORRESPONDING INTENSITIES (LOG E_{molar}) IN THE ULTRAVIOLET ABSORPTION SPECTRA OF ALKYL DERIVATIVES OF 1,2-BENZANTHRACENE (SOLVENT ETHANOL)

Derivative of 1,2-benzanthracene	M. p., °C.	Absorption data											
		A	B	C	D	E	F	G	H	I	I′	J	K
1,2-Benzanthracene[a]	160.5–	2540	2665	2765	2870	2995	3125	3275	3410	3580	3655	3755	3845
	161	4.56	4.60	4.85	4.95	3.99	3.63	3.80	3.87	3.69	3.41	2.73	3.07
1′-Methyl[b]	138.5–	2540	2675	2770	2875	2995	..	3260	3410	3585	3670	(3770)	3875
	139.2	4.50	4.68	4.89	4.90	4.00	..	..	3.88	3.81	3.48	2.74	3.20
4-Methyl[c]	124.1–	2580	2670	2785	2885	3015	..	3280	3420	3585	3650	3760	3850
	124.6	4.59	4.59	4.87	4.96	3.84	..	..	3.83	3.75	3.62	2.95	3.15
5-Methyl[d]	158.5–	(2625)	2695	2785	2890	3005	(3245)	3320	3460	3610	3675	3790	3860
	159	4.60	4.68	4.82	4.94	3.90	(3.75)	3.85	3.91	3.78	3.76	2.95	3.08
8-Methyl[e]	118–	2590	2690	2795	2900	3005	3160	3310	3460	3605	3670	3770	3865
	118.5	4.57	4.64	4.84	4.96	3.90	3.67	3.84	3.88	3.66	3.60	2.94	3.06
9-Methyl[f]		2580	2690	2790	2905	..	(3220)	3360	3515	(3670)	..	..	(3930)
		4.62	4.64	4.87	4.94	..	(3.66)	3.81	3.88	3.81	..	..	3.02
10-Methyl[d]	140.2–	2575	2705	2800	2915	3025	3210	3345	3545	3650	3720	3835	3895
	140.8	4.54	4.60	4.87	4.98	4.02	3.66	3.82	3.94	3.75	3.78	3.03	3.05
5,8-Dimethyl[g]	134.4–	2620	2715	2820	2925	..	3200	3360	3520	3625	3710	..	3865
	134.7	4.62	4.67	4.84	4.93	..	3.64	3.85	3.88	3.72	3.72	..	3.10
5,10-Dimethyl[d]	147–	2650	2725	2830	2945	3050	(3280)	3400	3580	3775	..	..	3925
	147.5	4.60	4.63	4.86	4.93	3.86	3.60	3.88	3.97	3.87	..	..	3.18
8,10-Dimethyl[g]	145.5–	2610	2730	2825	2950	3045	3235	3375	3560	3735	..	3830	3915
	146.5	4.57	4.59	4.78	4.96	4.03	3.71	3.89	3.97	3.77	..	3.12	3.08
9,10-Dimethyl[h]	122.7–	2625	2735	2850	2965	..	(3300)	3450	3640	3840	..	..	3900
	123.4	4.50	4.58	4.80	4.90	..	..	3.83	3.94	3.83	..	..	..

[a] Prepared by Dr. H. J. Creech by modification of method due to Bachmann, *J. Org. Chem.*, **1**, 349 (1936). [b] Fieser and Seligman, THIS JOURNAL, **60**, 170 (1938). [c] Fieser and Jones, *ibid.*, **60**, 1940 (1938). [d] Fieser and Newman, *ibid.*, **58**, 2376 (1936). [e] Fieser and Johnson, *ibid.*, **61**, 168 (1939). [f] Newman, *ibid.*, **59**, 1003 (1937). [g] Fieser and Johnson, *ibid.*, **61**, 1647 (1939). [h] Prepared by Mr. Webber by method due to Bachmann.

ciate these variations with the structural differences between the molecules but it can be concluded that substitution at the 9- and 10-positions seems to cause more loss of resolution than substitution elsewhere.

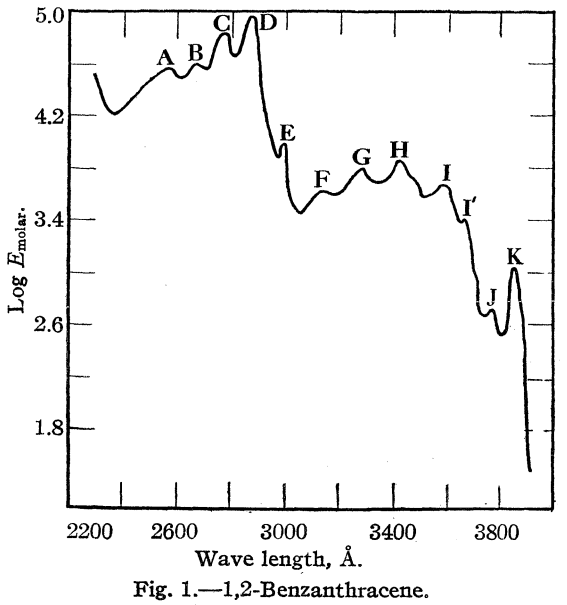


Fig. 1.—1,2-Benzanthracene.

The absorption curves of these various substances are not published since they are superficially very similar. The absorption spectrum of 1,2-benzanthracene itself is given in Fig. 1.

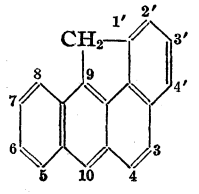
TABLE III

POSITIONS AND INTENSITIES OF THE ABSORPTION MAXIMA OF 1',9-METHYLENE-1,2-BENZANTHRACENE[a] (SOLVENT ETHANOL)

Wave length	Intensity	Wave length	Intensity
2565 Å.	(4.59)	3330	(3.89)
2720	(4.51)	3415	(3.81)
2805	(4.69)	3505	(3.93)
2890	(4.71)	3600	(3.73)
2930	(4.62)	3690	(3.87)
3060	(3.89)	(3775)[b]	(3.05)
3205	(3.64)	3870	(3.50)

[a] Fieser and Cason, THIS JOURNAL, **61**, 1740 (1939).
[b] Inflection only.

1',9-Methylene-1,2-benzanthracene. (I).—



(I)

Absorption measurements made on this compound show it to have a spectrum differing in many respects from that of the other derivatives (Fig. 2). The two bands C and D are here replaced by a system of one broad and two sharp maxima, all less intense. There is also more resolution in the longer wave region there being ten maxima resolved in the E–K range instead of eight. The act of bridge formation is not in itself sufficient cause for this change since cholanthrene and 20-methylcholanthrene show spectra of the normal type. Examination of Stuart models suggests that considerably more strain is present in the 1',9-methylene structure than in the 5,10-dimethylene bridge of cholanthrene and the changes produced in the spectrum may be associated with this condition.

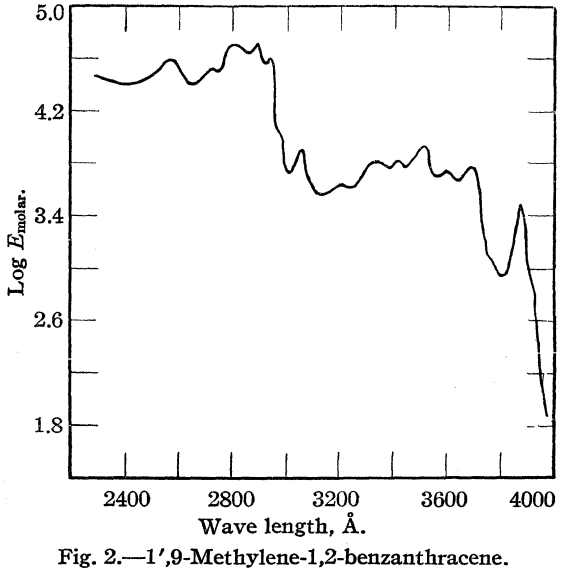


Fig. 2.—1',9-Methylene-1,2-benzanthracene.

Bathochromic Shifts Produced by Substitution.—The introduction of an alkyl group into an aromatic compound produces a shift of the absorption curve toward longer wave lengths (bathochromic shift). Klingstedt[10] found a shift of 820 cm.$^{-1}$ for toluene with respect to benzene and de Laszlo[11] observed shifts of 330 and 690 cm.$^{-1}$ for α- and β-methylnaphthalenes, respectively, in comparison with naphthalene.

An analysis of the alkyl 1,2-benzanthracenes shows that the shift produced differs very much according to the position of substitution. In making such an analysis the question arises as to what criterion should be taken in determining the relative shift. The displacement of each individual maximum may be measured (preferably on a frequency scale) and a mean value deduced but

(10) Klingstedt, *Compt. rend.*, **175**, 1065 (1921).
(11) De Laszlo, *Z. physik. Chem.*, **118**, 369 (1925).

TABLE IV

BATHOCHROMIC SHIFT OF BAND D AND THE CARCINOGENIC ACTIVITY AS INDICATED BY THE LATENT PERIOD IN TUMOR PRODUCTION IN MICE[a]

Derivative of 1,2-benzanthracene	Max., Å.	Δ Max., Å.	Activity: Subcutaneous	Activity: Skin Painting
1,2-Benzanthracene	2870	0	Inactive	Inactive
1'-Methyl-	2875	5	Inactive	Inactive
7-Methyl-	2880	10	1 Tumor in 39 weeks	Inactive
6,7-Dimethyl-	2880	10	Inactive	Very slightly active
6,7-Cyclopenteno-	2880	10	.....	About 43 weeks
4-Methyl-	2885	15	Active[b]	1 Papilloma
5-Methyl-	2890	20	27 Weeks	44 Weeks
6-Methyl-	2890	20	.....	44/102 Weeks
6-Isopropyl-	2895	25	.....	41 Weeks
8-Methyl-	2900	30	Inactive[b]	.....
9-Methyl-	2905	35	24 Weeks	.....
10-Methyl-	2915	45	14/18 Weeks	30 Weeks
10-Isopropyl-	2920	50	Inactive	Inactive
5,8-Dimethyl-	2925	55	.....	.....
5,6-Cyclopenteno-	2930	60	.....	26.4 Weeks
5,10-Dimethyl-	2945	75	15 Weeks	16 Weeks
8,10-Dimethyl-	2950	80	.....	.....
Cholanthrene	2950	80	13.5 Weeks	15.7 Weeks
(3,4-Benzpyrene)	2955	85	15.3 Weeks	19.1 Weeks
9,10-Dimethyl-	2965	95	Active	Very active
20-Methylcholanthrene	2970	100	13 Weeks	18 Weeks

[a] Fieser, *Am. J. Cancer*, **34**, 37 (1938). [b] Shear, private communication.

such a method is open to criticism as the widths of the bands vary considerably and with them the degree of accuracy possible in determining the exact position of the maximum; furthermore, as the number of bands which can be resolved in all the compounds is not the same, such a mean would have little physical significance. Band D is the most intense and is quite narrow and obviously corresponds to some major electronic excitation of the molecule. In view of this steepness, the position of the maximum can be determined more accurately than that of the other bands and it was therefore decided to compare the position of the maximum of this band only in the various derivatives.

In Table IV, column 2 the positions of the maximum of band D of twenty derivatives of 1,2-benzanthracene are arranged in increasing order of bathochromic shift. The values of the compounds in italics are interpolated from the graphs of Mayneord and Roe.[4]

Bathochromic Shift and Carcinogenic Activity.—Many of the alkyl and ace-1,2-benzanthracenes are carcinogenically active and it is interesting to examine whether any relation can be found between the spectrum of these compounds and their physiological action. An attempt to discover such a relation implies that the carcinogenic activity can be assessed quantitatively or at least that the compounds can be arranged in order of increasing carcinogenic potency; much attention has been given to this subject in the laboratories of Fieser,[5] Shear[6] and Cook.[7] The carcinogenic activity is often expressed in terms of the latent period between the commencement of the administration and the development of tumors in mice. In the case of three compounds which have been very thoroughly investigated, *viz.*, 1,2,5,6-dibenzanthracene, 20-methylcholanthrene and 3,4-benzpyrene it has been shown that many factors enter into the determination of this latent period. These include the genetic history, age and sex of the mouse, and the dosage, manner and medium of administration of the hydrocarbon. Cook has usually administered the compound by skin painting producing a carcinoma, while Shear has largely employed subcutaneous injection to give a sarcoma of the connective tissue.

The carcinogenic activity of most of these alkyl 1,2-benzanthracenes has so far been examined only in a superficial manner; determinations of the latent period prior to tumor production have been made on only ten or twenty mice and not necessarily under comparable conditions of genetic strain, age, sex or dosage, etc. The data at present available are summarized in Table IV (Fieser[5]) and it will be observed that some correlation can be traced between the carcinogenic activity and

the bathochromic shift of band D. Considering first the monomethyl derivatives, of the twelve possible isomers eight have been examined and the carcinogenically inactive 1′- and 7-methyl compounds show a very small shift (5, 10 Å.) whereas the 10-methyl compound, the most active of this group, has the largest shift (45 Å.). The 9,10-dimethyl compound, which is highly active, particularly with regard to skin painting, and cholanthrene both show large shifts (95, 80 Å.) while 20-methylcholanthrene which acts very rapidly on both subcutaneous and cutaneous tissue has the maximum shift of 100 Å. The introduction of a second alkyl group into an alkylaromatic hydrocarbon causes a further shift of the spectrum to longer wave lengths, yet in the feebly carcinogenic 6,7-dimethyl compound the shift is small (10 Å.), less than that of many of the monomethyl derivatives. The relative carcinogenic activities of the 6,7- and 5,6-cyclopenteno derivatives are also in agreement with their spectral shifts.

The correlation, however, is not without exceptions. The 10-isopropyl compound is inactive yet the bathochromic shift is quite large. Here there is a second factor introduced in the lengthening of the side chain and it is known that even the extreme lengthening of an alkyl chain may produce little change in the absorption of an attached chromophore (*cf.* the spectra of acetic and palmitic acids[12]) while its effect on the physiological properties may be profound. The 8-methyl compound is a more significant exception. It has failed to produce tumors when the crystalline substance was repeatedly injected into twenty mice over a period of ten months (Shear[13]).

3,4-Benzpyrene is included in Table IV in parentheses since although the short wave region of the spectrum is like that of 1,2-benzanthracene the longer wave part is different. The spectrum of 1,2,5,6-dibenzanthracene is quite different and cannot be included in this analysis. Of the carcinogenically active hydrocarbons not closely related to 1,2-benzanthracene, the 3,4-benzphenanthrene group is the most interesting, particularly the 2-methyl compound, which is very potent when applied to the skin[14] but apparently inactive subcutaneously.[13] The absorption spectrum of 3,4-benzphenanthrene differs considerably from that of 1,2-benzanthracene.[4]

The magnitude of these spectral shifts corresponds to relatively small differences in the absorption energy involved. The general similarity in shape and constancy of intensity among all the curves show that the presence or absence of an alkyl group can have only a minor influence on the electronic activations of the molecule associated with light absorption in this near ultraviolet region of the spectrum. On the other hand, the observed displacements are considerably greater than the experimental errors of measurement. At present the mode of action of a carcinogen is obscure and the great differences in activity among compounds of closely similar structure show that the controlling factors may be exceedingly subtle. The small spectral shifts and variations in carcinogenic activity may be independent consequences of some such common structural influence.

Acknowledgment.—The author wishes to thank Professor L. F. Fieser for his encouragement and advice during the progress of this research, the Commonwealth Fund for fellowship support and Dr. Hugh H. Darby for many valuable suggestions regarding the setting up of the apparatus. Funds for the installation of the spectrograph were derived from a grant to Professor Fieser from the National Advisory Cancer Council.

Summary

The ultraviolet absorption spectra of 1,2-benzanthracene and of ten mono and dimethyl derivatives have been examined and found to be closely similar in shape and intensity. Considerable variation is observed in the bathochromic shift of the position of the maximum of the most intense band and this appears to show some correlation with the variation in the carcinogenic activity of the hydrocarbons.

The spectrum of 1′,9-methylene-1,2-benzanthracene differs markedly from that of the other derivatives and this is considered possibly to be due to steric strain in the molecule.

The spectrographic equipment recently installed in these laboratories is also described.

CAMBRIDGE, MASS. RECEIVED JUNE 14, 1939

(12) Ley and Arends, *Z. physik. Chem.*, **B17**, 183 (1935).
(13) Private communication.
(14) Bachmann, Cook, Dansi, deWorms, Haslewood, Hewett and Robinson, *Proc. Roy. Soc.* (London), **B123**, 343 (1937).

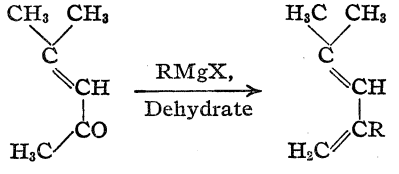
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Diene Synthesis of 2,3-Dialkyl-1,4-naphthoquinones Related to Vitamin K

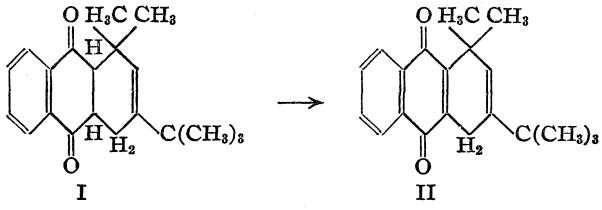
BY LOUIS F. FIESER AND CHARLOTTE W. WIEGHARD[1]

This research was undertaken with the idea of utilizing the reaction of α-naphthoquinone with dienes as a means of synthesizing compounds sharing with vitamins K_1 and K_2 the structural feature of a 1,4-naphthoquinone nucleus with alkyl substituents at the 2 and 3 positions. It soon became apparent from other observations in this Laboratory[2] that in the series of 2,3-dialkyl-1,4-naphthoquinones which have been assayed the antihemorrhagic activity of the first member (dimethyl) of the group is rather anomalous and that among the remaining compounds vitamin K activity begins to appear only when the alkyl side chains include a total of about ten carbon atoms. Preference was therefore given in the present work to the use of dienes of reasonably high molecular weight.

One scheme was to add a 1,1-dialkyl derivative of butadiene to α-naphthoquinone and convert the product to a 2,3-disubstituted naphthoquinone by isomerization and oxidation, for the presence of the *gem*-dialkyl group would counteract the normal tendency of the terminal ring to become aromatized with the formation of an anthraquinone. A satisfactory route to dienes of the desired type consists in the addition of a Grignard reagent to mesityl oxide and dehydration of the resulting carbinol.



The diene resulting from the use of the methyl Grignard reagent has already been added to α-naphthoquinone by Diels and Alder,[3] who converted the addition product as outlined above into 1,1,3-trimethyl-1,4-dihydroanthraquinone. On repeating their experiments a quinone was obtained of such widely different melting point as to suggest that a typographical error may have been made in their report. The substance was found by Dr. W. L. Sampson to be inactive in the chick assay at a dosage of 200 γ. A more promising case for present purposes consisted in the



introduction of a *t*-butyl group in the first step. The addition product I was obtained in a crystalline condition and easily isomerized and oxidized by treatment with alcoholic alkali and air and converted into the naphthoquinonoid substance II. A tertiary alkyl group has the advantage of preventing dehydration of the carbinol from occurring in more than one direction. This complication may have been involved in an experiment utilizing the carbinol[4] resulting from the reaction of mesityl oxide with ethylmagnesium bromide. The diene obtained on dehydration corresponded in boiling point with the material described by Abelmann[5] but gave no crystalline product when added to α-naphthoquinone.

A few attempts were made to employ 1,1,4,4-tetraalkylbutadienes in the synthesis without success. Suitable starting materials are available by the condensation of diethyl succinate with excess methyl[6] or ethyl[7] Grignard reagent and dehydration of the resulting glycols, as described for the first example by Faworsky.[8] The tetramethyl and tetraethyl compounds were both prepared but neither substance added readily to α-naphthoquinone and under forcing conditions extensive decomposition occurred.

A further scheme of synthesis is illustrated by the sequence of reactions starting with the addition of myrcene to α-naphthoquinone. The known addition product III[9] cannot be treated as above because of the ready conversion of the intermediate oxidation product into an anthraquinone under the conditions of its formation. The required partial dehydrogenation was accom-

(1) Department of Chemistry, Skidmore College.

(2) Fieser, Campbell and Fry, THIS JOURNAL, **61**, 2206 (1939); Fieser, Campbell, Fry and Gates, *ibid.*, **61**, 3216 (1939); Fieser, *ibid.*, **61**, 3467 (1939).

(3) Diels and Alder, *Ber.*, **62**, 2358 (1929).

(4) Jacquemoin, *Compt. rend.*, **198**, 483 (1934).

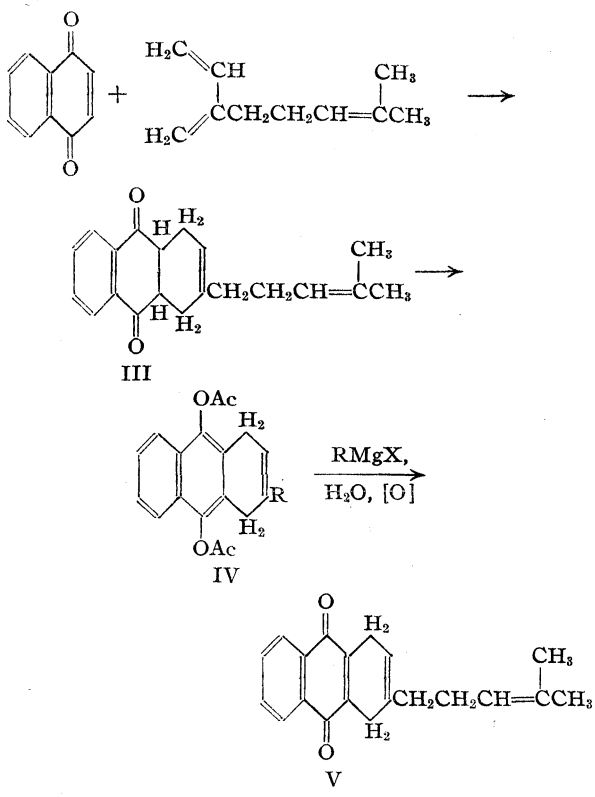
(5) Abelmann, *Ber.*, **43**, 1586 (1910).

(6) Harries, *Ann.*, **343**, 364 (1905).

(7) Valeur, *Compt. rend.*, **132**, 834 (1901).

(8) Faworsky, *J. prakt. Chem.*, **44**, 228 (1891).

(9) Arbusow and Abramow, *Ber.*, **67**, 1942 (1934).



plished successfully by conversion with acetic anhydride and pyridine into the diacetate IV, cleavage of this with methylmagnesium chloride, and oxidation of the liberated hydroquinone with silver oxide. 2-(∂-Methyl-γ-pentenyl)-1,4-dihydroanthraquinone (V) was thereby obtained in good yield as a crystalline yellow product.

Although 1,1-dimethyl-3-*t*-butyl-1,4-dihydroanthraquinone (II) and 2-(∂-methyl-γ-pentenyl)-1,4-dihydroanthraquinone (V) are comparable in molecular complexity with the antihemorrhagic 2-methyl-3-geranyl and 2-methyl-3-cinnamyl derivatives of α-naphthoquinone, neither substance showed vitamin K activity when assayed at 400 γ and 50 γ, respectively (W. L. Sampson).

Experimental Part[10]

1,1,3 - Trimethyl - 1,4 - dihydroanthraquinone.—**1,1,3-Trimethylbutadiene** was prepared essentially as described by Fellenberg.[11] From 50 g. of mesityl oxide and the reagent from 18 g. of magnesium and excess methyl chloride, refluxing in ether for one hour, there was obtained after two distillations 50 g. (86%) of the carbinol, b. p. 46° (14 mm.). This was dehydrated by distillation from 10 g. of potassium bisulfate at about 80–88°. The twice distilled diene boiled at 93°; yield, 27.5 g. (65%).

A mixture of 6 g. of the diene and 2 g. of α-naphthoquinone was refluxed for eight hours and the excess diene removed in vacuum. The residual yellow oil solidified on cooling, and two crystallizations from alcohol (Norite) gave 2 g. (62%) of colorless addition product, m. p. 119°, as reported by Diels and Alder.[3] This was dissolved in 10 cc. of hot alcohol and after adding one drop of 10% alcoholic potassium hydroxide, air was bubbled through the solution until the color changed from green to red to orange (ten minutes). The quinone separated in yellow plates and on recrystallization from alcohol formed yellow plates, m. p. 129–129.5°; yield 1.2 g. (60.5%). The melting point remained unchanged on recrystallization, and several preparations were made with the same results. Since Diels and Alder[3] report a very different m. p. (162°), the sample was analyzed. A cold alcoholic solution of the quinone acquires an intense greenish blue color on adding 10% alcoholic potassium hydroxide; the color fades slowly on standing, or rapidly on shaking with air, to a light orange.

Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.92; H, 6.39. Found: C, 81.12; H, 6.58.

1,1 - Dimethyl - 3 - *t* - butyl - 1,4 - dihydroanthraquinone (II).—In the first step, conducted essentially as described by Stevens,[12] the reagent prepared under nitrogen from 18 g. of magnesium, 70 g. of *t*-butyl chloride, and 600 cc. of ether was added with stirring to 40 g. of mesityl oxide in 300 cc. of ether and after refluxing for one hour the complex was decomposed with dilute acetic acid. The ether layer was washed neutral, washed with sodium chloride solution, dried with sodium sulfate, and evaporated. In the first distillation of the carbinol a 36-g. fraction, b. p. 85–105° (40 mm.), was collected; redistillation gave 23.4 g. (37%) of material, b. p. 94–95° (40 mm.). This fraction was distilled from 5 g. of potassium bisulfate and the cloudy distillate dried over sodium sulfate and distilled. There was obtained 13.3 g. (64%) of **1,1-dimethyl-3-*t*-butylbutadiene,** b. p. 58–59° (32 mm.).

For preparation of the addition product 12 g. of the diene was first heated with 4 g. of α-naphthoquinone without solvent at 100–110° for twenty-four hours. Some product crystallized on cooling, but the reaction was evidently incomplete and some decomposition had occurred (dark melt), and consequently 10 cc. of dioxane was added and heating continued for twenty-four hours longer. After evaporation in vacuum the viscous brown residue was triturated with 3 cc. of alcohol and the dark crystalline product obtained was recrystallized three times from alcohol using Norite, when glistening, colorless needles of the **addition product I** were obtained. The substance melts at 142–143°; yield 1 g. (13%).

Anal. Calcd. for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16. Found: C, 80.97; H, 8.09.

For isomerization and oxidation, 1 g. of the addition product was dissolved in 5 cc. of hot alcohol, a drop of 10% alcoholic potassium hydroxide was added, and air was bubbled through until the sequence of color changes reached an orange end-stage. The quinone crystallized on rubbing and the material, purified by two further crystallizations, formed yellow needles, m. p. 102–103°. The

(10) All melting points are corrected. Microanalyses by Lyon Southworth and Herbert S. Wight.

(11) Fellenberg, *Ber.*, **37**, 3578 (1904).

(12) Stevens, THIS JOURNAL, **57**, 1116 (1935).

yield of satisfactory material was 0.35 g. (35%). In the test with alcoholic potassium hydroxide in the cold, the quinone gives an intense blue changing slowly to yellow.

Anal. Calcd. for $C_{20}H_{22}O_2$: C, 81.59; H, 7.53. Found: C, 81.60; H, 7.62.

2 - (∂ - Methyl - γ - pentenyl) - 1,4 - dihydroanthraquinone (V).—The myrcene employed was obtained from a commercial terpene fraction of bay oil. About half of this distilled at 64–69° (20 mm., 1-m. column), and on redistillation of 250 cc. of this material the myrcene collected chiefly in a fraction boiling at 64.5–66° (20 mm.) and weighing 120 g. Semmler[13] reports the b. p. 67–68° at 20 mm. For identification a sample was converted into the maleic anhydride addition product, which corresponded in b. p. (188° at 8 mm.) and m. p. (34–35°) with the material described in the literature.[9,14]

The reaction between myrcene (30 cc.) and α-naphthoquinone (10 g.) was conducted by refluxing in dioxane (30 cc.) for twelve hours. After evaporation in vacuum the oily product was taken up in petroleum ether (b. p. 30–60°) and the solution was chilled and seeded with crystals obtained by cooling a dilute solution in petroleum ether to −70°. There was obtained 15.4 g. (83%) of cream colored crystalline product, m. p. 60–61°. Two crystallizations gave colorless crystals, m. p. 61–61.3°; yield 12 g. (64%). Arbusow and Abramow[9] found the m. p. 58–58.5°.

Anal. Calcd. for $C_{20}H_{22}O_2$: C, 81.59; H, 7.53. Found: C, 81.70; H, 7.66.

The **hydroquinone diacetate IV** was prepared by heating the addition product (12 g.) in acetic anhydride (20 cc.) and pyridine (4 cc.) for one hour on the steam-bath. The solution was cooled and stirred with dilute hydrochloric acid; with the hydrolysis of the excess anhydride the diacetate separated as a tan colored solid. This was taken into ether and the solution was washed free of acid, dried, and the solvent evaporated in vacuum. Three crystallizations from alcohol gave 13 g. (84%) of colorless needles having a fluorescent greenish tinge and melting at 121–122°.

Anal. Calcd. for $C_{24}H_{26}O_4$: C, 76.16; H, 6.93. Found: C, 76.34; H, 6.98.

For conversion to the quinone, 13 g. of the diacetate was added in ether solution to the Grignard reagent prepared from 12 g. of magnesium, 400 cc. of ether, and the required amount of methyl chloride. After refluxing for forty-five minutes the ether was largely displaced with benzene and refluxing was continued for one-half hour longer. The mixture was decomposed with ammonium chloride and hydrochloric acid and the yellow organic layer was washed, dried, and shaken for one-half hour with 3 g. of silver oxide and 20 g. of sodium sulfate. The filtered solution was evaporated, eventually under vacuum, leaving a residue of 7 g. (70%) of the quinone, m. p. 88–89°. Crystallized from alcohol, the substance formed glistening yellow plates, m. p. 89.8–90.8°. With alcoholic alkali the substance gives a red color changing rapidly on shaking with air to pale yellow.

Anal. Calcd. for $C_{20}H_{20}O_2$: C, 82.20; H, 6.89. Found: C, 82.25; H, 7.00.

Summary

As a route to 2,3-dialkyl-1,4-naphthoquinones of high molecular weight which might show vitamin K activity, a study has been made of the addition of suitable dienes to α-naphthoquinone and the partial dehydrogenation of the products. Two satisfactory syntheses were developed and applied to the preparation of C_{20}-quinones of the type desired. Neither of these substances shows activity.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASS. RECEIVED NOVEMBER 29, 1939

(13) Semmler, *Ber.*, **34**, 3126 (1901).
(14) Diels and Alder, *Ann.*, **470**, 65 (1929).

[CONTRIBUTION FROM THE SQUIBB INSTITUTE FOR MEDICAL RESEARCH, DIVISION OF ORGANIC CHEMISTRY]

Vitamin K-Active Derivatives of 2-Methyl-1,4-naphthohydroquinone

BY S. ANSBACHER, ERHARD FERNHOLZ AND M. A. DOLLIVER[1]

About six months ago we reported[2] that 2-methyl-1,4-naphthoquinone has a vitamin K potency of 1 unit[3] in about 0.5 γ. Simultaneously other investigators[4,5,6] published their work with this substance, and it is apparent that they then failed to observe the outstanding biological activity of this compound. However, the same authors,[7,8,9] and others[10,11] fully confirmed our results in more recent communications. Meanwhile we prepared and investigated several derivatives which are the object of the present report.

(1) Chemist at the Development Laboratory of E. R. Squibb & Sons, Brooklyn, N. Y.
(2) Ansbacher and Fernholz, THIS JOURNAL, **61**, 1924 (1939).
(3) Ansbacher, *J. Nutrition*, **17**, 303 (1939).
(4) Almquist and Klose, THIS JOURNAL, **61**, 1923 (1939).
(5) Fieser, Bowen, Campbell, Fry and Gates, Jr., *ibid.*, **61**, 1926 (1939).
(6) Thayer, Cheney, Binkley, MacCorquodale and Doisy, *ibid.*, **61**, 1932 (1939).
(7) Fieser, *ibid.*, **61**, 2559 (1939).
(8) Thayer, Binkley, MacCorquodale, Doisy, Emmett, Brown and Bird, *ibid.*, **61**, 2563 (1939).
(9) Almquist and Klose, *J. Biol. Chem.*, **130**, 787 (1939).
(10) Tishler and Sampson, THIS JOURNAL, **61**, 2563 (1939).
(11) Personal communication of September 25, 1939, from Dr. H. Dam of the University of Copenhagen, Denmark.

Experimental Part[12]

2 - Methyl - 1,4 - naphthohydroquinone - dipropionate.—A mixture of 10 g. of 2-methyl-1,4-naphthoquinone, 30 ml. of propionic acid, 100 ml. of propionic anhydride, 25 g. of zinc dust and 5 g. of fused sodium propionate was refluxed for thirty minutes in an oil-bath at 160–170°, then poured into water. An oily product separated and solidified on standing. It was removed by filtration and recrystallized from dilute methanol to a constant m. p. of 74–75°; yield 12 g. (72%).

Anal. Calcd. for $C_{17}H_{18}O_4$: C, 71.29; H, 6.34. Found: C, 71.48; H, 6.36.

The procedure followed for preparing the dipropionate is similar to the one used by Anderson and Newman[13] for the synthesis of the diacetate.

2 - Methyl - 1,4 - naphthohydroquinone - dibenzoate.—12.5 g. of 2-methyl-1,4-naphthohydroquinone was treated with 30 g. of benzoyl chloride in 60 g. of pyridine while cooling. After standing for one hour, the mixture was heated for thirty minutes at a bath temperature of 110–120° and poured into water. The resulting precipitate was collected by filtration and recrystallized from dilute acetone to a constant m. p. of 179°; yield 16.2 g. (59%).

Anal. Calcd. for $C_{25}H_{18}O_4$: C, 78.51; H, 4.97. Found: C, 78.71; H, 5.00.

A second crop of 9 g. (m. p. 174–176°) was obtained from the mother liquors, bringing the total yield to 25.2 g. (84%).

2 - Methyl - 1,4 - naphthohydroquinone - di - *n* - butyrate. Method A.—A mixture of 10 g. of 2-methyl-1,4-naphthoquinone, 30 ml. of butyric acid, 100 ml. of butyric anhydride, 5 g. of fused sodium butyrate, and 25 g. of zinc dust was refluxed for one hour in an oil-bath at 170–180°, then poured into water. As crystallization could not be induced, the oily product was extracted with ether, dried over anhydrous sodium sulfate and fractionated to give 12.5 g. of an oil distilling at 175–185° (1 mm.). The distillate solidified on cooling and stirring, and was recrystallized from dilute methanol to a constant m. p. of 52–53°; yield 10 g. (55%).

Anal. Calcd. for $C_{19}H_{22}O_4$: C, 72.57; H, 7.06. Found: C, 72.66; H, 7.31.

Method B. A mixture of 15 g. of *n*-butyryl chloride and 100 ml. of pyridine was added to 8.5 g. of 2-methyl-1,4-naphthohydroquinone and gently refluxed for one hour. After standing for one hour the mixture was poured into 800 ml. of water and the resulting oil extracted with ether. The ethereal solution was washed with 10% hydrochloric acid to remove pyridine, then freed from acid with water, and finally dried over anhydrous sodium sulfate. Fractionation gave 7.9 g. of an oil distilling at 190–195° (1.5 mm.). The distillate solidified on cooling and stirring. Recrystallization from dilute methanol yielded 3.5 g. of a compound melting at 52–53° and with no depression of melting point when mixed with the product resulting from method A.

2 - Methyl - 1,4 - naphthohydroquinone - di - isobutyrate.—Thirty grams of isobutyryl chloride in 75 ml. of pyridine was added to 19.5 g. of 2-methyl-1,4-naphthohydroquinone, the mixture allowed to stand for ninety minutes, then heated in an oil-bath at 120–135° for one hour, and finally poured into water. The solids thus obtained were removed by filtration, washed with water, and recrystallized from dilute methanol to a constant melting point of 73–74°; yield 24.6 g. (69%).

Anal. Calcd. for $C_{19}H_{22}O_4$: C, 72.57; H, 7.06. Found: C, 72.64; H, 7.02.

2 - Methyl - 1,4 - naphthohydroquinone - di - *n* - valerate.—Sixteen grams of 2-methyl-1,4-naphthohydroquinone was dissolved in 80 ml. of pyridine and treated dropwise while cooling and shaking with 30 g. of *n*-valeryl chloride. After standing for one hour the mixture was refluxed for one hour at a bath temperature of 120–130°, allowed to stand overnight and finally poured into water. The oily product was extracted with ether, the extract washed with water, 10% hydrochloric acid, and again with water. After being dried over anhydrous sodium sulfate, the ether was removed by distillation and the residual red oil was distilled three times under reduced pressure from a modified Claisen flask. The final product was a yellow oil distilling at 210° (1 mm.); yield 22 g. (70%).

Anal. Calcd. for $C_{21}H_{26}O_4$: C, 73.64; H, 7.66. Found: C, 73.43; H, 7.77.

After standing for some time, it crystallized and was recrystallized from dilute methanol to a constant melting point of 40–41°.

2 - Methyl - 1,4 - naphthohydroquinone - di - isovalerate.—Fifteen grams of 2-methyl-1,4-naphthohydroquinone was treated with 30 g. of isovaleryl chloride in 50 ml. of pyridine, then heated at a bath temperature of 130° for one hour. The mixture was poured into water and the resulting oil extracted with ether. The ethereal solution was washed with water, 10% hydrochloric acid, and again with water. After being dried over anhydrous sodium sulfate the ether was removed by evaporation and the residue was fractionated by three vacuum distillations from a modified Claisen flask. The final product was a yellow oil distilling at 185° (1 mm.); yield 14.2 g. (48%).

Anal. Calcd. for $C_{21}H_{26}O_4$: C, 73.64; H, 7.66. Found: C, 73.02; H, 7.44.

2-Methyl-1,4-dimethoxynaphthalene.—18.4 g. of 2-methyl-1,4-naphthohydroquinone was added to 53.6 g. of dimethyl sulfate in a flask equipped with a reflux condenser, mercury-seal stirrer, and a gas inlet tube. Nitrogen was passed through the apparatus while adding 1-ml. portions of a solution of 47.6 g. of potassium hydroxide in 100 ml. of water by way of the condenser. The mixture was then heated on the steam-bath for forty-five minutes, allowed to stand overnight, finally diluted to 500 ml. with water and extracted with ether. The extract was washed free from alkali with water, dried over anhydrous sodium sulfate and fractionated to yield 16.5 g. of an oily product distilling at 174–178° (18 mm.). The oil solidified on treatment with 50 ml. of 1 *N* sodium hydroxide and cooling. Recrystallization from petroleum ether gave a white crystalline product melting at 48–49°; yield 11.8 g. (55%).

Anal. Calcd. for $C_{13}H_{14}O_2$: C, 77.19; H, 6.98. Found: C, 77.09; H, 6.87.

The procedure followed for preparing the dimethyl ether

(12) Analyses by Dr. F. A. Smith, Chemist at the Development Laboratory of E. R. Squibb & Sons, Brooklyn, N. Y.

(13) Anderson and Newman, *J. Biol. Chem.*, **103**, 405 (1933).

is essentially the one outlined by Giral.[14] However, the product obtained by this investigator had a b. p. of 175–178° (18 mm.) and a m. p. of 23–24°.

Bio-assays.—The rapid assay procedure, carried out to date on more than 15,000 chicks, was employed for determining the vitamin K unit of the various naphthohydroquinone derivatives summarized in Table I. The method has been described in detail[3] and found applicable to the testing of concentrates,[3,15,16] synthetic vitamins[15] and synthetic substitutes.[2,15,17,18] Certain minor, but nevertheless important, points seem to warrant emphasis, since they were overlooked by other investigators when attempting to make use of a rapid assay procedure.

TABLE I

VITAMIN K UNIT OF METHYLNAPHTHOHYDROQUINONE AND ITS DERIVATIVES

Compound, 2-Methyl-1,4-	1 unit equals, γ
Naphthohydroquinone	0.5
Naphthohydroquinonediacetate	1
Naphthohydroquinonedipropionate	1
Naphthohydroquinonedibenzoate	1
Naphthohydroquinone-di-*n*-butyrate	1.25
Naphthohydroquinone-di-isobutyrate	5
Naphthohydroquinone-di-*n*-valerate	1.25
Naphthohydroquinone-di-isovalerate	3
Dimethoxynaphthalene	5

The medium employed for administering the test substances was cod liver oil in most of our experiments. Other oils, such as peanut or corn oil, are likewise satisfactory vehicles. However, the amount of the menstruum plays a decisive role. In accordance with the definition of our unit,[3] we administer fat-soluble test substances always in 0.10 ml. of oil. If a product is soluble in water, its potency can be determined with aqueous solutions. The 2-methyl-1,4-naphthoquinone is soluble in water to the extent of about 100 γ/ml.; it shows a biological response indicative of 1 unit in about 0.5 γ, irrespective of whether it is dissolved in 0.10 ml. of cod liver oil or 1 ml. of water. Incidentally, such aqueous solutions can be administered intravenously.

If a vitamin K experiment is carried out properly, the chicks become deficient within two weeks, no spontaneous cures occur, the blood clotting time of all the animals remains prolonged, and hemorrhages develop as a result of which death occurs. If a bird shows hemorrhages but has a normal or only slightly prolonged coagulation time after the depletion period, it undoubtedly has had access to vitamin K. There are chicks which will be more resistant to vitamin K deficiency than others, as already pointed out for birds with enlarged thyroid glands.[3] Furthermore, many investigators have commented on the apparent resistance of animals hatched during the summer months, and we have found that exposure of day-old chicks to freezing temperatures for about six hours, as a preliminary step to the depletion period, is a contributing factor to a high incidence of vitamin K deficiency. A biological assay properly conducted will permit the determination not only of the minimum effective dose, but also of the duration of the curative effect, summarized for the naphthohydroquinone derivatives in Table I and Table II, respectively.*

TABLE II

DURATION OF THE CURATIVE EFFECT OF THE VARIOUS COMPOUNDS

Compd.	Amount, γ	Hours
2-Methyl-1,4-naphthoquinone	0.75	72
	.50 (1 unit)	48
	.25	24
2-Methyl-1,4-naphthohydroquinonediacetate	1.5	72
	1.0 (1 unit)	48
	0.75	24
2-Methyl-1,4-naphthohydroquinonedipropionate	1.5	72
	1.0 (1 unit)	48
	0.75	24
2-Methyl-1,4-naphthohydroquinone-di-*n*-butyrate	1.5	72
	1.25 (1 unit)	48
	1.0	24

Discussion

Since 2-methyl-1,4-naphthohydroquinone may be oxidized easily to methyl-1,4-naphthoquinone, the equal potency of the two compounds was to be expected and has been mentioned already by Thayer, *et al.*[8] The mechanism of the biological effect of vitamin K active naphthohydroquinone derivatives has not been explained; it appears possible that an oxidation–reduction phenomenon is involved and certain data apparently substantiate such a hypothesis. The diacetate, dipropionate and dibenzoate esters are identical as far as potency, speed of action and period of efficacy within the animal body are concerned. This fact could be interpreted to mean that esters are

(14) Giral, *Anales soc. espan. fis quim.*, **31**, 861 (1933).

(15) Ansbacher, Fernholz and MacPhillamy, *Proc. Soc. Exp. Biol. Med.*, **42**, 655 (1939).

(16) Fernholz, Ansbacher and Moore, THIS JOURNAL, **61**, 1613 (1939).

(17) Fernholz and Ansbacher, *Science*, **90**, 315 (1939).

(18) Ansbacher and Fernholz, *J. Biol. Chem.*, **131**, 399 (1939).

(*) The detailed data of Tables I and II are included in the authors' reprints of this paper.

first saponified and then act in the form of methylnaphthohydroquinone. However, the potencies of the di-*n*-butyrate and di-*n*-valerate were found to be significantly greater than those of the corresponding iso-compounds with their inherent branched chains. This interesting observation may be explained by a difference in the rate of absorption, but it is also possible that these derivatives act as a whole and not in the form of a methylnaphthohydroquinone–methylnaphthoquinone equilibrium. Furthermore, the activity of the dimethyl ether is remarkably great, although in all probability this compound cannot be transformed to methylnaphthohydroquinone, considering the difficulty with which methyl ethers of phenols are split *in vitro*.

Our data confirm the results of Binkley, *et al.*,[19] namely: "In general, the activities of the diacetates of the 1,4-diols were about one-half that of the corresponding quinones." Most recently Doisy and his co-workers[20] stated, furthermore: "Only 1,4-naphthoquinones and compounds which upon oxidation in the organism might yield 1,4-naphthoquinones showed activity." In view of our observations above, particularly in conjunction with the vitamin K potency of phlorone, already reported,[18] it would seem that vitamin K activity is not confined solely to 1,4-naphthoquinones. Incidentally, anthraquinone appears to have a potency of one unit in about 2 mg.

(19) Binkley, Cheney, Holcomb, MacCorquodale, Thayer and Doisy, 98th Meeting, Am. Chem. Soc., Boston, Mass., September 12, 1939.

Summary

The preparation of several esters and an ether of 2-methyl-1,4-naphthohydroquinone is described.

The various derivatives were found to have different vitamin K potencies.

A discussion of the relationship between structure and vitamin K activity is presented.

(20) Doisy, MacCorquodale, Thayer, Binkley and McKee, Nat. Acad. Sci., Brown U. Meeting, October 23–25, 1939 [*Science*, **90**, 407 (1939)].

NEW BRUNSWICK, N. J. RECEIVED NOVEMBER 13, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE UPJOHN COMPANY]

Sulfanilamide Compounds. II. Arylidine Derivatives of N^1-Substituted Sulfanilamides

BY H. G. KOLLOFF AND JAMES H. HUNTER

In 1936 Buttle, Gray and Stephenson[1] reported N^1-phenylsulfanilamide to be as active against streptococcal infections in mice as sulfanilamide and on the basis of our preliminary tests N^1-(4-nitro)-phenylsulfanilamide[2] shows considerable activity against both streptococcal and pneumococcal infections. Since 1938 N^1-(2-pyridyl)-sulfanilamide[3] (Sulfapyridine, M. and B. 693) has attained a foremost position in the ranks of antibacterial agents.

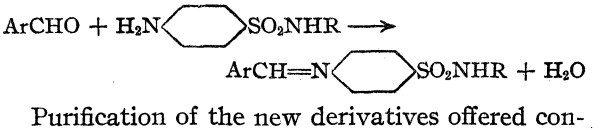
Goissedet, Despois, Galliot and Mayer[4] observed that some benzylidine sulfonamides were active and during the following year work along this line was continued by Gray, Buttle and Stephenson.[5]

The foregoing considerations suggested the preparation of a series of arylidine derivatives of the N^1-substituted sulfanilamides in order to ascertain in what respect their activity was generally affected by introducing an arylidine group.

For sake of comparison between structure and activity, the arylidine derivatives of the parent compound, sulfanilamide, have been included.

Sulfanilamide and sulfapyridine were obtained through commercial sources; N^1-phenylsulfanilamide was prepared according to Gelmo,[6] and for the preparation of N^1-(4-nitro)-phenylsulfanilamide the procedure of Webster and Powers[2] was successfully modified in that pyridine rather than dimethylaniline was used as a reaction medium.

The arylidine derivatives listed in Table I were prepared in 73% to practically quantitative yields by condensing the N^1-substituted sulfanilamides with the appropriate aldehyde in the absence of a solvent according to the equation



Purification of the new derivatives offered con-

(1) Buttle, Gray and Stephenson, *Lancet*, **1**, 1286 (1938).
(2) Webster and Powers, THIS JOURNAL, **60**, 1553 (1938).
(3) Whitby, *Lancet*, **1**, 1210 (1938).
(4) Goissedet, Despois, Galliot and Mayer, *Compt. rend. soc. biol.*, **121**, 1082 (1936).
(5) Gray, Buttle and Stephenson, *Biochem. J.*, **31**, 724 (1937).
(6) Gelmo, *J. prakt. Chem.*, [2], **77**, 374 (1908).

TABLE I

Substituted sulfanilamide[h]	Formula	M. p., °C. (uncor.)	N, % Calcd.	N, % Found	S, % Calcd.	S, % Found	Biologic activity[i] Strep.	Biologic activity[i] Pneumo.
Sulfanilamide	$C_6H_8N_2O_2S$						7.0	4.7
N^4-Benzylidine-	$C_{13}H_{12}N_2O_2S$[c,f]	176	10.77	10.60	12.30	12.83	7.0	4.7
N^4-(4-Methoxy)-benzylidine-	$C_{14}H_{14}N_2O_3S$[d,f]	192–3	9.66	9.99	11.03	11.68	4.7	4.5
N^4-(4-Dimethylamino)-benzylidine-	$C_{15}H_{17}N_3O_2S$[d,f]	226–7	13.84	14.39	10.55	11.01	7.0	2.5
N^1-Phenyl-	$C_{12}H_{12}N_2O_2S$[g]						3.8	0.3
N^4-Benzylidine-N^1-phenyl-	$C_{19}H_{16}N_2O_2S$[b]	175–75.5	8.28	8.34	9.47	9.61	2.8	1.0
N^4-(4-Methoxy)-benzylidine-N^1-phenyl-	$C_{20}H_{18}N_2O_3S$[a]	166	7.66	7.60	8.74	8.92	3.7	0.3
N^4-(4-Dimethylamino)-benzylidine-N^1-phenyl-	$C_{21}H_{21}N_3O_2S$[d]	231	11.08	10.92	8.44	8.65	4.5	0.5
N^1-(4-Nitro)-phenyl-	$C_{12}H_{11}N_3O_4S$[g]						2.3	3.0
N^4-Benzylidine-N^1-(4-nitro)-phenyl-	$C_{19}H_{15}N_3O_4S$[b]	192	11.02	11.25	8.40	8.61	7.0	3.3
N^4-(4-Methoxy)-benzylidine-N^1-(4-nitro)-phenyl-	$C_{20}H_{17}N_3O_5S$[e]	213.5	10.21	10.40	7.79	7.76	4.7	2.7
N^4-(4-Dimethylamino)-benzylidine-N^1-(4-nitro)-phenyl-	$C_{21}H_{20}N_4O_4S$[d]	231	13.20	13.42	7.54	7.49	5.2	5.2
N^1-(2-Pyridyl)-	$C_{11}H_{11}N_3O_2S$						6.8	7.0
N^4-Benzylidine-N^1-(2-pyridyl)-	$C_{18}H_{15}N_3O_2S$[e]	245–6	12.45	12.58	9.50	9.45	6.8	4.0
N^4-(4-Methoxy)-benzylidine-N^1-(2-pyridyl)-	$C_{19}H_{17}N_3O_3S$[e]	212–12.5	11.41	11.90	8.70	8.66	5.7	4.2
N^4-(4-Dimethylamino)-benzylidine-N^1-(2-pyridyl)-	$C_{20}H_{20}N_4O_2S$[e]	238.2–40	14.72	14.64	8.42	9.25	4.8	4.7

[a] From benzene. [b] From toluene. [c] From xylene. [d] From acetone–petroleum ether. [e] Washed with ether and acetone. [f] Prepared by Gray, Buttle and Stephenson.[5] [g] From dilute alcohol. [h] Nomenclature of Crossley, Northey and Hultquist, THIS JOURNAL, 60, 2217 (1938). [i] Results expressed on basis of average survival time, according to the method of Whitby.[3]

siderable difficulty because of both their slight solubility and their instability. When possible, the products were crystallized from benzene and its homologs or from an acetone–petroleum ether mixture. In some cases the crude products were simply washed with suitable solvents for removal of unreacted starting materials.

These arylidine derivatives, particularly the benzylidine and 4-methoxybenzylidine derivatives, hydrolyze easily. Some underwent hydrolysis merely by crystallization from dilute alcohol; for this reason water was excluded from the crystallizing media. A few compounds, N^4-(4-methoxy)-benzylidine-N^1-phenylsulfanilamide, for instance, decomposed when crystallized from high-boiling solvents such as toluene or xylene.

We are indebted to Dr. F. A. Eberly and Mr. E. A. Gibson[7] for the biological data herein reported.

These preliminary studies indicate that in general introduction of an arylidine group results in a slight, but not particularly significant, decrease in both the antistreptococcal and antipneumococcal activity; the latter was diminished to a greater extent than the former. In every instance the toxicity was found to be lowered.

(7) A detailed report of the biological study of these and other derivatives will be published elsewhere.

Further biologic studies are being made on certain compounds of this series where preliminary indications warrant.

Work on similar arylidine derivatives is now in progress in these Laboratories.

Experimental

N^4-Arylidine-N^1-substituted Sulfanilamides.—The following procedure for the preparation of **N^4-(4-methoxy)-benzylidine-N^1-(4-nitro)-phenylsulfanilamide** is typical of that used in preparing the derivatives given in Table I. Seven and forty-eight hundredths grams (0.055 mole) of anisaldehyde (Eastman Kodak Company, "Practical") was added to 14.6 g. (0.05 mole) of N^1-(4-nitro)-phenylsulfanilamide[2] (m. p. 166.5–167.5°) contained in a 500-cc. round-bottom flask, and the latter immersed one-half its depth in an oil or metal bath at 140–150°. After about five minutes the mixture liquefied and the orange-colored melt was stirred mechanically for fifteen minutes, at which time it had partially resolidified. Stirring was discontinued and the mixture heated for an additional one and three-fourths hours. Lumps of material were occasionally crushed during the heating. The crude product was cooled and thoroughly washed with five 50-cc. portions of ether; yield, 20.1 g. (98% of the theoretical). Nine grams of the crude product was crystallized from 400 cc. of xylene using a little decolorizing charcoal; yield, 5.7 g., m. p. 211–211.5° (uncorr.).

Summary

A detailed procedure is given for a general method of preparing N^4-arylidine sulfanilamides;

the preparation of N^4-(4-methoxy)-benzylidine-N^1-(4-nitro)-phenylsulfanilamide is described as an example.

On the basis of preliminary biological studies, introduction of the arylidine group causes some diminution in activity, and a significant decrease in toxicity.

KALAMAZOO, MICH. RECEIVED OCTOBER 25, 1939

[CONTRIBUTION FROM THE NICHOLS CHEMICAL LABORATORY OF NEW YORK UNIVERSITY]

Sulfanilyl Derivatives of Pyridine and Quinoline Amines

BY ROBERT WINTERBOTTOM

Since the discovery by Whitby[1] of the therapeutic action of 2-sulfanilamidopyridine, numerous compounds of similar structure have been prepared. This paper describes the preparation of sulfanilamides containing a pyridine or a quinoline ring. The sulfanilyl derivatives of 5, 6, 7, and 8 aminoquinoline[2] were published by Bobranski while this research was in progress. Their physical properties correspond with those of the same compounds prepared in this Laboratory. Although there are many references in the literature to 2-sulfanilamidopyridine, its detailed method of synthesis has never appeared; for this reason its preparation has been included.

The aminoquinolines, with the exception of 3-aminoquinoline, were prepared from the corresponding nitroquinolines by catalytic reduction using Raney nickel. The yields were slightly better than those obtained by using iron and acetic acid.[3] Attempts to prepare 7-nitroquinoline by nitration of quinoline with lithium nitrate in acetic anhydride[4] failed to give appreciable yields. Diacetyl orthonitric acid was tried because of its peculiar orienting effects but was ineffective. 7-Nitroquinoline, prepared by the Skraup reaction using metanitraniline, upon catalytic reduction gave an aminoquinoline corresponding in physical properties to that prepared by Hamer.[5] It melted at 74–75.5° and not at 189° as described by earlier workers.[6] 3-Aminoquinoline was prepared from the corresponding bromo compound by treatment with aqueous ammonia at 200°.[7]

The sulfanilamides were prepared by condensing recrystallized acetylsulfanilyl chloride with the appropriate amine in pyridine solution. 5-N^4-Acetylsulfanilamido-2-acetylaminopyridine was prepared from 5-amino-2-acetylaminopyridine by Bauer's[8] method employing acetone. A sample of 2-acetylamino-5-aminopyridine was obtained through the courtesy of the Pyridium Corporation. The crude acetyl derivatives were recrystallized from ethanol or propanol. In cases where no suitable solvent could be found, the crude products were washed and dried before analysis, or prepared by acetylation of the free amine. In all cases, except that of 2-N^4-acetylsulfanilamidopyridine, removal of the acetyl group was effected by boiling for a half hour with 12% hydrochloric acid. This treatment causes rupture of the sulfonamide linkage when applied to 2-N^4-acetylsulfanilamidopyridine. When the hydrolysis was carried out in alcoholic hydrochloric acid solution, the sulfonamide link remained intact.

Experimental Part

7-Aminoquinoline.—7-Nitroquinoline (10 g., 0.058 mole), dissolved in 100 cc. of acetone, was reduced in a low pressure Parr hydrogenator in the presence of 0.6 g. (0.001 mole) of Raney nickel. Reduction was complete in one hour. The acetone was then allowed to evaporate. The product separated as an oil which soon solidified. Upon recrystallization from water, light yellow needles were obtained; yield: 8 g. (95%), m. p. 74–75.5°.

The same procedure was utilized for 5- and 8-aminoquinoline, using ethanol as the solvent. Recrystallization from ligroin and petroleum ether have yields of 75 and 69%, respectively.

2-Sulfanilamidopyridine.—Acetylsulfanilyl chloride (10 g.) and 2-aminopyridine (4 g.) were dissolved in 34 cc. of acetone containing 5 cc. of pyridine. Upon standing overnight 5 g. of almost pure product separated as a white deposit. The filtrate upon dilution with water gave an additional 4 g. For analysis it was recrystallized from acetone as small white needles. Removal of the acetyl group was effected by treating 1 g. of the crude acetyl compound with 10 cc. of ethanol and 2 cc. of concd. hydro-

(1) Whitby, *Lancet*, **1**, 1210 (1938).
(2) Bobranksi, *Arch. Pharm.*, **277**, 75 (1938).
(3) Dikshoorn, *Rec. trav. chim.*, **48**, 153 (1929).
(4) Bacharach, *et al.*, *ibid.*, **52**, 413 (1933).
(5) Hamer, *J. Chem. Soc.*, **119**, 1434 (1921).
(6) Claus and Massau, *J. prakt. Chem.*, **48**, 174 (1893).
(7) Renshaw and Friedman, THIS JOURNAL, **61**, 3320 (1939).
(8) Bauer, *ibid.*, **61**, 613 (1939).

TABLE I

Compound[a]	M. p., °C. (corr.)	Formula	Nitrogen, % Calcd.	Found[b]
2-N^4-Acetylsulfanilamidopyridine	226–227	$C_{13}H_{13}N_3O_3S$	14.42	14.60
2-Sulfanilamidopyridine	190–191	$C_{11}H_{11}N_3O_2S$	16.86	16.68
3-N^4-Acetylsulfanilamidopyridine	272–275 dec.	$C_{13}H_{13}N_3O_3S$	14.42	14.14
3-Sulfanilamidopyridine	248–251 dec.	$C_{11}H_{11}N_3O_2S$	16.86	16.61
5-N^4-Acetylsulfanilamido-2-acetylaminopyridine	288–291 dec.	$C_{15}H_{16}N_4O_4S$	16.09	15.81
5-Sulfanilamido-2-aminopyridine	210–211	$C_{11}H_{12}N_4O_2S$	21.20	20.94
3-N^4-Acetylsulfanilamidoquinoline	250–253 dec.	$C_{17}H_{15}N_3O_3S$	12.31	12.23
3-Sulfanilamidoquinoline	185–186 dec.	$C_{15}H_{13}N_3O_2S$	14.04	14.20
5-N^4-Acetylsulfanilamidoquinoline[c]	256–258	$C_{17}H_{15}N_3O_3S$	12.31	12.52
5-Sulfanilamidoquinoline[c]	228–230	$C_{15}H_{13}N_3O_2S$	14.04	14.15
6-N^4-Acetylsulfanilamidoquinoline[c]	285–287	$C_{17}H_{15}N_3O_3S$	12.31	12.12
6-N^4-Acetylsulfanilamidoquinoline hydrochloride	238–240	$C_{17}H_{16}ClN_3O_3S$	11.12	11.06
6-Sulfanilamidoquinoline[c]	202–204	$C_{15}H_{13}N_3O_2S$	14.04	13.86
8-N^4-Acetylsulfanilamidoquinoline[c,d]	193–194	$C_{17}H_{15}N_3O_3S$	12.31	12.02
8-Sulfanilamidoquinoline[c,d]	194–195	$C_{15}H_{13}N_3O_2S$	14.04	13.87

[a] Nomenclature according to Crossley, Northey and Hultquist, THIS JOURNAL, 60, 2217 (1938). [b] Dumas. [c] Previously prepared by Bobranski.[2] [d] Previously prepared by A. D. Choudhury, *et al.*, *J. Ind. Chem. Soc.*, 14, 733 (1937).

chloric acid. After refluxing for twenty minutes, the reaction mixture was diluted with water and made basic with ammonium hydroxide. It was recrystallized from ethanol; yield, 0.67 g. (75%).

5 - N^4 - Acetylsulfanilamido - 2 - acetylaminopyridine.—Using the same procedure as above, 3.0 g. of 5-amino-2-acetylaminopyridine and 4.0 g. of acetyl sulfanilyl chloride gave 6.0 g. (94%) of crude 5-N^4-acetylsulfanilamido-2-acetylaminopyridine. This was converted to 5-sulfanilamido-2-aminopyridine by the same procedure used below for 3-sulfanilamidoquinoline.

3-Sulfanilamidoquinoline.—3-Aminoquinoline (2.5 g.) and acetylsulfanilyl chloride (4.0 g.) were dissolved in 30 cc. of dry pyridine. After heating for two hours on the steam-bath, the reaction mixture was poured into 400 cc. of cold water. The product separated as a white crystalline mass weighing 5.4 g. when dry. For analysis a small amount was washed successively with water and ethanol and dried at 100°. One gram of the crude acetyl compound was boiled for a half hour with 25 cc. of 12% hydrochloric acid. Upon cooling and neutralizing with ammonium hydroxide, the sulfonamide was obtained; yield 0.8 g. (91%). It was recrystallized from ethanol.

Summary

An improved method of preparation of the 5, 7, and 8-aminoquinolines as well as the preparation of certain sulfanilamido derivatives of pyridine and quinoline amines is described.

The results obtained by Bobranski[2] are confirmed.

NEW YORK, N. Y. RECEIVED OCTOBER 31, 1939

[CONTRIBUTION FROM THE BURROUGHS WELLCOME & CO. U. S. A. EXPERIMENTAL RESEARCH LABORATORIES]

Amines Related to 2,5-Dimethoxyphenethylamine.[1] I

BY RICHARD BALTZLY AND JOHANNES S. BUCK

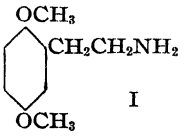
Preliminary pharmacological work has indicated that some amines containing the 2,5-dimethoxyphenyl group show activity comparable with that of similar phenolic amines, and also that they probably will be active orally. It therefore became important to prepare, for pharmacological examination, as complete a series as possible of amines (as hydrochlorides) containing the 2,5-dimethoxyphenethyl grouping, the optimal C–C–N side chain being present in all cases.

(1) This work is part of a joint research being carried out in collaboration with a pharmacological group at the above laboratories.

Six series of 2,5-dimethoxyphenethylamines were prepared, in each series the primary, secondary, tertiary and quaternary compounds being made. Included in the series are the analogs of practically all the known pharmacologically active amines containing the phenethyl group (that is, containing the C–C–N side chain).

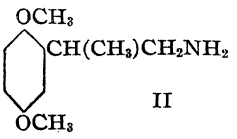
The present paper deals with the preparation and properties of the amines with no hydroxyl group in the side chain. One hydrochloride has been described previously.

The formulas of the primary amines are



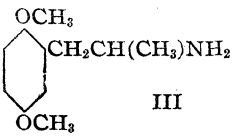
I

2,5-Dimethoxyphenethylamine



II

β-(2,5-Dimethoxyphenyl)-propylamine



III

β-(2,5-Dimethoxyphenyl)-isopropylamine

The syntheses of the first primary amine (I) and of the corresponding secondary amine have been described.[2] The starting material for the β-phenylpropylamine (II) was obtained by a Reformatzky reaction (2,5-dimethoxyacetophenone and ethyl bromoacetate). The remaining stages of the synthesis paralleled those of the first amine. The 2,5-dimethoxy-α-methylhydrocinnamic acid required for the third, β-phenylisopropylamine, was obtained by two methods, (a) by condensation of 2,5-dimethoxybenzaldehyde with ethyl α-bromopropionate, followed by reduction, and (b) by condensation of 2,5-dimethoxybenzaldehyde with diethyl malonate, followed by reduction, methylation, saponification and decarboxylation. Inaccessibility of the starting aldehyde deterred the authors from using the Claisen condensation with ethyl propionate, as this condensation in similar cases is wasteful and troublesome. The method of Bogert and Davidson[3] also was avoided, as in the authors' hands it gave discouraging results with dialkoxybenzaldehydes.

Secondary amines were obtained from the primary amines by the method of Decker.[2,4] The tertiary amines were prepared from the primary (or, better, secondary) amines by an adaptation of the Eschweiler reaction. Quaternary chlorides were obtained by the action of silver chloride on the methiodides of the tertiary amines.

Experimental

2,5-Dimethoxybenzaldehyde (gentisic aldehyde dimethyl ether) was prepared by the Gattermann method.[5] Amine hydrochlorides were all recrystallized, until pure, from absolute alcohol–ether mixture, sometimes with the addition of ethyl acetate. The solubilities of the hydrochlorides are all very similar, the compounds being readily soluble in water, alcohol, and methanol, and practically insoluble in less polar solvents. The melting points were determined on material dried for several hours at 100° *in vacuo*. All melting points are corrected.

2,5-Dimethoxyphenethylamine Hydrochloride.—The amine has been described previously.[2] The hydrochloride, made by the addition of absolute alcoholic hydrogen chloride to an ether solution of the amine, forms lustrous leaflets, melting at 139°.

Anal. Calcd. for $C_{10}H_{16}O_2NCl$: C, 55.15; H, 7.41. Found: C, 55.19; H, 7.37.

2,5-Dimethoxyphenethylmethylamine Hydrochloride.—This has been described previously.[2]

2,5-Dimethoxyphenethyldimethylamine Hydrochloride.—The above primary amine was converted into the tertiary amine by a modified Eschweiler reaction.[6,7,8] Nine grams of primary amine, 40 cc. of 36% formaldehyde solution and 0.1 cc. formic acid were heated for three hours at 125° in a sealed tube. The tertiary amine, b. p. 159° (23 mm.), was isolated in good yield and converted into the hydrochloride by adding alcoholic hydrogen chloride to the ether solution. The hydrochloride forms small, colorless plates, melting at 148°, and is rather hygroscopic.

Anal. Calcd. for $C_{12}H_{20}O_2NCl$: C, 58.63; H, 8.21. Found: C, 58.79; H, 8.25.

2,5-Dimethoxyphenethyltrimethylammonium Chloride.—The foregoing tertiary amine was converted, in ether solution, into the methiodide, which was filtered off, dissolved in water, and allowed to stand with silver chloride. After filtration, evaporation *in vacuo* and recrystallization, the chloride forms very hygroscopic lustrous plates, melting at 184–185°.

Anal. Calcd. for $C_{13}H_{22}O_2NCl$: C, 60.06; H, 8.54. Found: C, 60.28; H, 8.79.

2,5-Dimethoxy-β-methylcinnamic Acid.—2,5-Dimethoxyacetophenone and ethyl bromoacetate were condensed by the Reformatzky method, using a zinc–copper alloy. The resulting β-hydroxybutyric ester was dehydrated by phosphorus oxychloride to the β-methylcinnamic ester,[9,10] which was distilled, b. p. 140–143° (1.0 mm.). Saponification yielded the acid which crystallized from aqueous alcohol in slender prisms, melting at 113.5°.

Anal. Calcd. for $C_{12}H_{14}O_4$: C, 64.83; H, 6.35. Found: C, 64.82; H, 6.69.

β-(2,5-Dimethoxyphenyl)-butyric Acid.—The ester described above was reduced (platinum oxide and hydrogen) and then saponified. The resulting acid forms irregular crystals from ether–petroleum ether, melting at 79°.

Anal. Calcd. for $C_{12}H_{16}O_4$: C, 64.27; H, 7.20. Found: C, 64.62; H, 7.40.

β-(2,5-Dimethoxyphenyl)-butyramide.—The foregoing acid was heated in a stream of ammonia, at 220–230°, for two hours. Recrystallized from benzene the amide forms columnar prisms melting at 121°.

(2) Buck, THIS JOURNAL, **54**, 3661 (1932).
(3) Bogert and Davidson, *ibid.*, **54**, 334 (1932).
(4) Decker and Becker, *Ann.*, **395**, 362 (1913).
(5) Kauffmann and Burr, *Ber.*, **40**, 2352 (1907).
(6) Cf. Decker and Becker, *ibid.*, **45**, 2404 (1912); *Ann.*, **395**, 342 (1913).
(7) For an alternative method see Buck, Baltzly and Ide, THIS JOURNAL, **60**, 1789 (1938).
(8) The adaptation of Clarke and Gillespie, *ibid.*, **55**, 4571 (1933), appears to give some substitution with certain dimethoxy derivatives.
(9) Cf. Lindenbaum, *Ber.*, **50**, 1270 (1917).
(10) Cf. Woodruff and Pierson, THIS JOURNAL, **60**, 1075 (1938).

Anal. Calcd. for $C_{12}H_{17}O_3N$: C, 64.54; H, 7.68. Found: C, 64.76; H, 7.88.

β - (2,5 - Dimethoxyphenyl) - propylamine Hydrochloride.—The amine was obtained from the amide, in 45% yield, by the usual Hofmann procedure, using sodium hypochlorite. It boiled at 114° (1.0 mm.) and was converted into the hydrochloride by adding alcoholic hydrogen chloride to the ether solution. After recrystallization the hydrochlorite forms fine, colorless, felted needles melting at 149–150°.

Anal. Calcd. for $C_{11}H_{18}O_2NCl$: C, 56.99; H, 7.83. Found: C, 57.11; H, 8.03.

β - (2,5 - Dimethoxyphenyl) - propylmethylamine Hydrochloride.—The above primary amine was converted into the hydriodide of the secondary amine (m. p. 131°) by the Decker method (v. s.). The base, liberated from the hydriodide, was converted directly into the hydrochloride, which crystallizes in fine, colorless needles, melting at 146°.

Anal. Calcd. for $C_{12}H_{20}O_2NCl$: C, 58.63; H, 8.21. Found: C, 58.82; H, 8.07.

β - (2,5 - Dimethoxyphenyl) - propyldimethylamine Hydrochloride.—The tertiary amine may be prepared from the primary amine (or, better, from the secondary amine) by the Eschweiler methylation (v. s.). The amine was purified as the hydrochloride, which forms slender prisms, melting at 182–183°.

Anal. Calcd. for $C_{13}H_{22}O_2NCl$: C, 60.06; H, 8.54. Found: C, 60.33; H, 8.60.

β - (2,5 - Dimethoxyphenyl) - propyltrimethylammonium Chloride.—β - (2,5 - Dimethoxyphenyl) - propyldimethylamine (above) was treated with methyl iodide in ether solution to give the quaternary iodide (*i. e.*, the methiodide). Silver chloride converted the iodide (m. p. 139°) into the required chloride, which crystallizes in hygroscopic slender prisms. It forms a stable monohydrate, melting at 92°. After thorough drying, the chloride melts at 159–161° with discoloration.

Anal. Calcd. for $C_{14}H_{24}O_2NCl$: C, 61.37; H, 8.84. Found: C, 61.48; H, 9.18.

Diethyl 2,5-Dimethoxybenzalmalonate.—Diethyl malonate was condensed with 2,5-dimethoxybenzaldehyde in the presence of piperidine.[11] Saponification of a portion yielded an acid crystallizing in faint yellow leaflets from alcohol–benzene mixture. The acid melts at 183° (dec.). Kauffmann and Burr[5] prepared this acid by another method and gave the m. p. as 188° (dec.).

Anal. Calcd. for $C_{12}H_{12}O_6$: C, 57.12; H, 4.80. Found: C, 57.10; H, 5.13.

Diethyl 2,5-Dimethoxybenzylmalonate.—Catalytic reduction of the preceding ester yielded a nearly colorless oil, which was identified by saponifying a portion. The acid obtained, recrystallized from benzene, gave rhombic prisms melting at 156.5° (dec.).

Anal. Calcd. for $C_{12}H_{14}O_6$: C, 56.68; H, 5.55. Found: C, 57.03; H. 5.43.

2,5-Dimethoxybenzylmethylmalonic Acid.—The foregoing ester was methylated in the usual way (methyl iodide and sodium ethylate) and the product saponified. The resulting acid after crystallization from hexane forms fine, colorless crystals, melting at 143° (dec.).

Anal. Calcd. for $C_{13}H_{16}O_6$: C, 58.19; H, 6.02. Found: C, 58.35; H, 5.87.

α-Methyl-2,5-dimethoxyhydrocinnamic Acid.—This was obtained by heating the corresponding malonic acid (above) at 150°. After crystallization from ether–hexane mixture it forms a cream-colored powder melting at 59.5°.

Anal. Calcd. for $C_{12}H_{16}O_4$: C, 64.27; H, 7.20. Found: C, 64.39; H, 7.14.

α-Methyl-2,5-dimethoxyhydrocinnamide.—The amide was obtained by heating the corresponding hydrocinnamic acid (above) in a stream of ammonia at 220–230° for two hours. Recrystallized from benzene it forms a finely crystalline powder melting at 99°.

Anal. Calcd. for $C_{12}H_{17}O_3N$: C, 64.54; H, 7.68. Found: C, 64.58; H, 7.91.

The same amide was prepared, in poor yield by condensing ethyl bromopropionate with 2,5-dimethoxybenzaldehyde (Reformatzky method with ordinary zinc), dehydrating the resulting ester with phosphorus oxychloride, reducing the unsaturated ester catalytically, and then saponifying, and, finally, amidating the acid produced. The dehydration with phosphorus oxychloride or the subsequent distillation resulted in extensive polymerization, the yield of unsaturated ester being only about 20%.

β-(2,5-Dimethoxyphenyl)-isopropylamine Hydrochloride.—The Hofmann reaction on the foregoing amide was carried out as usual except that the amide was added dissolved in dioxane to the hypochlorite solution.[12] The yield of distilled amine (b. p. 137–140° (3 mm.)) was 70%. The hydrochloride, prepared in the usual way (v. s.), crystallizes in fine prisms melting at 117.5°.

Anal. Calcd. for $C_{11}H_{18}O_2NCl$: C, 56.99; H, 7.83. Found: C, 57.25; H, 7.89.

The same hydrochloride was also prepared, in very poor yield, by the catalytic reduction, in strongly acid alcohol, of 2,5-dimethoxynitropropenylbenzene.[13] The compound was isolated via the hydriodide, which forms prismatic needles, m. p. 138°.

Anal. Calcd. for $C_{11}H_{18}O_2NI$: C, 40.86; H, 5.62. Found: C, 40.94; H, 5.94.

β - (2,5 - Dimethoxyphenyl) - isopropylmethylamine Hydrochloride.—The primary amine (v. s.) was readily converted into the secondary amine by the Decker method.[6] The hydrochloride crystallizes in needle prisms, melting at 98.5°.

Anal. Calcd. for $C_{12}H_{20}O_2NCl$: C, 58.63; H, 8.21. Found: C, 58.52; H, 8.46.

β - (2,5 - Dimethoxyphenyl) - isopropyldimethylamine Hydrochloride.—The tertiary amine, b. p. 118–121° (0.5 mm.), was obtained by the Eschweiler methylation (v. s.) of the primary amine. The hydrochloride forms needles melting at 138–139°.

(11) *Cf.* Knoevenagel, *Ber.*, **31**, 2585 (1898).

(12) The use of dioxane to dissolve amides (using about one-third of the volume of the hypochlorite solution) greatly improves matters in cases where the amide is of low solubility. Cf. Woodruff and Conger, THIS JOURNAL, **60**, 465 (1938).

(13) Kauffmann, *Ber.*, **50**, 630 (1917).

Anal. Calcd. for $C_{13}H_{22}O_2NCl$: C, 60.06; H, 8.54. Found: C, 60.17; H, 8.39.

β - (2,5 - Dimethoxyphenyl) - isopropyltrimethylammonium Chloride.—The preceding tertiary amine was converted, in ether solution, into the methiodide (m. p. 142°), which on treatment with silver chloride gave the quaternary chloride. After crystallization, the chloride forms very hygroscopic, tiny, colorless prisms. After thorough drying (finally at 120° *in vacuo*) it melts at 203°.

Anal. Calcd. for $C_{14}H_{24}O_2NCl$: C, 61.37; H, 8.84. Found: C, 61.63; H, 8.81.

The authors wish to thank Mr. W. S. Ide for the many micro-analyses carried out during this work, and Dr. C. W. Ferry for the preparation of considerable amounts of 2,5-dimethoxybenzaldehyde.

Summary

As part of a series of 2,5-dimethoxyphenylalkyl- and alkanolamines, 2,5-dimethoxyphenethylamine hydrochloride, β-(2,5-dimethoxyphenyl)-propylamine hydrochloride and β-(2,5-dimethoxyphenyl)-isopropylamine hydrochloride, together with the corresponding secondary and tertiary amine hydrochlorides and the quaternary chlorides, have been prepared.

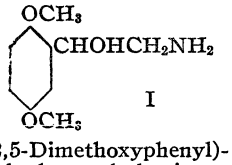
TUCKAHOE, NEW YORK RECEIVED OCTOBER 20, 1939

[CONTRIBUTION FROM THE BURROUGHS WELLCOME & CO. U. S. A. EXPERIMENTAL RESEARCH LABORATORIES]

Amines Related to 2,5-Dimethoxyphenethylamine.[1] II

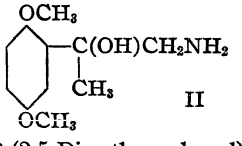
BY RICHARD BALTZLY AND JOHANNES S. BUCK

The work described below is a continuation and completion of that described in Part I.[2] The amines have the same structure as in the previous work but possess, in addition, a β-hydroxy group. As before, the primary, secondary, tertiary and quaternary compounds were made. The primary amines have the formulas



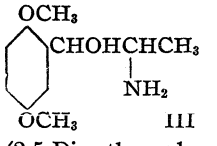
I

β-(2,5-Dimethoxyphenyl)-β-hydroxyethylamine



II

β-(2,5-Dimethoxyphenyl)-β-hydroxypropylamine



III

β-(2,5-Dimethoxyphenyl)-β-hydroxyisopropylamine

Secondary amines are denoted by "a," tertiary by "b," and quaternary salts by "c." The primary and secondary hydroxyethylamines and hydroxypropylamines (I, Ia, II, IIa) were prepared by the following series of reactions:

(R = 2,5-dimethoxyphenyl, Bz = benzyl)

$$RCOCH_3 \xrightarrow{Br_2} RCOCH_2Br \xrightarrow{(CH_2)_6N_4} RCOCH_2NH_2 \xrightarrow{PtO_2 + H_2} RCHOHCH_2NH_2 \quad (I)$$

$$RCHO \xrightarrow{CH_2BrCOOC_2H_5} RCHOHCH_2COOC_2H_5 \xrightarrow{NH_2NH_2} RCHOHCH_2CON_2H_3 \xrightarrow{HNO_2}$$

$$[RCHOHCH_2CON_3] \longrightarrow RCH(O{-}CO{-}NH)CH_2 \xrightarrow{HCl} RCHOHCH_2NH_2 \quad (I)$$

$$RCOCH_2Br(v.s.) \xrightarrow{BzNHCH_3} RCOCH_2NCH_3Bz \xrightarrow{PtO_2 + H_2} RCHOHCH_2NHCH_3 \quad (Ia)$$

$$RCOCH_3 \xrightarrow{CH_2BrCOOC_2H_5} RC(OH)(CH_3)CH_2COOC_2H_5 \xrightarrow{NH_2NH_2} RC(OH)(CH_3)CH_2CON_2H_3 \xrightarrow{HNO_2}$$

$$[RC(OH)(CH_3)CON_3] \longrightarrow RC(CH_3)(O{-}CO{-}NH)CH_2 \xrightarrow{HCl} RC(OH)(CH_3)CH_2NH_2 \quad (II)$$

$$RCOCH_2NCH_3Bz(v.s.) \xrightarrow{CH_3MgI} RC(OH)(CH_3)CH_2NCH_3Bz \xrightarrow{PtO_2 + H_2} RC(OH)(CH_3)CH_2NHCH_3 \quad (IIa)$$

The corresponding tertiary amines and quaternary salts were prepared as follows:

(1) This work is part of a joint research being carried out in collaboration with a pharmacological group at the above laboratories.

(2) Baltzly and Buck, THIS JOURNAL, 62, 161 (1940).

$$NCCH_2N(CH_3)_2 \xrightarrow{RMgBr} RCOCH_2N(CH_3)_2 \xrightarrow{PtO_2 + H_2} RCHOHCH_2N(CH_3)_2\ (Ib) \xrightarrow{CH_3I}$$

$$RCHOHCH_2N(CH_3)_3I \xrightarrow{AgCl} RCHOHCH_2N(CH_3)_3Cl \quad (Ic)$$

$$RCOCH_2N(CH_3)_2(v.s.) \xrightarrow{CH_3MgI} RC(OH)(CH_3)CH_2N(CH_3)_2\ (IIb) \xrightarrow{CH_3I}$$

$$RC(OH)(CH_3)CH_2N(CH_3)_3I \xrightarrow{AgCl} RC(OH)(CH_3)CH_2N(CH_3)_3Cl \quad (IIc)$$

The primary amine of the third (hydroxyisopropylamine) series (III) was prepared by Hartung's[3] method, by the reduction of α-isonitroso-2,5-dimethoxypropiophenone. The secondary amine (IIIa) and the tertiary amine (IIIb) were prepared, by a method similar to that of Hyde, Browning and Adams,[4] from α-bromo-2,5-dimethoxypropiophenone. From the tertiary amine, the quaternary chloride was prepared, via the methiodide.

It is assumed, pending further investigation, that the hydroxyisopropylamine group (III, IIIa, IIIb, IIIc) has the ephedrine, rather than the ψ-ephedrine, configuration. The relatively high melting points and the methods of preparation support this view.

Experimental

β-(2,5-Dimethoxyphenyl)-hydracrylic Hydrazide.—2,5-Dimethoxybenzaldehyde and ethyl bromoacetate were condensed by the Reformatzky method[2,5,6] to give ethyl β-(2,5-dimethoxyphenyl)-hydracrylate. This ester, obtained in 80% yield, is a viscous yellow oil, b. p. 164–167° (1.0 mm.). The ester was converted into the hydrazide, which, crystallized from alcohol–benzene mixture, formed glossy needles melting at 161.5°.

Anal. Calcd. for $C_{11}H_{16}O_4N_2$: C, 54.97; H, 6.72. Found: C, 55.19; H, 6.80.

5-(2,5-Dimethoxyphenyl)-oxazolidone-2.—Prepared by the Curtius[7] rearrangement from the hydrazide (v. s.) this crystallizes from benzene in colorless needles, m. p. 107°.

Anal. Calcd. for $C_{11}H_{13}O_4N$: C, 59.17; H, 5.87. Found: C, 59.38; H, 5.80.

β-(2,5-Dimethoxyphenyl)-β-hydroxyethylamine Hydrochloride (I).—Cleavage of the preceding oxazolidone[7] by cold concd. hydrochloric acid gave the desired amine hydrochloride. It forms fine colorless needles melting at 158.5°, and is very soluble in water, readily soluble in hot alcohol, moderately soluble in cold alcohol, sparingly soluble in ethyl acetate, and practically insoluble in non-polar solvents. Similar solubilities are shown by the other hydroxyamine hydrochlorides of this series, which may be crystallized conveniently from absolute alcohol solution by the addition of ether or ethyl acetate or both.

Anal. Calcd. for $C_{10}H_{16}O_3NCl$: C, 51.37; H, 6.91. Found: C, 51.24; H, 6.92.

(3) Hartung, U. S. Patent 1,989,093.

(4) Hyde, Browning and Adams, THIS JOURNAL, **50**, 2287 (1928).

(5) Cf. Lindenbaum, *Ber.*, **50**, 1270 (1917).

(6) Cf. Woodruff and Pierson, THIS JOURNAL, **60**, 1075 (1938).

(7) Cf. Schroeter, German Patent 220,852.

This amine also may be prepared by the reduction of 2,5-dimethoxyphenacylamine hydrobromide, prepared from 2,5-dimethoxyphenacyl bromide and hexamethylenetetramine by the procedure of Mannich and Hahn.[8] Hydrobromic acid was used for the hydrolysis so as to obtain a homogeneous hydrohalide. The amino ketone hydrobromide so prepared forms yellowish prisms, melting at 195° (dec.).

Anal. Calcd. for $C_{10}H_{14}O_3NBr$: C, 43.46; H, 5.11. Found: C, 43.60; H, 5.31.

2,5-Dimethoxyphenacylmethylbenzylamine.—2,5-Dimethoxyphenacyl bromide was added as a solid to twice its equivalent amount of methylbenzylamine[9] in absolute ether, with occasional shaking. After standing overnight, the methylbenzylamine hydrobromide formed was filtered off and the amino ketone precipitated as hydrochloride by the addition of absolute alcoholic hydrogen chloride. The hydrochloride forms a light yellow oil which soon crystallizes. On recrystallization (absolute alcohol–ether) it forms nearly colorless prisms melting at 167.5°.

Anal. Calcd. for $C_{18}H_{22}O_3NCl$: C, 64.38; H, 6.61. Found: C, 64.36; H, 6.73.

β-(2,5-Dimethoxyphenyl)-β-hydroxyethylmethylamine Hydrochloride (Ia).—The foregoing amino ketone hydrochloride is readily reduced (PtO_2 and hydrogen) in alcohol solution, yielding the desired amine hydrochloride, the benzyl group being eliminated as toluene.[10] The hydrochloride crystallizes in fine, felted needles, melting at 151.5°.

Anal. Calcd. for $C_{11}H_{18}O_3NCl$: C, 53.31; H, 7.33. Found: C, 53.62; H, 7.43.

β-(2,5-Dimethoxyphenyl)-β-hydroxypropylmethylamine Hydrochloride (IIa).—2,5-Dimethoxyphenacylmethylbenzylamine (v. s.), liberated from the hydrochloride, was dried, in ethereal solution, over potassium carbonate. The ether solution was added to an excess of methylmagnesium iodide. The reaction mixture was worked up as usual and the base liberated by ammonia, extracted with ether, the ether dried over potassium carbonate, and the hydrochloride precipitated by adding alcoholic carbonate chloride. The hydrochloride formed an uncrystallizable yellow sirup, probably due to a certain amount of dehydration. The sirup was reduced catalytically (reaction rather slow) and the desired amine hydrochloride isolated from the solution. It forms silky needles, melting at 158–159°.

(8) Mannich and Hahn, *Ber.*, **44**, 1542 (1911).

(9) Prepared by catalytic reduction of benzylidenemethylamine. Zaunschirm, *Ann.*, **245**, 279 (1888); *cf.* Emde, *Arch. Pharm.*, **247**, 351 (1909).

(10) The reductive removal of the N-benzyl group (mentioned in British Patent 318,488) is a very useful and convenient reaction, especially when, as in the present case, the method of Hyde, Browning and Adams (*loc. cit.*) proves unmanageable. The same process might profitably be used for the secondary amine (IIIa). Reductive removal of O-benzyl groups is a familiar procedure.

Anal. Calcd. for $C_{12}H_{20}O_3NCl$: C, 55.05; H, 7.71. Found: C, 55.11; H, 7.94.

β - Methyl - β - (2,5 - dimethoxyphenyl) - hydracrylic Acid.—2,5-Dimethoxyacetophenone was condensed with ethyl bromoacetate (zinc–copper alloy); after the usual washings, saponification and acidification gave the hydroxy acid, which crystallizes from benzene–petroleum ether in platelets, melting at 121–122°.

Anal. Calcd. for $C_{12}H_{16}O_5$: C, 59.98; H, 6.72. Found: C, 60.17; H, 6.77.

β - Methyl - β - (2,5 - dimethoxyphenyl) - hydracrylic Hydrazide.—The preparation of this hydrazide gave considerable trouble, due to the tendency of the compounds in this series to dehydrate when distilled or subjected to acids. Finally it was found that a 27% yield of hydrazide (reckoned on the starting ketone) could be obtained by treating the crude washed, but not distilled, ester from the Reformatzky reaction with hydrazine hydrate in alcohol. Nothing isolable was obtained when the ester was distilled or prepared from the acid. After considerable purification, the hydrazide was obtained as needles, m. p. 112°.

Anal. Calcd. for $C_{12}H_{18}O_4N_2$: C, 56.66; H, 7.14. Found: C, 56.83; H, 7.24.

5 - Methyl - 5 - (2,5 - dimethoxyphenyl) - oxazolidone-2.—The oxazolidone was obtained in excellent yield from the hydrazide, by the Curtius rearrangement.[7] It crystallizes from benzene in colorless prisms, melting at 159°.

Anal. Calcd. for $C_{12}H_{15}O_4N$: C, 60.74; H, 6.38. Found: C, 60.91; H, 6.66.

β - (2,5 - Dimethoxyphenyl) - β - hydroxypropylamine Hydrochloride (II).—The preceding oxazolidone was dissolved in concd. hydrochloric acid. After the evolution of carbon dioxide had ceased, excess acid was removed under reduced pressure at around room temperature. The yield of the amine salt is practically quantitative, but if higher temperatures are used other products make their appearance. The hydroxyamine salt, after recrystallization, forms flat-sided prisms, melting at 174°.

Anal. Calcd. for $C_{11}H_{18}O_3NCl$: C, 53.31; H, 7.33. Found: C, 53.57; H, 7.39.

2,5 - Dimethoxyphenacyldimethylamine.—Bromohydroquinone dimethyl ether[11] was converted into the Grignard reagent and dimethylaminoacetonitrile[12] added. The reaction mixture was decomposed with acid, the ether layer separated, and the base liberated by ammonia. After extraction with ether, the extract was washed, dried, and treated with alcoholic hydrogen chloride. The hydrochloride so obtained, after recrystallization, forms nearly colorless prisms, m. p. 171° (dec.).

Anal. Calcd. for $C_{12}H_{18}O_3NCl$: C, 55.48; H, 6.99. Found: C, 55.76; H, 7.17.

β - (2,5 - Dimethoxyphenyl) - β - hydroxyethyldimethylamine Hydrochloride (Ib).—This hydrochloride is readily obtained by the reduction (PtO_2 and hydrogen), in alcohol solution, of the above amino ketone hydrochloride. When recrystallized, it forms fine, colorless, needle-like prisms melting at 155°.

(11) Noelting and Werner, *Ber.*, **23**, 3246 (1890).

(12) Von Braun, *ibid.*, **40**, 3933 (1907).

Anal. Calcd. for $C_{12}H_{20}O_3NCl$: C, 55.05; H, 7.71. Found: C, 55.28; H, 7.98.

β - (2,5 - Dimethoxyphenyl) - β - hydroxyethyltrimethylammonium Chloride (Ic).—The methiodide of the foregoing tertiary amine was prepared in the usual way, and converted into the chloride by silver chloride. It forms slender prisms, melting at 185–186°.

Anal. Calcd. for $C_{13}H_{22}O_3NCl$: C, 56.60; H, 8.05. Found: C, 56.33; H, 7.99.

β - (2,5 - Dimethoxyphenyl) - β - hydroxypropyldimethylamine Hydrochloride (IIb).—This tertiary amine was prepared by the action of methylmagnesium iodide on 2,5-dimethoxyphenacyldimethylamine (v. s.) and was converted into the hydrochloride by alcoholic hydrogen chloride. It forms stout, almost colorless rhombs, melting at 176.5°.

Anal. Calcd. for $C_{13}H_{22}O_3NCl$: C, 56.60; H, 8.05. Found: C, 56.58; H, 7.76.

β - (2,5 - Dimethoxyphenyl) - β - hydroxypropyltrimethylammonium Chloride (IIc).—The quaternary salt was prepared from the preceding tertiary amine via the methiodide and silver chloride. After recrystallization it forms stout, colorless prisms, melting at 213.5°.

Anal. Calcd. for $C_{14}H_{24}O_3NCl$: C, 57.99; H, 8.33. Found: C, 58.06; H, 8.63.

α - Isonitroso - 2,5 - dimethoxypropiophenone.—2,5-Dimethoxypropiophenone[13] was converted into the isonitroso compound by Hartung's[3] method. After recrystallization from benzene–heptane mixture, the compound forms pale yellow leaflets, melting at 97–98°.

Anal. Calcd. for $C_{11}H_{13}O_4N$: C, 59.17; H, 5.87. Found: C, 59.25; H, 5.86.

β - (2,5 - Dimethoxyphenyl) - β - hydroxyisopropylamine Hydrochloride (III).—The above isonitroso compound was readily reduced by palladized charcoal in absolute alcohol containing hydrogen chloride. The product crystallizes in columnar prisms, melting at 175–176° (dec.).

Anal. Calcd. for $C_{11}H_{18}O_3NCl$: C, 53.31; H, 7.33. Found: C, 53.42; H, 7.34.

2,5 - Dimethoxy - α - methylaminopropiophenone.—2,5-Dimethoxy-α-bromopropiophenone was prepared by bromination of 2,5-dimethoxypropiophenone in chloroform solution (*cf.* 5). The bromo ketone was added to a large excess of methylamine in absolute ether. After standing overnight at 0°, the precipitated methylamine hydrobromide was filtered off, and the filtrate evaporated to dryness under reduced pressure, at room temperature or below. The residue was dissolved in ether and absolute alcoholic hydrogen chloride added. The hydrochloride still contains some methylamine salts, which are removed by repeated recrystallization. The pure amino ketone hydrochloride forms colorless prisms melting at 172–173° (dec.).

Anal. Calcd. for $C_{12}H_{18}O_3NCl$: C, 55.48; H, 6.99. Found: C, 55.48; H, 7.22.

β - (2,5 - Dimethoxyphenyl) - β - hydroxyisopropylmethylamine Hydrochloride (IIIa).—Catalytic reduction of the foregoing amino ketone hydrochloride yielded the

(13) Johnson and Hodge, THIS JOURNAL, **35**, 1014 (1913).

desired hydroxyamine hydrochloride, which crystallizes in fine, colorless needles, m. p. 170°.

Anal. Calcd. for $C_{12}H_{20}O_3NCl$: C, 55.05; H, 7.71. Found: C, 55.33; H, 7.91.

2,5 - Dimethoxy - α - dimethylaminopropiophenone.—The method of Hyde, Browning and Adams[4] gave very good results in this case. It was necessary, in order to remove dimethylamine completely, to wash the ether solution of the base with water. The tertiary amino ketones of this type are reasonably stable. The hydrochloride crystallizes in slender, practically colorless prisms, melting at 154–156° (dec.).

Anal. Calcd. for $C_{13}H_{20}O_3NCl$: C, 57.00; H, 7.37. Found: C, 56.89; H, 7.57.

β - (2,5 - Dimethoxyphenyl) - β - hydroxyisopropyldimethylamine Hydrochloride (IIIb).—Catalytic reduction of the preceding α-dimethylaminopropiophenone gave the desired compound. The hydrochloride crystallizes in fine, colorless needles, melting at 198° (dec.).

Anal. Calcd. for $C_{13}H_{22}O_3NCl$: C, 56.60; H, 8.05. Found: C, 56.52; H, 8.25.

β - (2,5 - Dimethoxyphenyl) - β - hydroxyisopropyltrimethylammonium Chloride (IIIc).—The methiodide, prepared from the above tertiary base, was converted into the chloride by the silver chloride method. After recrystallization, the chloride forms fine, colorless, felted needles, melting at 221–223° (dec.).

Anal. Calcd. for $C_{14}H_{24}O_3NCl$: C, 57.99; H, 8.33. Found: C, 58.08; H, 8.62.

Melting points are all corrected. Those for the hydrochlorides were determined on material dried *in vacuo* at 100° for several hours. The authors wish to make the same acknowledgments to Mr. W. S. Ide and Dr. C. W. Ferry as were made in Part I.

Summary

The projected series of 2,5-dimethoxyphenylalkyl- and alkanolamines has been completed by the preparation of the alkanolamines, β-(2,5-dimethoxyphenyl)-β-hydroxyethylamine hydrochloride, β-(2,5-dimethoxyphenyl)-β-hydroxypropylamine hydrochloride, and β-(2,5-dimethoxyphenyl)-β-hydroxyisopropylamine hydrochloride, together with the corresponding secondary and tertiary amine hydrochlorides and the quaternary chlorides.

TUCKAHOE, NEW YORK RECEIVED OCTOBER 20, 1939

[CONTRIBUTION FROM THE SYPHILIS DIVISION OF THE DEPARTMENT OF MEDICINE, JOHNS HOPKINS MEDICAL SCHOOL, BALTIMORE, MARYLAND, AND THE UNITED STATES PUBLIC HEALTH SERVICE, WASHINGTON, D. C.]

A Modified Bart Reaction

BY G. O. DOAK

Indirect methods for preparing sulfonic and sulfamido substituted arsonic acids are tedious and give low yields. Although Oneto[1] recently has succeeded in preparing *p*-sulfophenyl- and *p*-sulfamidophenylarsonic acids by means of the Bart reaction, in this Laboratory this method failed with the corresponding *m*- and *o*- compounds. The alcoholic Bart reaction described by Scheller[2] has received but scant attention in the literature.[3a,b] When this modification proved successful in this Laboratory with both *p*- and *m*-sulfamidophenylarsonic acids, it was extended to include other arsonic acids, difficult to prepare by the customary Bart procedure. It was found that while anilines substituted in the ring by nitro, carboxy, or sulfamido groups gave excellent results, the reaction failed with 2,6- and 3,5-dimethylanilines. It also failed with metanilic acid. When applicable, the method gave higher yields, was less time consuming, and gave a product more easily purified than the customary Bart procedure.

Experimental Part

The amine, 0.1 mole in 250 cc. absolute alcohol with 10 g. of sulfuric acid and 28 g. arsenous chloride cooled to 0°, was diazotized with a saturated aqueous solution of the calculated amount of sodium nitrite, using starch–iodide paper to protect the end-point. Then, and not before, 1 g. of cuprous bromide[4] was added, the mixture thoroughly stirred, warmed to 60° until no more nitrogen was evolved, and then distilled with steam. The separated arsonic acid was recrystallized.

***p*-Sulfamidophenylarsonic Acid.**—This compound was obtained in 57% yield from sulfanilamide, crystallizing from water in small needles.

Anal. Calcd. for $C_6H_8NO_5SAs$: As, 26.7. Found: As, 26.8.

***m*-Sulfamidophenylarsonic Acid.**—*m*-Aminobenzenesulfonamide, 0.2 mole, gave 32.7 g. (58% yield) of *m*-sulfamidophenylarsonic acid, which crystallized from water in warty aggregates. When placed in a bath at 215° and the temperature slowly raised, it melted at 218–219°, but

(1) Oneto, THIS JOURNAL, 60, 2058 (1938); 61, 2105 (1939).

(2) Scheller, French Patent 624,028, *Chem. Zentr.*, 98, II, 229 (1927).

(3) (a) Steinkopf, *J. prakt. Chem.*, 128, 63 (1930); (b) Cherline and Iscoubovitch, *Bull. soc. chim.*, [5] 1, 1367 (1934).

(4) Cuprous bromide was found to give slightly better yields than the cuprous chloride as recommended by Scheller.

resolidified, probably to the anhydride, which charred without melting. It was extremely resistant to hydrolysis. After heating in a pressure bottle with concentrated hydrochloric acid at 100°, the compound was recovered unchanged, and it was only partially hydrolyzed with cold concentrated sulfuric acid after twenty-four hours.

Anal. Calcd. for $C_6H_8NO_5SAs$: As, 26.7. Found: As, 26.3.

m-**Nitrophenylarsonic Acid.**—*m*-Nitroaniline, 138 g. (1 mole) gave 133.5 g. (54% yield) of *m*-nitrophenylarsonic acid, after one recrystallization from water.

3-Nitro-4-methylphenylarsonic Acid.—2-Nitro-4-aminotoluene gave a 40% yield of 3-nitro-4-methylphenylarsonic acid by the modified method.

m-**Carboxyphenylarsonic Acid.**—*m*-Aminobenzoic acid gave a 76% yield by the modified procedure.

Analyses of these last three substances for arsonic acid gave percentages of arsenic in close agreement with the theoretical requirements.

Attempted Preparation of *m*-Sulfophenylarsonic Acid.—When metanilic acid was subjected to the modified Bart reaction, no crystals separated from the aqueous solution. An attempt to isolate the compound by means of the barium salt yielded only *m*-phenolsulfonic acid. Similarly, 2,6-dimethyl- and 3,5-dimethylanilines gave only the corresponding xylenols when subjected to the modified Bart reaction. In the case of the 2,6- compound, this failure cannot be due to any steric factor, since 2,6-dimethylphenylarsonic acid was prepared in a 30% yield by the usual Bart procedure.

The advantage of the modified Bart procedure may be shown by the following percentage yield figures, the first figure in each case corresponding to the ordinary procedure and the second figure to the modified one: *p*-sulfamido,[1] 25, 57; *m*-sulfamido, 0, 58; *m*-nitro,[5a] 28, 54; 3-nitro-4-methyl,[5b] 15.5, 40; *m*-carboxy,[5a] 36.6, 76.

Summary

The method of Scheller for the preparation of arsonic acids by an alcoholic Bart reaction has been tried with a series of aromatic amines. With sulfamido-, carboxy-, or nitro-substituted amines the reaction gave larger yields of the arsonic acid than the usual Bart procedure, but with two dimethylanilines and metanilic acid, the modification did not prove applicable.

(5) (a) Bart, *Ann.*, **429**, 55 (1922); (b) Jacobs, Heidelberger and Rolf, THIS JOURNAL, **40**, 1580 (1918).

BALTIMORE, MARYLAND RECEIVED SEPTEMBER 25, 1939

[CONTRIBUTION FROM THE SYPHILIS DIVISION OF THE DEPARTMENT OF MEDICINE, JOHNS HOPKINS MEDICAL SCHOOL BALTIMORE, MARYLAND, AND THE UNITED STATES PUBLIC HEALTH SERVICE, WASHINGTON, D. C.]

The Preparation of Phenylarsenoxides in Relation to a Projected Study of their Chemotherapeutic Activity. I. Monosubstituted Derivatives

BY G. O. DOAK, HARRY EAGLE, AND H. G. STEINMAN

There is now a considerable body of evidence to show that the chemotherapeutic action of arsonic acids and arseno compounds is due to their conversion *in vivo* to the corresponding arsenoxide. Thus, Voegtlin and Smith[1] concluded that both the arsonic acids and the arseno compounds are not in themselves trypanocidal but become active only after conversion to the arsenoxides in the animal body. Further, Tatum and Cooper[2] have shown that "Mapharsen," 3-amino-4-hydroxyphenylarsenoxide, while much more toxic, actually possesses a higher therapeutic index than neoarsphenamine. More recently, Eagle[3] has shown that although the arsphenamines are directly treponemicidal *in vitro*, that activity is primarily due to their rapid oxidation in solution by molecular oxygen, and is either absent or minimal if the experiment is carried out under nitrogen.

While considerable work has been done in attempting to correlate the chemical structure and chemotherapeutic activity of arsonic acids and arseno compounds, the arsenoxides themselves have received much less attention. The present investigation was therefore undertaken in an attempt to correlate the chemical structure of the arsenoxides with their treponemicidal activity, using as the test organism *Treponema pallidum*, the causative agent of syphilis. Although the majority of investigators have hitherto used trypanosomes in testing arsenicals, compounds active against one species of trypanosome will not necessarily be active against *T. pallidum*,[4] or even against another species of trypanosome.[5] The chemical preparation and properties of the arsenoxides will be presented here; data relating to their treponemicidal activity, toxicity, and potential therapeutic utility will be published elsewhere.

The initial series consisted of the parent com-

(1) Voegtlin and Smith, *J. Pharmacol.*, **15**, 475 (1920).
(2) Tatum and Cooper, *ibid.*, **50**, 198 (1934).
(3) Eagle, *ibid.*, **66**, 423 (1939).
(4) Ehrlich and Hata, "The Experimental Chemotherapy of Spirilloses," Redman Co., New York, 1911, p. 126; Probey and McCoy, *U. S. Publ. Health Repts.*, **45**, 1716 (1930).
(5) Kuhs and Tatum, *J. Pharmacol.*, **61**, 451 (1937).

pound, phenylarsenoxide, the *o*-, *m*-, and *p*-monosubstituted methyl, carboxy, chloro, nitro, amino, and hydroxy derivatives, the *o*- and *p*-sulfophenyl arsenoxides, and *o*-iodophenyl-arsenoxide. For twelve of these compounds, work done in this Laboratory has merely confirmed previous descriptions in the literature. The *m*-chloro, *m*-amino, *m*-hydroxy, *o*-sulfo, and *o*-iodo compounds have not been previously reported. We have also obtained additional data on the three nitro arsenoxides, and slightly different results from those reported in the literature with the *o*-hydroxy and *o*-chloro compounds. The arsenoxides were prepared by reduction of the known arsonic acids in hydrochloric acid solution with sulfur dioxide and potassium iodide, followed by hydrolysis of the resulting dichloroarsine with ammonia or sodium bicarbonate. In the case of the sulfonic acids, hydrobromic acid was used in order to obtain the less soluble dibromoarsines.

There was a marked tendency for the arsenoxides to separate as sirups, particularly in the case of the meta compounds. In certain cases, these could be crystallized by the method suggested by Blicke and Smith,[6] but in other cases even this method failed to yield a crystalline compound. Except in a few cases, the arsenoxides did not melt, but charred above 250°, or softened without giving a definite melting point.

o-, *m*-, and *p*-nitrophenylarsonic acids reduced by sulfur dioxide in the usual manner gave the corresponding dichloroarsines, which yield the arsenous acids on hydrolysis with alkali.[7,8,9] It has been suggested that the presence of the nitro group prevents loss of water from the arsenous acid to form the arsenoxide. We found, however, that the *o*- and *p*-nitro compounds yielded the arsenoxides when reduced in suspension in dilute hydrochloric acid. The meta compound, however, gave only the arsenous acid. *o*-Nitro-phenylarsenoxide (or the arsenous acid) showed a curious anomaly in its pharmacological behavior, in that it dissolved in alkali to form a deep brown solution which no longer showed either the toxicity or activity of the typical arsenoxides. Unlike other arsenoxides, it could not be reprecipitated from such solutions with acid. When the alkaline solution was poured into a large excess of acetone, an oil formed which crystallized after standing for several days at −25°. Although these crystals analyzed for the composition $(NO_2C_6H_4As(ONa)_2 \cdot 2H_2O$, it seems unlikely that this is the correct formula, for when buffered with bicarbonate, the compound could not be titrated with iodine. By exposing *o*-nitrophenylarsenoxide to sunlight, Karrer[10] obtained a brown compound which he believed to be the *o*-nitrosoarsonic acid, formed by migration of one oxygen atom from the nitrogen to the arsenic. The compound we obtained, unlike Karrer's compound, did not give an insoluble magnesium salt under any conditions. It is accordingly unlikely that it is an arsonic acid. The remarkable color change on dissolving the arsenoxide in alkali suggests quinoid formation.

(6) Blicke and Smith, THIS JOURNAL, **51**, 3479 (1929).
(7) Bart, *Ann.*, **429**, 55 (1922).
(8) Kalb, *ibid.*, **423**, 39 (1921).
(9) Michaelis and Loesner, *Ber.*, **27**, 263 (1894).

Experimental Part

p-Nitrophenylarsenoxide.—*p*-Nitrophenylarsonic acid was precipitated in a finely divided state by the addition of dilute hydrochloric acid to a 10% aqueous solution of the sodium salt. When reduced with sulfur dioxide and potassium iodide, the arsenoxide was obtained as a white solid, in contrast to the yellow *p*-nitrophenylarsenous acid.

Anal. Calcd. for $C_6H_4NO_3As$: As, 35.2; N, 6.6. Found; As, 35.1; N, 6.7.

o-Nitrophenylarsenoxide.—The reduction of 10 g. of sodium *o*-nitrophenylarsonate in a similar manner gave *o*-nitrophenylarsenoxide as a light yellow powder.

Anal. Calcd. for $C_6H_4NO_3As$: As, 35.2; N, 6.6. Found: As, 35.1; N, 6.2.

The **disodium salt**, which may have a quinoid structure, was prepared by the addition of acetone to an alkaline solution of the arsenoxide. The oily precipitate crystallized after several days at −25°. These crystals tended to become oily on exposure to air, and it was difficult to wash free from alkali.

Anal. Calcd. for $C_6H_4NO_4Na_2As \cdot 2H_2O$: As, 24.2; Na, 14.8; water, 11.6. Found: As, 23.5; Na, 15.2; loss at 100°, 10.3.

The reduction of *m*-nitrophenylarsonic acid by the same method gave only *m*-nitrophenylarsenous acid,[9] which did not lose water at 100°.

Anal. Calcd. for $C_6H_6NO_4As$: As, 32.4; N, 6.1. Found: As, 32.7, N, 6.1.

m-Aminophenylarsenoxide.—The reduction of 10 g. of *m*-aminophenylarsonic acid in concentrated hydrochloric acid gave the dichloroarsine hydrochloride as a white crystalline solid. On the addition of ammonia, this gave the oxide as an amorphous solid, which was purified by dissolving in dilute hydrochloric acid and again precipitating with ammonia. Although the compound could be crystallized from alkaline solution by the addition of saturated salt solution, it was difficult to wash the crystals free from salt because of their solubility. It is soluble in acids, alkali, water, excess ammonium hydroxide, and organic solvents. It softened at 62° (cor.) without giving a definite melting point.

(10) Karrer, *ibid.*, **47**, 1783 (1914).

Anal. Calcd. for C_6H_6ONAs: As, 40.9. Found: As, 40.8.

***m*-Hydroxyphenylarsenoxide.**—The *m*-dichloroarsine, obtained as a yellow oil, was dissolved in ether and neutralized with sodium carbonate solution. The ether layer was dried with anhydrous sodium sulfate and evaporated. The sirupy arsenoxide thus obtained contained two moles of water which were lost only after heating at 150° for twelve hours. The resulting compound was a brittle, pulverulent mass.

Anal. Calcd. for $C_6H_5O_2As \cdot 2H_2O$: As, 34.0. Found: As, 34.2. Calcd. for $C_6H_5O_2As$: As, 40.7. Found: As, 40.9.

***o*-Hydroxyphenylarsenoxide.**—This compound, previously described by Kalb[8] as the anhydride, was obtained as the crystalline arsenoxide when the dichloroarsine was treated with ammonia. It melted at 182–184° (cor.) and gave no coloration with ferric chloride. If a drop of hydrogen peroxide was added to a solution of the oxide containing ferric chloride, a deep wine color was produced, characteristic of *o*-hydroxyphenylarsonic acid.

Anal. Calcd. for $C_6H_5O_2As$: As, 40.7. Calcd. for $C_{12}H_8O_3As_2$: As, 42.8. Found: As, 40.5.

***m*-Chlorophenylarsenoxide.**—The dichloroarsine, obtained as a yellow oil, gave the oxide as a sirup on treatment with sodium bicarbonate solution. It could not be crystallized by the method of Blicke and Smith. When dissolved in alcohol and poured into ice water, the oxide separated as a white powder which again became sirupy on removal of the water.

Anal. Calcd. for C_6H_4OClAs: As, 37.0. Found: As, 36.6.

***o*-Chlorophenylarsenoxide.**—This compound, recently described by Hiratuka,[11] who gives a melting point of 140–150°, was obtained by reduction of the arsonic acid in methyl alcohol and precipitation of the dichloroarsine with water. Subsequent treatment with ammonia gave the oxide as an amorphous solid, purified by dissolving in sodium hydroxide solution and reprecipitating with dilute hydrochloric acid. The resulting compound was a white powder. It softened at 208° (cor.) without giving a definite melting point.

(11) Hiratuka, *J. Chem. Soc. Japan.*, **58**, 1051 (1937); *C. A.*, **33**, 157 (1939).

Anal. Calcd. for C_6H_4OClAs: As, 37.0. Found: As, 36.8.

Sodium Salt of *o*-Sulfophenylarsonic Acid.—*o*-Sulfophenylarsonic acid was isolated by Barber[12] as the barium salt in 90–95% yield by treating *o*-iodophenylarsonic acid with sodium sulfite and precipitating the barium salt with barium chloride. We have prepared the disodium salt in 95% yield by refluxing the iodoarsonic acid with sodium sulfite, making the resulting solution just acid to litmus, and precipitating with alcohol. The compound was recrystallized by dissolving in water and again precipitating with alcohol.

Anal. Calcd. for $C_6H_5O_6SAsNa_2 \cdot H_2O$: As, 21.3; Na, 13.4; water, 5.2. Found: As, 21.5; Na, 12.7; loss at 100°, 5.1.

Sodium Salt of *o*-Sulfophenylarsenoxide.—The disodium salt described in the preceding paragraph, 10 g. in hydrobromic acid solution, was reduced, and the solution evaporated to 30 cc., when the dibromoarsine crystallized from the solution. After recrystallization, this was treated with sodium hydroxide, made acid to litmus with hydrochloric acid, and evaporated to dryness. The arsenoxide was separated from the sodium bromide by successive extractions with absolute alcohol.

Anal. Calcd. for $C_6H_4O_4SAsNa$: As, 27.7. Found: As, 27.9.

***o*-Iodophenylarsenoxide.**—*o*-Iodophenylarsonic acid reduced in the usual manner and treated with sodium hydroxide gave *o*-iodophenylarsenoxide as a white powder. It softens at 263° and melts at 267°.

Anal. Calcd. for C_6H_4OIAs: As, 25.5. Found: As, 25.3.

Summary

A series of monosubstituted phenylarsenoxides has been prepared with a view to studying their action against *Treponema pallidum*. Five new compounds have been described, and additional data have been obtained on some of the known arsenoxides.

BALTIMORE, MD. RECEIVED SEPTEMBER 25, 1939

(12) Barber, *J. Chem. Soc.*, 2047 (1930).

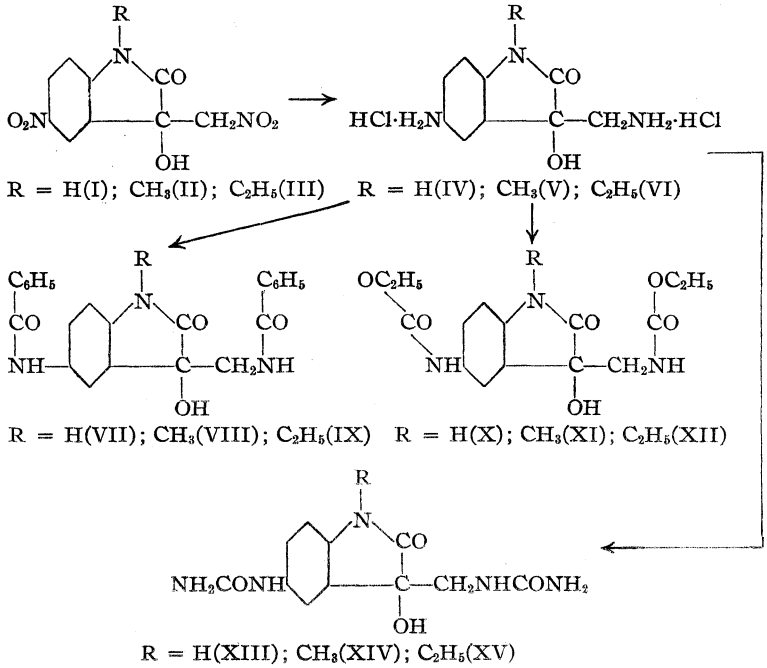
[CONTRIBUTION FROM NICHOLS LABORATORY OF NEW YORK UNIVERSITY]

Ethanolamines of the Oxindole Series

BY RAYMOND B. CRAWFORD[1] AND H. G. LINDWALL

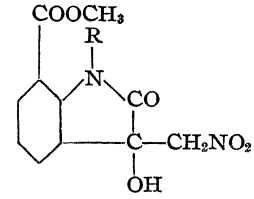
It has been reported previously[2] that isatin and N-alkylated isatins will condense with nitromethane to yield products of the type 3-hydroxy-3-nitromethyl-oxindole; these products, upon reduction, yield the respective 3-hydroxy-3-aminomethyl-oxindoles. That work has now been extended in order to obtain similar compounds containing salt-forming groups in the benzenoid ring of the oxindole structure.

CHART I



Isatin, 1-methylisatin, and 1-ethylisatin were nitrated in the 5-position by the method of Calvery, Noller and Adams.[3] The resulting nitroisatins were then condensed with nitromethane using diethylamine as the catalyst.[2] All three of these condensation products were reduced to the corresponding di-amino compounds readily, by the action of tin and hydrochloric acid (see Chart I). These di-amino compounds upon treatment with benzoyl chloride, ethyl chloroformate, and potassium cyanate, formed, respectively, the corresponding di-benzoyl, diurethan, and di-urea derivatives.

A similar study of derivatives of 7-carboxy-isatin was made. The 7-carboxy-isatin has been prepared by Sandmeyer[4] and by Rupe and Guggenbuhl[5] from anthranilic acid by the chloral hydrate and hydroxylamine method. Since Waldmann[6] has shown that a purer product can be obtained by using methyl anthranilate as the starting material, his procedure was followed in preparing the 7-carboxy-isatin and the 1-methyl- and 1-ethyl-analogs. The 7-carboxy-isatins thus obtained were then esterified and the esters were used in the condensation reactions with nitromethane. In this way the following compounds were obtained



R = H(XVI); CH_3(XVII); C_2H_5(XVIII)

Of these condensation products, compound XVI was subjected to treatment with tin and concentrated hydrochloric acid, and yielded 3-hydroxy-3-aminomethyl-7-carboxy-oxindole hydrochloride (XIX). Compound XIX formed benzoyl (XX), urethan (XXI), and urea (XXII) derivatives.

Several of the products will be tested for physiological activity.

Experimental Part

Compounds I, II, and III.—5-Nitro-isatin (or 1-methyl-5-nitro-isatin or 1-ethyl-5-nitro-isatin) (15 g.) was suspended in absolute ethyl alcohol (15 cc.) containing 10 g. of nitromethane, and the mixture was cooled to −15°. Then diethylamine (15 drops) was added with stirring. After standing at −15° for two hours, 1 cc. of glacial acetic acid was added and the solvent was partially removed

(1) From the dissertation presented by Raymond B. Crawford to the Faculty of the Graduate School of New York University in candidacy for the degree of Doctor of Philosophy, June, 1938.

(2) Conn and Lindwall, THIS JOURNAL, **58**, 1236 (1936).

(3) Calvery, Noller and Adams, *ibid.*, **47**, 3059 (1925).

(4) Sandmeyer, *Helv. Chim. Acta*, **2**, 234 (1919).

(5) Rupe and Guggenbuhl, *ibid.*, **10**, 926 (1927).

(6) Waldmann, *J. prakt. Chem.*, **147**, 338 (1937).

TABLE I

PROPERTIES AND ANALYSES OF COMPOUNDS

	Derivative	Crystals and color	Crude yield, %	M. p., °C.	Formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Nitrogen Calcd.	Nitrogen Found.	Chlorine Calcd.	Chlorine Found	Water Calcd.	Water Found
					3-Hydroxy-3-nitromethyl-5-nitro-oxindoles										
I	...	...	57	145–147	$C_9H_7O_6N_3$	42.70	42.85	2.79	3.11	...	...	...	...	...	...
II	1-Methyl-	Light yel. prisms	82	153	$C_{10}H_9O_6N_3$	44.95	44.78	3.39	3.58	...	...	...	...	...	...
III	1-Ethyl-	Stout yel. prisms	72	134–135	$C_{11}H_{11}O_6N_3$	46.98	47.23	3.94	4.21	...	...	...	...	...	...
					3-Hydroxy-3-aminomethyl-5-amino-oxindole di-hydrochlorides										
IV	...	White glossy plates	72	>300	$C_9H_{13}O_2N_3Cl_2$	40.62	40.32	4.92	4.95	15.79	15.72	26.64	26.40	...	...
	Picrate of IV	Yel. prisms	...	198 dec.	...	...	...	..	..	...	...	...	...	...	...
V	1-Methyl-	...	80	170–173	$C_{10}H_{15}O_2N_3Cl_2$	...	...	..	..	...	...	25.31	28.18	...	...
	Picrate of V	Yel. brown plates	...	201–203 dec.	...	...	...	..	..	...	...	...	...	...	...
VI	1-Ethyl-	Needles	40	137–137.5	$C_{11}H_{17}O_2N_3Cl_2 \cdot 2H_2O$	40.01	40.15	6.41	6.64	12.73	12.53	21.47	21.48	10.91	10.78
	Picrate of VI	Yel. plates	...	179–180	...	...	...	..	..	...	...	...	...	...	...
					3-Hydroxy-3-benzoylaminomethyl-5-benzoylamino-oxindoles										
VII	...	White needles	100	200–201	$C_{23}H_{19}O_4N_3$	68.82	68.58	4.77	5.28	...	...	...	...	...	...
VIII	1-Methyl-	White needles	100	249–251	$C_{24}H_{21}O_4N_3$	69.38	69.01	5.09	5.46	10.11	9.53	...	...	...	...
IX	1-Ethyl-	White needles	100	227–227.5	$C_{25}H_{23}O_4N_3$	69.92	70.66	5.40	5.26	...	...	...	...	...	...
					3-Hydroxy-3-ethylcarbamidomethyl-5-ethylcarbamido-oxindoles										
X	...	White prisms	100	154	$C_{15}H_{19}O_6N_3$	...	...	..	..	12.46	12.21	...	...	...	...
XI	1-Methyl-	White needles	100	171–172	$C_{16}H_{21}O_6N_3$	54.69	54.83	6.02	6.14	...	...	...	...	...	...
XII	1-Ethyl-	White needles	100	183	$C_{17}H_{23}O_6N_3$	55.88	55.92	6.34	5.87	...	...	...	...	...	...
					3-Hydroxy-3-uramidomethyl-5-uramido-oxindoles										
XIII	...	White needles	90	Chars	$C_{11}H_{13}O_4N_5$	47.31	47.34	4.99	5.00	...	...	...	...	...	...
XIV	1-Methyl-	White needles	90	213–214	$C_{12}H_{15}O_4N_5$	...	...	..	..	23.88	23.92	...	...	...	...
XV	1-Ethyl-	White needles	90	224–225	$C_{13}H_{17}O_4N_5$	50.81	50.46	5.58	5.82	...	...	...	...	...	...
					3-Hydroxy-3-nitromethyl-7-carbomethoxy-oxindoles										
XVI	...	White silky	...	159–161.5	$C_{11}H_{10}O_6N_2$	49.62	49.32	3.79	3.65	10.52	10.34	...	...	...	...
XVII	1-Methyl-	White prisms	80	138–139	$C_{12}H_{12}O_6N_2$	51.43	51.18	4.31	4.36	10.00	9.99	...	...	...	...
XVIII	1-Ethyl-	White prisms	60	96–97.5	$C_{13}H_{14}O_6N_2$	53.06	52.87	4.80	4.62	...	...	...	...	...	...
					3-Hydroxy-3-aminomethyl-7-carboxy-oxindole hydrochloride										
XIX	...	White needles	80	187–188	$C_{10}H_{11}O_4N_2Cl$	46.43	46.26	4.38	4.03	10.86	10.53	13.71	13.85	...	...
					3-Hydroxy-3-benzoylaminomethyl-7-carboxy-oxindole										
XX	...	White prisms	53	240–241	$C_{17}H_{14}O_5N_2$	62.63	62.75	4.33	4.39	8.60	8.18	...	...	...	...
					3-Hydroxy-3-ethylcarbamidomethyl-7-carboxy-oxindole										
XXI	...	White needles	45	217–218	$C_{13}H_{14}O_6N_2$	53.06	53.03	4.80	4.85	9.52	9.42	...	...	...	...
					3-Hydroxy-3-uramidomethyl-7-carboxy-oxindole										
XXII	...	White	42	218–219	$C_{11}H_{11}O_5N_3$	49.81	49.57	4.48	4.92	15.84	15.90	...	...	...	...

under vacuum at 30°, the product separated and recrystallized from ethyl alcohol (I), or (II and III) from glacial acetic acid.

Compounds IV, V, and VI from I, II, and III, respectively.—Compound I (or II or III) (25.3 g.) was suspended in 100 cc. of concentrated hydrochloric acid and mossy tin (41.6 g.) was added slowly, keeping the temperature below 60°. In one-half hour all of the nitro compound had gone into solution. Then 50 cc. of concentrated hydrochloric acid and 41.6 g. of mossy tin were added and the mixture was boiled for twenty hours. The unused tin was then filtered off, the solution was diluted to 1600 cc. with water, and tin was removed as the sulfide. The product was obtained by evaporation to dryness on the steam-bath. Purification of IV was by dissolving in water and saturating with hydrogen chloride; of VI by crystallization from alcohol; V could not be recrystallized.

The Benzoyl Derivatives of IV, V, and VI (VII, VIII, and IX).—Compound IV (or V or VI) (0.5 g.) was dissolved in 10 cc. of water and 1 g. of sodium carbonate and 1.5 g. of benzoyl chloride were added. The product separated after standing two hours at room temperature; recrystallized from ethyl alcohol.

The Urethan Derivatives of IV, V, and VI (X, XI, and XII).—Compound IV (or V or VI) (0.5 g.) was dissolved in 10 cc. of water and 1 g. of sodium carbonate and 0.7 g. of ethyl chloroformate were added. The products were crystallized from ethyl alcohol.

The Urea Derivatives of IV, V, and VI (XIII, XIV and XV).—Compound IV (or V or VI) (1.0 g.) was dissolved in 7 cc. of water and 1 g. of potassium cyanate dissolved in 3 cc. of water was added. The crystalline product separated after twelve hours standing in ice; in each case the product was recrystallized from water after treatment with bone coal.

Compounds XVI, XVII and XVIII.—Nitromethane (9 g.) and 7-carbomethoxy-isatin (12 g.) were placed in 12 cc. of absolute ethyl alcohol and the mixture was cooled to −15°. Diethylamine (15 drops) was added with stirring. The mixture was held at −15° for one hour, and part of the solvent was then removed to cause fairly complete separation of XVI. Compounds XVII and XVIII were prepared, respectively, by substituting 1-methyl-7-carbomethoxy-isatin and 1-ethyl-7-carbomethoxy-isatin in this procedure.

Compound XIX (from XVI).—Compound XVI (9.5 g.) was suspended in 50 cc. of concentrated hydrochloric acid and mossy tin (17 g.) was added slowly, keeping the temperature below 60°. After boiling the mixture for two hours it was diluted with water and tin was removed as the sulfide. The solution was evaporated until a solid separated; it was recrystallized from ethyl alcohol. Treatment of XIX with benzoyl chloride yielded **compound XX**; with ethyl chloroformate, **compound XXI**; with potassium cyanate, **compound XXII.**

Summary

Oxindole and N-alkylated-oxindole derivatives have been prepared in which the 3-position holds the hydroxyl and the aminomethyl groups, and the 5- or 7-position is occupied, respectively, by the amino or carboxyl group. For certain of these products benzoyl, urethan, and urea derivatives are described.

UNIVERSITY HEIGHTS
NEW YORK, N. Y.

RECEIVED JULY 1, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, NEW YORK UNIVERSITY]

Sulfides and Sulfones of Pyridine and Quinoline

BY A. R. SURREY AND H. G. LINDWALL

The similarity of therapeutic effect to sulfanilamide of the dinitro- and diaminodiphenyl sulfides and sulfones,[1,2,3] suggested the preparation of like compounds in the pyridine and quinoline series.

The chemotherapy of these diphenyl compounds[4,5] showed that while some of them possess greater activity than sulfanilamide, in general they have a greater toxicity. The introduction of the pyridine ring in sulfanilamide not only enhances the activity but also adds desirable features absent from sulfanilamide. Encouraging results were obtained with certain other pyridine compounds[6] including the dihydrobromide of 2,2′-dipyridyl sulfide. Recently, sulfonamides of some aminoquinolines have been synthesized.[7] It therefore seemed desirable to prepare pyridine and quinoline analogs of the dinitro and diamino diphenyl sulfides and sulfones.

5,5′-Dinitro 2,2′-dipyridyl sulfide (I) has been prepared by the action of sodium sulfide on 2-chloro-5-nitropyridine. This is essentially the method used by Nietzki and Bothof[8] for the preparation of the diphenyl analog. The diquinolyl sulfides (IV) and (V) (see Table I) were prepared in the same way starting with 5-chloro-8-nitro-

(1) Buttle, *Lancet*, 1331 (1937).
(2) E. Fourneau, J. and MMe. J. Trefouel, F. Nitti and D. Bovet, *Bull. acad. méd.*, **118**, 210 (1937).
(3) H. Bauer and S. M. Rosenthal, *U. S. Public Health Rpts.*, **53**, 40 (1938).
(4) A. DeM. Welch, *J. Pediatrics, II*, no. 2, 159 (1937).
(5) G. W. Raiziss, L. W. Clemence, M. Severac and J. C. Moetsch, THIS JOURNAL, **61**, 2763 (1939).
(6) J. A. Kolmer, H. Brown and G. W. Raiziss, *J. Pharmacol.*, **61**, 253 (1937).
(7) Bobranski, *Arch. Pharm.*, **277**, 75 (1939).
(8) Nietzki and Bothof, *Ber.*, **27**, 3261 (1894).

TABLE I

PROPERTIES AND ANALYSES OF COMPOUNDS

Sulfide	M. p., °C.	Formula	Nitrogen, % Calcd.	Found	Carbon, % Calcd.	Found	Hydrogen, % Calcd.	Found
I 5,5′-Dinitro-2,2′-dipyridyl	136–137	$C_{10}H_6N_4O_4S$	20.14	20.13	...	...	..	..
II 5,5′-Diamino-2,2′-dipyridyl	130–131.5	$C_{10}H_{10}N_4S$	25.69	25.53	55.05	54.96	4.59	4.74
III 5,5′-Diacetylamino-2,2′-dipyridyl	265–266.5	$C_{14}H_{14}N_4O_2S$	18.54	18.52	...	...	..	..
IV 8,8′-Dinitro-5,5′-diquinolyl	280–281	$C_{18}H_{10}N_4O_4S$	14.81	14.92	57.14	57.47	2.64	2.91
V 5,5′-Dinitro-8,8′-diquinolyl	288.5–290	$C_{18}H_{10}N_4O_4S$	14.81	14.79	57.14	57.40	2.64	2.62
Sulfone								
VI 5,5′-Dinitro-2,2′-dipyridyl-	218.5–220.5	$C_{10}H_6N_4O_6S$	18.06	18.20	...	...	..	..
VII 5,5′-Diamino-2,2′-dipyridyl-	238–239	$C_{10}H_{10}N_4O_2S$	22.40	22.14	48.00	48.42	4.00	4.30
VIII 5,5′-Diacetylamino-2,2′-dipyridyl-	276–278	$C_{14}H_{14}N_4O_4S$	16.77	16.69	...	...	..	..
IX 5,5′-Dinitro-8,8′-diquinolyl-	260[a]	$C_{18}H_{10}N_4O_6S$	13.66	13.73	52.68	53.06	2.44	2.37

[a] Begins to decompose at 245°, completely black at 260°.

quinoline and 8-chloro-5-nitroquinoline, respectively. The latter were made from the corresponding chloroquinolines by nitration. The dinitrodipyridylsulfone (VI) was prepared by oxidation of (I) with potassium dichromate. 5,5′-Dinitro-8,8′-diquinolylsulfone (IX) was formed from (V) by oxidation with chromic acid.

Reduction of the dinitrodipyridyl compounds (I and VI), to yield the corresponding amino compounds (II and VII), was carried out using stannous chloride. Two forms of 5,5′-diamino-2,2′-dipyridyl sulfide were obtained, one melting at 80–81°, the other at 130–131.5°. By heating the lower melting compound in the oven at 90° the higher melting variety was obtained. Both gave the same diacetylamino derivative (III). A calculated amount of stannous chloride was used in the reduction of (VI) to give 5,5′-diamino-2,2′-dipyridylsulfone (VII). An excess of stannous chloride reduced the sulfone group to give (II).

Certain of these compounds will be tested to determine their therapeutic effect.

Experimental Part

I, IV and V.—To a nearly saturated solution of 2-chloro-5-nitropyridine (or 5-chloro-8-nitroquinoline or 8-chloro-5-nitroquinoline) in hot alcohol was added a slight excess of a saturated aqueous solution of sodium sulfide. In each case the reaction mixture turned red and heat was evolved. After the initial reaction had subsided, the solution was refluxed for four hours on the steam-bath. The product which separated was filtered and washed with alcohol; yield: (I) 73%, yellow needles from alcohol; (IV) 90%, small yellow needles from acetone and water; (V) 85%, small orange crystals from pyridine.

5,5′-Dinitro-2,2′-dipyridylsulfone (VI).—A solution of 6 g. of potassium dichromate in 80 cc. of water was added with shaking to a solution of 4.5 g. of I in 80 cc. of water and 60 cc. of concd. sulfuric acid. In a short time a fine white precipitate began to separate. After all the dichromate solution had been added, the reaction mixture was allowed to stand for a few minutes and then diluted with four times its volume of water. The precipitate was filtered and washed with water until a clear filtrate was obtained, and then dried; yield, 4.5 g. (90%). The material crystallized from propyl alcohol in small white needles.

II and VII.—Compound I (or VI) (3 g.) was added slowly with cooling to a solution of 24 g. (or 14 g.) of stannous chloride in 30 cc. (or 17 cc.) of concd. hydrochloric acid. The solution was then heated on the steam-bath for one hour. The clear solution was allowed to cool and the tin salt which separated was filtered. To a solution of the tin salt in a small amount of water, 40% sodium hydroxide was added until the solution was strongly alkaline. The brown oil which separated was cooled until it solidified and then was filtered. The crude amine was dissolved in hot water and treated with bone black: yield, (II) 68%; (VII) 67%. Both were obtained as white needles after repeated recrystallizations from water.

5,5′-Diacetylamino-2,2′-dipyridyl Sulfide (III).—Compound II (0.5 g.) was added to 10 cc. of acetic anhydride. Heat was evolved and the diacetylamino compound (III) separated as a fine white powder. The product was purified by dissolving in alcohol, treating with bone black and allowing most of the alcohol to evaporate; yield, almost quantitative.

5,5′-Diacetylamino-2,2′-dipyridylsulfone (VIII).—Compound VII (0.5 g.) was added to 10 cc. of acetic anhydride. The solution was warmed until all of the amine went into solution. On cooling, light yellow needles separated out. The material was purified by recrystallizing from water.

5,5′-Dinitro-8,8′-diquinolylsulfone (IX).—Chromic acid (1.0 g.) was added to a solution of 1.0 g. of V in 30 cc. of glacial acetic acid. After the initial vigorous reaction, which was induced by warming, the solution was refluxed for fifteen minutes and then poured into ice. A yellow precipitate separated; yield, 0.6 g. (54%); small yellow needles from acetone.

Summary

Methods are described for the preparation of the 5,5′-dinitro, the 5,5′-diamino, the 5,5′-diacetylamino-2,2′-dipyridyl sulfides, and their respective sulfones, as well as the 5,5′-dinitro-8,8′-diquinolyl sulfide and its sulfone, and the 8,8′-dinitro-5,5′-diquinolyl sulfide.

UNIVERSITY HEIGHTS
NEW YORK, N. Y.

RECEIVED NOVEMBER 13, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, THE UNIVERSITY OF TEXAS]

A Quantitative Test for Biotin and Observations Regarding its Occurrence and Properties

BY ESMOND E. SNELL, ROBERT E. EAKIN AND ROGER J. WILLIAMS

In the course of studies on biotic acid[1] we found that vitamin B_6 serves as a yeast nutrilite[2] and were led to introduce the pure vitamin into our basal culture medium. (The effect of vitamin B_6 on yeast was independently discovered elsewhere at the same time.[3]) In this modified basal medium, yeast became much more sensitive to addenda of small amounts of liver preparations. Shortly after this, through the kindness of Professor Kögl, we were furnished with a sample of biotin, and a few tests demonstrated that in this medium the yeast was responding specifically to biotin.

Some of the observations reported herein were made before we were aware that biotin was the physiologically active substance involved.

Experimental Procedure

The yeast used in this test was isolated in pure culture from a cake (pound goods) of Fleischmann yeast, and was carried thereafter on molasses–agar slants as previously described.[4] Several cultures isolated from this source were found interchangeable for this purpose. The basal medium contains: C. P. sucrose 20 g., $(NH_4)_2SO_4$ 3 g., KH_2PO_4 2 g., $MgSO_4 \cdot 7H_2O$ 0.25 g., $CaCl_2 \cdot 2H_2O$ 0.25 g., H_3BO_3 1 mg., $ZnSO_4$ 1 mg., $MnCl_2$ 1 mg., $TlCl_3$ 1 mg., $FeCl_3$ 0.5 mg., $CuSO_4 \cdot 5H_2O$ 0.1 mg., KI 0.1 mg., *l*-aspartic acid 0.1 g., inositol 5 mg., β-alanine 0.5 mg., thiamin 20 γ and vitamin B_6 20 γ, all added to one liter of distilled water.

Addenda to the basal medium are dissolved in 2 ml. of water in 50-ml. Erlenmeyer flasks and sterilized by steaming for five minutes. After cooling, 10 ml. of the (previously sterilized) basal medium containing 0.02 mg. of suspended yeast is pipetted into each flask which is set unstoppered and without agitation in an incubator at 30° for the growth period of approximately sixteen hours. Very clean glassware is essential for proper results.

At the end of the growth period the yeast suspension is diluted with 10 ml. of saturated aqueous chlor thymol and shaken mechanically for three to five minutes. The amount of yeast present is determined by use of a thermocouple-galvanometer set-up.[5] The same instrument is used to gage the seeding in the basal medium at the start, the concentration being determined indirectly from a heavy suspension from which the proper aliquot is taken. We have found it convenient to use a box type galvanometer with lamp and scale enclosed, and to adjust so that it reads zero when basal medium alone is interposed between the light and the thermocouple, and 100 when an opaque object is interposed. This instrument is superior for this purpose to available photoelectric colorimeters.

Blank cultures (no addenda) and cultures containing known amounts of biotin (0.000025 to 0.00025 γ) are run simultaneously with the unknowns, and the amounts of biotin in the unknown sample are read off the standard curve, in which galvanometer readings are plotted against the known amounts of biotin (either pure or in a standardized extract) added.

Experimental Results

In Fig. 1 are plotted the results of parallel tests of a crude liver preparation and a biotin solution. The two curves are parallel through a wide range. At relatively high concentrations both curves flatten out and do not diverge strikingly. This parallelism means that when the test is applied to such an extract, values obtained at different dosage levels agree, which is true of extracts generally, as is illustrated by data presented below (Table II). This strongly indicates that the test is specific.

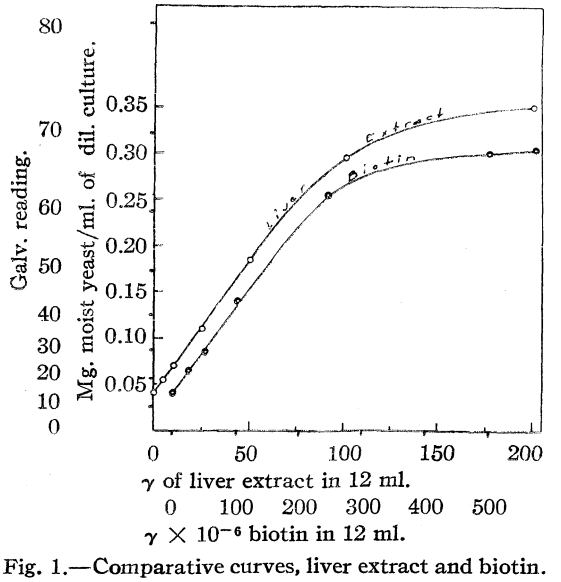


Fig. 1.—Comparative curves, liver extract and biotin.

Under our test conditions biotin gives a response at an exceedingly low dosage. Kögl,[6] speaking of biotin, says "it can be detected in the yeast test even at a dilution of 1 in 4×10^{11}." From Fig. 1 it is seen that in our test a concentra-

(1) Eakin and Williams, *J. Biol. Chem.*, **128**, xxiii (1939).
(2) Eakin and Williams, THIS JOURNAL, **61**, 1932 (1939).
(3) Schultz, Atkin and Frey, *ibid.*, **61**, 1931 (1939).
(4) Williams, Wilson and Von der Ahe, *ibid.*, **49**, 229 (1927).
(5) Williams, McAlister and Roehm, *J. Biol. Chem.*, **83**, 315 (1929).
(6) Kögl, *Proc. Roy. Soc.* (London), **B124**, 1 (1937).

tion of 1 in 5×10^{11} increased the galvanometer reading from 16 to 22. This is considerably greater than the least detectable amount. The advantage of a small dosage in a test of this kind is evident. To get a *measurable* response, less than 0.1 mg. of extracted material (5 γ or more in the case of autolyzed liver extracts) must be added to a 12-ml. culture. The chance of introducing other physiologically active substances which might interfere with the test is thus minimized, and the specificity of the test is ensured.

The active substance concerned in our test has the known properties of biotin. Its activity is not destroyed by heating with normal alkali at 100°, and it withstands refluxing with acidic methanol (*cf.* Table III). The latter procedure brings about esterification but the ester is physiologically active.[7] Biotic acid is destroyed by this treatment. All of the well recognized yeast nutrilites are placed in the basal medium (in this medium β-alanine completely replaces pantothenic acid) and so far as we are aware no known or postulated substance can replace biotin in this test.

Vitamin B_6 must be present in the medium before any significant effect of biotin can be demonstrated. This is illustrated in Table I. The

TABLE I

EFFECT OF BIOTIN IN PRESENCE AND ABSENCE OF VITAMIN B_6

Addition to medium per flask, γ	Galvanometer readings on basal medium: Without vitamin B_6	Containing vitamin B_6
0.0	36.0	30.3
.00003 biotin	38.8	38.8
.00007 biotin	40.0	50.2
.00015 biotin	39.8	58.0
.00300 biotin	38.1	69.1
5.0 liver preparation	39.0	39.2
10.0 liver preparation	38.6	49.4
20.0 liver preparation	36.0	57.0
40.0 liver preparation	31.8	66.0
100.0 liver preparation	25.0	70.0

situation here is somewhat analogous to that with rats, where the presence of vitamin B_6 is necessary before the "filtrate factors" show their full effect.[8,9,10]

The test of Kögl involving a growth response from heavy seeding of "Rasse M" yeast seems not to be as specific as the one we have described. It has been indicated[7] that a crude extract in high dosage gives a 600% increase under his growth conditions, whereas pure biotin causes only a 300% increase. From the published assays[11] it is not clear whether the specificity of the test can be ensured by holding the dosages down to low levels, since assay values at different dosage levels are not given.

In the test investigated by Robbins and Schmidt[12] involving the organism *Ashbya gossypii*, no claim for specificity is made and the authors state that their results are "suggestive only." At different dosage levels the materials did not show the same relative potency, indicating that toxic and/or stimulating principles were influencing the results.

Data on Assays.—For further information regarding the quantitative distribution of biotin, assays on the materials listed below were carried out. Clear water extracts were obtained by autoclaving the material (finely ground if necessary) for ten minutes at 15 lb. (1 atm.) pressure with a large volume of water. If necessary the extract obtained was clarified by filtering with filter-cel. Casein samples were hydrolyzed with sulfuric acid and the $SO_4^=$ ion removed with Ba^{++} for assay. Examples are given in Table II showing comparative results at different dosage levels. In Table III single values are given for the sake of brevity. Liberation of biotin by autolysis of liver tissue is

TABLE II

COMPARATIVE RESULTS OF BIOTIN ASSAYS AT DIFFERENT TESTING LEVELS

Material	Fresh material tested (as extract), γ	Dry wt. in extract added, γ	Biotin found, γ	Biotin content found: Fresh substance, γ per g.	Solids in extract, γ per g.
Autolyzed	30	4.5	0.000020	0.67	4.46
Liver I	100	15.0	.000065	.65	4.33
(37°, 24	200	30.0	.000132	.66	4.40
hr., 10% suspension)			Av.	.66	4.4
Unauto-	500	15.5	.000015	.030	0.97
lyzed	1000	31.0	.000032	.032	1.03
Liver I	3000	93.0	.000073	.024	0.78
			Av.	.029	.93
"Liquid	50	1.5	.000025	.50	16.7
Manure"	150	4.5	.000070	.47	15.7
	500	15.0	.000230	.46	15.3
			Av.	.48	15.9
Egg Yolk I	50	1.7	.000015	.30	8.8
	150	5.1	.000045	.30	8.8
	500	17.0	.000137	.27	7.9
			Av.	.29	8.5

(7) Kögl and Tönnis, *Z. physiol. Chem.*, **242**, 43 (1936).
(8) Lepkovsky, Jukes and Krause, *J. Biol. Chem.*, **115**, 557 (1936).
(9) Lepkovsky, *ibid.*, **124**, 125 (1938).
(10) Edgar, El Sadr and Macrae, *Biochem. J.*, **32**, 2200 (1938).
(11) Kögl and Hasselt, *Z. physiol. Chem.*, **243**, 189 (1936).
(12) Robbins and Schmidt, *Bull. Torrey Botan. Club*, **66**, 139 (1939).

TABLE III

BIOTIN CONTENT OF VARIOUS MATERIALS

Material	Biotin content, γ per g.
Cane molasses (Hawaiian Blackstrap)	2.1
Cane molasses (Cuban Blackstrap)	1.7
Beet molasses I	0.06
Beet molasses II	.9
Urine (liquid)	.09
Urine (solids)	2.0
Whey (liquid)	0.12
Whey (solids)	2.5
Egg white (fresh)	0.05
Egg yolk II (fresh)	.37
Egg yolk II (autolyzed 24 hr.)	.35
Yeast (moist, autolyzed)	.13
Beacon Dog Meal	.53
Casein, purified (Eimer & Amend, free of Vitamin "B")	.002
Casein, technical	.125
Potato (fresh)	.010
Autolyzed liver II (solids)	3.89
Autolyzed liver II (refluxed 1 hr. with *N* NaOH)	3.87
Autolyzed liver II (refluxed 1 hr. with 3% HCl in CH_3OH)	3.89

clearly demonstrated and indicates that biotin is bound up with liver proteins or other colloids, an observation apparently not previously made. In the assays of Kögl and Hasselt on animal tissues,[11] livers appeared to be mediocre biotin sources. Had autolysis been carried out, results would doubtless have been different. Whether other tissues yield more biotin on autolysis is not known. Egg yolk extracts are not increased in biotin content by "autolysis."

In this connection it is interesting to note that casein contains considerable amounts of biotin; purification greatly decreases the amount present.[13]

Manure (and also urine) is a relatively rich source of biotin, but according to our tests it is not as rich as indicated by the tests of Robbins and Schmidt,[12] who judged the extract to be nearly 300 times as rich (on a dry weight basis) as egg yolk.

In view of its properties, occurrence and high physiological activity, the "growth substance" described in 1935[14] may have been biotin. The test organism used in its study became less and less sensitive on subculture and finally was lost. This "growth substance" was removed from casein and other proteins with difficulty.

The absolute values for the biotin content of materials given in Tables II and III are based upon the preparation which Professor Kögl kindly sent us and upon a limited number of samples and should not be accepted as final. If this standard preparation deteriorated during shipment or before use, then values given would be too high. Relative values would not, of course, be affected.

Destruction by Nitrous Acid.—Before we were aware that the active principle in liver extract was biotin, tests revealed that it was destroyed rapidly by nitrous acid.

Following the method of Dunn and Schmidt,[15] we investigated the rate at which the active principle in a liver autolysate was inactivated by standing at 23° in the presence of a given concentration of glacial acetic acid and sodium nitrite. Aliquots were removed and diluted to stop the reaction at time intervals noted in Table IV. Results are compared with those obtained by Dunn and Schmidt[15] for the rate of reaction of α, β and γ amino groups. Only 94% of the activity of the liver could be destroyed by this treatment; the residual activity may arise from the hydroxyl compound which presumably is formed. Assuming this to be true, and recalculating on this basis, it readily is seen that inactivation occurs at a rate most characteristic of α-amino acids. The destructive action of nitrous acid was later confirmed on a small sample of Kögl's biotin. Biotin may therefore be an α-amino acid. Its liberation from tissues by autolysis, the biological activity of its methyl ester and inactivity of its acetyl derivative[7] coupled with its destruction by nitrous acid, all point toward the significance of this amino group in determining its physiological activity.

TABLE IV

EFFECT OF NITROUS ACID ON BIOTIN ACTIVITY OF A LIVER CONCENTRATE AND ON AMINO ACIDS AT 23°

	Biotin		% Amino N liberated from amino acids[a]		
Time, min.	% Destruction	% Destruction (recalcd.)	α-Alanine	β Alanine	γ-Amino-*n*-valeric acid
0.0	0	0	0	0	0
.5	42	45	..	..	..
1.0	75	80	55	57	20
2.0	88	94	..	..	..
3.0	..	..	99	90	58
4.0	94	100	..	..	..
5.0	..	..	100	97	78
7.0	..	..	..	100	..
9.0	..	..	..	..	95
10.0	94	100	..	..	100
30.0	94	100	..	..	..

[a] Taken from data of Dunn and Schmidt.[15]

(13) The biotin content of hydrolyzed casein has been pointed out before: *cf.* Snell and Williams, THIS JOURNAL, **61**, 3594 (1939).

(14) Williams and Christensen, *Science*, **82**, 178 (1935).

(15) Dunn and Schmidt, *J. Biol. Chem.*, **53**, 401 (1922).

We gladly acknowledge the generous support of this work by The Rockefeller Foundation and Standard Brands, Inc., of New York.

Summary

A sensitive and accurate assay for biotin is described which involves the growth of a strain of *Saccharomyces cerevisiae* from a small seeding. Under the test conditions the response of this organism to biotin is quantitative within a concentration range from 0.00002 to about 0.001 γ of biotin. Assay results on crude extracts agree well at different levels within this range, and the curves obtained are very similar to those obtained with pure biotin. Assay results on a number of natural materials are given.

The effectiveness of biotin under these conditions depends to a large extent on the presence of vitamin B_6 (and of β-alanine) in the medium. Biotin in liver concentrates is destroyed by nitrous acid at a rate which indicates that it may be an α-amino acid.

AUSTIN, TEXAS RECEIVED NOVEMBER 28, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE UNIVERSAL OIL PRODUCTS COMPANY]

Catalytic Hydration of Acetylene and of Some Alkylacetylenes[1]

BY RAYMOND E. SCHAAD AND VLADIMIR N. IPATIEFF

Previously sulfuric acid, sulfuric acid with mercury salts, and the latter composite in the presence of organic solvents have been used as catalysts in the hydration of acetylene and of alkylacetylenes to acetaldehyde and ketones, respectively, as reviewed and described by Thomas, Campbell and Hennion.[2] For the hydration of acetylene several patents claim a similar use of phosphoric acid and mercury salts,[3] and of phosphoric acid on charcoal with[4] and without[5,6] added metals.

In the present work solid phosphoric acid polymerization catalyst[7,8,9] was found to catalyze hydration of butyne-1 rather than its polymerization, the water required for the hydration being removed from the catalyst which was thereby decreased in activity. Continuous hydrations of this and of other alkynes, including acetylene, propyne, pentyne-1, pentyne-2, hexyne-1, and heptyne-1, were effected without rapid decrease in catalyst activity by simultaneous passage of the hydrocarbon and steam through a heated tube containing the granular solid catalyst.

Acetaldehyde formed when steam and acetylene or mixtures of steam with acetylene and ethylene or nitrogen were passed through a tube containing solid phosphoric acid catalyst at 260–300° and atmospheric pressure. Some higher boiling products also formed apparently by condensation of acetaldehyde in the presence of the catalyst.

The different alkylacetylenes tried, both monoalkyl and dialkyl derivatives, underwent hydration to ketones in the presence of solid phosphoric acid catalyst at 204° and atmospheric pressure. Butyne-1 was hydrated also at 150°. Condensation of some of the ketone to oils of relatively high boiling point and refractive index accompanied its formation. By this hydration reaction propyne yielded acetone, butyne-1 formed 2-butanone, pentyne-1 and pentyne-2 each gave 2-pentanone, hexyne-1 produced 2-hexanone and heptyne-1 yielded 4-heptanone. The latter result indicates isomerization possibly involving migration of the triple bond along the carbon chain of heptyne-1 before hydration occurred producing 4-heptanone.

Experimental Part

Sources of Acetylene Hydrocarbons.—Acetylene from a commercial cylinder was purified from acetone vapors by passing through three scrubbers containing 96% sulfuric acid and then through a soda lime tower before use in the hydration experiments. Propyne was prepared following Hennion[10] and butyne-1 was produced according to the

(1) Presented before the Division of Organic Chemistry at the 98th meeting of the American Chemical Society, Boston, Mass., Sept. 12, 1939.

(2) Thomas, Campbell and Hennion, THIS JOURNAL, **60**, 718 (1938).

(3) I. G. Farbenindustrie A.-G., British Patent 460,862 (Feb. 5, 1937).

(4) Walter, U. S. Patent 2,098,842 (Nov. 9, 1937).

(5) Eberhardt, U. S. Patent 2,093,146 (Sept. 14, 1937).

(6) I. G. Farbenindustrie A.-G., French Patent 46,616 (July 11, 1936).

(7) Ipatieff, U. S. Patents 1,993,512–13 (Mar. 5, 1935); 2,018,065–6 (Oct. 22, 1935); 2,020,649 (Nov. 12, 1935); 2,057,433 (Oct. 13, 1936); 2,060,871 (Nov. 17, 1936).

(8) Ipatieff and Schaad, U. S. Patents 2,120,702 (June 14, 1938); 2,157,208 (May 9, 1939).

(9) Universal Oil Products Co., British Patents 437,188 (Oct. 14, 1935); 463,272 (Mar. 25, 1937); 463,864 (Apr. 7, 1937); 464,671–2 (Apr. 19, 1937); French Patent 797,584 (April 29, 1936).

(10) Hennion, Meeting of the Indiana Academy of Science, Manchester, Indiana, November 5, 1937.

TABLE I

HYDRATION OF ALKYLACETYLENES IN THE PRESENCE OF SOLID PHOSPHORIC ACID CATALYST AT 204°

Hydrocarbon	B. p., °C.	Ketone	B. p., °C.	d^{20}_4	$n^{20}D$	Semicarbazone, m. p., °C.	2,4-Dinitrophenylhydrazone, m. p., °C.
Propyne	−23 to −22	Acetone	56– 60	0.789	...	183	...
Butyne-1	+8	2-Butanone	72– 82	.806	1.380	138–9	114–6
Pentyne-1	39–40	2-Pentanone	96–104	.818	1.392	103–4	142–4
Pentyne-2	55	2-Pentanone	99–107	.830	1.395	106–8	142–4
Hexyne-1	71	2-Hexanone	125–131	.814	1.401	116–7	107–8
Heptyne-1	98.5–99.5	4-Heptanone	150–153	.818	1.410	117–8	74–5

method published by Hurd and Meinert.[11] The pentyne-1, pentyne-2, hexyne-1, and heptyne-1 were purchased from the University of Notre Dame.

Apparatus and Procedure.—When hydrating a liquid alkylacetylene, water and the acetylene hydrocarbon were dropped simultaneously at constant rates from burets into the upper end of a vertical Pyrex tube (10 mm. inside diam. × 90 cm.) containing the solid phosphoric acid catalyst (7.0 or 14.0 g. of 6-10 mesh particles) and surrounded by an insulated, electrically heated, aluminum bronze block furnace (60 cm. long) provided with a thermoregulator which maintained the temperature constant to within ±2°. The exit end of the catalyst tube was attached by a ground glass joint to an ice-cooled Pyrex receiver connected through a calcium chloride drying tube to a trap cooled by solid carbon dioxide and acetone.

When the alkylacetylene used was gaseous, it was passed from a weighed aluminum bomb through a calibrated flowmeter and thence to the top of the catalyst tube, the rest of the apparatus and procedure being the same as described. In the experiments on acetylene purified by sulfuric acid the amount of this gas entering and leaving the catalyst chamber (of 100 g. catalyst capacity) was measured by means of wet-test meters through which acetylene had been passed previously to saturate the water contained in them.

The trap cooled by solid carbon dioxide remained empty during the experiments on liquid alkylacetylenes, it collected small amounts of unreacted hydrocarbon in the experiments with gaseous alkylacetylenes and collected the main part of the acetaldehyde as an aqueous solution in the runs on the hydration of acetylene. In experiments on the alkylacetylene, the reaction products and water were collected mainly in the ice-cooled receiver from which the aqueous layer was removed by a pipet, and the main ketone layer and that obtained by salting-out the aqueous layer with potassium carbonate were combined, dried over anhydrous sodium sulfate or potassium carbonate and later distilled. These ketone fractions were characterized by their physical properties and by preparation of semicarbazones and 2,4-dinitrophenylhydrazones.

Distillation of the aqueous aldehyde solution, produced from acetylene, separated acetaldehyde with 20–22° boiling point from the excess of water used in the experiment, the higher boiling oily condensation products having been separated previously from the heavier lower layer of aqueous acetaldehyde solution.

Reaction between Acetylene and Water.—Formation of acetaldehyde from mixtures of approximately equal molecular proportions of acetylene and water began at about 260° under atmospheric pressure in the presence of solid phosphoric acid catalyst. At 300° hydration was more rapid in the equimolecular mixture and at the beginning of the experiment as much as 70% of the entering acetylene reacted. Of the acetylene consumed at the beginning of the reaction, about one-third yielded acetaldehyde and one-half produced higher boiling materials which apparently consisted of acetaldehyde condensation products containing crotonaldehyde and relatively high boiling aromatic hydrocarbons.

After the catalyst was in use for twenty-one hours and the absorption of acetylene had decreased to approximately 30% per pass, the cata yst was reactivated by heating in dry air at 500° for sixteen hours, followed by steaming at 260° for sixteen hours. Following this treatment the test was continued with 70% initial absorption of acetylene which dropped to 30% at the end of twenty-three hours and continued at that value for twenty-two hours more. The acetaldehyde yield reached 56% of the theoretical on the basis of the acetylene consumed with 9% accompanying condensation during this twenty-two hour period in which a reaction mixture consisting of two moles of water to one mole of acetylene was contacted with the reactivated catalyst. In all these acetylene hydration experiments the reaction mixture was in contact with the catalyst for an average time of 4.3 to 5.5 seconds.

Acetaldehyde from Acetylene–Ethylene and Acetylene–Nitrogen Mixtures.—Acetylene mixed with approximately an equal molecular proportion each of steam and ethylene, and with one proportion of steam and one-half proportion of nitrogen, also underwent hydration to acetaldehyde in the presence of solid phosphoric acid catalyst. Ethylene was not consumed, but apparently acted only as a diluent as was the case with nitrogen. These tests were made at an average contact time in the range of 5.0 to 5.7 seconds on both fresh, reactivated, and used catalysts. On the basis of the acetylene consumed, fresh catalyst gave the lowest yield of acetaldehyde and the highest production of oily condensation products; while used catalyst gave more acetaldehyde and less condensation products.

Hydration of Alkylacetylenes.—Propyne, butyne-1, pentyne-1 and -2, hexyne-1, and heptyne-1 underwent hydration in the presence of solid phosphoric acid catalyst and steam at 204° under atmospheric pressure and yielded acetone, 2-butanone, 2-pentanone, 2-hexanone, and 4-heptanone, respectively, as shown in Table I.

In addition to ketone formation by hydration of the different alkylacetylenes, there was also a production of small amounts of oils with relatively

(11) Hurd and Meinert, THIS JOURNAL, 52, 4544 (1930); 53, 289 (1931).

high boiling points and refractive indices. These were probably ketone condensation products but no attempt was made to identify them because of the small quantities available.

There were also indications that isomerization of alkylacetylenes involving migration of the triple bond occurred in contact with the catalyst. Thus the liquid products recovered from an experiment on butyne-1 (b. p. + 8°) contained a small quantity of material which may have been butyne-2 as it boiled at 25–30°, was insoluble in water, gave no reaction with semicarbazide hydrochloride, and turned red on contact with sulfuric acid, as is characteristic of butyne-2.

The materials available were insufficient to show whether pentyne-1 and pentyne-2 isomerized into each other. It is probable that each of these may hydrate to the same ketone without isomerization.

The fact that heptyne-1 hydrated to 4-heptanone is evidence that isomerization of this alkylacetylene occurred before hydration.

The authors are indebted to Mr. G. L. Hervert for assistance in conducting the hydration experiments.

Summary

Catalytic hydration of acetylene and of six alkylacetylenes has been accomplished readily by passing a mixture of the hydrocarbon and steam over a solid phosphoric acid-containing catalyst under atmospheric pressure at 260–300° for acetylene and at 150–204° for the alkylacetylenes.

CHICAGO, ILLINOIS RECEIVED NOVEMBER 10, 1939

[CONTRIBUTION FROM THE LABORATORY OF THE NORTHERN COKE RESEARCH COMMITTEE, NEWCASTLE-UPON-TYNE, ENGLAND]

Crystallite Growth during Carbonization

BY H. E. BLAYDEN, H. L. RILEY AND A. TAYLOR

The following is a description and discussion of further results obtained in a detailed X-ray and chemical study of the changes which occur in the solid phase during the carbonization of various carbonaceous materials. We already have described[1] the results of our study of the carbonization in the temperature range 400–1300° of cellulose and of a Northumberland coal. This work now has been extended in the case of cellulose to 2000° and also to the carbonization of two South Wales anthracites, an American anthracite, lignin and an Irish peat. Although the investigations are still incomplete and because of this their presentation must in some ways be tentative, the results already obtained appear to be of sufficient interest to justify publication at this stage. The demand for new knowledge of this kind need not be emphasized, for the fuller understanding of the molecular mechanism of the combustion and the reactivity of solid carbonaceous fuels demands more complete and fundamental information of their ultimate structure and of the effect of temperature, in the presence and absence of catalysts, upon this structure.

The Hull–Debye–Scherrer method of X-ray analysis has provided a means of obtaining this more detailed information. From the broadening of the diffraction lines in the X-ray powder photographs of the so-called "amorphous" carbons compared with the lines in the X-ray spectrum of macrocrystalline graphite, it is possible to calculate the average dimensions of the crystallites present (assumed to be cylindrical). This method already has been employed for this purpose by Koch-Holm,[2] Lowry and Bozorth,[3] U. Hofmann and co-workers,[4] Berl,[5] Corriez[6] and others. The magnitude of the results reported is affected by the particular method of computation used and to some extent also by the X-ray technique employed. This should be borne in mind when comparing the results of different investigators. The method and technique employed by us, which have already been described in detail,[1] are believed to be in closest keeping with the most recent developments of X-ray crystallographic analysis. Although, in the present state of our knowledge, it is not possible to claim any high order of fundamental accuracy, it is probable

(1) Blayden, Riley and Taylor, *J. Chem. Soc.*, 67 (1939).

(2) Koch-Holm, *Wiss. Veroff. Siemens Konzern*, **6**, 188 (1927).

(3) Lowry and Bozorth, *J. Phys. Chem.*, **32**, 1524 (1928).

(4) Hofmann and Wilm, *Z. Elektrochem.*, **42**, 504 (1936).

(5) Berl, Andress, Reinhardt and Herbert, *Z. physik. Chem.*, **A158**, 273 (1932).

(6) Corriez, "Contribution à l'étude des variétés noires du carbone," Les Presses Universitaires de France, Paris, 1937.

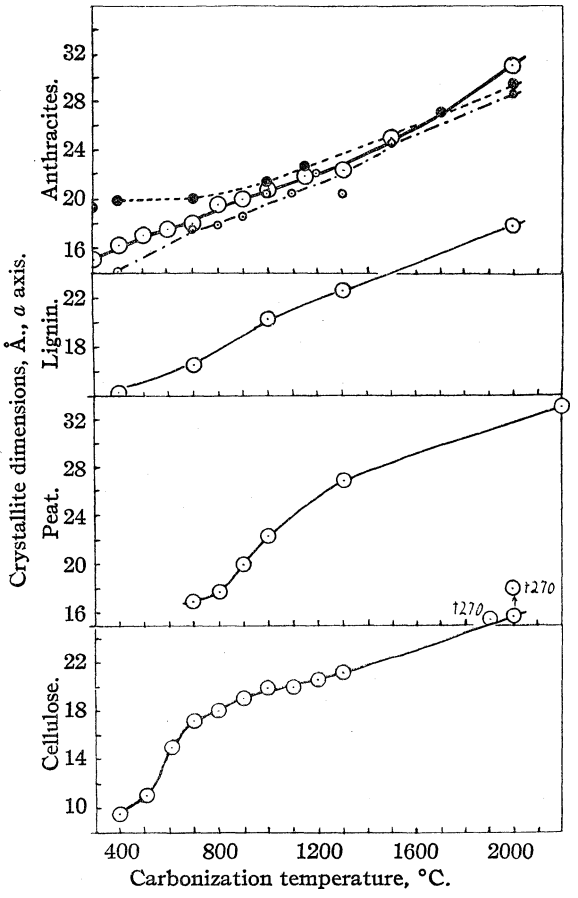


Fig. 1.—The influence of carbonizing temperature on *a* dimensions of crystallites. The results marked t270 for cellulose refer to samples which had been maintained for 270 minutes at the temperature shown. –⊙—⊙–, South Wales anthracite C527; -·⊙·-⊙·-, South Wales anthracite C607; –⊙---⊙–, American anthracite C618.

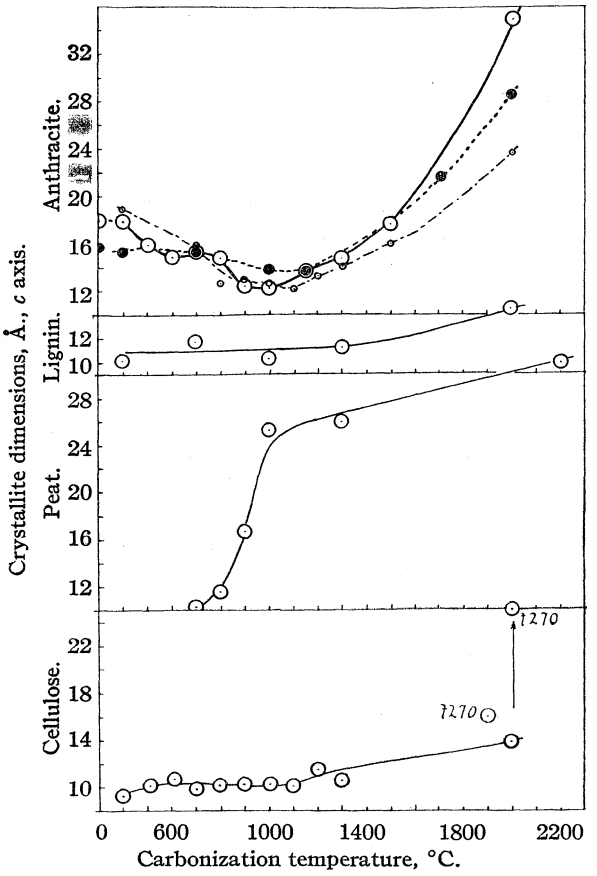


Fig. 2.—The influence of carbonizing temperature on *c* dimensions of crystallites. The results marked t270 for cellulose refer to samples which had been maintained for 270 minutes at the temperatures shown. –⊙—⊙–, South Wales anthracite C527; -⊙·-·-⊙-, South Wales anthracite C607; –⊙----⊙–, American anthracite C618.

that the results are relatively correct to within 10%.

The general picture of crystallite growth during carbonization which it is possible to form from our own observations and the work of other investigators, particularly U. Hofmann, is as follows. Crystallite growth as a result of processes occurring in the condensed phase with rise of temperature can be divided into three stages. *Stage 1:* from ordinary temperatures to approximately 700°.—In this temperature range the process is essentially one of aromatic condensation or aromatization, the main feature of the growth being the lateral extension of the hexagon layer planes of the graphite crystallites with little or no growth of the crystallites at right angles to the layer planes (*c* direction). That aromatization starts at relatively low temperatures when entirely non-aromatic substances are used has been demonstrated by Smith and Howard.[7] The experiments of Juettner[8] on the formation of mellitic acid from carbon show in a striking way the fundamental significance of 700° in relation to carbonization. *Stage 2:* from 700° to the temperature at which thermal recrystallization commences.—In this temperature range the *c* dimension remains constant and the *a* dimension (average diameter of cylindrical crystallites) increases slowly with rise in temperature. The most obvious explanation of this continued lateral growth of the layer planes appeared to be that the volatile matter still remaining in the carbon at 700° provided the carbon atoms for further aromatization. The results reported in the present paper, however, throw some doubt upon the validity of this

(7) Smith and Howard, THIS JOURNAL, 59, 234 (1937).
(8) Juettner, *ibid.*, 59, 1472 (1937).

simple explanation, for when the carbonization is carried to temperatures at which the residue is practically 100% carbon, the linear (*a*) dimensions of the crystallites continue to increase with temperature at the same rate as at lower temperatures. *Stage 3:* from the point at which thermal recrystallization commences upward.—During carbonization, at a more or less definite temperature, the *c* dimension, *i. e.*, the average number of layer planes in the crystallites, begins to increase rapidly. This type of growth which begins in certain cases sharply may be referred to conveniently as "thermal recrystallization," for it undoubtedly involves crystallites growing at the expense of their neighbors. Probably this type of growth is susceptible to "catalytic" influences perhaps due to inorganic substances present. In certain cases it begins at surprisingly low temperatures.

For purposes of comparison we propose to refer to the type of growth shown in the carbonization of cellulose as "normal," *viz.: Stage 1*, more or less rapid increase of the *a* dimension, *c* dimension constant; *Stage 2*, an equal or less rapid increase in the *a* dimension, *c* dimension constant; *Stage 3*, a relatively sharp onset of rapid growth in the *c* direction at a relatively high temperature. We have reason to believe that when growth departs from this "normal" type, extraneous factors are present and in seeking to elucidate these, it is possible that new and fundamental light will be thrown upon the process of crystallite growth and the structure of carbon.

The results obtained in the case of two South Wales anthracites, an American anthracite from the Pennsylvania southern coal field, a lignin prepared from soft wood and an Irish peat, are summarized in Fig. 1 (*a* dimensions) and Fig. 2 (*c* dimensions). The results obtained with cellulose previously reported[1] together with results obtained at higher temperatures, have been included for comparison purposes. Details of the X-ray and analytical results are given in Tables I–V.

Anthracites.—Ten-gram samples of the anthracites, graded between 60 and 100 I. M. M. sieves were carbonized in an atmosphere of nitrogen at 5°/min. up to the required temperature, the product being maintained at the final temperature for ten minutes and allowed to cool in nitrogen. This procedure was adopted for the preparation of cokes up to 1300°. A specially constructed carbon tube resistance furnace which operated in vacuum was employed for the preparation of the cokes at temperatures above 1300°. The rate of heating in this furnace could not be controlled so precisely as in the low temperature furnace as it was necessary occasionally to slow down the rate of heating in order to prevent the powdered charge being blown out of the tube due to the too rapid evolution of gas in the vacuum. The carbons heated to high temperatures in the carbon tube vacuum furnace were given a preliminary carbonization in nitrogen up to 1000° in the wire resistance tube furnace. In order to prevent the appearance of lines due to ash on the X-ray photograph the samples were thoroughly extracted after carbonization by boiling with 20% hydrochloric acid followed by two evaporations with hydrofluoric acid, then by another treatment with hydrochloric acid. This was usually sufficient to reduce the amounts of crystalline ash constituents to such an extent that no trace of ash lines was visible on the powder photographs. The coals and cokes after this treatment contained appreciable amounts of very firmly adsorbed hydrochloric acid (*vide infra*). To remove this it was necessary to heat the sample in vacuum to 110°. Duplicate chemical analyses were made and powder photographs taken from which crystallite dimensions were computed by the method already described.

The *a* dimension-carbonizing temperature curves obtained with these anthracites are interesting in several respects. In stage 1, the anthracite curves are consistently higher than the bituminous coal curve already reported. It is noteworthy that the American anthracite itself (95.92% C) and the cokes prepared from it up to 700° all give *a* dimensions greater than the corresponding samples prepared from the two Welsh anthracites (92.50 and 93.64% C). These results are in accord with the views of Bone and coworkers and others upon the relationship between coal rank and the development of "benzenoid" characteristics. Another interesting feature which could perhaps have been anticipated from the experiments of Juettner[8] is that the crystallite *a* dimensions for the two Welsh anthracite 700° cokes (18.0 and 17.6 Å.) and the *a* dimension of a corresponding bituminous coal coke crystallite

TABLE I

EXAMINATION OF S. WALES ANTHRACITE C527

Analysis of C527: ash, 1.0 (dry coal basis); C, 93.64; H, 2.75 (dry, ash-free basis).

Carbonization temp., °C.	Analysis (dry, ash-free basis) C, %	H, %	Crystallite size, Å. *a*-axis	*c*-axis	Interatomic dist., Å.	Interlayer plane dist., Å.
400	92.35	2.80	16.3	17.8	1.38	3.41
500	92.36	2.76	16.6	15.9	1.38	3.44
600	92.40	2.50	17.6	14.9	1.38	3.45
700	92.38	2.25	18.0	15.4	1.38	3.50
800	93.40	1.54	19.6	14.8	1.38	3.54
900	94.10	0.84	20.0	12.4	1.38	3.52
1000	94.74	.83	20.6	12.3	1.38	3.60
1150	96.90	.46	21.8	13.7	1.38	3.55
1300	98.32	.23	22.4	14.8	1.37	3.46
1500	..	..	25.0	17.6	1.39	3.47
2000	99.44	..	31	35	1.41	3.38

TABLE II

EXAMINATION OF S. WALES ANTHRACITE C607

Analysis of C607: ash, 4.0 (dry coal basis); C, 92.50; H, 3.37 (dry, ash-free basis).

Carbonization temp., °C.	Analysis (dry, ash-free basis) C, %	H, %	Crystallite size, Å. *a*-axis	*c*-axis	Interatomic dist., Å.	Inter layer plane dist., Å.
400	92.20	3.20	14.2	19.0	1.38	3.40
700	93.12	2.37	17.6	15.7	1.38	3.45
800	94.34	1.55	18.0	12.7	1.38	3.53
900	95.34	0.97	18.7	12.8	1.38	3.60
1000	95.84	.63	20.6	12.6	1.38	3.60
1100	96.66	.44	20.5	12.2	1.38	3.54
1200	97.76	.28	22.2	13.3	1.39	3.60
1300	97.82	.18	20.5	14.0	1.38	3.59
1500	98.56	.05	24.8	16.0	1.39	3.51
2000	99.26	..	28.7	23.8	1.40	3.41

TABLE III

EXAMINATION OF AMERICAN ANTHRACITE C618

Analysis of C618: ash, 2.95 (dry coal basis); C, 95.92; H, 1.93 (dry, ash-free basis).

Carbonization temp., °C.	Analysis (dry, ash-free basis) C, %	H, %	Crystallite size, Å. *a*-axis	*c*-axis	Interatomic dist., Å.	Inter layer plane dist., Å.
400	95.96	1.67	20.0	15.4	1.39	3.44
700	95.70	1.61	20.0	15.4	1.38	3.43
1000	..	..	21.4	13.8	1.39	3.54
1150	98.14	0.40	22.6	13.7	1.39	3.53
1700	99.62	..	27.6	21.5	1.39	3.44
2000	..	..	29.6	28.5	1.40	3.42

(18.2 Å.) are approximately the same while the American anthracite 700° coke gives a value only slightly greater (20.0 Å.). It is also perhaps significant that in stage 2, the growth curves of all four coals are approximately concurrent.

As far as our knowledge goes at present it would appear that the extent to which the lateral growth of a crystallite can occur in the earlier stages of carbonization must be governed primarily by two factors, *viz.* (1) the number of graphite nuclei present in the parent material or formed during carbonization, around which aromatic condensation occurs, and (2) the chemical nature of the carbonaceous material, *e. g.*, substances containing much oxygen would be expected, when carbonized, to give off a larger proportion of volatile matter and, other things being equal, to form smaller crystallites. The remarkable similarity of the *a* dimension of the 700° coke crystallites prepared from quite diverse substances suggests that other and possibly more fundamental factors control crystallite growth in stage 1.

The *c* dimension growth curve (Fig. 2) shows a very different state of affairs from that obtaining with the cellulose, lignin and Northumberland coal. Whereas with the latter the *c* dimension remains constant over a considerable range of carbonizing temperature this is not so with the anthracites. The Welsh anthracite crystallites contain on the average 6 layer planes and the American anthracite 5.6. At a carbonizing temperature of 400° the *c* dimension begins to decrease and at 900° reaches a value corresponding to an average of approximately 4.5 layer planes. As the temperature is further increased the crystallites show a pronounced growth in the *c* direction. This phenomenon is not quite so pronounced with the American as with the Welsh anthracites.

It already has been pointed out[1] that the *c* spacing is an inverse function of the *c* dimension. This fact provides an interesting and independent check of the crystallite size determinations. In Fig. 3, *c* dimension has been plotted against *c* spacing for a large number of crystallites and it will be seen that the anthracite results fall on a smooth curve drawn through these points.

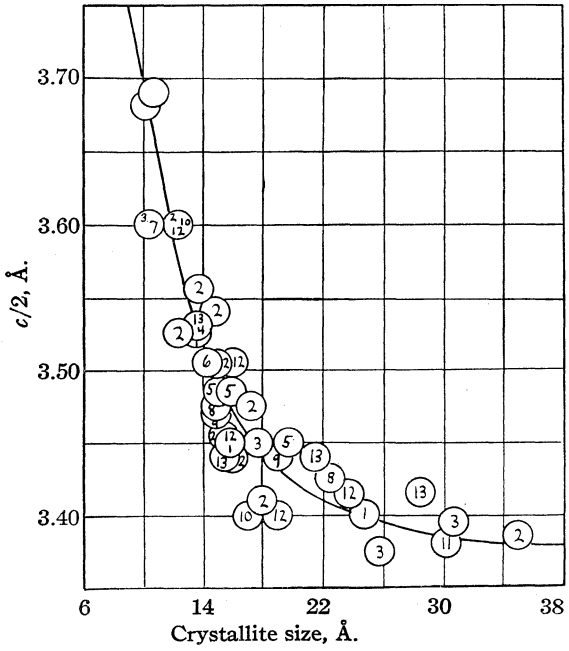
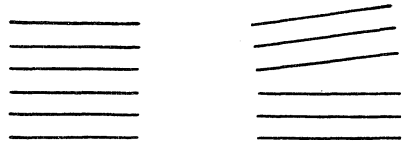


Fig. 3.—Variation of interplanar distances with crystallite size in *c* direction: 1, cellulose carbons; 2, S. W. anthracite C527; 3, peat; 4, coke C518; 5, coke C383; 6, lignin; 7, wood; 8, coke C526; 9, coke C528; 10, coke C458; 11, pentadiene carbon; 12, S. W. anthracite C607; 13, American anthracite C618.

It is apparent from Fig. 1 that the lateral growth of the layer planes as the temperature increases is much too small to account for the decrease of the *c* dimension by the lateral growth of certain

of the layer planes at the expense of others. The most probable explanation appears to be that rise of temperature causes disruption of the original anthracite crystallites in the manner shown in Fig. 4. It is possible that this phenomenon is connected with the decrepitation which occurs when many anthracites are heated rapidly, for if the above explanation is correct then rise of temperature will be accompanied by a disruption of the crystallites and a consequent anisotropic expansion along the *c*-axis which would be sufficient to cause decrepitation.



(a) Original anthracite layer planes.

(b) Probable disorder introduced into the anthracite crystallite by heating to 500–900°.

Fig. 4.

The question naturally arises as to why this crystallite disruption occurs with the anthracites studied and not with the Northumberland coal and several other bituminous coals upon which preliminary tests have been made. Although a much greater number of coals must be examined before this question can be answered, the following points are worthy of consideration. Theoretical considerations have been advanced[9] which indicate the possibility of bonding hydrogen atoms or ions between the layer planes of the graphite crystal lattice. Anthracite has been reported to have an adsorptive power greater than coals of lower rank for both carbon dioxide[10] and methane.[11] These facts suggest that the disruption of the anthracite crystallites on heating, may be connected with the desorption of interstitially adsorbed gas, probably hydrogen. The fact that gas evolution and crystallite disruption commence at approximately the same temperature supports this hypothesis.

Lignin.—The lignin used was prepared from soft wood sawdust by Klason's method[12] and cokes were made from it in the manner already described. It will be seen from Fig. 1 that in stage 1 the lignin coke crystallites show an *a* dimension growth curve very similar to that of the anthracites. This is probably a reflection of the fact that the lignin itself contains highly condensed aromatic molecules[13] arranged in a lattice which must in many respects be similar to that of a graphite crystallite.[14]

TABLE IV

EXAMINATION OF LIGNIN

Analysis of lignin: ash, 0.59 (dry basis); C, 65.70; H, 4.57 (dry, ash-free basis).

Carbonization temp., °C.	Analysis (dry, ash-free basis) C, %	H, %	Crystallite size, Å. *a*-axis	*c*-axis	Interatomic dist., Å.	Interlayer plane dist., Å.
400	76.01	3.38	14.3	10.3	1.38	3.60
700	91.72	1.73	16.6	11.8	1.38	3.69
1000	96.62	0.57	20.4	10.4	1.37	3.69
1300	98.90	.20	22.6	11.2	1.37	3.75
2000	..	..	27.9	14.3	1.40	3.51

In other respects the lignin crystallite growth curves can be considered normal. The preparation of lignin involved the extraction of wood with strong mineral acid which removed not only the cellulose but also the major part of the inorganic constituents. The cokes were thus prepared from a material relatively low in ash. This is probably connected with the fact that thermal recrystallization as evidenced by the rapid increase of the *c* dimension only sets in at relatively high temperatures (*vide infra*).

Peat.—The Irish peat employed was from Turraun, and its properties already have been described in detail.[15] Owing to its ash content and the difficulty of eliminating this from the cokes prepared at low temperatures by acid extraction, it has not yet been possible to prepare X-ray photographs, for stage 1 of the growth curves, sufficiently free from ash lines to permit of their use in crystallite size determinations. The results recorded are from 700° upward. The growth curves are entirely anomalous. The growth of the *a* dimension between 700 and 1300° is considerably greater than that recorded for the other materials studied. More surprising is the rapid growth of the *c* dimension which occurs between 700 and 1000°. This is not an isolated result. Preliminary experiments have shown that

(9) Balfour, Riley and Robinson, *J. Chem. Soc.*, 456 (1936). See also Lowry, THIS JOURNAL, **46**, 824 (1924); *J. Phys. Chem.*, **33**, 1332 (1929).

(10) Sinkinson and Turner, *Ind. Eng. Chem.*, **18**, 602 (1926).

(11) Coppens, *Ann. Min. Belg.*, **37**, 173 (1936).

(12) Klason, *Chem. Rev.*, **14**, 117 (1934).

(13) Fuchs, *Brennstoff-Chem.*, **9**, 178 (1928); Fischer, *Abh. Kohle*, **6**, 277 (1923).

(14) Sedletzky and Brunowsky, *Kolloid Z.*, **73**, 90 (1935).

(15) D. S. I. R., Fuel Research Board, Technical Paper No. 4.

other Irish peats behave similarly. Two explanations of this phenomenon suggest themselves. The anomalous growth may be due to either (a) something inherent in the organic structure of the peat material or (b) a catalytic effect. (a) appears unlikely for the following reasons: (1) the anomalous growth in the *c* direction is not shown by cellulose, lignin or a sample of soft wood; (2) the X-ray photographs of the cokes give no indication that their organic structures are fundamentally different from those of other carbonaceous materials; (3) the anomalous growth is not prevented by carbonizing in high vacuum instead of nitrogen. The evidence in favor of (b) is as follows: (1) the ash content of the peat is higher than that of the other carbonaceous materials employed; (2) the ash is probably intimately associated with the organic matter, for acid extraction fails to remove it completely; (3) the carbonaceous material remaining after extraction of the original peat with boiling concentrated or dilute (2%) hydrochloric acid behaves normally and does not show the rapid growth in the *c* direction at low temperatures. Such treatment might, however, besides extracting ash, also bring about an alteration in the nature of the organic matter present; (4) attempts to promote growth in the *c* direction at low temperatures by the pretreatment of ash-free cellulose with iron and alkali salts so far have been unsuccessful. At higher temperatures (1600°), inorganic additions have a very pronounced effect, promoting very rapid growth.[16] Details of these experiments will be published at a later date.

TABLE V

EXAMINATION OF IRISH PEAT C445

Analysis of Irish peat: ash, 3.5 (dry basis); C, 57.22; H, 5.27 (dry, ash-free basis).

Carbonization temp., °C.	Analysis (dry, ash-free basis) C, %	H, %	Crystallite size, Å. *a*-axis	*c*-axis	Interatomic dist., Å.	Interlayer plane dist., Å.
400	76.35	3.92	..	..	..	..
700	90.12	1.76	17.0	10.3	1.38	3.60
800	91.80	1.20	17.8	11.5	1.38	3.58
900	93.88	0.68	20.0	16.7	1.39	3.45
1000	95.70	.56	22.4	25.2	1.39	3.36
1300	97.94	.27	27.4	25.8	1.39	3.38
2200	99.4	..	32.8	30.8	1.38	3.39

Although at present it is not possible to put forward a definite explanation of this phenomenon, these results suggest the possibility of rendering the carbon atoms in the graphite crystallites highly mobile at relatively low temperatures with a consequent enhancement of their reactivity.[17]

The pronounced falling off in the rate of growth in the *c* direction at 1000° may be due either to (a) the elimination of the catalyst by volatilization or (b) change in the degree of contact of individual crystallites, brought about by the pronounced growth which already has occurred.[18]

Crystallite Growth at High Temperatures.—With temperatures up to 1300°, a carbonization rate of 5° per minute and heating for ten minutes at the final temperature provides sufficient time for maximum growth. No appreciable further growth was detected when cellulose cokes were heated for an additional period of five hours at the maximum temperature. The nature of the growth occurring at temperatures greater than 1600° may be of a different character from that occurring at lower temperatures. The results obtained with cellulose show that after carbonizing at 5° per minute the retention of the specimen at the final temperature for several hours brings about considerable further crystallite growth.

The form of the *c* dimension curves of the anthracites, which were carbonized in the presence of their ash, compared with the corresponding curves for cellulose and lignin both of which were subjected to a preliminary acid extraction, suggests that the inorganic constituents must play an important role in the growth process at high temperatures.

The Adsorption of Hydrochloric Acid by Coals and Cokes.—The anomalous nature of the ultimate analyses of the cokes prepared from the anthracites after extraction with hydrochloric and hydrofluoric acids led us to investigate the adsorption of hydrochloric acid by these substances. It was discovered that both the coals and the cokes adsorb considerable quantities of hydrochloric acid which is not eliminated by several hours of heating in vacuum at 110°. That this adsorbed hydrochloric acid replaces some of the inherent water in the air dried coals is shown by the following results.

	%
(a) Increase in weight of anthracite after extraction with hydrochloric acid	2.11 (dry coal basis)
(b) Chlorine content of anthracite after extraction with hydrochloric and hydrofluoric acids	2.28 (dry coal basis)

(16) *Cf.*, however, statements of Arsem, *Trans. Am. Electrochem. Soc.*, **20**, 105 (1911).

(17) *Cf.* investigations of Hedvall, *Z. Elektrochem.*, **45**, 83 (1939).

(18) Wesselowsky and Pertzov, *Z. anorg. Chem.*, **216**, 228 (1934).

	%
(c) Moisture content of the air dried anthracite before extraction with hydrochloric acid	2.5
(d) Moisture content of the air dried anthracite after extraction with hydrochloric acid	0.5

The hydrochloric acid contents of a series of cokes after extraction with this acid and subsequent drying at 110° are shown in Table VI.

TABLE VI

ADSORPTION OF HYDROCHLORIC ACID

Carbonization temp., °C.	HCl adsorbed, % of dry substance			
	Anthracites C527	C607	Lignin	Irish peat
400	0.83	1.50	0.43	2.38
500	1.07	..	..	..
600	0.72	..	..	..
700	.59	1.60	.74	3.18
800	.51	1.45	..	1.96
900	.72	1.51	..	0.91
1000	.09	0.71	.04	.92
1100	..	.49	..	..
1150	.19	..	..	..
1200	..	.06	..	..
1300	..	..	Trace	1.18

It will be seen (Table VI) that the amount of adsorbed hydrochloric acid passes through a maximum with the 700° coke, which is significant in view of the results of other investigations on adsorptive power.[7]

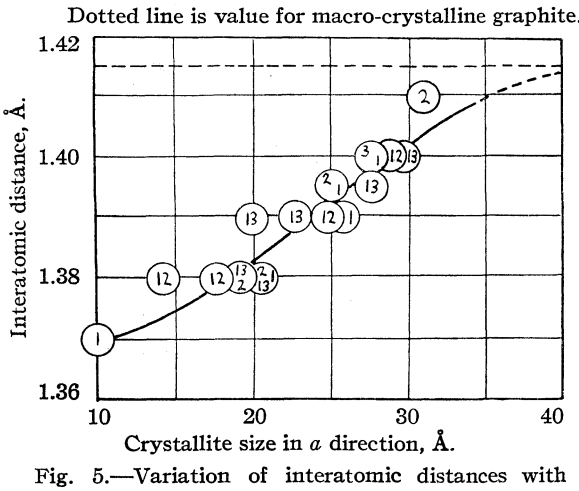


Fig. 5.—Variation of interatomic distances with crystallite size in *a* direction: 1, cellulose carbons; 2, S. W. anthracite C527; 3, peat; 4, coke C518; 5, coke C383; 6, lignin; 7, wood; 8, coke C526; 9, coke C528; 10, coke C458; 11, pentadiene carbon; 12, S. W. anthracite C607; 13, American anthracite C618.

Variation of C–C Spacing with Crystallite Size.—It already has been pointed out that the *c* spacing is an inverse function of the number of layer planes in the crystallite. The C–C spacing in the layer planes also shows an interesting variation with crystallite size. The C–C spacing in the layer planes of macrocrystalline graphite is 1.415 Å., while in the microcrystalline carbons already studied it is approximately 1.37–1.38 Å. The measurements recorded in this paper indicate that the latter value increases as the crystallites grow. Figure 5 shows the C–C spacing plotted against the *a* dimension of the layer plane.

Conclusion.—It is apparent from the above results that investigations of this kind are likely to throw considerable light upon the ultimate nature of coals and "amorphous" carbons and upon the changes which these substances undergo on heating. The investigation already has revealed a number of quite unexpected results and it would therefore at this stage be unwise to theorize as there is still a host of very diverse carbonaceous materials, both synthetic and natural, to be studied.

The authors are indebted to the Northern Coke Research Committee for permission to publish this paper, to Dr. F. S. Sinnatt (Director, Fuel Research Board, D. S. I. R.) and the Amalgamated Anthracite Co., Wales, for samples of peat and anthracite, respectively, and to Dr. A. C. Fieldner (U. S. Bureau of Mines) and the Lehigh Navigation Coal Co., Pa., for samples of the American Anthracite. They also record their thanks to Messrs. J. Gibson, B. Sc. and J. Almond for assistance with the analyses.

Summary

The investigations of crystallite growth during carbonization in the temperature range 400–1300°[1] have now been extended to include one American and two Welsh anthracites, lignin and an Irish peat, and carbonization temperatures up to 2200°. The anthracites and the peat all show interesting anomalies in their crystallite growth curves. The anthracite crystallites show a decrease in the *c* dimension as the carbonization temperature is increased from 400 to 900°. This has been interpreted as due to disruption of the crystallites. The peat coke crystallites show a very rapid growth in the *c* direction between 700 and 1000° which is probably due to a catalytic effect.

The significance of the results obtained is discussed in detail.

NEWCASTLE-UPON-TYNE, ENGLAND
RECEIVED SEPTEMBER 18, 1939

[CONTRIBUTION FROM THE MORLEY CHEMICAL LABORATORY, WESTERN RESERVE UNIVERSITY]

Thermodynamic Properties of the Hexyl Alcohols. III. 2-Methylpentanol-3 and 3-Methylpentanol-3

BY FRANK HOVORKA, HERMAN P. LANKELMA AND ABRAHAM E. AXELROD

This paper represents the third[1,2] of a series of investigations being carried out in this Laboratory dealing with the relation between the physical properties and chemical constitution of the hexyl alcohols, and concerns the vapor pressure, viscosity, surface tension, density and refractive index of 2-methylpentanol-3 and 3-methylpentanol-3.

Experimental

Preparation of Materials.—2-Methylpentanol-3 was prepared from ethyl bromide and isobutyraldehyde by the Grignard synthesis.[3] 3-Methylpentanol-3 was obtained from the Eastman Kodak Co. and further purified.

Purification.—The fractionating columns employed for the initial and final distillations have been described previously.

"Drierite"[4] was used as the drying agent for both alcohols. The alcohols were allowed to stand over the "Drierite" for two weeks, filtered, and then fractionally distilled.

The alcohols were considered pure when the final boiling point range did not exceed 0.02°.

Apparatus and Procedure for Determining Physical Constants.—The apparatus and the procedures used in this research are those described by Hovorka, Lankelma and Stanford.[2]

All of the instruments used in the surface tension, density, and viscosity measurements were recalibrated before determinations were made.

Discussion of Results

Vapor Pressure.—The vapor pressure data are tabulated in Table I, column 5.

The summary of the values calculated from the vapor pressure data is given in Table II. The constants of the Rankine equation are designated as A, B, and C. The vapor pressures calculated from the Rankine equation agree quite closely with the observed values.

The values of the Trouton constant are considerably higher than the normal value of 21 and indicate varying degrees of association. These high values correspond with those found by Hovorka, *et al.*,[1,2] for the hexanols thus far reported.

Viscosity.—The viscosity data are collected in Table I, column III. The relationship between chemical structure and viscosity is an obscure one since the curves of viscosity *vs.* temperature possess different slopes and even tend to cross each other. This fact has been noted previously. It is significant to observe, however, that the temperature *vs.* viscosity curves for the two hexanols under observation tend to approach the same value at 60° and that from 60 to 130°, the two hexanols have practically the same viscosity values. This behavior may be interpreted by assuming that the molecular aggregation of the alcohols is the same in the temperature interval 60–130°.

Stewart[5] has shown that there are two types of association found among alcohols. According to his theory, both of the hexanols under investigation are associated side by side, the spacing corresponding to one molecular length. Assuming that association takes place through the hydroxyl group, the shielding effect upon the association forces should be approximately the same in both cases. This observation is borne out by the fact that the slopes of the viscosity *vs.* temperature and the density *vs.* temperature curves are practically the same in the temperature interval 60–130°, thus pointing to the fact that the breakdown of these association complexes with temperature is approximately the same for both hexanols.

Plots of Raman's equation[6] and Andrade's[7] equation for 2-methylpentanol-3 yielded perfectly symmetrical curves instead of the straight lines which are to be expected if the equations held. In the case of 3-methylpentanol-3, the plot of the Andrade equation showed a decided break in the higher temperature range. A similar break occurs in the same temperature range when the specific volumes of 3-methylpentanol-3 are plotted against temperature. The constants

(1) Hovorka, Lankelma and Naujoks, THIS JOURNAL, **55**, 4820 (1933).
(2) Hovorka, Lankelma and Stanford, *ibid.*, **60**, 820 (1938).
(3) Pickard and Kenyon, *J. Chem. Soc.*, **101**, 620 (1912).
(4) Hammond and Withrow, *Ind. Eng. Chem.*, **25**, 1112 (1933).
(5) Stewart, *Phys. Rev.*, **24**, 919 (1927).
(6) C. V. Raman, *Nature*, **111**, 532 (1923).
(7) E. N. Andrade, *Phil. Mag.*, **17**, 497, 698 (1934).

TABLE I

SURFACE TENSION, VISCOSITY, DENSITY, VAPOR PRESSURE, AND REFRACTIVE INDEX

Temp., °C.	Surface tension, dynes	Abs. viscosity	Abs. density	Vapor press., mm.	Index of refraction	Parachor	Eötvös constant	Total surface energy, ergs
			A. 2-Methylpentanol-3					
5.0	25.72	0.10174	0.83713	...	....	274.7	..	...
15.0	24.95	.05768	.82911	...	1.4189	275.2	1.58	47.14
25.0	24.14	.03640	.82064	6.0	1.4148	275.8	1.59	49.49
35.0	23.33	.02400	.81182	10.5	1.4100	276.4	1.81	47.99
45.0	22.45	.01675	.80300	20.0	1.4049	276.8	1.84	50.76
55.0	21.55	.01230	.79346	36.0		277.3	1.88	50.76
65.0	20.64	.00928	.78380	63.0		277.9	2.01	51.41
75.0	19.70	.00729	.77362	103.8		278.1	2.14	52.77
85.0	18.72	.00589	.76295	163.0		278.6	2.10	54.50
95.0	17.69	.00485	.75173	247.0		279.1	2.07	53.78
105.0	16.75	.00409	.73987	364.0		279.9	2.38	53.05
115.0	15.70	.00355	.72787	520.0		280.0	2.47	56.84
125.0	14.61	.00315	.71860	719.0		280.1	2.42	57.62
126.0	...	...	...	744.2		...	..	...
128.0	...	...	...	790.0		...	..	...
			B. 3-METHYLPENTANOL-3					
5.0	24.63	0.07341	0.83861	...	....	271.2	..	...
15.0	23.93	.04565	.82866	...	1.4123	272.5	1.20	44.14
25.0	23.27	.03040	.81903	18.0	1.4079	273.6	1.32	42.94
35.0	22.55	.02150	.80911	23.8	1.4038	275.0	1.57	44.43
45.0	21.74	.01545	.79864	38.0	1.3990	276.1	1.78	47.51
55.0	20.85	.01175	.78808	61.0		276.9	1.82	49.73
65.0	19.95	.00920	.77705	92.0		277.8	2.00	50.39
75.0	19.00	.00731	.76588	139.5		278.5	2.07	52.40
85.0	18.02	.00600	.75447	211.0		279.3	2.02	52.41
95.0	17.03	.00498	.74265	310.8		280.0	2.59	51.68
105.0	15.97	.00425	.73057	450.5		280.0	2.49	59.05
115.0	14.87	.00366	.71860	632.0		279.9	2.54	57.53
120.0	...	...	...	740.0		...	..	...
121.0	...	...	...	762.8		...	..	...
123.0	...	...	...	810.0		...	..	...

TABLE II

SUMMARY OF VALUES CALCULATED FROM VAPOR PRESSURE DATA

Substance	A	B	C	Max. devn. +	Max. devn. −	Av. devn.	Heat of vapn.[a]
2-Methylpentanol-3	−5078.0	−16.9262	59.6217	0.28	1.4	−0.40	10,624
3-Methylpentanol-3	−2013.4	− 1.0840	5.1802	1.15	2.14	− .03	10,057

	Boiling point, °C.[b]	Trouton's constant
2-Methylpentanol-3	126.68° ± 0.02	26.6
3-Methylpentanol-3	120.91° ± .02	25.5

[a] These are average values calculated from the slope of the curve obtained by plotting log P against $1/T$. [b] Boiling point values were obtained by interpolation from the vapor pressure curves.

of the Andrade equation were evaluated by the method of least squares and the viscosities calculated. The constants and the deviations of the calculated from the observed viscosities are given in Table III. The symmetrical nature of these deviations is very evident. The above observations are in accordance with those previously found.

TABLE III

CONSTANTS FOR THE EQUATION $nv^{1/3} = Ae^{c/VT}$

	$A \times 10^{-6}$	C	Maximum deviation +	Maximum deviation −
2-Methylpentanol-3	17.34	2804	15.2	25.6
3-Methylpentanol-3	36.12	2493	13.3	14.6

Bingham and co-workers[8,9] have proposed various methods for the calculation of the degree of association of liquids which are based upon the premise that fluidities are additive and that, accordingly, liquids should be compared at temperatures of equal fluidity. The association

(8) Bingham and Spooner, *J. Rheol.*, **3**, 228 (1932).
(9) Bingham and Darral, *ibid.*, **1-2**, 174 (1929-31).

factors of 2-methylpentanol-3 and 3-methylpentanol-3 have been calculated from Bingham's "atomic constants" and are given in Table IV.

Refractive Index.—Using the values given by Eisenlohr[10] for the atomic refractive constants of carbon, hydrogen and oxygen, we have calculated the molecular refractive power of 2-methylpentanol-3 and 3-methylpentanol-3. These values are compared in Table V with those calculated from the Lorenz–Lorentz formula.

TABLE IV

CALCULATION OF ASSOCIATION FROM FLUIDITY

200 rhes			300 rhes		
Calcd. temp., °A.	Obsd. temp., °A.	X	Calcd. temp., °A.	Obsd. temp., °A.	X
2-Methylpentanol-3					
271.1	367.0	1.36	305.5	393.0	1.28
3-Methylpentanol-3					
271.1	369	1.37	305.5	396.0	1.29

TABLE V

MOLECULAR REFRACTIVE POWER

	Lorenz–Lorentz equation	Summation of atomic constants
3-Methylpentanol-3	30.74	31.44
2-Methylpentanol-3	31.15	31.44

Surface Tension.—The surface tension data are collected in Table I, column 2.

The values of the Eötvös constant, parachor, and total surface energy were calculated over the entire temperature range and are tabulated in Table I. The general trend of these values is the same as that found by Hovorka, Lankelma and Stanford.[2] In all cases the values are those of associated substances.

(10) F. Eisenlohr, *Z. physik. Chem.*, **75**, 585 (1911).

If, according to Sidgwick, the parachor is to be used as a criterion for the degree of association, it is seen that 3-methylpentanol-3 is slightly more associated than 2-methylpentanol-3 at the lower temperature, and that both hexanols are more associated than those previously studied.

The critical constants have been calculated from the Ramsay–Shields equation and are given in Table VI. A large decrease in the values with increase in temperature is readily apparent.

TABLE VI

CRITICAL TEMPERATURES

Alcohol	T	°C.	T	°C.
2-Methylpentanol-3	364.7	(25–35)[a]	296.6	(115–125)
3-Methylpentanol-3	402.4	(25–35)	283.4	(105–115)

[a] The values in parentheses show the two temperatures used to calculate the critical temperatures in question.

Summary

1. The preparation and purification of two hexyl alcohols, 2-methylpentanol-3 and 3-methylpentanol-3, have been described.

2. The surface tension, density, viscosity and vapor pressure have been determined over the temperature range from 5° to the boiling point. The refractive index has been determined from 15 to 45°.

3. The average heat of vaporization and the constants for Rankine's equation have been calculated from vapor pressure data.

4. The parachor, Eötvös constant, total surface energy, and critical constants have been calculated from surface tension data.

CLEVELAND, OHIO RECEIVED OCTOBER 30, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY, GENERAL ELECTRIC COMPANY]

The Determination of Organic Peroxides

BY HERMAN A. LIEBHAFSKY AND WILLIAM H. SHARKEY

Because of possible explosion hazards,[1] and for other reasons, a rapid, accurate method for determining organic peroxides was needed in connection with a synthesis involving the distillation of large amounts of *n*-butyl ether. A modification of iodometric methods already in the literature[2] seemed most likely to meet the following requirements: (1) a reaction system homogeneous even during the titration; (2) a negligible blank; (3) liberation of iodine complete in less than ten minutes; (4) accuracy to within two drops of 0.01 *N* solution.

Simple experiments showed that homogeneity and rapid iodine liberation both can be obtained in glacial acetic acid. Separation into two phases, which occurs more readily with *n*-butyl than with ethyl ether, is avoided at room temperature if less than 8 cc. of water is added to 5 cc. of *n*-butyl ether dissolved in 25 cc. of the acid. The blank, however, is a more serious problem, especially since there is no guarantee that the reaction between oxygen and iodide (the "oxygen error"), which gives rise to the blank, will proceed independently of the reaction between peroxide and iodide. Numerous trials, which cannot be described in detail, showed the blank to be unreproducible but always too high when oxygen was present, even though light was rigorously excluded between mixing and titration. It was found that the blank could be eliminated satisfactorily by adding about 1.5 g. of sodium bicarbonate to the reaction mixture; the carbon dioxide produced is effective not only because it is heavier than air, but also because it is liberated within the reaction mixture, which it thus frees of oxygen.

The logical order of mixing is acetic acid, sodium bicarbonate, potassium iodide solution. With this sequence no appreciable iodine need be formed provided the acetic acid contains enough water to ensure vigorous effervescence before the iodide solution is added. Unfortunately, this amount of water retards the reaction between peroxide and iodide more than is desirable and leads to a rapid exhaustion of the bicarbonate. The reaction mixture was accordingly prepared as follows. To 25 cc. of glacial acetic acid and approximately 1.5 g. of sodium bicarbonate in a glass-stoppered flask, 1 cc. of potassium iodide solution (0.4 g./cc.) is added. The mixture usually becomes faintly yellow. 0.01 *N* thiosulfate is now added, two drops at a time, with gentle swirling, until the color is that of the end-point. (It is safer to take the end-point as the faintest yellow perceptible to the eye; starch is an unsatisfactory indicator in this system.) Because the reaction between sodium thiosulfate and iodine does not seem to be instantaneous in this medium, there is danger of adding too much thiosulfate unless ten seconds or so intervene between successive additions. When no further deepening of the iodine color occurs, the sample for the peroxide determination (in our case usually 5 cc. of *n*-butyl ether) is added, the flask is stoppered and placed in a dark cabinet for five minutes, and the iodine titrated thereafter with standard 0.01 *N* sodium thiosulfate solution. The flask is subsequently replaced in the cabinet for a similar time; if no further iodine formation occurs, the titration is satisfactory. This analytical method, which already has proved useful for the determination of other peroxides, was tested specifically on hydrogen peroxide dissolved in glacial acetic acid, on benzoyl peroxide in the same solvent, and on the peroxides in *n*-butyl ether. In the two former cases, the volume of thiosulfate solution was within approximately 0.1 cc. of that known to be equivalent to the amounts of the

(1) Rieche, *Z. angew. Chem.*, **44**, 896 (1931), gives the earlier literature. For recent correspondence on the subject, see *Chemistry and Industry*, **14**, 421, 580 and 964 (1936).

(2) (a) Rowe and Phelps, THIS JOURNAL, **46**, 2078 (1924); (b) Marks and Morrell, *Analyst*, **54**, 503 (1929); (c) Van Winkle and Christiansen, *J. Am. Pharm. Assoc.*, **18**, 1247 (1929); (d) Wheeler, *Oil and Soap*, **9**, 89 (1932); (e) Green and Schoetzow, *J. Am. Pharm. Assoc.*, **22**, 412 (1933); (f) French, Olcott, and Mattill, *Ind. Eng. Chem.*, **27**, 724 (1935). None of these methods meets all the requirements listed above.

A few experiments with cadmium iodide added to our reaction mixtures showed that its use detracted from our method. It appears to have been introduced (*cf.* (g) "U. S. Pharmacopoeia," 9th ed., 1916; and refs. 2a, 2c, and 2e) to minimize iodine liberation by oxygen in the qualitative test for peroxides in pharmaceutical ether, and then retained in the corresponding quantitative methods. It acts, through complex ion formation, to reduce the iodide concentration, but it is not very effective in dilute solution [Bates and Vosburgh, THIS JOURNAL, **60**, 137 (1938)]. However useful it may be in qualitative tests, its value in quantitative determinations is doubtful since a lower iodide concentration means a longer time for complete reduction of the peroxide, other things being equal. Certainly it appears to have no place in a method where the blank is negligible.

peroxides used; in the latter case, the analysis was considered satisfactory because samples permitted to stand for different times gave concordant results.

With this analytical method available, the observations of Table I were made on peroxide formation in *n*-butyl ether.

TABLE I

No.	Description of the ether	$10^3 \times$ peroxide normality
1	Stood in laboratory for several days	2.1
2	Exposed no. 1 to 2537 Å. (not monochromatic) for 30 min.	7.1
3	Exposed no. 1 to 3650 Å. (not monochromatic) for 30 min.	7.1
4	Left no. 3 near window for 1 day	8.5
5	No. 1 several days later	3.3
6	Refluxed no. 5 for 15 min.	0.9
7	Refluxed no. 6 for 15 min. longer	0.5
8	Fresh supply of ether	4.6
9	Bubbled oxygen for 15 min. through boiling no. 8 ether	24.6
10[a]	Bubbled oxygen for 45 min. longer through boiling no. 9 ether	66

[a] Intermediate values omitted. For an unknown reason, one of these was lower than the preceding value. This anomaly could not be reproduced.

The indications are that (1) exposure to ultraviolet radiation increases the peroxide concentration; (2) daylight is also effective; (3) refluxing destroys the peroxides; (4) bubbling oxygen through the boiling ether rapidly produces them. For the 5-cc. samples used, the average titration error (*ca.* 0.1 cc. of 0.01 *N* solution) corresponds to a peroxide concentration of $0.2(10^{-3})$ *N*.

Rates of Reactions.—During work on the analytical method, several observations on rates of reactions in glacial acetic acid containing water in varying amounts were made. These observations were confirmed in simple experiments, the results of which are given here in the hope that someone will find them sufficiently interesting to extend the investigations.

Owing to serious overstepping of the end-point, the titration of thiosulfate and iodine solutions in glacial acetic acid as a medium often gave erratic results when the amount of water in solution was small. The following experiment illustrates the difficulty involved: 100 cc. of glacial acetic acid and 1 cc. of 0.01 *N* sodium thiosulfate are thoroughly mixed, 0.6 cc. of 0.008 *N* tri-iodide solution is then added, and the solution shaken. Its color begins to disappear immediately, but the rate of disappearance decreases markedly with time. After several minutes, the solution is still colored; but it becomes colorless immediately upon being shaken with 10 cc. of water. If 10 cc. of water is added initially to the 100 cc. of acid, no appreciable persistence of color is observed. An experiment employing a photoelectric spectrophotometer confirmed these visual observations. The simplest, though by no means the only, explanation is that sodium thiosulfate and iodine do not react instantaneously in glacial acetic acid.

A crude measure of the rates at which various peroxides are reduced by iodide in glacial acetic acid was obtained in experiments carried out as follows. The peroxide solution was blown into the reaction mixture prepared as for the peroxide analysis, the initial time being observed on a suitable timer. A number of seconds later, when appreciable iodine formation had occurred, 0.01 *N* thiosulfate solution was added rapidly until the mixture was decolorized, at which point the final time was estimated. From the volume of thiosulfate solution required, the volume of thiosulfate, *a*, (determined on another sample) equivalent to the peroxide added to the reaction mixture, and the reaction time (in minutes), a first order rate constant, *k*, was calculated from the equation

$$kt = 2.3 \log \frac{a}{a - x}$$

The unproved assumption that the reaction is first order with respect to peroxides in this medium is based on reasonable analogy.[3] To measure the effect of added water on these reactions, a corresponding series of experiments with 3 cc. of water initially present in the reaction mixture was performed. The results are summarized in Table II. With the exception indicated, each value is the average of three rough determinations. In aqueous solution, with 0.1 *M* iodide and 1 *N* acid, *k* at 25° would be approximately[3b] $0.1(0.7 + 10.5) = 1$. More precise work of this kind should shed some light on acetic acid as a reaction medium and on any kinetic relationships of the organic

TABLE II

Peroxide	H_2O_2 in HOAc	Bz_2O_2 in HOAc	Peroxides in *n*-Bu_2O
k (no added water)	10[a]	1.9	2.5
k (3 cc. added water)	1.6	0.9	0.9

[a] Order of magnitude based on a single observation. Iodide concentration for these experiments, roughly 0.1 *M*.

(3) (a) Mohammad and Liebhafsky, THIS JOURNAL, **56**, 1680 (1934); (b) Liebhafsky and Mohammad, *ibid.*, **55**, 3977 (1933).

peroxides to hydrogen peroxide; that some simple relationships may exist is obvious from the above data.

Summary

A modified iodometric method for the determination of organic peroxides is described.

Certain observations have been made on the formation and decomposition of peroxides in *n*-butyl ether.

When tri-iodide solution is added to excess sodium thiosulfate in glacial acetic acid, the color fades at a measurable rate. The addition of water of course causes the fading to become practically instantaneous.

Crude rate measurements show that benzoyl peroxide and the peroxides in *n*-butyl ether are about equally reactive toward iodide in glacial acetic acid, and not much less reactive than hydrogen peroxide in the same medium. The addition of water retards all three reactions about equally.

SCHENECTADY, NEW YORK RECEIVED NOVEMBER 10, 1939

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

The Dipole Moments and Structures of Chlorine Compounds of Germanium, Chromium, Selenium and Tellurium

BY C. P. SMYTH, A. J. GROSSMAN AND S. R. GINSBURG

The dipole moments of monochloro and dichlorogermane, chromyl chloride, diphenylselenium dichloride and tellurium tetrachloride have been measured with the object of studying the structures of the molecules and obtaining information as to the magnitudes of the bond moments in the molecules. The moments were obtained with the apparatus and methods previously described,[1,2] with the exception of that of monochlorogermane, which was measured in the vapor state by Mr. R. H. Wiswall, Jr., the dielectric constants being determined at three temperatures so close together that the moment was calculated by subtracting a calculated molar refraction from the polarization. The experimental measurements on solutions of dichlorogermane in carbon tetrachloride carried out by Dr. George L. Lewis already have been published and discussed elsewhere. The value of the moment is included in Table II for comparison with that of monochlorogermane.

Preparation of Materials

Benzene[1] and carbon tetrachloride[2] were purified as in the work previously described.

Monochloro- and Dichlorogermane.—A kilogram of germanite containing 6% of germanium dioxide was obtained from the Foote Mineral Company and treated according to a procedure described by Professor J. H. Müller of the University of Pennsylvania in a communication to Professor N. H. Furman of Princeton University, to both of whom the authors wish to express their gratitude. By this procedure germanium was extracted from its ore as the tetrachloride, which was then hydrolyzed to form the dioxide. After the reduction of the latter in an atmosphere of hydrogen, it was combined with magnesium. The resulting germanide, treated with hydrochloric acid in an atmosphere of hydrogen, gave monogermane, which was purified by fractionation and mixed with an equal volume of hydrogen chloride over aluminum chloride as a catalyst according to the method of Dennis and Judy.[3] The resulting monochlorogermane and dichlorogermane were separated by fractionation at low temperatures, between 2 and 3 cc. of monochlorogermane and 1 cc. of dichlorogermane being obtained in the liquid form. In spite of careful fractionation, the samples could not be regarded as very pure. The stability of the monochlorogermane was sufficient to permit of its measurement in the vapor state over a limited temperature range, while decomposition of the dichlorogermane was rendered negligible by measurement in dilute solution.

Chromyl Chloride.—The compound was prepared by the method given by Henderson and Fernelius[4] and distilled at reduced pressure in an apparatus which had been dried by thorough baking.

Diphenylselenium Dichloride.—Material from the Eastman Kodak Company was recrystallized from dry benzene and dried in a vacuum desiccator.

Tellurium Tetrachloride.—Twenty-eight grams of C. P. tellurium in the form of sticks was placed in a distilling apparatus, which was then evacuated and baked. The gently heated tellurium was treated with a slow stream of dry chlorine, which converted it first into a black amorphous mass of tellurium dichloride and then into the white, crystalline tetrachloride. The latter was distilled into a side-arm where it gave an amber liquid, which solidified to white crystals.

(1) Lewis and Smyth, *J. Chem. Phys.*, **7**, 1085 (1939).

(2) Lewis and Smyth, THIS JOURNAL, **61**, 3063 (1939).

(3) Dennis and Judy, *ibid.*, **51**, 2321 (1929).

(4) Henderson and Fernelius, "Inorganic Preparations," McGraw-Hill Book Co., Inc., New York N. Y., 1935, p. 143.

Experimental Results

The dielectric constants ϵ and densities d of the solutions containing mole fraction c_2 of the polar solute and the polarizations, P_1 of the solvent and P_2 of the polar solute, are given in Table I. Table II gives values of the molar refractions MR_D for the D sodium line, calculated as the sum of atomic refractions obtained from Landolt–Börnstein or calculated from refraction data in the literature. The errors in MR_D are too small to have appreciable effect upon the values of the moments except in the case of chromyl chloride, the moment of which is enclosed in parentheses because of its uncertainty. The succeeding columns of Table II list the polarizations P_∞ obtained by extrapolating the P_2–c_2 curves to infinite dilution, except in the case of monochlorogermane, where P_∞ was obtained from measurements of the vapor at several different pressures, and the dipole moments μ. The measurements on diphenylselenium dichloride were made at 50° in order to take advantage of the greater solubility at the higher temperature.

TABLE I

DIELECTRIC CONSTANTS, DENSITIES AND POLARIZATIONS

c_2	ϵ	d	P_2
Carbon Tetrachloride–Chromyl Chloride (t = 25°)			
0.00000	2.236	1.5836	(28.35 = P_1)
.04836	2.258	1.5986	30.36
.09677	2.283	1.6171	30.13
Benzene–Diphenylselenium Dichloride (t = 50°)			
0.00000	2.224	0.8484	(26.67 = P_1)
.01110	2.403	.8679	289.0
.01786	2.505	.8782	281.6
Benzene–Tellurium Tetrachloride (t = 25°)			
0.00000	2.276	0.8729	(26.68 = P_1)
.00761	2.352	.8903	165.8
.00981	2.372	.8947	164.1
.01189	2.389	.8991	159.7

TABLE II

MOLAR REFRACTIONS, POLARIZATIONS AND DIPOLE MOMENTS

Substance	MR_D	P_∞ (t°)	$\mu \times 10^{18}$
GeH_3Cl	16.93	111.0(3.4°)	2.06
		105.0(14°)	2.03
		99.4(24°)	2.00
		Mean value	2.03
GeH_2Cl_2	21.8	123(25°)	2.21
CrO_2Cl_2	26	30.6(25°)	(0.47)
$(C_6H_5)_2SeCl_2$	74	301.2(50°)	3.47
$TeCl_4$	35	167(25°)	2.54

Discussion of Results

As germanium tetrachloride has been found by means of electron diffraction[5] to be tetrahedral, it is practically certain that monochloro and dichlorogermane are approximately tetrahedral. This means that, with inductive effects neglected, the resultant of the moments associated with the three hydrogen–germanium bonds in the monochlorogermane molecule should be equal to the moment of one bond and should lie in the line of the germanium–chlorine bond moment, that is, (H–Ge) + (Ge–Cl) = μ_{GeH_3Cl}, where the symbols in parentheses represent the bond moments. Also 1.15 (H–Ge) + 1.15 (Ge–Cl) = $\mu_{GeH_2Cl_2}$. If the bond moments depended wholly on intrinsic electronegativities of the two bonded atoms and were uninfluenced by induction, resonance effects and possible unknown factors, the moments of tetrahedral molecules like these germanes should be independent of the central atom and should depend simply on the differences in electronegativity of the attached atoms. This would mean that both methyl chloride and monochlorogermane would have the same moment as hydrogen chloride, 1.05×10^{-18}. The large effect of complicating factors in raising the carbon–chlorine, –bromine, and –iodine bond moments above the values to be expected on the basis of hydrogen bond moments has been pointed out previously.[6] It is evidently even greater in the case of the germanium–chlorine bond moments, as shown by the large moments of these chlorogermanes. In the case of the chlorosilanes[7] and silicobromoform,[2] the complicating factors seem to compensate one another to such an extent that the moments are not far from the values to be expected on the basis of hydrogen bond moments. The value of the moment of monochlorogermane is in accordance with the ideas previously presented[2] in connection with the relation of the moment of dichlorogermane to the moments of carbon, silicon and tin compounds. As the H–C moment is only about 0.3 and as the H–Ge moment is undoubtedly lower than this, possibly, acting in the opposite direction, it may be concluded that the Ge–Cl moment is about 2, or larger than this by the amount of the Ge–H moment.

For comparison of the moments of the two

(5) Brockway, *Rev. Modern Phys.*, **8**, 231 (1936).

(6) Smyth, *J. Phys. Chem.*, **41**, 209 (1937); THIS JOURNAL, **60**, 183 (1938).

(7) Brockway and Coop, *Trans. Faraday Soc.*, **34**, 1429 (1938).

chlorogermanes, it is desirable to use the gas value 2.34 calculated empirically[2] for dichlorogermane from the solution value given in Table II. In the absence of mutual induction between the dipoles in the molecule, the tetrahedral angle 110° requires a ratio 1.15 between the moment of GeH_2Cl_2 and that of GeH_3Cl as between the moments of the corresponding compounds of carbon, silicon and tin.[6] The observed ratios are: for CH_2Cl_2 and CH_3Cl, 0.85; for SiH_2Cl_2 and SiH_3Cl, 0.91; for GeH_2Cl_2 and GeH_3Cl, 1.15; and for $(C_2H_5)_2SnCl_2$ and $(C_2H_5)_3SnCl$, 1.12, as compared to 1.02 for $(CH_3)_2CCl_2$ and $(CH_3)_3CCl$. Increase in size of the central atom of the tetrahedral molecule with consequent increase in the distance between the attached dipoles evidently decreases the mutual inductive effects of these dipoles, as would be expected.

A moment value as small as that found for chromyl chloride is necessarily uncertain when determined in solution because of neglect of atomic polarization as well as possible solvent effect. The uncertainty of the value in Table II is increased by an uncertainty of 2 cc. in the molar refraction. It is certain, however, that the moment is little larger than 0.5 and probable that it is between 0.5 and 0. If the molecule were tetrahedral and the bond moments unaffected by complicating factors, the moment should be 1.15 times the difference between the Cr–O and the Cr–Cl bond moments. The former bonds are more or less semipolar and should, therefore, have moments not far from 3, although they may have a considerable amount of double bond character, which would lower the moments somewhat. The Cr–Cl bond may be written as a normal covalent bond, but it must be remembered that the Sn–Cl bond was found[6] to have a moment not less than 3.1. It is, therefore, not only reasonable to suppose that the Cr–Cl moment may be of this magnitude but necessary to conclude that it is at least almost as large as this in order to account for the small moment of the CrO_2Cl_2 molecule since the Cr–O moment would be large even if it possessed a good deal of double bond character. The distortion of the tetrahedral structure of this molecule indicated tentatively by electron diffraction,[8] according to which the O–Cr–O angle is about 105° and the Cl–Cr–Cl angle about 113°, would increase the moment of the molecule if the Cr–O moment is greater than the Cr–Cl moment. A large Cr–Cl moment also accounts for the difference between the small CrO_2Cl_2 moment and the considerable value 1.86 found[9] for SO_2Cl_2, which is due to the difference between the fairly large moment of the more or less semipolar S–O bonds and the small moment 0.5 of the normal covalent S–Cl bonds.

The molecules of diphenylselenium dichloride and tellurium tetrachloride present essentially the same structural problem when treated according to the methods used by Pauling.[10] One might expect to find hybridized sp^3 orbitals, which would give a regular tetrahedral structure with the selenium or tellurium atom at its center, or sp^2d orbitals, which would give a square structure around the central selenium or tellurium atom. Either of these two structures could be reconciled with the moment found for diphenylselenium dichloride, but both would obviously give zero moment for tellurium tetrachloride in contrast to the large value observed. If the $TeCl_4$ molecule were tetrahedral in form and had zero dipole moment, the substance should be soluble in carbon tetrachloride and probably in carbon bisulfide and heptane, in all three of which it was found to be too insoluble to permit of dipole moment measurements. Also its boiling point, instead of being 414°, should not be far from the region 60–114°, in which the boiling points of the symmetrical tetrahedral molecules of carbon, silicon, germanium and tin tetrachloride lie. The symmetrical tetrahedral titanium tetrachloride boils at 136.4°. The symmetrical tetrahedral structure for tellurium tetrachloride would thus be ruled out on the score of its boiling point and solubility in the absence of other evidence. The markedly greater solubility of the compound in benzene than in carbon tetrachloride, carbon bisulfide or heptane suggests the possibility of the formation of an intermolecular compound with the solvent, but the solubility, about 0.012 mole fraction of tellurium tetrachloride at 25°, is still so small that it cannot be regarded as evidence of compound formation, the occurrence of which would probably give rise to a considerable moment. Consequently, we feel sufficient confidence in the moment of the tellurium tetrachloride molecule to rule out both the regular tetrahedral and the square structures for it and also for the diphenylselenium dichloride molecule.

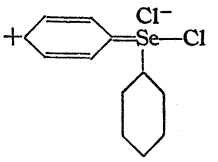
(8) Palmer, THIS JOURNAL, **60** 2360 (1938).

(9) Smith, *Proc. Roy. Soc.* (London), **138**, 154 (1932).

(10) See Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1939.

According to a treatment of directed valence communicated to us by Professor G. E. Kimball of Columbia University, the tellurium tetrachloride molecule should be an unsymmetrical tetrahedron, which would, of course, possess a moment. An analogous unsymmetrical tetrahedral structure would be indicated for diphenylselenium dichloride. Professor Linus Pauling, who has very kindly read this manuscript, suggests, in view of the moments possessed by these two compounds, that "the configuration is similar to that of PCl_5 and related molecules; that is, that the four bonds and one unshared pair occupy the five corners of a trigonal bipyramid. The unshared pair would probably occupy one of the equatorial positions rather than one of the apical positions." Such a structure would give an unsymmetrical tetrahedral arrangement of the four atoms or groups attached to the central atom, somewhat different from that given by Kimball's treatment.

In order to give rise to molecular moments as large as those observed, the Se–Cl and Te–Cl moments would have to be much larger than the values, 0.6 and 0.9, respectively, calculated on the basis of the electronegativities of the elements.[11] Comparison with the As–Cl value 1.64 and the Sb–Cl value 2.6 suggests 1.2 and 2.3 as possible values for Se–Cl and Te–Cl, respectively, the higher values probably arising from induced shifts of charge. The small moment of the C–Se bond, 0.9, calculated from that of diphenyl selenide cannot contribute largely to the moment of diphenylselenium dichloride, but the high value of this latter moment may be due, at least in part, to the occurrence of resonance with contributions from twelve polar structures such as



The writers wish to express their indebtedness to Mr. R. H. Wiswall, Jr., for measuring the monochlorogermane and to Dr. J. Y. Beach and Professors G. E. Kimball and Linus Pauling for their advice on the structures of diphenylselenium dichloride and tellurium tetrachloride.

Summary

The dipole moment of monochlorogermane has been measured in the vapor state and the moments of chromyl chloride, diphenylselenium dichloride and tellurium tetrachloride have been measured in solution. The ratio of the moment of monochlorogermane to the previously published value of dichlorogermane shows that the large size of the germanium atom largely eliminates induction between two chlorines attached to it. The considerable value of the moment of the molecule shows that the Ge–Cl bond moment is about 2 or greater than this by the amount of the small Ge–H moment. The very small moment of chromyl chloride shows that the Cr–Cl bond is of the same magnitude as the more or less semipolar Cr–O moment and probably, therefore, as large as 3.

The large moments found for diphenylselenium dichloride and tellurium tetrachloride indicate unsymmetrical tetrahedral structures for their molecules. The Se–Cl and Te–Cl bond moments necessary to produce such moments are much larger than those calculated as the electronegativity differences between the elements.

(11) See ref. 6 and ref. 10, p. 64.

PRINCETON, NEW JERSEY RECEIVED NOVEMBER 8, 1939

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

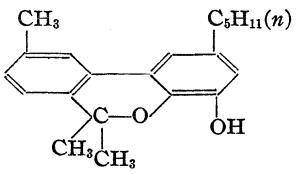
Structure of Cannabidiol, a Product Isolated from the Marihuana Extract of Minnesota Wild Hemp. I

BY ROGER ADAMS, MADISON HUNT, AND J. H. CLARK[1]

(IN COLLABORATION WITH THE TREASURY DEPARTMENT, NARCOTICS LABORATORY, WASHINGTON, D. C., AND DR. S. LOEWE, DEPT. OF PHARMACOLOGY, CORNELL UNIVERSITY MEDICAL COLLEGE)

Marihuana is the term commonly used in the United States to represent those portions of the *Cannabis sativa* or hemp plant which are capable of inducing somatic and psychic changes in humans. It is also familiarly known as hashish, bhang, charas, and ganja. The activity of an extract of the plant is found to vary widely, and to be dependent on the source of the hemp. Previous investigators, for the most part, have studied the resin obtained by working up hashish of Indian origin from the variety of hemp known as *Cannabis indica*. In this investigation, Minnesota wild hemp, cut after flowering had begun and before the seed had "set" in the female tops, was used as a raw material. It was extracted with ethanol and the so-called "red oil" containing the active principle or principles was obtained by distillation under diminished pressure.

Numerous investigators have studied the active red oil from *Cannabis sativa* and *indica* but only a single pure substance other than nonacosane has yet been isolated from the mixture of products present. This was called cannabinol by Wood, Spivey and Easterfield,[2] and was purified through its crystalline acetate. They assigned the formula $C_{21}H_{26}O_2$. This formula was confirmed and the constitution investigated by Cahn,[3] who proposed structure I in which the positions of the hydroxyl and *n*-amyl groups are uncertain.



I

Cannabinol is very toxic but has no marihuana activity. A knowledge of the structure of this compound is significant, however, due to the fact that the active red oil, even though derived from various sources, gives an analysis not substantially different from that of pure cannabinol.

When the red oil from Minnesota hemp was treated to isolate cannabinol according to methods previously suggested, no crystalline cannabinol acetate[3] or *p*-nitrobenzoate[4] could be isolated. Since the red oil contained substances with phenolic groups as shown by qualitative tests, other reagents for phenols were studied. This resulted in observing that a crystalline 3,5-dinitrobenzoyl derivative could be isolated in yields which corresponded to about 33% of the purified red oil used. Analysis indicated this derivative to be a *bis*-3,5-dinitrobenzoate of a dihydric phenol of the formula $C_{21}H_{30}O_2$ or $C_{21}H_{32}O_2$, the analysis not allowing distinction between them. It was readily purified. Upon ammonolysis of the purified *bis*-3,5-dinitrobenzoate by means of ammonia in toluene, the isolation of a pure compound was accomplished. It proved to have one of the two empirical formulas suggested above and has been given the name cannabidiol. It has none of the physiological activity typical of marihuana. The product is optically active, $[\alpha]_D$ $-119°$, and gives a very strong alkaline Beam test somewhat different from and more intense than that exhibited by purified red oil. Numerous other color tests applied to cannabidiol and purified red oil are given in Table I. It is obvious that the colors given by the red oil are dependent in part on substances other than cannabidiol.

By comparison with the formula of cannabinol, it is obvious that cannabidiol contains merely four or six more hydrogen atoms. The presence of two hydroxyls, presumably phenolic, is shown by the *bis*-3,5-dinitrobenzoate derivative and further was confirmed by the preparation of a crystalline *bis*-*m*-nitrobenzene sulfonate, a dimethyl ether, and a Zerewitinoff determination.

Methylation by means of repeated treatments with excess methyl iodide in acetone and potas-

(1) An abstract of a thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry. Solvay Process Company Fellow, 1939–1940.

(2) Wood, Spivey and Easterfield, *J. Chem. Soc.*, **69**, 539 (1896); **75**, 20 (1899).

(3) Cahn, *ibid.*, 986 (1930); 630 (1931); 1342 (1932); 1400 (1933). See also Bergel, *Ann.*, **482**, 55 (1930); **493**, 250 (1932). An excellent review of the literature dealing with the chemical constituents of *Cannabis sativa* is given in an article by Blatt, *J. Wash. Acad. Sci.*, **28**, 465 (1938).

(4) Work, Bergel and Todd, *Biochem. J.*, **33**, 123 (1939).

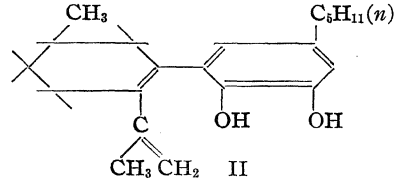
TABLE I

COLOR REACTIONS OF CANNABIDIOL AND OF PURIFIED RED OIL

Test	Red oil	Cannabidiol	References
Beam test 5% ethanolic KOH	Reddish violet, yellowish brown on acidification	Deep violet, yellow on acidification	*C. A.*, **6**, 1952 (1912). Wellcome, *Trop Res. Labs. Khortoum*, 4th Rept. (B), 25.
Duquenois test acetaldehyde, vanillin–HCl	Opaque blue after several minutes	Clear pale blue, deepening on standing	*J. Egypt. Med. Assoc.*, **21**, 224 (1938) [*C. A.*, **32**, 5993 (1938)].
Ghamrawy test *p*-dimethylaminobenzaldehyde	Deep red; on dilution with water changes to deep purple	Bright red; on dilution with water changes to bluish green	*J. Egypt. Med. Assoc.*, **20**, 193 (1937) [*C. A.*, **32**, 4724 (1938)].
Ethanolic $FeCl_3$	No color	No color	*Pharm. Acta Helv.*, **1**, 210 (1926) [*C. A.*, **21**, 2050 (1927)].
Millon's reagent	Red and precipitate in cold	Red and precipitate in cold	Same
Ammoniacal $AgNO_3$	Reduces slightly in cold, readily when hot	Very slight reduction in cold, slow reduction when hot	Same
Fehling's soln.	Reduces slowly in cold, readily when hot	Reduces very slowly when hot, no reduction in cold	Same
Formaldehyde–H_2SO_4	Dark brown	Very deep red	*The Analyst*, **36**, 540 (1911).[a]
Opianic acid–H_2SO_4	Bright red changing to brown	Bright red	*Ber.*, **20**, 874 (1887).[a]
Alloxan–H_2SO_4	Deep red changing to brown	Bright red	*Chem. Zentr.*, **73**, I, 631 (1902).[a]
Acetic acid	No color	No color	*Pharm. Acta Helv.*, **1**, 210 (1926).
H_2SO_4	Brown	Pale orange, fading to pale yellow	Same
Acetic anh.–H_2SO_4	Brown	Light brown	Same
$CHCl_3$–H_2SO_4	Brown in acid layer	Brilliant brown red in acid layer	Same
$Ca(OCl)_2$	Yellowish red	No reaction	*Ann.*, **68**, 95 (1848).[a]
$CHCl_3$–10% aq. KOH	Dark red in aqueous layer	Red in aqueous layer	*Z. anal. Chem.*, **56**, 286 (1917).[a]
$NaNO_2$–dil. H_2SO_4	No reaction	No reaction	*Ber.*, **7**, 248 (1874).[a]

[a] Tests have not previously been used on red oil. References are to the description of the tests on simply polyhydroxy benzenes.

sium carbonate resulted finally in formation of a dimethyl ether. Oxidation with permanganate in acetone gave *n*-caproic acid, which represents strong evidence for an *n*-amyl group in a phenolic ring. From these few facts alone, it may be concluded that one-half of the molecule of cannabidiol probably corresponds to the right-hand half of cannabinol (I). However, both hydroxyls are free in the cannabidiol so that the possibility of a pyran ring such as exists in cannabinol is excluded. On the assumption that the cannabidiol resembles cannabinol in entirety, the other half of the cannabidiol molecule may be postulated as a partially hydrogenated methylisopropylbenzene nucleus. Thus, formula II expresses satisfactorily the available experimental facts.



II

If the correct formula is $C_{21}H_{30}O_2$ (II), then two double bonds or the equivalent must be present. The positions assigned them in II are essentially fortuitous as no sound evidence has yet been revealed whereby to place them. The possibility of one double bond and a three-, four-, or five-membered ring, such as occurs in many terpenes, is not excluded. On the other hand, if the formula of cannabidiol is $C_{21}H_{32}O_2$, only one double bond in the left-hand ring can be present. The analyses of cannabidiol and its derivatives, the esters and ether, do not make possible a definite conclusion about the formula though $C_{21}H_{30}O_2$ agrees somewhat more uniformly with the analyses and, therefore, appears the more likely. Hydrogenation experiments, which should lead to the detection of one or two double bonds, have as yet proven indecisive. It is hoped, however, that a

careful reduction study now under way may clarify the question of unsaturation.

Red oil probably contains other products closely related to cannabinol or cannabidiol in structure, such as partially hydrogenated cannabinols, isomers of cannabidiol, or molecules like cannabidiol with less unsaturation. A large number of closely related compounds is possible. The active marihuana principle or principles may be among this group of substances. On the other hand, the possibility of the presence in red oil of a very potent active compound, entirely unrelated structurally to cannabinol or cannabidiol, is not excluded.

Experimental

The hemp used in these experiments grew wild in Minnesota during the season of 1938. It was cut in August, after flowering had begun but before seed had "set" in the female tops. It was stored for six weeks in a room where a fan assured circulation of air in order to dry it completely. No molding occurred. The material was then beaten and shaken to remove the coarse stems which amounted to about one-third of the total dry weight. The stems were discarded and the relatively fine material that remained was extracted with 95% ethanol in the manner described below.

Four 20-gallon (75-liter) crocks, each holding approximately 23 lb. (10 kg.) of material, were set up in series for countercurrent extraction. Each crock held approximately 61 liters of solvent of which about 41 liters were withdrawn at each transfer, the remainder being retained by the hemp. Once the process had become uniform in operation, the extract received from crock no. 4 at each transfer reached a concentration of approximately 2 g. per 100 cc. Transfers were made once or twice a day as conditions warranted. The most concentrated extract thus obtained was passed to a concentrator where most of the solvent was "flashed off" under vacuum. It was never heated above 50°. The evaporation was carried out at about 30°. The concentrated solution contained in this case 23.1 g. of solids per 100 cc. and 1 cc. was equivalent to 4.13 g. of hemp extracted. The operations just described were carried out by Dr. John R. Matchett and his assistants in the Narcotics Laboratory of the Treasury Department, Washington, D. C. They kindly furnished us with a generous supply of ethanol extract.

The red oil from these extracts was obtained as follows. Into a 1-liter Claisen flask, with a wide short neck, filled with glass wool was poured ethanolic extract until two-thirds full. The bath temperature was raised gradually from 90–140° while the pressure was diminished slightly. The ethanol distillate was discarded and the flask again filled to two-thirds capacity. This process was repeated until a maximum of 1600 cc. of extract had been added and all the ethanol was distilled. The temperature was then gradually raised to 200° and when distillation of the last traces of ethanol ceased, the bath was lowered to 180° and the pressure gradually reduced to 30 mm. Great care was necessary to prevent the liquid from foaming over. The temperature was gradually raised to 200° (30 mm.) until distillation ceased. The bath was then cooled to 170° and the pressure reduced to 2–5 mm. The residual product was then distilled. Considerable care was necessary to keep the bath at the lowest temperature at which the oil distilled regularly since there was a particular tendency to foam when the superheating was excessive. The material distilled between 100–220° (3 mm.) with the bath temperature at 170–310°; yield 180–200 g.

This crude red oil was dissolved in 500 cc. of petroleum ether (b. p. 30–60°) and extracted twice with water. The aqueous extract was saved and worked up for water-soluble materials. The petroleum ether layer was distilled and the residue fractionated through a good column with an outside heating unit. The first fraction boiled at 115–150° (2 mm.) (bath temperature 190–210°); yield, 70–80 g. The second fraction boiled at 150–175° (2 mm.) (bath temperature 215–225°); yield 25–35 g. The residual material in the flask was removed while still hot by dissolving in ethanol and filtering from the glass wool. The ethanol was removed and the product distilled from a 250-cc. flask, b. p. 175–195° (2 mm.) (bath temperature 220–270°); yield 90–110 g. This last material was considered as purified red oil.

Cannabidiol *bis*-3,5-Dinitrobenzoate.—A solution of 50 g. of purified red oil, b. p. 175–195° (2 mm.), in 200 cc. of dry pyridine was poured rapidly with shaking and cooling on 85 g. of 3,5-dinitrobenzoyl chloride. The mixture was heated on a steam cone for two hours with occasional shaking and was then poured into ice and hydrochloric acid (200 cc. of concentrated hydrochloric acid, 500 cc. of ice). It was filtered or decanted and the insoluble material was washed several times with dilute hydrochloric acid. The residue was dissolved in 600 cc. of benzene and filtered. The insoluble material consisted mainly of 3,5-dinitrobenzoic acid.

The benzene solution was washed with dilute hydrochloric acid, then with aqueous sodium bicarbonate and finally with water. Considerable trouble was encountered with emulsions which broke with difficulty. The benzene was evaporated and the residue was dissolved in 500 cc. of dry ether. This solution was treated with norit (20 g.), filtered, and then concentrated to 300 cc. On cooling in an ice–salt mixture with constant stirring, crystallization set in. After one hour, the product was filtered and washed with cold dry ether. It was purified by recrystallizing from 800 cc. of a mixture of methanol and methyl acetate (2:1); white rods, m. p. 106–107° (corr.).

Anal. Calcd. for $C_{21}H_{28}(OCOC_6H_3(NO_2)_2)_2$: C, 59.82; H, 4.88; N, 7.97. Calcd. for $C_{21}H_{30}(OCOC_6H_3(NO_2)_2)_2$: C, 59.64; H, 5.15; N, 7.95. Found: C, 59.74; H, 5.00; N, 7.96. *Rotation.* 0.057 g. made up to 5 cc. with acetone at 27° gave α_D −1.73°; l, 2; $[\alpha]^{27}D$ −76°.

Cannabidiol.—A solution of 50 g. of cannabidiol *bis*-3,5-dinitrobenzoate in 100 cc. of toluene was placed in the glass liner of a high pressure bomb. The mixture was cooled by dry-ice and about 100 cc. of liquid ammonia passed into it. The liner was then placed in the bomb and the cover quickly fastened. The bomb was allowed to stand for five hours at room temperature. At the end of that time the excess ammonia was allowed to escape and the product, which had set to a solid mass, was digested with 400 cc.

of petroleum ether (b. p. 60–110°). The solid 3,5-dinitrobenzamide was filtered and washed with two 50-cc. portions of petroleum ether. Filtrate and washings were combined and extracted six times with 150-cc. portions of boiling water to remove the last traces of 3,5-dinitrobenzamide. The petroleum ether was then evaporated and the residue distilled, b. p. 187–190° (2 mm.) (bath temperature 220°), d^{40}_4 1.040; $n^{20}D$ 1.5404. Cannabidiol is a pale yellow resin; yield 17–19 g.

Anal. Calcd. for $C_{21}H_{30}O_2$: C, 80.21; H, 9.62. Calcd. for $C_{21}H_{32}O_2$: C, 79.69; H, 10.19. Found: C, 80.08, 80.29; H, 9.87, 9.41. *Rotation.* 0.0378 g. made up to 5 cc. with 95% ethanol at 28° gave α_D −0.90°; *l*, 1; $[\alpha]^{28}D$ −119°.

A Zerewitinoff determination showed two active hydrogens.

Cannabidiol is soluble in all common organic solvents, ether, benzene, ethanol, methanol, chloroform, and petroleum ether, but insoluble in water and 10% hot or cold aqueous sodium hydroxide.

That no rearrangement or deep-seated decomposition had taken place by this method of hydrolysis was demonstrated by the fact that the product readily could be reconverted in essentially quantitative yields to the same *bis*-3,5-dinitrobenzoate.

Cannabidiol *bis*-*m*-Nitrobenzene Sulfonate.—To a solution of 0.2 g. of cannabidiol in 5 cc. of dry pyridine, 0.35 g. of *m*-nitrobenzene sulfonyl chloride was added. The mixture was warmed on a steam cone for one hour and was then poured into ice and hydrochloric acid. The product was filtered, washed with dilute hydrochloric acid, aqueous sodium bicarbonate and then with water. It was purified by recrystallization from ethanol: white rods, m. p. 119–120° (corr.); yield 0.17 g. This same derivative could be obtained directly from purified red oil.

Anal. Calcd. for $C_{21}H_{28}(OSO_2C_6H_4NO_2)_2$: C, 57.87; H, 5.30; N, 4.09. Calcd. for $C_{21}H_{30}(OSO_2C_6H_4NO_2)_2$: C, 57.70; H, 5.58; N, 4.08. Found: C, 57.72; H, 5.49; N, 4.39.

Cannabidiol Dimethyl Ether.—A solution of 11.25 g. of cannabidiol in 75 cc. of acetone was refluxed for four hours with 12 g. of methyl iodide and 15 g. of anhydrous potassium carbonate. A deep purple color present at the beginning of the reaction had changed to a pale yellow at the end of this time.

The potassium carbonate was filtered, washed with ether, and the filtrate and washings combined. The solution becomes cloudy due to the precipitation of salts dissolved in the acetone. About 300 cc. more of ether was added and the mixture extracted with water. The solvent was then removed and the product distilled. Five cuts of approximately equal volume were taken since temperature changes were not significant. The refractive indices of these fractions ranged from 1.5330 to 1.5372, indicating that some reaction had taken place but that the product was not homogeneous.

The distillate was dissolved again in acetone, treated with excess methyl iodide and potassium carbonate and refluxed for periods of ten, twelve, forty-eight, and sixty hours. After each treatment the progress of the reaction was followed by the refractive index as described above. At the end of a total of one hundred and thirty-four hours of refluxing the refractive index of the main portion of the distillate was found to have reached a constant value. The material thus obtained was a pale yellow oil, much less viscous than cannabidiol; b. p. 175–177° (3 mm.) (bath temperature 200°); yield 3.3 g.; n^{20} D 1.5254; d^{20}_4 0.9823.

Anal. Calcd. for $C_{21}H_{28}(OCH_3)_2$: C, 80.65; H, 10.01; OCH_3, 18.12. Calcd. for $C_{21}H_{30}(OCH_3)_2$: C, 80.17; H, 10.53; OCH_3, 18.02. Found: C, 80.52; H, 10.08; OCH_3, 18.2. *Rotation.* 0.0535 g. made up to 5 cc. with 95% ethanol at 28° gave α_D −1.42°; *l*, 1; $[\alpha]^{28}D$ −133°.

Cannabidiol dimethyl ether is insoluble in water, difficultly soluble in cold 95% ethanol, and readily soluble in petroleum ether, acetone, and ether.

An attempt was made to prepare the monomethyl ether by refluxing cannabidiol in acetone solution for eight hours with over twice the theoretical amounts of methyl iodide and potassium carbonate. The product was worked up as described above and carefully fractionated. That portion of the distillate which seemed, on the basis of refractive indices, to be homogeneous was found to give a very satisfactory value for methoxyl content, but a consistently poor value for carbon. The material was a clear viscous oil, b. p. 177–179° (2 mm.) (bath temperature 200–210°); $n^{20}D$ 1.5311.

Anal. Calcd. for $C_{21}H_{29}O(OCH_3)$: C, 80.44; H, 9.82; OCH_3, 9.45. Calcd. for $C_{21}H_{31}O(OCH_3)$: C, 79.94; H, 10.37; OCH_3, 9.39. Found: C, 79.67, 79.50; H, 9.65, 9.79; OCH_3, 9.41. *Rotation.* 0.0455 g. made up to 5 cc. with 95% ethanol at 26° gave α_D −2.14; *l*, 2; $[\alpha]^{26}D$ −118°.

Oxidation of Cannabidiol.—To a solution of 5 g. of cannabidiol in 25 cc. of acetone was added a saturated solution of 8 g. of potassium permanganate in 50% aqueous acetone and 5 g. of sodium bicarbonate. The mixture was heated for thirty minutes on a steam-bath. Ethanol was added to remove the last traces of the permanganate, the mixture filtered and acidified with hydrochloric acid. The acid solution was extracted with ether and the ether solution in turn extracted with aqueous sodium bicarbonate.

The aqueous sodium bicarbonate solution was acidified with hydrochloric acid and extracted with ether. The ether solution was dried over anhydrous magnesium sulfate, the solvent removed and the product distilled. It boiled at 200–203° (750 mm.) and weighed 1.15 g. (64% based on one molecule of *n*-caproic acid per molecule of cannabidiol). The anilide was prepared for identification purposes, m. p. 95–96°, and proved to be identical with an authentic sample of *n*-caproanilide.

Summary

A new compound, cannabidiol, present in the purified red oil of *Cannabis sativa* has been isolated through the *bis*-3,5-dinitrobenzoate. This diester is a crystalline, easily purified compound. Ammonolysis of it gives cannabidiol which has the formula $C_{21}H_{30}O_2$ or $C_{21}H_{32}O_2$, the former probably being the correct one.

Cannabidiol is oxidized to *n*-caproic acid, methylated with difficulty to a dimethyl ether and

converted to a *bis-m*-nitrobenzenesulfonate. It is concluded that this substance is closely related to cannabinol in structure. Half the molecule is probably a dihydroxy *n*-amylphenyl, the other half probably an unsaturated alicylic nucleus.

URBANA, ILLINOIS RECEIVED DECEMBER 4, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, COLUMBIA UNIVERSITY]

The Preparation and Properties of 3(α),11-Dihydroxy-12-ketocholanic Acid

BY BERNARD B. LONGWELL[1] AND O. WINTERSTEINER

The isolation of naturally occurring steroids in which an oxygen atom is believed to occupy position 11[2,3,4] renders of interest the study of model substances in which ring C carries a functional group in this, and only in this, position.

The original aim of this investigation was to prepare 3,11-dihydroxycholanic acid by elimination of the keto group of 3,11-dihydroxy-12-ketocholanic acid, which has been described recently by Marker and Lawson.[5] Although this object has not been accomplished, we are reporting here the preparation and properties of the starting compound because our results not only extend but in some points fail to confirm the work of these authors. Their procedure is essentially analogous to that of Wieland and Posternak[6] for the preparation of 11-hydroxy-12-ketocholanic acid. They[5] acetylated 3-hydroxy-12-ketocholanic acid, and then brominated it in position 11. The bromo acid was hydrolyzed to 3,11-dihydroxy-12-ketocholanic acid. Neither of the two intermediates was isolated. In our hands this abbreviated procedure failed to yield the end-product in crystalline form. We found it necessary to conduct the reaction in two separate steps. We furthermore had to modify the method of bromination in order to limit the reaction to a substitution with only one bromine atom. Although the bromo acid thus obtained was amorphous and its bromine content still slightly too high, its hydrolysis yielded the desired 3,11-dihydroxy-12-ketocholanic acid without any difficulty. The over-all yield from 3-hydroxy-12-ketocholanic acid was over 50%, whereas Marker and Lawson obtained in 35% yield a product which melted 9° lower than ours.

In order to eliminate any doubt regarding the site of the new hydroxyl group, the monobromo acid was subjected to debromination with anhydrous sodium acetate in analogy to the experiment of Barnett and Reichstein[7] on 11-bromo-12-ketocholanic acid. The ultraviolet absorption spectrum of the resulting compound (m. p. 201°) exhibited a maximum at 241 mμ (ϵ = 9000, solvent alcohol), which is characteristic for α,β-unsaturated ketones. The unsaturated compound is, therefore, $\Delta^{9,11}$-3-acetoxy-12-ketocholenic acid. Furthermore, the acid 3-succinate of methyl 3,11-dihydroxy-12-ketocholanate was oxidized with chromic acid to the corresponding 11,12-diketone. The ultraviolet absorption spectrum of the resulting compound is similar to that reported by Barnett and Reichstein for methyl 11,12-diketocholanate (maximum at 284 mμ, ϵ = 135; minimum at 250 mμ, ϵ = 80, solvent alcohol). Saponification of the diketo ester failed to yield a crystalline compound.

When we tried to repeat the preparation of the 3-monoacetate of 3,11-dihydroxy-12-ketocholanic acid described by Marker and Lawson, we observed that the reaction takes a more complicated course than the report of these authors indicates. Our acetylation product showed the same melting point (268°) as their monoacetyl derivative, but the analysis indicated the loss of a molecule of water as well as the esterification of one hydroxyl group. We are unable to explain the considerable discrepancy between the carbon value of our analyses and that reported by Marker and Lawson, but it must be pointed out that the values assigned in their paper to the monoacetyl acid, $C_{26}H_{40}O_6$, with which their experimental figures agree, are incorrectly calculated (C, 70.5; H, 8.8, instead of C, 69.60; H, 8.99). Furthermore, our substance, in contradistinction to the starting compound, is insoluble in aqueous sodium carbonate. Hydrolysis at room temperature

(1) Commonwealth Fund Fellow, 1938–1939.

(2) Reichstein, *Ergeb. der Vitamin- und Hormonforschung*, **1**, 334 (1938).

(3) Marker, Kamm, Crooks, Oakwood, Wittle and Lawson, THIS JOURNAL, **60**, 210 (1938).

(4) Tschesche and Bohle, *Ber.*, **69**, 793, 2497 (1936).

(5) Marker and Lawson, THIS JOURNAL, **60**, 1334 (1938).

(6) Wieland and Posternak, *Z. physiol. Chem.*, **197**, 17 (1931).

(7) Barnett and Reichstein, *Helv. Chim. Acta*, **21**, 926 (1938).

with standard alkali resulted in the neutralization of two equivalents of base and recovery of the original acid. The neutral compound is, therefore, either an 11-(or 12-enol)-lactone or a dimolecular anhydride, more likely the latter.[8] When the compound was boiled for an hour with 33% acetic acid, an acid extractable with aqueous sodium carbonate and melting at 106° was obtained in good yield. According to the analysis, which conforms with $C_{26}H_{40}O_6 \cdot 1/2H_2O$, this acid represents, in all probability, the true monoacetate of 3,11-dihydroxy-12-ketocholanic acid.

Besides the anhydride, which can be obtained in 20–30% yield by direct crystallization of the acetylated material, an acidic product, which would not crystallize, was formed in the acetylation reaction. Analyses and titration data indicated that this product is a diacetyl derivative of the starting acid. When the acetylation reaction was conducted in pyridine, this acidic substance was the only reaction product.

Both the anhydride and the amorphous diacetoxy acid yielded the starting acid on alkaline hydrolysis. Careful comparison of the specific rotations of the two hydrolysis products and of the original preparation revealed no significant differences. This finding precludes the possibility that the simultaneous formation of neutral and acidic reaction products on treatment with acetic anhydride is due to the existence of two 11-epimers in the original preparation, one of which might be amenable to acetylation at C_{11} under the conditions employed.

All our attempts to prepare keto derivatives of 3,11-dihydroxy-12-ketocholanic acid have been unsuccessful. The preparations of the semicarbazone, the hydrazone, and the oxime were essayed, but in each case the starting material was recovered unchanged. Marker and Lawson claimed to have prepared a semicarbazone melting at 232° in 18% yield, but no analysis of the product is reported. We have experienced consistent failures in our attempts to prepare this semicarbazone by the method of Marker and Lawson. We also tried, without success, to let the acid react with semicarbazide acetate in cold pyridine solution, in boiling butyl alcohol, and in alcohol at 190° in a bomb tube. Apparently the steric hindrance exerted by the groups on the adjoining carbon atoms is too great to permit reaction with the 12-keto group.

Treatment of the acid with hydrazine hydrate and sodium ethylate at 200° resulted in the formation of a compound, m. p. 162°, with two oxygen atoms less than the starting product. Obviously the keto group at C_{12} had been eliminated, but at the same time the hydroxyl at C_{11} was lost by a dehydration reaction.

Experimental

3-Hydroxy-12-ketocholanic acid was obtained in good yield from desoxycholic acid by the method of Kaziro and Shimada[9] as modified by Cortese,[10] m. p. 162–163°. The 3-acetyl derivative was prepared by treatment with acetic anhydride in pyridine, m. p. 197–198°. The sample for analysis was dried *in vacuo* at 110°.

Anal. Calcd. for $C_{26}H_{40}O_5$: C, 72.18; H, 9.32. Found: C, 72.01; H, 9.18.

3(α)-Acetoxy-11-bromo-12-ketocholanic Acid.—Five grams of 3(α)-hydroxy-12-ketocholanic acid was refluxed for one hour in a mixture of 15 cc. of glacial acetic acid and 2.5 cc. of acetic anhydride. The reaction mixture, after dilution to 50 cc. with glacial acetic acid, was treated with 0.7 cc. of bromine in 40 cc. of glacial acetic acid. The solution was stirred mechanically during the dropwise addition of the bromine, which required three to four hours. The temperature was maintained at 50–60° during this period and thereafter for four to five hours, while stirring was continued. After cooling to room temperature, 250 cc. of water was added slowly with stirring. The reddish-yellow gum which separated was dissolved in 350 cc. of 95% ethanol, and this solution was poured slowly into 2450 cc. of water. The resulting milky suspension formed a flocculent precipitate upon the addition of 16 cc. of glacial acetic acid. On filtering and washing once with a solution of ethanol, water and acetic acid (3.5, 24.5, and 0.16 parts, respectively), and twice with water, 5.82 g. of the amorphous bromo acid was obtained, which melted with decomposition at 159°. The sample for analysis was dried *in vacuo* at 110°.

Anal. Calcd. for $C_{26}H_{39}O_5Br$: Br, 15.62. Found: Br, 16.1, 16.3, 16.86.

3(α),11-Dihydroxy-12-ketocholanic Acid.—The bromo acid (5.82 g.) was refluxed for twenty minutes in 115 cc. of 20% methyl alcoholic potassium hydroxide solution. The hydrolysate was poured into 1150 cc. of ice water. On acidification with hydrochloric acid a flocculent precipitate formed, which was separated by filtration and washed with water; yield 4.4 g. It was dissolved in 325 cc. of hot 95% ethanol and 825 cc. of water was added to the hot solution. On slow cooling a crystalline precipitate formed; yield 2.94 g. Several recrystallizations from aqueous ethanol yielded plates, m. p. 202°, $[\alpha]^{24}D$ +65.7° (2.5% in 95% alcohol). Further recrystallization from 95% ethanol produced blunt rods, m. p. 205°, $[\alpha]^{27}D$

(8) Professor Reichstein (private communication) has observed the formation of dimolecular anhydrides, which could be hydrolyzed with acetic acid, on acetylation of hydroxy acids of a similar type. We are highly indebted to him for this information.

(9) Kaziro and Shimada, *Z. physiol. Chem.*, **249**, 220 (1937).

(10) Cortese, unpublished experiments. The coöperation of Dr. Cortese in permitting us the use of his method prior to publication is gratefully acknowledged.

+67.1° (1.3% in 95% alcohol). The sample for analysis was dried *in vacuo* at 110°.

Anal. Calcd. for $C_{24}H_{38}O_5$: C, 70.9; H, 9.42; neut. equiv., 406. Found: C, 70.8; H, 9.41; neut. equiv. (115.4 mg.), 412.

Methyl 3(α),11-Dihydroxy-12-ketocholanate.—An ether solution of 20 mg. of the acid was treated with diazomethane in ether. After two hours in the refrigerator, the excess diazomethane was removed by gentle heating and the ether was washed with 5% sodium carbonate solution and with water. Evaporation of the ether yielded 18.7 mg. The ester crystallized from methanol in triangular plates, m. p. 157°. The sample for analysis was dried *in vacuo* at 110°.

Anal. Calcd. for $C_{25}H_{40}O_5$: C, 71.39; H, 9.59. Found: C, 70.97; H, 9.36.

3(α),11-Diformoxy-12-ketocholanic Acid.—A solution of 69.8 mg. of the acid, m. p. 202°, in 0.5 cc. of 98–100% formic acid, was allowed to stand at room temperature for twenty-four hours. When 0.4 cc. of 95% ethanol and 1.1 cc. of water were added, an oil separated out which was extracted quickly with ether. The residue of the washed and dried ether solution was freed from traces of formic acid *in vacuo*. After several recrystallizations from aqueous ethanol, needles were obtained, m. p. 146–148°. The sample for analysis was dried *in vacuo* at 110°.

Anal. Calcd. for $C_{26}H_{38}O_7$: C, 67.51; H, 8.28. Found: C, 67.41; H, 8.43.

Acetylation of 3(α),11-Dihydroxy-12-ketocholanic Acid.—A solution of 678 mg. of the acid (m. p. 199–201°) in 21 cc. of acetic anhydride was boiled under reflux for one and one-half hours. The acetic anhydride was decomposed with ice water. The gummy, white precipitate was centrifuged, washed, and dissolved in a minimal amount of hot 95% ethanol. A crystalline precipitate formed on standing overnight in the refrigerator. This was removed by centrifuging and washed with 95% ethanol and ether (116 mg.). The supernatant and washings were poured into 50 cc. of water and thoroughly extracted with ether. The ether solution was then extracted exhaustively with 5% sodium carbonate solution, then with water and brought to dryness (257 mg.).

The combined sodium carbonate extracts were acidified with hydrochloric acid and extracted with ether. The residue from the washed and dried ether yielded 431 mg.

The yields of alkali insoluble and alkali soluble fractions represent approximately a 50% partition, a finding which was uniform in several experiments. In this experiment 17% of the starting material was obtained as the crystalline anhydride. In other experiments yields of 27, 32, and 26% were obtained.

The Crystalline Anhydride.—The crystalline product from the acetylation reaction was purified by recrystallization from 95% ethanol, m. p. 268°. It crystallized in fine, white needles, soluble in hot 95% alcohol and insoluble in ether and aqueous alkali. The sample for analysis was dried *in vacuo* at 110°.

Anal. Calcd. for $C_{26}H_{38}O_5$: C, 72.52; H, 8.90. Found: C, 72.18; H, 8.78. C, 72.11; H, 8.84. C, 72.14; H, 8.89. *Titration.* A solution of 14.5 mg. (0.0337 millimole) in absolute alcohol reacted neutral to phenolphthalein. Standard alkali was added and the excess titrated back after forty-four hours. Alkali neutralized: calculated, 0.067 milliequiv.; found, 0.0668 milliequiv. The titration mixture was acidified and extracted with ether. The ether was washed with water and evaporated, and the residue was crystallized from aqueous ethanol, m. p. 203–204°. $[\alpha]^{24}D$ +67.2° (0.33% in 95% alcohol).

3(α)-Acetoxy-11-hydroxy-12-ketocholanic Acid.—A solution of 18 mg. of the anhydride (m. p. 268°) in 6 cc. of 33% acetic acid was boiled under reflux for one hour. The reaction mixture was extracted with ether and the ether in turn extracted with 5% sodium carbonate solution. The alkaline extract was worked up in the usual way; yield, 14.4 mg. This product crystallized from aqueous ethanol in needles, m. p. 106°. The sample for analysis was dried *in vacuo* at 61°.

Anal. Calcd. for $C_{26}H_{40}O_6 \cdot {}^1/_2H_2O$: C, 68.24; H, 9.03. Found: C, 68.35; H, 9.14.

The Acidic Fraction from the Acetylation Reaction.—Efforts to crystallize the acidic fraction from the original separation of the acetylation mixture were unsuccessful. The sample for analysis was dried *in vacuo* at 110°.

Anal. Calcd. for $C_{28}H_{42}O_7$: C, 68.54; H, 8.63. Found: C, 68.47; H, 9.41.

In the hope that the ester might be obtained in crystalline form the compound was esterified with diazomethane. An oily product which could not be crystallized was obtained.

Titration. A solution of 41.8 mg. of the ester (0.0828 millimol.) in absolute methanol was neutral to phenolphthalein. Standard alkali was added and the excess titrated back after sixty hours. Alkali neutralized: calculated, 0.2485 milliequiv.; found, 0.2247 milliequiv. A solution of 55.3 mg. (0.1096 millimol.) was treated similarly. Alkali neutralized: calculated, 0.3288 milliequiv.; found, 0.352 milliequiv.

The acid was recovered from the titration mixture by extraction with ether, and was crystallized from aqueous ethanol, m. p. 203–204°; $[\alpha]^{23}D$ +63.4° (0.68% in 95% alcohol). All later runs yielded preparations with the higher value (+67°).

Acetylation in Pyridine.—A solution of 54 mg. of the starting acid in 2 cc. of pyridine was treated with 1.8 cc. of acetic anhydride. After standing overnight at room temperature, the acetic anhydride was decomposed with water, and the reaction products taken up in ether. The ether solution was washed with 5% hydrochloric acid, and then extracted with 5% sodium carbonate solution. Upon acidification and extraction with ether the alkaline extract yielded 63 mg. of a colorless oil. The sample for analysis was dried *in vacuo* at 110°.

Anal. Calcd. for $C_{28}H_{42}O_7$: C, 68.55; H, 8.62. Found: C, 68.55; H, 8.50.

$\Delta^{9,11}$-3(α)-Acetoxy-12-ketocholenic Acid.—A solution of 400 mg. of the amorphous bromo acid and 200 mg. of fused sodium acetate in 2.5 cc. of glacial acetic acid was heated in a bomb tube at 185–190° for seventeen hours. The acetic acid of the reaction mixture was partially neutralized with sodium carbonate, and the reaction products were extracted with ether. The ether solution was filtered to remove tar, and then extracted with 5% sodium car-

bonate solution. A precipitate separated in the alkaline solution, which was removed by centrifuging. The aqueous solution of the precipitate was acidified with hydrochloric acid, and extracted with ether. The ether extract, after washing and drying, yielded 98.5 mg. Since the residue did not crystallize well, it was subjected to three additional precipitations as the sodium salt. The acid finally obtained on decomposition of the latter was crystallized from aqueous ethanol until the melting point became constant at 201°. The sample for analysis was dried *in vacuo* at 110°.

Anal. Calcd. for $C_{26}H_{38}O_5$: C, 72.52; H, 8.90. Found: C, 72.63; H, 9.00.

Acid Succinate of Methyl 3(α)-Hydroxy-11,12-diketocholanate.—A solution of 275 mg. of crystalline methyl 3,11-dihydroxy-12-ketocholanate and 655 mg. of succinic anhydride in 10 cc. of dry pyridine was allowed to stand at room temperature for twenty hours. It was then heated under reflux at 135° (bath temperature) for one-half hour. The reaction mixture was poured into water and extracted with ether. After removal of the pyridine by repeated washing with 5% hydrochloric acid, the ether was evaporated. The residue was dissolved in 7.5 cc. of glacial acetic acid, 0.5 cc. of water and 100 mg. of chromic acid added. After standing at room temperature for twenty hours, the reaction mixture was diluted with water and extracted with ether. The ether solution was then extracted with 5% sodium carbonate solution, which, after removal of the acetic acid, resulted in the precipitation of the reaction product as the sodium salt. This was converted into the free acid in the usual way (76 mg.). Crystallization from 80% methanol yielded plates, m. p. 194–196°. The sample for analysis was dried *in vacuo* at 110°.

Anal. Calcd. for $C_{29}H_{42}O_8$: C, 67.16; H, 8.16. Found: C, 66.65; H, 8.39.

Saponification with alkali did not yield any crystallizable products.

Attempted Preparation of the Semicarbazone.—A solution of 100 mg. of 3(α),11-dihydroxy-12-ketocholanic acid, 110 mg. of semicarbazide hydrochloride and 110 mg. of potassium acetate in 2.4 cc. of 83% ethanol was refluxed for fifteen hours, and then worked up in the usual way. After recrystallization, 86.5 mg. of the starting acid was recovered, m. p. 200–202°. Attempts to prepare the semicarbazone in pyridine solution, by refluxing in butyl alcohol, and by heating at 190° in a bomb tube, were similarly unsuccessful. Furthermore, all efforts to prepare the hydrazone and the oxime met with failure.

Treatment of 3(α),11-Dihydroxy-12-ketocholanic Acid with Sodium Ethylate and Hydrazine Hydrate.—A mixture of 500 mg. of the acid, 500 mg. of sodium in 17.5 cc. of absolute alcohol, and 2.5 cc. of hydrazine hydrate was heated in a bomb tube at 197–200° for eight hours. The reaction mixture was poured into water, acidified with hydrochloric acid, and extracted with ether. The ether was washed with water, dried over sodium sulfate, and evaporated to yield an oil which could not be crystallized. The entire product was dissolved in 17 cc. of pyridine together with 1.275 g. of succinic anhydride, and was heated under reflux at 130–135° (bath temperature) for one hour. After cooling, the reaction mixture was poured into water and extracted with ether. The ether solution was extracted with 5% sodium carbonate solution, and the alkali soluble material recovered in the usual way (600 mg.). Crystallization from aqueous ethanol yielded 78 mg. of plates melting at 227° with decomposition. The sample for analysis was dried *in vacuo* at 110°.

Anal. Calcd. for $C_{23}H_{42}O_6$: C, 70.85; H, 8.92. Found: C, 70.80; H, 8.75.

Titration. 17.93 mg. (0.0378 millimol.); neutralization equivalent, calculated 237; found 241. After subsequent saponification with excess alkali, calculated 0.0377 milliequiv.; found 0.0370 milliequiv. of base neutralized.

Saponification of the acid succinate with 0.1 *N* sodium hydroxide produced an acid which softened at 135° and melted at 162–163°. The sample for analysis was dried *in vacuo* at 110°.

Anal. Calcd. for $C_{24}H_{38}O_3$: C, 76.96; H, 10.25. Calcd. for $C_{24}H_{38}O_3 \cdot {}^1/_2H_2O$: C, 75.15; H, 10.35. Found: C, 75.63; H, 10.48.

The analyses reported in this paper were performed by Mr. William Saschek.

Summary

The procedure of Marker and Lawson for the preparation of 3,11-dihydroxy-12-ketocholanic acid has been modified so as to give better yields. The intermediate 11-bromo acid was isolated in amorphous form. The position of the new substituent group was confirmed by conversion of the bromo acid into $\Delta^{9,11}$-3-hydroxy-12-ketocholenic acid, and of the dihydroxy acid into the acid 3-succinate of methyl 3-hydroxy-11,12-diketocholanate. The acetyl derivative of 3,11-dihydroxy-12-ketocholanic acid described by Marker and Lawson is actually a neutral compound, that is, either a 3-acetoxy lactone or a dimolecular anhydride. On hydrolysis with acetic acid this substance yields the true 3-acetoxy-11-hydroxy-12-keto-cholanic acid. The 11-hydroxy group is also capable of acylation as evidenced by the preparation of a crystalline diformyl and of an amorphous diacetyl derivative.

All attempts to prepare the semicarbazone of 3,11-dihydroxy-12-ketocholanic acid, described by Marker and Lawson, as well as other ketone derivatives, failed. Treatment of the acid with sodium ethylate and hydrazine hydrate at 200° resulted in elimination of both oxygen atoms in ring C.

NEW YORK, N. Y. RECEIVED NOVEMBER 15, 1939

[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH]

Semiquinone Radicals of the Thiazines

BY L. MICHAELIS, M. P. SCHUBERT AND S. GRANICK

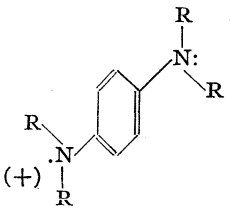
The formation of semiquinone radicals as intermediary reduction products in reversibly reducible dyestuffs, although considered an exceptional phenomenon some years ago, has now been recognized to occur so frequently that the differences in the behavior of various reversible dyestuffs can be looked upon only as quantitative, not qualitative. Among the more familiar classes of reversible dyestuffs it is only the thiazines and oxazines in which formation of semiquinones has not yet been demonstrated experimentally. This paper is to fill in this gap.

The general ideas about stability of semiquinone radicals have been clarified so far that one may start the topic by predicting the conditions under which the formation of semiquinones of these dyestuffs should be most conspicuous and then testing the theory by experiment. To increase the stability of a free radical it has to be put into such a state of its various possible levels of acidic ionization as to bring about equivalent resonance. This term requires some comment.

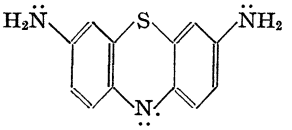
An equivalent resonance is a resonance between two limiting structures which are quite equivalent, that is to say, which, if written by the customary structural formulas, are indistinguishable except for orientation of the molecule as a whole in space. Two types of equivalent resonance may be distinguished. One of them occurs in the regular quinonoid dyestuffs, containing one benzenoid ring (or two) and one quinonoid ring. The resonance consists in the ambiguity as to which ring is the quinonoid one and which is the benzenoid. This resonance stretches over two rings (or three, in the triphenylmethane dyes) and may be designated as quinone–benzene resonance.

The other type of equivalent resonance occurs in the semiquinone radicals. It is restricted, or at least it may be restricted, to a single ring. There is one unpaired electron, and the ambiguity as to the place of this electron on writing down a structural formula is what underlies the resonance. An equivalent resonance occurs when there is a pair of possible structural formulas, or "limiting states," which are indistinguishable. There may be several pairs of equivalent limiting structures as has been recently discussed for Wurster's radicals.[1] An equivalent resonance has a greater stabilizing effect than a non-equivalent one.[2]

In speaking of equivalence, it is not necessary that it refer to the whole molecule. It is sufficient if there is equivalence only with respect to that part of the molecule within which the exchange of electrons resulting in resonance takes place. So, in a Wurster's radical (I), resonance stretches from one N atom across the conjugated double bonds of the ring to the other N atom.[3] The four R's may be different atoms or atom groups without appreciably diminishing the stabilizing of resonance, *provided each N is combined with two R's.*



(I)



(II)

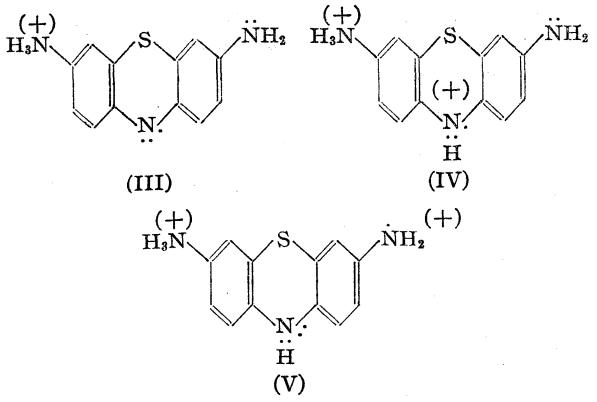
These ideas may be applied to the thionine radical. Its simplest structural formulation is (II), with an odd electron at the N. It resembles the diphenyl-nitrogen radical. In this state, there is no resonance of the equivalent type,[4] since the bridge N and the amino N are bonded to a different number of atoms. Yet equivalence can be produced by adding protons to the N atoms. In a slightly acid solution, one of the two NH_2 groups will attach a proton (III). This does not improve the stability. However, when in a more acid solution a second proton is attached, it will prefer a position such as to bring about equivalent resonance (IV). This structure would be in equivalent resonance with (V), since (IV) can be changed to (V) by moving electrons only, keeping all nuclei in place. Another pair of equivalent resonating limiting states would be (VI) and

(1) L. Michaelis, M. P. Schubert and S. Granick, THIS JOURNAL, **61**, 1981 (1939).

(2) See, for instance, L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, New York, 1939.

(3) In all formulas, letters stand for atomic kernels, not for full atoms; a dash, or a pair of dots for an electron pair; a single dot is an unpaired electron.

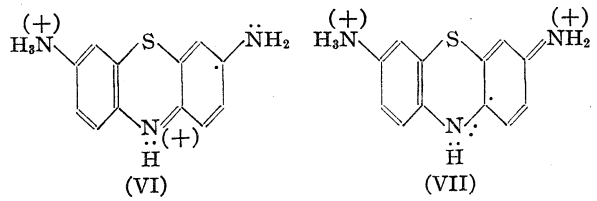
(4) The regular resonance within each benzene ring may be neglected for the present purpose.



(III) (IV)

(V)

(VII), which also arise from (IV) by shifting electrons only. The left-hand ring does not take



(VI) (VII)

part in the resonance. The right-hand ring is benzenoid in the pair IV, V; it is quinonoid in the pair VI, VII. Both the resonance IV, V, and the resonance VI, VII, are equivalent, since there are two N atoms attached to the right-hand ring, and each of these N atoms is attached to two more atoms, and there is no steric hindrance with respect to coplanar arrangement. This radical may be considered as a Wurster's radical (I), in which the two right-hand R's are H, and of the two left-hand R's one is H, the other an aromatic ring, attached furthermore by the S-bridge.

For a regular Wurster's radical, a slightly acid solution is sufficient to bring about the state of equivalent resonance, namely, the singly charged cation. For thionine, a doubly charged cation is the necessary condition for equivalent resonance. For this reason a much higher acidity will be requisite to bring about the most stable form of the thionine radical than for a regular Wurster's radical, not only because any second constant of ionization is liable to be weaker than a first one, but also because the basicity of the bridge N atom between two aromatic rings, such as in diphenylamine, is very weak.

It would be interesting to compare this state of affairs for the thiazines with that of indamines and indophenols.[5] This discussion will be reserved for a later review of the whole problem.

(5) G. Schwarzenbach and L. Michaelis, THIS JOURNAL, **60**, 1667 (1938).

The condition predicted for obtaining a possibly stable semiquinone radical from thionine is a rather strongly acid solution. This prediction is confirmed by experiment. The range of acidity necessary for the purpose is rather high, so high indeed that it was never included in the experimental works of previous authors, either for dyestuffs of this class,[6] or for any other, for the obvious reason that extremely strong acid solutions present difficulties with respect to the measurement and even the definition of *p*H. The knowledge of *p*H has so far always been desirable for a rational interpretation in problems concerned with oxidation potentials. We have to work in a range of just such an inconveniently extreme acidity as can no longer be safely measured in terms of the *p*H scale, namely, in 10 to 25 *N* sulfuric acid or in almost concentrated hydrochloric acid. The radical obtained by partial reduction of thionine in such an acid solution is yellow, has very distinct absorption bands (Figs. 5 and 6) in the blue region of the visible spectrum, which fortunately do not overlap with the bands of the oxidized form of the dye.

The degree of separation of the two steps of reduction depends very greatly on the acidity; in a 25 *N* sulfuric acid solution the separation is so complete that the potential curve shows a definite jump at 50% reduction and in the second half of the titration the pure yellow color of the radical appears without being overshadowed by the intense bluish-green color of the quinonoid form. Spectroscopically, the radical can be detected even in mixture with the quinonoid form under not too unfavorable conditions. At the end-point of reductive titration all color disappears, the leuco dye being colorless.

The radical derived from methylene blue is spectroscopically quite similar to that of thionine. Its formation, at least to an easily recognizable extent, requires a still higher acidity than in the case of thionine. It is striking that the methylation of the amino groups of thionine does not cause any distinct shift of the absorption bands of the radical.

As acidity decreases, the formation of the radical is very rapidly diminished. However, even in neutral solution it never vanishes entirely. Here, the radical must have a structure lacking equivalent resonance, and be less stable. Yet

(6) W. M. Clark, B. Cohen and H. D. Gibbs, *Publ. Health Report*, **23** 1131 (1925).

even then it is not a labile molecule inclined to undergo irreversible destruction, but perfectly stable in time to such an extent as is compatible with its equilibrium with the quinonoid dye and the leuco dye. The smallness of the concentration of this form of the radical in equilibrium with the large amount of an intensely colored substance would be sufficient to make its detection by optical methods difficult. Moreover, this form of the radical having no equivalent resonance may not be expected to exhibit any, or at least any appreciable, absorption in the visible spectrum.

Oxazines seem to behave quite similarly. Preliminary optical observation on commercial Capri blue, in the partially reduced state, showed absorption bands quite similar to those of the thiazines, but displaced toward longer wave lengths. The degree of acidity to attain this condition must be still higher.

Thiazines, particularly methylene blue, have been very much used as catalysts for oxidation, especially respiration. They increase the rate of respiration of slowly respiring cells such as erythrocytes. It has been the tendency of the authors to correlate such an effect of a dye with its faculty of being reduced in successive univalent steps.[7] Such an occurrence had not yet been demonstrated previously for the thiazine dyes. Now the suggestion concerning the mechanism of the catalytic effect of these dyestuffs is supported.

Experimental Part

1. **Preparations.**—Thionine (Lauth's violet), was prepared by dissolving 18 g. (0.1 mole) of *p*-phenylenediamine dihydrochloride in 3 liters of cold 3 *M* hydrochloric acid saturated with hydrogen sulfide. Half of a solution of 180 g. of ferric chloride hexahydrate in 400 cc. of water was stirred in, the mixture aerated to remove hydrogen sulfide and then the other half of the ferric chloride solution added. The mixture was set on ice, the precipitate filtered off and extracted with 1600 cc. of boiling water. The filtered solution is chilled and 40 cc. of 6 *M* hydrochloric acid is added, precipitating the product in crystalline condition. The product is recrystallized similarly, yield 2.5 g. The product is dried in a desiccator over calcium chloride, ground up finely and again dried over calcium chloride at 1 mm. pressure. *Anal.* Calcd. for $C_{12}H_{10}N_3SCl\cdot H_2O$: N, 14.91; S, 11.37; Cl, 12.60. Found: N, 15.03; S, 11.43; Cl, 12.37. Nitrogen by micro Dumas gave very low results but Kjeldahl determinations were satisfactory when stannous chloride was added before the digestion.

Methylene blue is prepared similarly except that 20 g. (0.1 mole) of *p*-aminodimethylaniline is dissolved in 1 liter of cold 3 *M* hydrochloric acid. The dye is salted out at the end of the reaction with 300 g. of sodium chloride. It is recrystallized twice from 400 cc. of boiling water, yield 4 g.

The essential claim as to the purity of methylene blue is that it should not be contaminated with less methylated thiazines which easily arise from it in alkaline solutions. The non- or less-methylated thiazines not being quaternary bases, can be extracted from an alkaline aqueous solution by benzene, staining it red. If a methylene blue solution is made alkaline with sodium hydroxide, it stains benzene red because it quickly decomposes. On choosing a proper *p*H one can obtain a condition where the free base of the less methylated compounds is extractable and still no decomposition of methylene blue is noticed for a sufficiently long time. When a 1 to 1000 solution, say of thionine or toluidine blue, in phosphate buffer of *p*H 7.5 is extracted with an equal volume of benzene by vigorously shaking for ten seconds, the benzene, after separating it from the aqueous phase, is pink. When methylene blue is treated in the same way the result depends on its purity. The best preparation obtained from outside (kept in the laboratory for some years) produced a very faint pink tint; our own preparation left benzene quite colorless. In a mixture of our preparation of methylene blue with commercial toluidine blue the latter could be detected easily in a proportion 1 to 50. At 1 to 100 the test was doubtful.

Every author working with methylene blue has had trouble in obtaining a really satisfactory elementary analysis. This may be due to the fact that the water of crystallization easily changes from 1 to 2 molecules, perhaps also 3.

Well ground samples were dried in vacuum over calcium chloride but difficulty was encountered on attempting to weigh out samples as moisture was rapidly absorbed, so the product was allowed to come to equilibrium with the air for a day. Then analysis agreed best with a dihydrate. *Anal.* Calcd. for $C_{16}H_{18}N_3SCl\cdot 2H_2O$: N, 11.80; Cl, 9.97; S, 9.00. Found: N, 11.31; Cl, 10.18; S, 9.19. Some of this material was converted to the iodide by dissolving 1.5 g. in 200 cc. of warm water and adding a solution of 7 g. of sodium iodide in 50 cc. of water. The crystalline product was recrystallized from 400 cc. of hot water. *Anal.* Calcd. for $C_{16}H_{18}N_3SI\cdot 2H_2O$: N, 9.40; I, 28.40; S, 7.16. Found: N, 9.24; I, 28.42; S, 7.45.

2. **Technique of Potentiometric Titration.**—Working with extremely acid solutions entails the difficulties ensuing from the liquid junction potential in a much higher degree than usual. The easiest method of examining the drift of the liquid junction potential in time is this. The potential of an acid solution such as 10 *N* sulfuric acid, at the hydrogen electrode, against a potassium chloride saturated calomel half cell is measured. The contact is established by an agar bridge such as presently will be described (Fig. 1). The end of the agar bridge is first kept above the level of the acid solution, hydrogen is bubbled for a sufficient length of time, then contact is established by pushing the agar bridge down. Any drift of the potential can be ascribed entirely to the drift of the liquid junction potential. The observations made in this way caused us to adopt the following procedure as a routine method.

(7) L. Michaelis and C. V. Smythe, *Ann. Rev. Biochem.*, 1938.

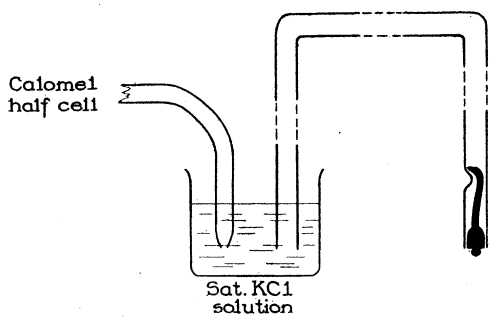


Fig. 1.—Agar bridge.

The calomel half cell and the acid solution are connected by an agar bridge. This consists of a cylindrical, properly bent glass tube, the ends not tapering. At the time when the tube was being filled with the hot liquid agar (3% agar, saturated with potassium chloride), the one end, to be used for contact with the solution in the electrode vessel, had been tightly closed with a ground glass stopper so as to leave only a minute capillary cylindrical agar film for contact. The stopper is locked by a hook fitting into a groove of the tube. This kind of agar tube has been used for many years in this Laboratory. When a freshly prepared agar tube is used as a bridge for extremely acid solutions, there is an enormous drift of potential in the negative direction. After a few hours, the drift becomes much smaller. Now the agar tube is kept for a day under saturated potassium chloride solution. When being used again, the drift subsides after fifteen to thirty minutes so much as to amount to about only one millivolt or even much less, during the period of time carrying the titration from 25 to 75% reduction. Such an agar tube, if kept under saturated potassium chloride solution when not in use, can be used over and over again. To be sure, it never will be in the same condition in parallel experiments but each experiment yields a satisfactory titration curve except for the fact that any reference to a standard potential is impossible. Neither can the oxidation–reduction potential be referred to that of the normal hydrogen electrode, nor can the potential of the solution at the hydrogen electrode be used for the computation of *p*H. We shall, for obvious reasons, use as reference point for each titration curve the potential at its 50% point of reduction. No other specification is required in order to derive the semiquinone formation constant k from the shape of the titration curve. The acidity will be expressed in terms of the normality of the acid, whereby of course one renounces any rational statement as to the relationship of acidity to semiquinone formation constant. What is certain from the experimental data is only that k becomes larger with increasing acidity. In 26 N sulfuric acid, k attains the very high value of 1000; with decreasing acidity it rapidly decreases to values < 1.

The reducing agent used for titrating the dye in such acid solution was titanous chloride. For instance, 0.07 cc. of the commercial solution of titanous chloride in strong hydrochloric acid was diluted with 10 cc. of sulfuric acid of the same concentration as the dye solution; the concentration of acid was varied from 9 to 26 N sulfuric acid. Titrations were carried out in a stream of purified nitrogen.

The other titrations, within the usual range of *p*H, were performed as usual. A very good method appeared to be reductive titration with leuco-Rosindulin GG. If conditions of solubility permitted, it was dissolved in a buffer of the same kind as used for the dye to be titrated; otherwise it was dissolved in pure water to such a concentration as to change the volume of the solution during the titration by not more than 2%, rendering any change in *p*H or ionic strength during the titration negligible.

Results

The results obtained in strongly acid solutions are best presented in the form of diagrams (Figs. 2, 3, 4) with their legends. It is clearly seen that the potential curves become steeper with increasing acidity and, from a certain acidity on, there appear in addition to the point of inflection in the midpoint, two more inflection points, symmetrically located. An acidity higher than 26 N sulfuric acid cannot be used because in this case the end-point becomes unsharp due to overlapping of the potential of the dye with that of the reducing agent. When there is no such overlapping, the curves are symmetric around the midpoint of titration. Figure 2 shows that the shape of the curve remains entirely unchanged by varying the initial concentration of the dye in the ratio 1 to 4. This is evidence for the fact that the intermediate compound is a free radical, and that no dimerization of the radical takes place, at least in the concentration range used.

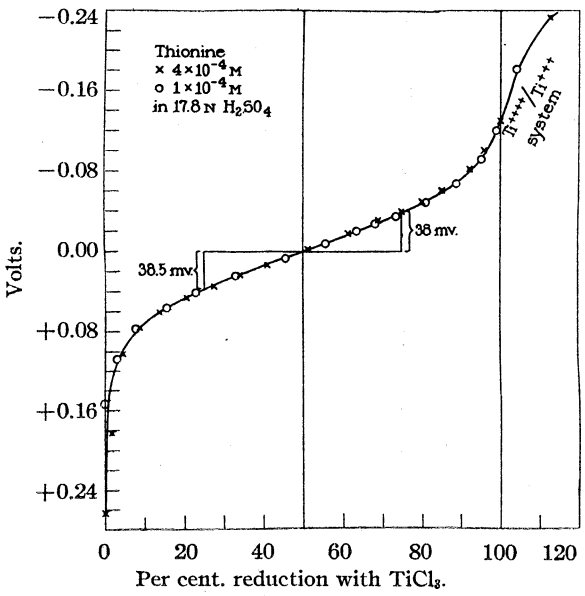


Fig. 2.—Showing independence of potential of the initial concentration of the dyestuff.

According to theory[8] there should be only one

(8) L. Michaelis and M. P. Schubert, *J. Biol. Chem.* **119**, 133 (1938).

point of inflection at 50% reduction, whenever the semiquinone formation constant k is $\leqq$ 16 or, what is the same, whenever the index potential E_i is $\leqq$ 40 millivolts. This expectation is verified as Fig. 3 shows. This is another evidence in justification of the interpretation of the titration curves.

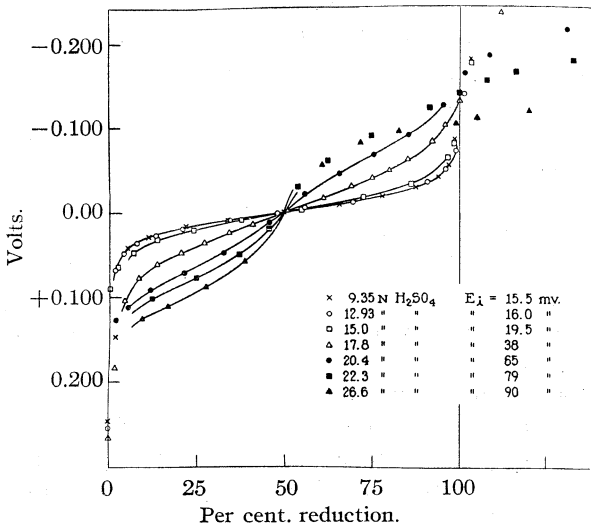


Fig. 3.—Reductive titration curves of thionine in sulfuric acid of varied normality. Reduction by titanous chloride dissolved in sulfuric acid, of the same normality as the dye solution. The drawn out curves are interpolations between all acceptable experimental points. Acceptable points are those in which no overlapping with the potential range of Ti^{++++}/Ti^{+++} occurs. The more concentrated the acid the closer are the potential ranges of Ti and the dye. Appreciable overlapping takes place only for the two highest concentrations of the acid and even here only in the second half of titration. All the other curves show sharp end-points of titration. The point × at 50.0% reduction stands not only for 9.35 N sulfuric acid, but also for 26.6 N. The flattest curve is the one for 9.35 N sulfuric acid. The points for 12.93 N sulfuric acid are distinguishable from the latter on a plot of larger scale. In the scale used here they are so close that no special curve for them has been drawn to avoid crowding. The index potentials, E_i, of the left and the right halves of each curve are equal to each other, in the worst case within one millivolt. For the two highest concentrations of sulfuric acid only the left hand E_i can be determined, and this is possible only because here the 50% point of titration is recognizable due to the fact that the point of inflection at 50% is very distinct. Lateral points of inflection, in addition to the point of inflection at 50% reduction, according to theory, should occur only if $E_i >$ 40 mv. This expectation is verified here.

The results obtained in the ordinary range of pH as established by buffers are shown in Tables II and IV. All titration curves were symmetric around the midpoint of titration, indicated by the fact that the difference of potential at 25% reduction and 50%, and the difference between 50 and 75%, are equal within at least three-tenths of a millivolt and usually better. The symmetry obtains not only from 25 to 75% but throughout the whole potential range as far as quickly established and reproducible potentials are obtained.

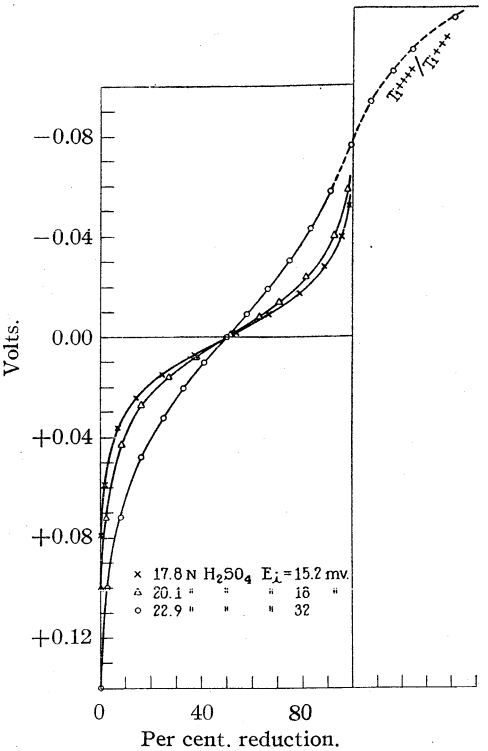


Fig. 4.—Reductive titrations of methylene blue in sulfuric acid of varied normality. Reduction by titanous chloride. The curves become steeper with increasing acidity. To reach the same degree of steepening, a higher concentration of acid is needed than for thionine. Even for the highest concentration of acid used here, the separation is not great enough to cause the appearance of the two lateral points of inflection in accordance with the fact that E_i does not reach the value 40 mv. Still higher concentrations of acids cannot be used because the overlapping of the potential ranges of the dye and Ti becomes too great. For all lower concentrations of acid, the end point is sharp.

This shows that the specimens of the dyes are not contaminated with any measurable amount of some other dyestuff of slightly different normal potential, in which case the overlapping would cause asymmetry. Furthermore, it shows that the molecular size of the oxidized and the reduced form is the same. The fact that all index poten-

TABLE I

REDUCTIVE TITRATIONS IN STRONGLY ACID SOLUTION OF THIONINE, 2×10^{-4} M WITH $TiCl_3$, AT 30°

H_2SO_4, N	Index potential, E_i, mv., from 25 to 50%	50 to 75%	Semiquinone formation constant, k	Ratio of semiquinone to total dye in the half-reduced state, $(s/a)_{max.}$	Spect. evidence for the semiquinone in the partially (about 80%) reduced state
9.35	15.5	15.3	0.02[a]	0.06[a]	No bands visible
12.9	16.0	16.0	.05	.10	Faint bands just visible in the spectroscope
15.0	19.3	19.7	.35	.24	Bands visible and color of radical just noticeable by the unaided eye
17.65	31.4	32.8	6	.55	Bands visible in spectroscope, and yellow color visible with unaided eye
17.80	38.0[b]	38.5[b]	14	.64	
	39.0[c]	39.0[c]			
20.4	64	66	160	.81	
22.3	78	80	420	.85	
26.6	95	85	1000	.94	

[a] These figures may be too small if there were any drift of liquid junction potential during the titration even to the amount of only a few tenths of a millivolt. For all the other experiments a similar error in E_i would influence the evaluation of k and $(s/a)_{max.}$ only very slightly. [b] Concentration of dye 1×10^{-4} M. [c] 4×10^{-4} M.

TABLE II

REDUCTIVE TITRATION OF THIONINE WITH LEUCOROSINDULIN GG IN VARIOUS BUFFERS AT 30°

Concn. of thionine $\times 10^4$ M	Buffer	pH	E_m	E_i	
1.0	2.5 cc. 1 N HCl + 25 cc. 0.2 M KCl to 50 cc. total vol.	1.41	+0.1967	14.6	15.0
1.0	Citrate	1.79	+0.1622	14.9	15.2
1.0	Citrate	2.07	+ .1375	14.9	15.2
1.0	Acetate	3.76	− .0141	15.5	15.5
0.2	Acetate	4.62	− .0768	16.1	15.7
.8	Acetate	4.62	− .0785	15.7	15.7
2.0	Acetate	4.62	− .0788	15.5	15.6
2.0	Acetate	4.62	− .0796	15.7	15.5
1.0	Acetate	4.77	− .0882	15.8	16.0
1.0	Acetate	5.34	− .1208	14.7	15.0
2.0	Phosphate	6.91	− .1805	15.7	(15.8)[a]
0.7	Phosphate	7.08	− .1817	(14.8)[b]	(14.8)[b]
.7	Phosphate	7.48	− .1950	15.0	(15.5)[b]
.2	Veronal	7.83	− .208	Slight drifts, impairing accuracy of E_i	
.3	Veronal	8.03	− .210		
.2	Veronal	8.22	− .2198		

[a] Not quite trustworthy because of beginning precipitation of the leuco dye. [b] Not trustworthy because of slight drift due to insolubility of leuco dye.

TABLE III

REDUCTIVE TITRATIONS IN STRONGLY ACID SOLUTIONS OF METHYLENE BLUE 2×10^{-4} M WITH $TiCl_3$, AT 30°

H_2SO_4, N	Index potential, E_i		Semiquione formation constant, k	Ratio of semiquinone to total dye in the half reduced $(s/a)_{max.}$	
17.8	14.7[a]	14.5[a]	0.001[a]	0.015[a]	No optical evidence for radical
20.1	18.0	17.8	.25	.20	Yellow color just visible near the end of titration
22.9	31.0	32	6	.55	Yellow color directly visible in the second half of titration

[a] These figures may be too small; see footnote (*a*) to Table I.

TABLE IV

REDUCTIVE TITRATION OF METHYLENE BLUE WITH LEUCOROSINDULIN GG IN BUFFER SOLUTION, AT 30°

Concn. of methylene blue $\times 10^4$	Buffer	pH	E_m	E_i	
1.0	Citrate	1.85	+0.1240	16.6	16.8
1.0	Citrate	3.68	− .0395	16.4	16.4
1.0	Acetate	3.78	− .0482	16.2	16.0
1.0	Acetate	4.42	− .1027	16.2	16.2
0.5	Acetate	4.62	− .1182	15.6	15.6
1.0	Veronal	7.92	− .2632	(14.3)	Not reliable, drift toward the end

tials are always in the neighborhood of their possible minimum values of 14 millivolts and never decrease to any lower value shows that both the dye and the leuco dye are always present in the monomeric form and no measurable polymerization either of the dye or of the leuco dye occurs within the low concentration range chosen. This fact is important to emphasize since there are some observations, spectrophotometric by Holmes,[9] for a great number of dyestuffs, both spectrophotometric and potentiometric for thiazines and oxazines by Clark and Cohen[10] and by Cohen and Preisler[11] which have been tenta-

(9) W. C. Holmes, *Ind. Eng. Chem.*, **16**, 35 (1924).

(10) W. M. Clark and B. Cohen, *Publ. Health Rep.*, **40**, 1131 (1925).

(11) B. Cohen and P. W. Preisler, *Publ. Health Rep.*, Suppl. No. 92 (1931).

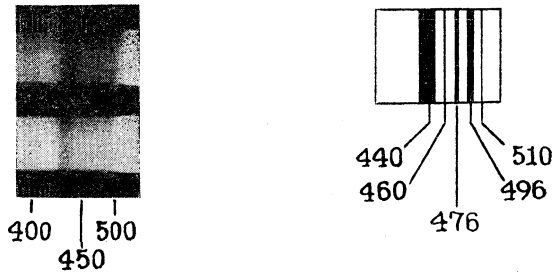


Fig. 5.—Absorption bands of the semiquinone of thionine, as existing in 20 N sulfuric acid, the dye being reduced to approximately 75% by titanous chloride. The two spectrum photographs (by Dr. Lavin) are with various lengths of exposure. The other spectrum is a schematized sketch to show the finer structure more clearly than in the photograph. Wave lengths are in mμ. On direct visual inspection with the hand spectroscope, the 496 band is strongest rather than the 440 band.

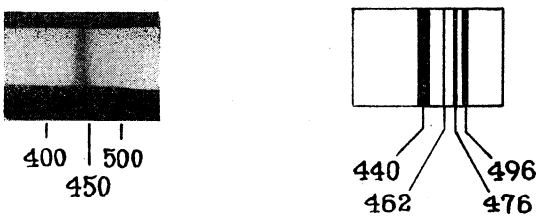


Fig. 6.—Absorption bands of the semiquinone of methylene blue. Conditions were the same as in Fig. 5.

tively interpreted as evidence that the dyestuffs in higher concentration might partially form higher molecular aggregates. This is certainly not so for thionine and methylene blue in such a concentration range as used in our experiments.[12] The potentials are stable, there is no evidence for any decomposition, not even for methylene blue, except in alkaline solution, where the accuracy of the experiments with this dyestuff suffers anyhow from the extremely slight solubility of the leuco dye. The index potential both for thionine and methylene blue in solutions from pH 4 to 7 may be estimated as about 16 millivolts; in any case decidedly not less than 15 mv. Using the methods of calculation previously described,[13] the relationship between the index potential E_i, the semiquinone formation constant k, and the maximum fraction of semiquinone to total dye is

E_i	= 15.0	15.5	16.0
k	= 0.01	0.02	0.05
$s/a_{max.}$	= .05	.065	.10

In a very wide pH range around neutrality, the dye in its half-reduced state contains not less than 5%, probably approximately 10%, as semiquinone. This should be considered as ample to account for the efficiency of the radical in establishing the reversibility of the system and its catalytic effect. It is in agreement with the behavior of other cationic dyestuffs presenting more favorable experimental conditions that k, though rapidly diminishing with increasing pH, does not vanish entirely, but remains constant from a certain pH on. This is due to the fact that the convergence of the E_1 and E_2 curves (normal potential of the lower, and of the higher step of oxidation) with increasing pH gives way to parallelism at the pH corresponding to an ionization constant of the radical.

As additional evidence that index potentials close, but not quite equal, to the theoretical minimum value of 14.3 millivolts are trustworthy within a few tenths of a millivolt, a titration experiment with a univalent oxidation system was performed in which according to the theory no other E_i value than 28.6 mv. can ever be obtained and any deviation must be ascribed to technical insufficiency. A solution of 3×10^{-4} gram atom of iron per liter in the form of ferric ammonium sulfate in a solvent 0.01 M in hydrochloric acid and 1 M in a neutral salt (potassium chloride in one experiment, sodium chloride in another) was titrated with leuco-rosindulin, dissolved in water, in such a concentration that the titration from 25 to 75% reduction required as little as 0.7 cc. for 50 cc. of the solution to be titrated. The change in ionic strength caused hereby during the titration may be considered as quite negligible. The graphic evaluation of the index potentials was as shown; a and b are compu-

	E_i			
	a		b	
Expt. with 1 N KCl	28.6	28.6	28.5	28.7
Expt. with 1 N NaCl	28.6	28.3	28.9	28.7

tations based on different estimations as to the endpoint of titration, this difference being taken as

(12) It can be confirmed that even in a range of low concentrations (from 5×10^{-6} to 150×10^{-6} M) Beer's law is not obeyed. In low concentration, thionine has essentially one band at 593 mμ; and it emits a fluorescence band at about 640. As concentration increases, gradually a second band around 556 develops, and fluorescence diminishes. In alcohol, the effect of increased concentration, both on the decrease of fluorescence, and on the development of the second band, is quite considerably weaker. There is some intermolecular interaction, stronger in water than in alcohol, to the effect that the probability of an unexcited molecule absorbing 556 is increased, as the probability of an excited molecule emitting 640 is decreased. This phenomenon should not be correlated with any change in size of the molecular unit of the dye. This, of course, can be asserted only for our dyestuffs and within the concentration range used.

(13) Summarized by L. Michaelis and M. P. Schubert, *Chem. Rev.*, **22**, 437 (1938).

large as was reasonably compatible with the experimental data. These experiments suggest that any deviation of the index potential exceeding by 2 or 3 tenths of a millivolt its expected theoretical minimum value may be taken as real.

It should now be our task to plot the three normal potentials against *p*H, showing all bends corresponding to the various ionization constants of the dye in each of its three levels of reduction, as shown in many previous cases. This cannot be accomplished satisfactorily because one cannot express either the acidity of highly concentrated sulfuric acid solutions in terms of *p*H or refer the normal potentials to the standard hydrogen electrode. Here we are faced with a problem of a much more general scope, concerning both the scale of oxidation–reduction potentials, and the scale of acidity, to which we intend to devote a special study.

Summary

A semiquinone radical is shown to exist as a univalent reduction product for thionine and for methylene blue. In equilibrium with the dye and the leuco dye, it can exist only to a few per cent. of the total dye *in maximo* over the whole *p*H range covered by the customary buffers. In very strongly acid solution, such as from 10 to 26 *N* sulfuric acid, it is stable to a much higher extent and can be identified by an analysis of the reductive titration curve of the dye and by its color, which is yellow with distinct absorption bands in the blue. The semiquinone formation constant *k* reaches for thionine the value 1000 in 26.6 *N* sulfuric acid but rapidly decreases to values < 1 in less acid solutions. For methylene blue, this constant reaches in 22.9 *N* sulfuric acid only the value 6. In a wide *p*H range around neutrality, *k* is for both dyestuffs approximately 0.05. The greater stability of the radical in very acid solution is ascribed to the formation of a bivalent cation having a structure, exhibiting equivalent resonance, of the same type as a Wurster radical.

The existence of this radical is correlated with the reversibility of oxidation–reduction of thiazines, and with their catalytic effect in biological oxidations.

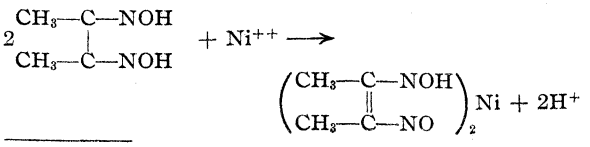
NEW YORK, N. Y. RECEIVED NOVEMBER 1, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE INSTITUTE OF TECHNOLOGY OF THE UNIVERSITY OF MINNESOTA]

Amperometric Titrations. II. The Titration of Nickel with Dimethylglyoxime Using the Dropping Mercury Electrode as Indicator Electrode

BY I. M. KOLTHOFF AND A. LANGER

In a previous paper[1] the general characteristics of amperometric titrations and the titration of lead with dichromate or chromate have been described. It is expected that many of the modern organic precipitants will be useful in the amperometric titration of several metals, especially since many of these organic reagents are specific for a limited number of inorganic ions. In the present paper the amperometric titration of nickel with dimethylglyoxime is described, using the dropping mercury electrode as indicator electrode. In ammoniacal and weakly acid medium dimethylglyoxime reacts with nickel to form the insoluble red, microcrystalline precipitate of nickel dimethylglyoxime.



(1) I. M. Kolthoff and Y. D. Pan, THIS JOURNAL, **61**, 3402 (1939).

Besides nickel, only palladium and platinum form slightly soluble compounds with dimethylglyoxime. Several metal ions, such as cobalt and ferrous iron, react with the glyoxime to form soluble complexes and may interfere in the titration of nickel. The interference by other metals has been considered in this paper.

Experimental

The general set-up was similar to that described in a previous paper.[1] The current was measured with a d'Arsonval galvanometer, the sensitivity of which could be changed with an Ayrton shunt. In a few instances a microammeter was used. A saturated calomel electrode connected with the titration cell by means of an agar salt bridge served as an external anode. The applied e. m. f. was measured with the aid of a potentiometer. In most practical work, in which the applied e. m. f., as a rule, has to be known only within 0.05 to 0.1 volt, a suitable voltmeter can be used instead. The reagent was added from a calibrated microburet of the shape given in Fig. 1. The arrangement allowed the storage and the introduction of

the reagent into the titration cell in the absence of air.[2] Before the titration air was removed from the cell by means of a current of nitrogen. For further details, see the previous publication.[1]

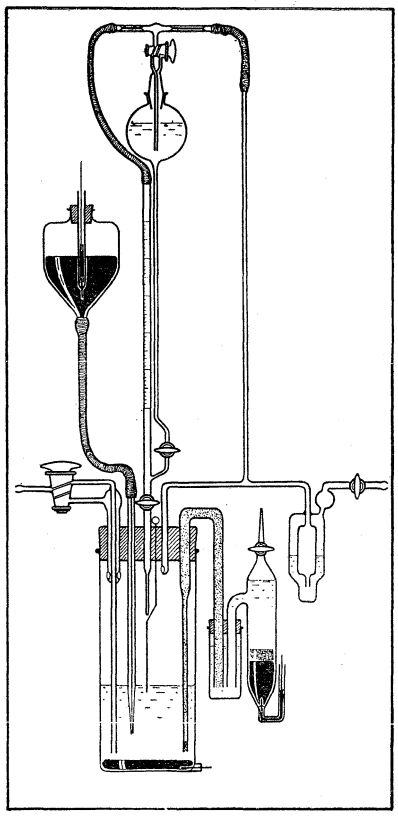


Fig. 1.—Cell allowing the titration to be carried out in the absence of air. The terminal of the agar bridge is made of sintered glass. The gas can pass through or above the solution.

Chemicals Used.—All chemicals used were of C. P. quality. If necessary they were further purified by recrystallization. The stock nickel solution was standardized by classical methods. A 0.1 *M* stock solution of dimethylglyoxime in 96% alcohol was prepared. When protected from evaporation this solution could be kept for more than six months without changing its titer.

Performance of the Titration.—A measured volume (as a rule 50 ml.) of the standard nickel solution in the proper medium was introduced into the cell, nitrogen was passed through for fifteen to twenty minutes, the proper e. m. f. was applied to the cell and the current was measured. Successive amounts of the alcoholic dimethylglyoxime solution were added from the microburet. After each addition the contents of the cell were mixed by passing nitrogen through for half a minute and the current was recorded after it had become constant (two to three minutes). The tip of the capillary was placed close to the bottom of the cell, as the red precipitate had the tendency to agglomerate near or at the surface of the solution. No trouble due to obstruction of the capillary was noticed. In all cases the values of the current, corrected for the volume change, were plotted against the amount of reagent added.

(2) Comp. J. Heyrovsky, "Physikalische Methoden der analytischen Chemie," Bd. II, Akademische Verlagsgellschaft, Leipzig, 1936, p. 284; also M. Spálenka, *Coll. Czechoslov. Chem. Commun.*, **11**, 146 (1939).

Experimental Results

The most suitable titration medium for nickel was found to be an ammoniacal solution. Consequently, current voltage curves (polarograms) of nickel and dimethylglyoxime were determined at different concentrations in order to find the most suitable range of values of the applied e. m. f. between which the titrations have to be carried out. In Fig. 2 the current–voltage curve of 0.004 *M* nickel chloride in 0.1 *M* ammonium chloride and 0.5 *M* ammonia is given. The wave

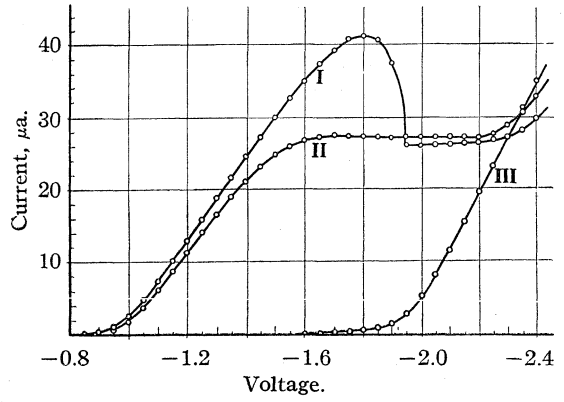


Fig. 2.—Current–voltage curves, temp. 19°, drop time 2.6 sec.: I, 0.004 *M* nickel chloride in 0.1 *M* ammonium chloride and 0.5 *M* ammonia; II, same after addition of three drops of 10% gelatin; III, blank.

is drawn out and shows a pronounced maximum (curve I). This maximum can be eliminated by the addition of a trace of gelatin[3] (0.001%), as is evident from curve II; but the wave remains drawn out. In Fig. 3 the current–voltage curves of 0.001, 0.002 and 0.003 *M* solutions of dimethylglyoxime in 0.5 *M* ammonia and 0.1 *M* ammonium chloride are given with the current–voltage curve of the medium alone (curve 1). With the 0.001 *M* dimethylglyoxime solution a diffusion current was obtained at applied values of the e. m. f. between 1.93 and 2.17 volt (curve 2); the 0.002 *M* solution showed a distinct maximum (curve 3), while the 0.003 *M* solution (curve 4) did not give any indication of a diffusion current. At these higher concentrations the current–voltage curve of

(3) Comp. J. J. Lingane; Thesis, University of Minnesota, 1938; I. M. Kolthoff and J. J. Lingane, *Chem. Rev.*, **24**, 1 (1939).

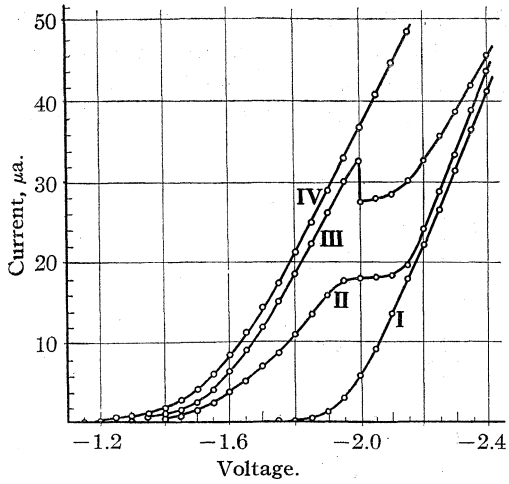


Fig. 3.—Current–voltage curves, temp. 22°, drop time 2.8 sec.: I, 0.1 *M* ammonium chloride and 0.5 *M* ammonia; II, with 0.001 *M* dimethylglyoxime; III, with 0.002 *M*; IV, with 0.003 *M*.

the reagent coincided smoothly with the decomposition current of the medium at higher applied e. m. f. In Fig. 3b it is shown that at an applied e. m. f. of 1.85 volt the dimethylglyoxime current was proportional to the concentration when the latter was smaller than 0.002 *M*. The current

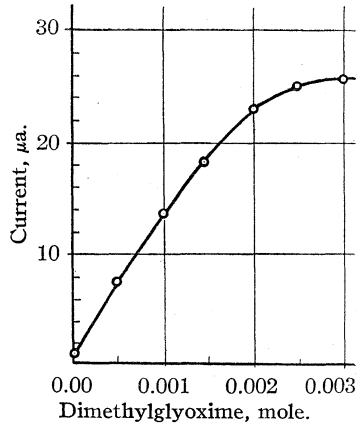


Fig. 3b.—Current at applied voltage of −1.85 v. at different concentrations of dimethylglyoxime in 0.1 *M* ammonium chloride and 0.5 *M* ammonia; temp. 22°, drop time 2.8 sec.

increased only slightly with further increase of the dimethylglyoxime concentration. An applied e. m. f. of 1.85 volt was therefore selected in the performance of the titration. As alcohol was added with the introduction of the reagent, the diffusion current of nickel was determined at $E_{appl.}$ = 1.85 v. in the above medium in the presence of different amounts of alcohol. The diffusion current of nickel remained practically unaltered at alcohol concentrations smaller than 12%.

In Fig. 4 are given the data obtained in the titration of a 0.005 *M* nickel solution in 0.1 *M* ammonium chloride and 0.5 *M* ammonia with 0.1 *M* dimethylglyoxime at an applied e. m. f. of 1.85 v. The ordinate gives the values of the current and the abscissa the volume of reagent added. In the titrations the point of intersection was found after addition of 5.00 to 5.03 ml. of reagent. The results are accurate and precise.

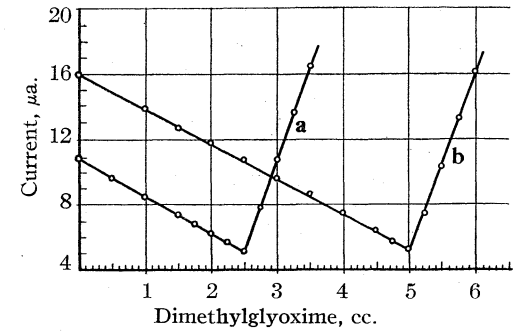


Fig. 4.—Titration curves of 50 ml. of (a) 0.0025 *M*, (b) 0.005 *M*, nickel chloride solutions in 0.1 *M* ammonium chloride and 0.5 *M* ammonia at an applied e. m. f. −1.85 v. with 0.1 *M* dimethylglyoxime; temp. 25°, drop time 2.5 sec.

The concentrations of ammonia and ammonium chloride could be changed within wide limits without affecting the results. Keeping the ammonium chloride concentration equal to 0.1 *M* the residual current at the point of intersection increased only slightly with increasing concentration of ammonia. In 0.5 *M* ammonia it was only 0.85 microampere, in 1 *M* ammonia 1.2, and in 2 *M* ammonia 1.3 microampere. A few data obtained in the titration of 50 ml. of 0.004 *M* nickel chloride with 0.1 *M* dimethylglyoxime in the neighborhood of the end-point are given in Fig. 5. It is seen that in all cases the point of intersection was found after addition of 4.00 ml. of reagent. An increase of the ammonium chloride concentration resulted in a marked increase of the current at the point of intersection. In 0.1 *M* chloride and 0.5 *M* ammonia it was found equal to 0.88 microampere, but in 1 *M* ammonium chloride and 0.5 *M* ammonia it was found equal to 2.2 microamperes. Larger amounts of ammonium chloride apparently increase the solubility of the nickel dimethylglyoxime. In general, it is recommend-

able to keep the ammonium chloride concentration smaller than 0.5 M.

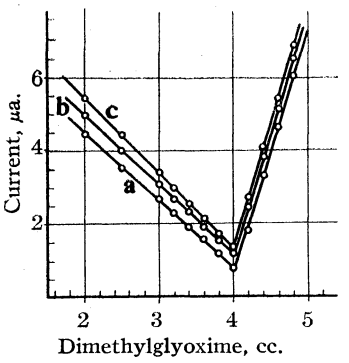


Fig. 5.—Titration curves of 50 ml. of 0.004 M nickel chloride in 0.1 M ammonium chloride and (a) 0.5 M ammonia, (b) 1.0 M ammonia, (c) 2.0 M ammonia solution with 0.1 M dimethylglyoxime at an applied e. m. f. of −1.85 v.; temp. 23°, drop time 3.1 sec.

In Fig. 6 are given the data obtained at various applied e. m. f.'s in the titration of 50 ml. of 0.004 M nickel in 0.1 M ammonium chloride and 0.5 M ammonia. The best results were obtained at an applied e. m. f. of 1.6 to 1.9 v. At an applied e. m. f. of 2.0 v. the current at the end-point was relatively great (5.3 microamp.) corresponding to the current of the medium at this voltage. The data obtained at an applied e. m. f. of 1.4 volts varied in an irregular way. These irregularities are caused by stirring effects which are responsible for the occurrence of the maximum

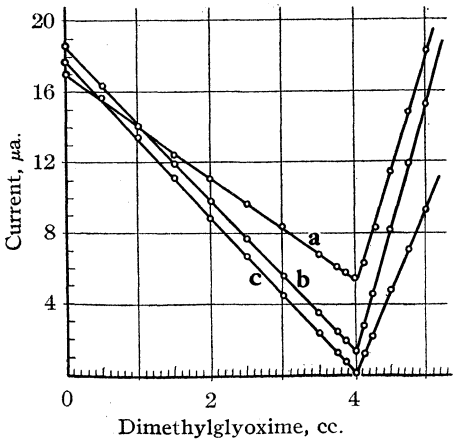


Fig. 6.—Titration curves of 50 ml. of 0.004 M nickel chloride in 0.1 M ammonium chloride and 0.5 M ammonia solution with 0.1 M dimethylglyoxime at an applied e. m. f. of (a) −2.0 v., (b) −1.8 v., (c) −1.6 v.; temp. 25°, drop time 3.1 sec.

in the nickel curve (see Fig. 2). The stirring effect and also the irregularities were eliminated by the elimination of the maximum as is evident from the results shown in Fig. 7. In this titration

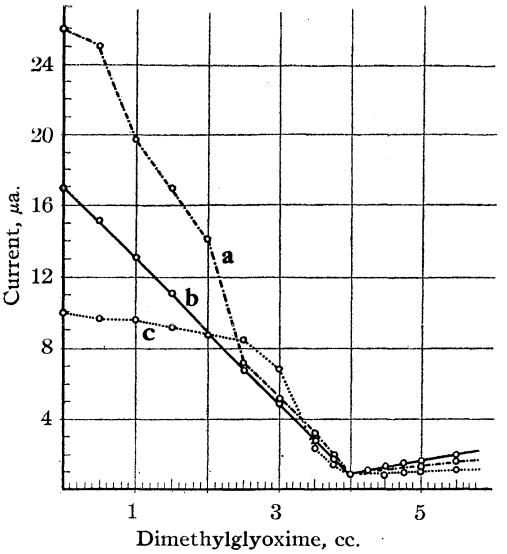


Fig. 7.—Titration curves of 50 ml. of 0.004 M nickel chloride in 0.1 M ammonium chloride and 0.5 M ammonia solution with 0.1 M dimethylglyoxime at an applied e. m. f. of (a) −1.4 v., (b) −1.4 v. and addition of 1 ml. of 1% gelatin, (c) −1.2 v.; temp. 25°, drop time 3.1 sec.

the maximum was eliminated by the addition of 1 ml. of 1% gelatin. The precipitation line was found to be straight until the end-point. After passing the end-point the current increased only slightly, as at an $E_{\text{appl.}}$ of 1.4 v. the currents of dimethylglyoxime solutions were very small (see Fig. 3), although proportional to the concentration of the reagent. The data obtained at an applied e. m. f. of 1.2 v. were very irregular (see Fig. 7) for the same reason as at $E_{\text{appl.}}$ of 1.4 v. A great number of titrations was carried out with 50 ml. of a nickel solution (in 0.1 M ammonium chloride, and 0.5 M ammonia at $E_{\text{appl.}}$ = 1.85 v.) the concentration of which was varied between 0.01 and 0.001 M. The results were precise and accurate within 0.4%. Titrations were also carried out with more dilute solutions, using a 0.01 M solution of dimethylglyoxime as reagent. Some data obtained in the titration of 0.0001 M, 0.0002 M and 0.0004 M nickel solutions are given in Fig. 8.

In these highly dilute solutions the solubility of the precipitate at and near the end-point is distinctly noticeable. However, by plotting the

TABLE I

TITRATION OF 50 ML. OF 0.004 *M* NICKEL CHLORIDE SOLUTION IN 0.1 *M* AMMONIUM CHLORIDE AND 0.5 *M* AMMONIA WITH 0.1 *M* DIMETHYLGLYOXIME (t = 2.8 SEC.; TEMP. = 24° C.)

Reagent added, ml.	0.00	1.00	2.00	3.00	3.20	3.40	3.80	3.90	4.00	4.10	4.20	4.40
Current (corr.) μa.	18.90[a]	13.96[a]	9.66[a]	5.52[b]	4.58[b]	3.64[b]	2.01[b]	1.64[b]	1.50[b]	2.82[b]	4.56[b]	6.44[b]

[a] Galvanometer at 0.01 sensitivity. [b] At 0.1 sensitivity.

TABLE II

TITRATION OF VARYING AMOUNTS OF NICKEL

Ni taken, mg.	29.34	18.80	14.67	11.74	5.87	2.93	1.76	1.17	0.58
Rel. error, %	+0.14	+0.16	+0.30	±0.25	+0.75	−0.3	−1.2	+0.25	−1.0

measurements more than 20 to 40% removed from the equivalence point it is possible to get sufficient data to construct the two straight lines. Although the drop time of the mercury changed somewhat during the titration (up to 10% near the end-point) it was possible to titrate the 0.0001 *M* nickel solution with an accuracy of 1–2%. Solutions more dilute than 0.0001 *M* could not be titrated with a reasonable accuracy, as the solubility effect became too great. The above titrations all have been carried out with a 50-ml. volume of the nickel solution. The accuracy is hardly affected by taking smaller volumes. We have titrated 10-ml. portions containing 0.06 to 0.30 mg. of nickel with an accuracy of 2–3%. By making the proper changes in the apparatus and using still smaller volumes it is possible to use the method for the micro titration of nickel, when the concentration of the nickel is greater than 0.0001 *M* and the volume corrections are considered.

In Table I is given as an illustration the current (corrected for the change of the volume) in the titration of a 0.004 *M* nickel chloride solution.

In Table II is given a summary of some results obtained in the titration of 50-ml. volumes containing varying amounts of nickel. Extensive investigations have been carried out in which attempts were made to titrate the nickel in acetate buffers and in sodium acetate instead of in ammoniacal medium. Although under certain conditions useful results could be obtained in the titration of larger quantities of nickel, the results, quite generally, were much better in ammoniacal medium. For this reason details will not be reported.

Interference by Other Metal Ions.—Metal ions which are electroreduced at the applied e. m. f. used in the titration of nickel interfere when present in larger quantities, even if they do not form complexes with the reagent. It is possible to compensate the current caused by the electroreduction of the foreign metal ions, but the readings of the current during the titration become less accurate due to the relatively large fluctuations of the current during the formation of a drop of mercury. In general the concentration of foreign ions which are reduced at the applied voltage and which do not react with the reagent should not be many times greater than that of the nickel. It is expected that a stationary electrode may have advantages over the dropping electrode in this respect.

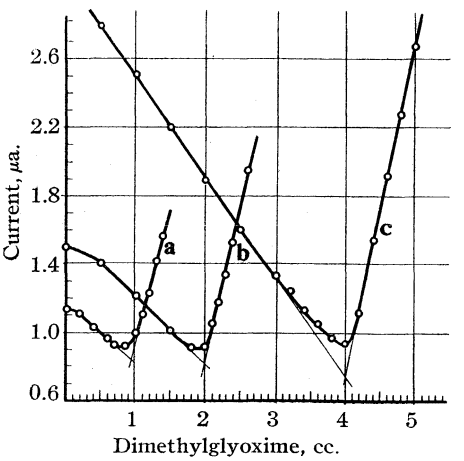


Fig. 8.—Titration curves of 50 ml. of (a) 0.0001 *M*, (b) 0.0002 *M*, (c) 0.0004 *M*, nickel chloride in 0.1 *M* ammonium chloride and 0.5 *M* ammonia solution at an applied e. m. f. of −1.85 v.; temp. 23°, drop time 2.5 sec.

Interference by Cobalt.—A special study was made of the interference caused by cobalt. Cobalt in ammoniacal solution yields a diffusion current at the applied e. m. f. used in the titrations. Moreover, it yields a soluble complex with the dimethylglyoxime. Upon addition of small amounts of the alcoholic reagent to a dilute ammoniacal cobalt solution at an applied e. m. f. of 1.85 v., the current was found to increase in a linear way with the dimethylglyoxime concentration (see Fig. 9). Apparently, the soluble com-

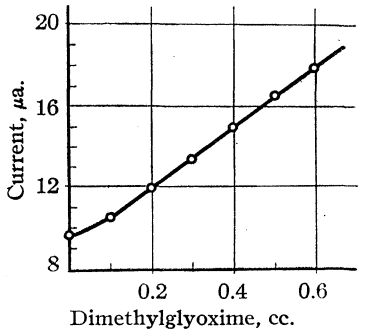


Fig. 9.—Titration curve of 50 ml. of 0.004 *M* cobalt chloride in 0.1 *M* ammonium chloride and 0.5 *M* ammonia solution with 0.1 *M* dimethylglyoxime at an applied e. m. f. of −1.85 v.; temp. 25°, drop time 2.1 sec.

plex seems to be electroreducible at the applied voltage. Although not expected from this behavior, it was found that small amounts of cobalt interfered with the titration of nickel. Some results are given graphically in Fig. 10. When the ratio of cobalt to nickel in the 0.004 *M* nickel solution was greater than 1:20, the end-point could not be found with accuracy. With larger amounts of cobalt the current changed in a highly irregular way during the titration; and increased from the very beginning. In sodium acetate or in acetate buffers containing 50% of alcohol better results were obtained, but no useful procedure was found for the titration of nickel in the presence of larger quantities of cobalt. Although nickel yields a good current–voltage curve with a diffusion current in cyanide solution, it was found

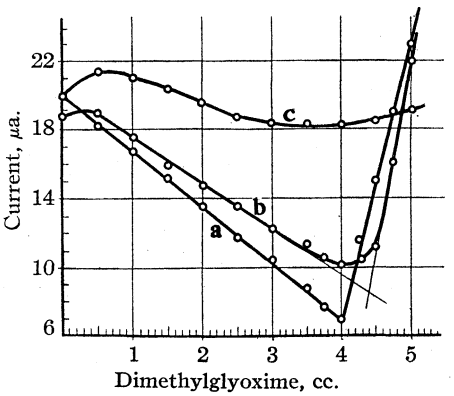


Fig. 10.—Titration curves of 50 ml. of 0.004 *M* nickel chloride in 0.1 *M* ammonium chloride and 0.5 *M* ammonia solution at an applied e. m. f. of −1.85 v. in presence of (a) 0.0002 *M* cobalt chloride, (b) 0.0004 *M*, (c) 0.001 *M*; temp. 25°, drop time 3.1 sec.

that the nickel dimethylglyoxime does not separate from such a medium when little nickel is present. On the other hand it was found that although nickel (and cobalt) do not yield a diffusion current in a solution which was 0.05 *M* in sodium pyrophosphate (see Fig. 11), the nickel complex precipitated readily from such a medium.

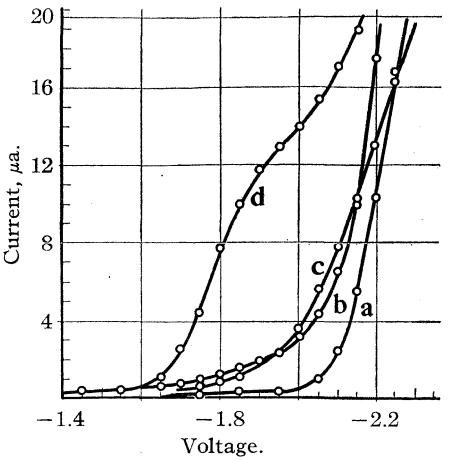


Fig. 11.—Current–voltage curves of: (a) 0.05 *M* sodium pyrophosphate, (b) with 0.004 *M* nickel chloride, (c) with 0.004 *M* cobalt chloride, (d) with 0.004 *M* dimethylglyoxime; temp. 25°, drop time 2.5 sec.

When a nickel titration was carried out in 0.05 *M* sodium pyrophosphate at an applied e. m. f. of 1.7, the titration lines had a slope as given in Fig. 12.

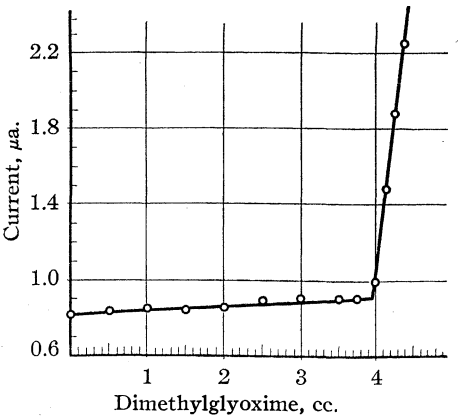


Fig. 12.—Titration curve of 50 ml. of 0.004 *M* nickel chloride in 0.05 *M* sodium pyrophosphate solution with 0.1 *M* dimethylglyoxime at an applied e. m. f. of −1.7 v.; temp. 24°, drop time 2.5 sec.

The end-point could be found with an accuracy of 1–2%. Again, however, relatively small amounts of cobalt interfered. When the amount of cobalt

is more than 5% that of the nickel, it is necessary to remove it by chemical separation. Satisfactory results were obtained by removing the cobalt as potassium cobaltinitrite. To the solution, acidified with acetic acid, was added a large excess of potassium nitrite. After the precipitate had settled it was filtered and washed (or an aliquot part of the filtrate was taken), and the filtrate was evaporated to dryness in the presence of enough hydrochloric acid to remove all of the nitrite. The latter interferes with the nickel titration as it is electroreduced at the applied e. m. f. used in the titrations. The nickel was titrated in ammoniacal medium at an applied voltage of 1.65 in the presence of 1 ml. of 1% gelatin. Taking mixtures with a ratio of cobalt to nickel of 10 to 1, results were obtained which were accurate to within 0.5%. Even when the ratio was 100 to one the results were entirely satisfactory.

Interference by Other Metal Ions.—Metal ions, such as ferric iron, aluminum and chromium, which are precipitated in ammoniacal medium can be present in small quantities (about double the amount of nickel). When present in larger quantities low results are found, as the hydrous oxides adsorb nickel. The errors found in the titration of 50 ml. of 0.004 *M* nickel in the presence of 1 ml. of 0.1 *M* solutions of ferric iron, aluminum, chromium and manganese, respectively, were −0.25, −0.5, −2.5, and +0.8%. Larger amounts of the above ions must be removed by classical chemical methods. We have applied the nickel titration to the determination of nickel in nickel steel. After dissolving the sample, oxidation of the iron and reprecipitation from ammoniacal medium in the presence of ammonium chloride, the nickel content was found to be 3.44%, in good agreement with the value 3.47% given by the Bureau of Standards. It is simpler to remove the iron by the ammonium benzoate method.[4] The residue of the solution of the steel (1.16 g.) after oxidation and evaporation was taken up in 0.1 *N* hydrochloric acid, dilute ammonia was added until beginning turbidity, then 5 ml. of glacial acetic acid and 100 ml. of 10% ammonium benzoate. After boiling for five minutes the precipitate was filtered and washed with dilute ammonium benzoate in 30% acetic acid. The filtrate and washings were evaporated, the residue taken up in ammonium chloride and ammonia and the whole diluted to 250 ml. in a volumetric flask. Fifty-ml. portions were titrated with 0.1 *M* dimethylglyoxime. As an average from four titrations the nickel content was found to be equal to 3.48 ± 0.04%.

Cadmium and zinc do not react with the dimethylglyoxime, but they are reduced at the applied e. m. f. at which the titration is carried out. Still, it was found possible to titrate 0.004 *M* nickel solutions in the presence of the same amounts of cadmium and zinc with an accuracy of 1%.

Cupric copper was found to interfere badly. It has to be removed from the solution before titrating the nickel.

Solubility of Nickel Dimethylglyoxime.—An attempt has been made to determine the solubility of the red precipitate in various solutions polarographically. The determination should be carried out at an applied e. m. f. at which both nickel and dimethylglyoxime yield a diffusion current. At such an e. m. f. the diffusion current of nickel is: $i_{d_{Ni}} = k_{Ni}C_{Ni}$, and of dimethylglyoxime $i_{d_{D.G.}} = k_{D.G.}C_{D.G.}$ The k values can be determined empirically by determining the diffusion currents of nickel and dimethylglyoxime at different concentrations. It is then simple to calculate the solubility from the current measured with the saturated solution (1 Ni + 2 D.G.). Unfortunately, it was hardly possible to find in the various media a suitable value of the applied e. m. f. at which nickel and dimethylglyoxime (or one of them) yield the diffusion current. The best results were obtained with an acetate buffer of *p*H 4.05 (0.03 *M* in sodium acetate) at an applied e. m. f. of 1.45 v. The results corresponded to a solubility of 9.5 mg. of nickel dimethylglyoxime per liter. The other results are not reported as they are highly approximate for the reasons mentioned above.

Summary

1. The amperometric titration of nickel in ammoniacal medium with an alcoholic solution of dimethylglyoxime, using the dropping mercury electrode as indicator electrode, yields accurate and precise results.

2. The method is especially useful for the titration of very dilute nickel solutions, good results being obtained in a concentration range between 0.01 and 0.0001 *M*.

3. The interference by other metal ions is

(4) I. M. Kolthoff, V. A. Stenger and B. Moskovitz, THIS JOURNAL, 56, 812 (1934).

discussed. Procedures are described for the determination of nickel after removal of large amounts of cobalt and of iron. The procedure given for the determination of nickel in nickel steels yields good results.

MINNEAPOLIS, MINN. RECEIVED OCTOBER 30, 1939

[CONTRIBUTION FROM THE STERLING CHEMISTRY LABORATORY, YALE UNIVERSITY]

Some Alkamine Esters of Disubstituted Methylcarbamic Acids

BY JOHN J. DONLEAVY AND JAMES ENGLISH, JR.

Most prominent among the various types of simple amines exhibiting local anesthetic properties are the benzohydrylamines. Amines of this type ($C_6H_5CH(NH_2)R$) were first found to be active local anesthetics by Ogata[1] and further study by Fourneau and his collaborators led to the development of a whole series of extremely active local anesthetics including numerous alkoxy-substituted benzohydrylamines.[2] Certain compounds of analogous structure have been studied in this Laboratory and found to be quite active although rather irritating. Experience has shown that in some cases[3] mixed, or aliphatic–aromatic, types are often more active than the diaryl or benzohydrylamine derivatives themselves. Hence typical examples of each of these classes were included in the present investigation.

It was thought possible that the introduction of groups on the nitrogen atom in compounds of this type might act to decrease the irritation produced in the test animals and among the groups considered for this purpose was the COOR group. The present paper describes the preparation of several types of disubstituted methylcarbamates in which R is an aminoalkyl group. It was thought that such compounds might combine the high activity of the benzohydrylamines with that of the amino alcohol carbamates, which are known to be local anesthetics.[4]

The compounds prepared were of the type $R_1R_2CHNHCOO(CH_2)_nNR_2$ where R_1 and R_2 are either aromatic or aliphatic radicals. Two methods of preparation have been worked out for the isocyanate intermediate in the synthesis of the type in which R_1 and R_2 are both aromatic. The first is based on a modification of the Curtius reaction of acid azides as developed by Naejeli.[5] This involves the reaction of an acid chloride with sodium azide in dilute acetone solution to give the isocyanate which is immediately treated with the appropriate amino alcohol to give a substituted carbamate. The second method, which was applied also to the aliphatic compounds, consists of the preparation of the isocyanate by the reaction of the alkyl bromide with silver isocyanate and treating this in turn with an amino alcohol. The compounds prepared are listed in Table I.

The pharmacological data will appear elsewhere[6]; it may be said here that the compounds are highly active local anesthetics of toxicity comparable to cocaine; they are somewhat irritating, however.

Experimental

Diphenylmethyl Isocyanate.—Fifteen grams of diphenylmethyl bromide was placed in a flask equipped with a reflux condenser and a mechanical stirrer, care being taken to protect the mixture from moisture at all times. One hundred cc. of anhydrous ether was then added and 12 g. of silver cyanate introduced. The mixture was refluxed and stirred for three hours and refluxing continued overnight. After filtering from the silver bromide, the ether was removed and the product distilled. Diphenylmethyl isocyanate boils at 148° (4 mm.). The yield is 80% of the theoretical.

Amino Alcohol Carbamates.—A dry ether solution of the above isocyanate was treated with the calculated quantity of the desired amino alcohol. The solution was refluxed for three hours to ensure completion of the reaction. On passing dry hydrogen chloride into the cold reaction mixture the hydrochloride of the basic urethan precipitated in a fairly pure state. The products can be recrystallized from dry acetone. They are nicely crystalline salts soluble in water and somewhat hygroscopic.

Amino Alcohol Carbamates from Diphenylacetyl Chloride.—Twelve grams of diphenylacetyl chloride was dissolved in 80 cc. of acetone and the solution cooled to 0°.

(1) R. Ogata, *J. Pharm. Soc. Japan*, **456**, 81 (1920).

(2) M. Valette, *Bull. soc. chim.*, (4) **47**, 289 (1930); C. Torres, *ibid.*, (4) **37**, 1591 (1925); Y. Bonnard and J. M. Bulif, *ibid.*, (4) **49**, 1303 (1931).

(3) E. R. Bockstahler, private communication.

(4) A. D. Boese and R. T. Major, THIS JOURNAL, **57**, 175 (1935).

(5) C. Naejeli and A. Tyabji, *Helv. Chim. Acta*, **16**, 350 (1933).

(6) The authors are indebted to J. H. Weatherby and H. R. Hulpieu and the Pitman-Moore Company for carrying out the pharmacological tests.

TABLE I

SUBSTITUTED ALKAMINE METHYLCARBAMATES

	M. p., °C.	Nitrogen, % Calcd.	Found
$(C_6H_5)_2CHNHCOOCH_2CH_2N(C_2H_5)_2\cdot HCl$	179	7.75	7.63
$(C_6H_5)_2CHNHCOOCH_2CH_2CH_2N(C_2H_5)_2\cdot HCl$	183	7.45	7.26
$(C_6H_5)_2CHNHCOOCH_2CH_2N(C_4H_9)_2HCl$	136	6.70	6.53
$(C_6H_5)_2CHNHCOOCH_2CH_2N\langle CH_2CH_2 \rangle CH_2\cdot HCl$	119	Cl, 9.69	9.58
$(C_6H_5)(CH_3)CHNHCOOCH_2CH_2N(C_2H_5)_2$	B. 178 (5 mm.)	8.60	8.82
$(C_6H_5)(CH_3)CHNHCOOCH_2CH_2CH_2N(C_2H_5)_2$	B. 164 (3 mm.)	8.24	8.29
$(CH_3)_2CHNHCOOCH_2CH_2N(C_2H_5)_2HCl$	114	11.76	11.65

To this was added a saturated aqueous solution of sodium azide and the mixture shaken and cooled in ice for one-half hour. An excess of cold water was then added and the solution extracted at once with ether; the ether extract, after drying briefly over calcium chloride, was filtered and treated with the calculated quantity of the desired amino alcohol. The solution was refluxed for two hours, the ether removed and the residue heated at 100° under diminished pressure to remove unchanged amino alcohol. The free base thus obtained was taken up in dry ether and a stream of dry hydrogen chloride passed into the solution. The hydrochloride precipitated at once and was filtered and recrystallized from acetone. The yield was 64% of the theoretical.

Amino Alcohol Esters of α-Phenylethylcarbamic Acid.—Eighteen grams of α-phenylethyl bromide dissolved in 100 cc. of anhydrous ether was stirred and refluxed with 15 g. of dry silver cyanate for six hours and refluxing continued overnight without stirring. At the end of this time the silver salts were filtered off and the ether evaporated. The residual oil could be distilled under reduced pressure; in this way 10.5 g. of phenylethyl isocyanate (72%) b. p. 96° (18 mm.) was obtained. This was converted to the amino alcohol carbamates by refluxing in ether solution with an amino alcohol as in the case of the diphenylmethyl isocyanate above. The esters so prepared gave hydrochlorides that were extremely hygroscopic and difficult to purify and hence these compounds were purified by distillation of the free bases. For purposes of pharmacological testing the light yellow oils thus obtained were suspended in water and the calculated amount of hydrochloric acid added to give a solution of the hydrochlorides.

β-Diethylaminoethyl Ester of Isopropylcarbamic Acid.—Twenty-four grams of isopropyl bromide in 200 cc. of anhydrous ether was refluxed for forty-eight hours with 30 g. of silver cyanate, after which time the appearance of the suspended salts seemed to have changed. Twenty grams of β-diethylaminoethanol was then added and the mixture refluxed for three hours longer. After filtering from the silver salts and removing the ether, the residue was fractionated *in vacuo*. There was obtained 10 g. of a colorless viscous oil, b. p. 123–125° (5 mm.), consisting of the pure amino alcohol carbamate. When this was treated in dry ether solution with hydrogen chloride there was obtained a crystalline hydrochloride which was purified by crystallization from acetone.

Summary

1. A method has been described for the preparation of alkamine esters of the type $\frac{R_1}{R_2}$>CHNHCOOR.

2. A series of esters has been prepared in which R_1 and R_2 are phenyl or methyl groups and R is an amino alkyl group.

3. Those compounds in which R_1 and R_2 are both phenyl exhibit marked local anesthetic activity.

NEW HAVEN, CONNECTICUT

RECEIVED NOVEMBER 10, 1939

[CONTRIBUTION FROM THE STERLING CHEMISTRY LABORATORY, YALE UNIVERSITY]

The Synthesis of Some Alkamine Esters of Alkylthiobenzoic Acids

BY JOHN J. DONLEAVY AND JAMES ENGLISH, JR.[1]

Among the numerous synthetic local anesthetics that have been prepared, those which are found most effective from a practical point of view are the *p*-aminobenzoic acid alkamine esters of the procaine type. Much experimental work has been carried out in an effort to improve the characteristics of these compounds and to correlate structure and physiological activity in this series. A considerable portion of this work has been directed toward modification of the amino alcohol portion of the molecule.[2]

It has been found, however, that the introduction of groups other than the amino group into the benzene ring of this class of compounds may increase their efficiency as local anesthetics. Alkoxy groups, for example, when introduced into the novocaine molecule are reported to increase the activity of this compound as a local anesthetic.[3] Indeed, investigation has shown that the alkoxy group may replace the nuclear amino group in aminobenzoic acid alkamine esters, in some cases increasing the activity of the resulting compound beyond that of the corresponding amino derivative.[4]

There are very few data in the literature on the effect of sulfur-containing groups on the pharmacological properties of local anesthetics and no data on the effect of alkylthio groups in this connection have appeared. In a few instances local anesthetics have been prepared which contain sulfur groupings[5] and these have been found superior to the oxygen analogs in these cases.

In view of the above facts it seemed worth while to prepare a series of alkylthio-substituted benzoic acid alkamine esters in order to determine whether such compounds possess local anesthetic activity and thus to establish the value of the alkylthio grouping in this series. By utilizing several different alkylthio groups as well as several amino alcohols it was hoped that some connection between structure and physiological action could be established in this series of compounds.

The method found most practical for the introduction of the alkylthio group into the benzoic acid nucleus is a modification of that of Leuckart[6] involving the reaction of a diazonium salt with potassium ethyl xanthate and direct alkylation of the reaction mixture. The alkylthiobenzoic acids prepared in this way from the corresponding aminobenzoic acids were converted to the acid chlorides and these were treated with the desired amino alcohol to give the alkamine ester. The basic esters were converted to the hydrochlorides for pharmacological testing.

The detailed report of the local anesthetic behavior of these compounds will be presented elsewhere.[7] It may be said that the compounds reported here are all less toxic than procaine. Furthermore, many of them surpass this local anesthetic in duration of anesthesia when tested on the rabbit cornea. The *o*- and *m*-ethylthio and methylthio compounds are more active than the corresponding *p*-derivatives.

Experimental

Alkylthiobenzoic Acids.—The aminobenzoic acid (ortho, meta, para) was diazotized in the usual manner with sodium nitrite and hydrochloric acid and the resulting diazonium salt solution poured into a hot (70°), freshly prepared solution of one mole of potassium ethyl xanthate containing sufficient sodium carbonate to neutralize the acid in the diazonium salt solution. After the reaction was over, as indicated by the cessation of the evolution of gases, the mixture was cooled. It was then treated with 1.1 moles of sodium hydroxide and one mole of diethyl or dimethyl sulfate. In the case of the higher members of the series two moles of the alkyl halide and an equivalent amount of sodium hydroxide in five times its weight of 70% alcohol was used. The mixture was then refluxed for five hours to complete the alkylation. On acidifying with hydrochloric acid, the crude alkylthiobenzoic acid was obtained in a form pure enough for use in subsequent operations. The yields ranged from 80 to 100% of the theoretical quantity. The pure alkylthiobenzoic acids are best prepared by recrystallization from dilute acetic acid. The compounds are white or slightly yellow crystalline solids, practically insoluble in water and soluble in organic solvents.

(1) This communication describes work done by James English, Jr., in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry.

(2) S. Fränkel, "Arzneimittelsynthese," Berlin, 1927, p. 387.

(3) German Patents 512,723, 511,467 (1930).

(4) E. A. Wildman and L. Thorpe, U. S. Patent 1,193,650 (1915); C. Rohman and B. Scheurle, *Arch. Pharm.*, **274**, 110 (1936); A. R. McIntyre and R. F. Sievers, *J. Pharmacol.*, **61**, 107 (1937).

(5) H. L. Hansen and L. S. Fosdick, THIS JOURNAL, **55**, 2872 (1933); German Patent 239,310; C. F. Lischer and C. N. Jordan, *ibid.*, **59**, 1623 (1937); S. A. Karjala and S. M. McElvain, *ibid.*, **55**, 2966 (1933).

(6) R. Leuckart, *J. prakt. Chem.*, [2], **41**, 179 (1890).

(7) The authors are indebted to J. H. Weatherby, H. R. Hulpieu and the Pitman-Moore Company for carrying out the pharmacological testing.

TABLE I

ALKYLTHIOBENZOIC ACIDS AND CHLORIDES

	Methyl		Ethyl		*n*-Propyl		*n*-Butyl	
	m-	*o*-	*m*-	*p*-	*o*-	*m*-	*o*-	*m*-
Acids								
M. p., °C.	129	134	98	145	121	104	98	103
S, Calcd.	[b]	[a]	16.00[c]	[d]	16.32	16.32	15.24	15.24
% Found			16.06		16.14	16.19	14.98	14.97
Chlorides								
B. p., °C.	123	133	127	118	145	138	151	147
Press., mm.	8	3	3	3	3	3	3	3

[a] Previously reported m. p. 134°, German Patent 203,388 (1908). [b] Th. Zincke and J. Müller, *Ber.*, **46**, 775 (1913). [c] Monohydrate. [d] K. Auwers and C. Beger, *ibid.*, **27**, 1739 (1894).

Acid Chlorides.—To the dried alkylthiobenzoic acid prepared as above, there was added the calculated quantity of phosphorus pentachloride. A vigorous reaction ensued, and after this subsided the mixture was refluxed for one-half hour to complete the reaction. The phosphorus oxychloride was removed by distillation under reduced pressure and the product distilled. The alkylthiobenzoyl chlorides distill without decomposition at pressures below 5 mm. but on standing for some days they decompose slowly. They are light yellow, viscous oils which turn darker on standing.

Alkamine Esters.—A dry ether solution of the acid chloride prepared as above was treated with a mixture of one molecular quantity of the desired amino alcohol and an excess of pyridine (about 2 moles). After refluxing for three hours the mixture was poured into a cold dilute solution of sodium carbonate and the basic ester extracted with ether. The ether was then dried over sodium sulfate and removed in the usual manner. The products were distilled under reduced pressure. Hydrochlorides of these esters were prepared by passing dry hydrogen chloride into a dry ether solution of the free base. The precipitated salt was filtered and recrystallized from dry acetone. The pure salts are white crystalline compounds, somewhat hygroscopic, especially if not quite pure. The lower members of the series are readily soluble in water; the solubility diminishes with increase in the size of the alkyl groups on sulfur and in the amino alcohol portion of the molecule.

TABLE II

ALKAMINE ESTERS

	B. p. °C.	Mm.	Hydrochloride m. p., °C.	Nitrogen, % Calcd.	Found
***o*-Ethylthiobenzoates**					
β-Diethylaminoethyl	158	3	128	4.42	4.46
γ-Diethylaminopropyl	184	3	121	4.24	4.23
β-Piperidinoethyl	197	3	134	Cl, 10.54	10.55
β-Dibutylaminoethyl	187	3	116	3.75	3.83
***o*-*n*-Propylthiobenzoates**					
β-Diethylaminoethyl	176	3	123	4.24	4.22
γ-Diethylaminopropyl	182	3	87	4.02	4.03
β-Piperidinoethyl	190	3	128	Cl, 10.12	10.31
β-Dibutylaminoethyl	208	3	93	3.62	3.57
***o*-*n*-Butylthiobenzoates**					
β-Diethylaminoethyl	180	2	117	4.06	4.00
γ-Diethylaminopropyl	193	2	96	3.90	3.81
β-Piperidinoethyl	198	2	120	Cl, 9.72	9.85
β-Dibutylaminoethyl	193	3	107	3.49	3.37
***m*-Methylthiobenzoates**					
β-Diethylaminoethyl	185	5	153	4.63	4.62
γ-Diethylaminopropyl	190	4	149	4.42	4.38
***m*-Ethylthiobenzoates**					
β-Diethylaminoethyl	163	2	135	4.42	4.34
γ-Diethylaminopropyl	170	3	125	4.24	4.13
β-Piperidinoethyl	173	3	139	Cl, 10.54	10.65
***m*-*n*-Propylthiobenzoates**					
β-Diethylaminoethyl	172	2	110	4.24	4.32
γ-Diethylaminopropyl	183	3	94	4.06	3.98
β-Piperidinoethyl	182	3	116	Cl, 10.12	10.24
***m*-*n*-Butylthiobenzoates**					
β-Diethylaminoethyl	200	4	110	4.06	3.97
γ-Diethylaminopropyl	194	3	96	3.90	3.97
β-Piperidinoethyl	198	3	114	Cl, 9.72	9.95
***p*-Ethylthiobenzoates**					
β-Diethylaminoethyl	160	3	166	4.42	4.54
γ-Diethylaminopropyl	185	3	138	4.24	4.20

All nitrogen analyses in Table II were done by the Kjeldahl method on a semimicro scale. Chlorine analyses are reported for those compounds not suited to this method.

Summary

1. A general method of preparation of a series of alkylthiobenzoic acids has been described.

2. A series of alkamine esters of these acids has been prepared by action of their acid chlorides on a series of amino alcohols.

3. Preliminary pharmacological investigation has shown these compounds to possess marked local anesthetic activity and low toxicity.

NEW HAVEN, CONNECTICUT

RECEIVED NOVEMBER 10, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. LXXXV. Oxidation of Sarsasapogenin Acetate with Potassium Permanganate

BY RUSSELL E. MARKER AND EWALD ROHRMANN

Although the oxidative degradation of the side chain of the steroidal sapogenins using chromic anhydride has been rather extensively investigated, especially with sarsasapogenin, only a few studies have been reported concerning the effect of other oxidizing agents upon the side chain. Several investigators[1,2,3] have studied the action of nitric acid on the side chain and observed that this reagent tends to yield C_{22} lactones. Simpson and Jacobs[2] observed that the side chain of sarsasapogenin is inert to sodium hypobromite. We have substantiated this observation. This is in accordance with the apparent inertness of the side chain in alkaline solutions.

With the hope of gaining further information concerning the nature of the side chain, we have made a brief study of the action of potassium permanganate on sarsasapogenin acetate.

Sarsasapogenin acetate, when treated with potassium permanganate in acetic acid solution at 20°, is readily oxidized to yield the C_{22} keto acid,[4] the C_{22} lactone[5] and sarsasapogenoic acid. Almost identical results were obtained when the reaction was carried out at 50–70°. We find that sarsasapogenoic acid acetate and the C_{22} lactone acetate are relatively inert to potassium permanganate in acetic acid and appear to give none of the C_{22} keto acid. The C_{19} dibasic acid[6] was not encountered in the permanganate oxidation, indicating that permanganate under the conditions used has less tendency to further oxidize a ketonic carbonyl group with subsequent ring rupture than is the case with chromic anhydride.

In striking contrast to the action of permanganate on sarsasapogenin acetate in acid solution is the great stability of the sapogenin to this reagent in neutral or alkaline medium. Sarsasapogenin acetate was unaffected by heating with potassium permanganate in a pyridine–aqueous sodium carbonate medium. The substance also was unaffected by boiling with a pyridine solution of potassium permanganate. These results show further that the sapogenin side chain is non-reactive in alkaline or neutral medium in contrast to its reactivity in acidic medium.[7]

The results on the oxidation of sarsasapogenin acetate with permanganate raise some interesting questions relative to the mechanism of the side chain oxidation. The great ease of the formation of the C_{22} keto acid, the lactone and sarsasapogenoic acid and the fact that neither the lactone nor the C_{22} keto acid are formed from permanganate oxidation of sarsasapogenoic acid,[8] suggests that the oxidation may proceed through the formation of two intermediates. The extreme lability of these intermediates to further oxidation apparently results in carbon–carbon cleavages under relatively mild conditions.

We wish to thank Parke, Davis and Company for their generous help and assistance in the various phases of this work.

Experimental Part[9]

To a solution of 1 g. of sarsasapogenin acetate in 100 cc. of acetic acid at 20° was added 50 cc. of 1 *N* aqueous potassium permanganate solution. The temperature was maintained at 18 to 20° for fifteen hours, after which the mixture was diluted with water and extracted with ether. The ethereal extract was washed well with water and then with 3% sodium hydroxide solution.

Evaporation of the ether solution containing the neutral products gave a sirup which was hydrolyzed with hot ethanolic potassium hydroxide. Dilution of the resulting solution with water gave a slight precipitate which was taken up in ether and discarded. The aqueous alkaline solution was acidified with hydrochloric acid and the precipitated material taken up in ether. After sublimation in high vacuum at 160–180° the product was crystallized from ether–pentane to give white needles, m. p. 198–200°. This gave no depression with an authentic sample of sarsasapogenin lactone, m. p. 198.5–200°.

Anal. Calcd. for $C_{22}H_{34}O_3$: C, 76.25; H, 9.7. Found: C, 76.2; H, 10.0.

The sodium hydroxide washings containing the acidic fraction from the oxidation was heated on the steam-bath for fifteen minutes to complete the hydrolysis. Acidification of the cooled solution with hydrochloric acid yielded a white solid which was taken up in ether and crystallized from this solvent to give 225 mg. of white crystals. The product was recrystallized from methanol to give a product,

(1) Windaus and Linsert, *Z. physiol. Chem.*, **147**, 275 (1925).
(2) Simpson and Jacobs, *J. Biol. Chem.*, **109**, 573 (1935).
(3) Simpson and Jacobs, *ibid.*, **110**, 565 (1935).
(4) Marker and Rohrmann, THIS JOURNAL, **61**, 1285 (1939).
(5) Farmer and Kon, *J. Chem. Soc.*, 414 (1937).
(6) Marker and Rohrmann, THIS JOURNAL, **61**, 2722 (1939).
(7) Marker and Rohrmann, *ibid.*, **61**, 846 (1939).
(8) Marker and Rohrmann, *ibid.*, **61**, 2072 (1939).
(9) Micro-analyses by Dr. John R. Adams, Jr., of this Laboratory.

m. p. 286–288° dec. This gave no depression with a sample of the C_{22} keto acid previously described, m. p. 285–287°.

Anal. Calcd. for $C_{22}H_{34}O_4$: C, 72.9; H, 9.5. Found: C, 72.6; H, 9.7.

The filtrate remaining after removal of the above acid was evaporated and the sirup crystallized from aqueous acetone to give 150 mg. of white crystals, m. p. 185°. The product was recrystallized from ether–pentane as white plates, m. p. 186–188°. This gave no depression with an authentic sample of sarsasapogenoic acid, m. p. 187–189°.

Anal. Calcd. for $C_{27}H_{42}O_5$: C, 72.6; H, 9.5. Found: C, 72.4; H, 9.7.

Similar results were obtained when the oxidation was carried out at 50–70° for two hours.

A solution of sarsasapogenoic acid acetate in acetic acid when treated with aqueous potassium permanganate for three hours at 25° gave no evidence of oxidation. Some oxidation appeared to take place at 70–80° but the only product which could be isolated after mild alkaline hydrolysis was sarsasapogenoic acid.

A solution of sarsasapogenin lactone acetate in acetic acid when heated with aqueous potassium permanganate for one hour and then allowed to stand at 25° for eight hours yielded no acidic products and the lactone acetate was recovered essentially unchanged.

A solution of 1 g. of sarsasapogenin acetate in 50 cc. of pyridine was mixed with a solution of 1 g. of potassium permanganate and 2 g. of sodium carbonate in 30 cc. of water and 20 cc. of pyridine. After heating for one hour at 70° there was no evidence of oxidation. Sarsasapogenin acetate when refluxed for two hours with a pyridine solution of potassium permanganate showed no noticeable evidence of oxidation.

Summary

1. Sarsasapogenin acetate upon oxidation with potassium permanganate yields the C_{22} keto acid, the C_{22} lactone and sarsasapogenoic acid.

STATE COLLEGE, PENNA. RECEIVED NOVEMBER 22, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS, PENNSYLVANIA STATE COLLEGE, AND THE RESEARCH LABORATORIES OF PARKE, DAVIS AND COMPANY]

Sterols. LXXXVI. Desoxotestosterone and its Conversion to Testosterone

BY R. E. MARKER, E. L. WITTLE AND B. F. TULLAR

Various isomers and epimers of testosterone, such as $\Delta^{5,6}$-androstenol-17-one-3, dehydroandrosterone, *cis*-testosterone, etc., have been prepared in an attempt to obtain greater hormone activity or to learn more of the specificity of testosterone. In this connection it seemed of interest to prepare less oxygenated substances, such as desoxotestosterone and desoxoandrostenedione, which might be converted to testosterone or related substances by oxidation within the body and thus show hormone activity. That such an oxidation is conceivable might be expected from the ease of preparation of 7-keto-cholesteryl acetate from cholesteryl acetate in the laboratory and in the present work by a similar conversion of desoxotestosterone to testosterone. This paper describes the preparation of desoxotestosterone and related experiments.

The starting material, cholesterol, was converted to $\Delta^{5,6}$-cholestene by known processes[1] and after protection of the double bond by bromine the latter compound was oxidized by chromic acid to remove the side-chain. The $\Delta^{5,6}$-androstenone-17 so formed was isolated from the oxidation mixture as the insoluble semicarbazone and the carbonyl group was then regenerated by hydrolysis with dilute sulfuric acid. The insolubility of cholestene dibromide in acetic acid during the oxidation was overcome by the use of carbon tetrachloride and this procedure, together with the absence of substituents in ring A of the sterol molecule, facilitated the oxidation. Reduction of $\Delta^{5,6}$-androstenone-17 with sodium and alcohol gave the hydroxy compound (I) which was converted to the hydrochloride by treatment with dry hydrogen chloride in the cold. Regeneration of the double bond by refluxing this compound with alcoholic potassium acetate gave a mixture of desoxotestosterone (II) and the original $\Delta^{5,6}$-androstenol-17 (I), the former predominating. This mixture could not be separated by direct crystallization, recalling the preparation of the so-called "*allo*"-cholesterol, m. p. 117°,[2] by this method, a substance which was later shown to be a mixture of the true *allo*-cholesterol and cholesterol.[3]

The hydroxy compounds were separated by crystallization of the acetates prepared from this mixture and hydrolysis of the pure acetates. While these isomeric acetates show a depression in melting point when mixed, the hydroxy com-

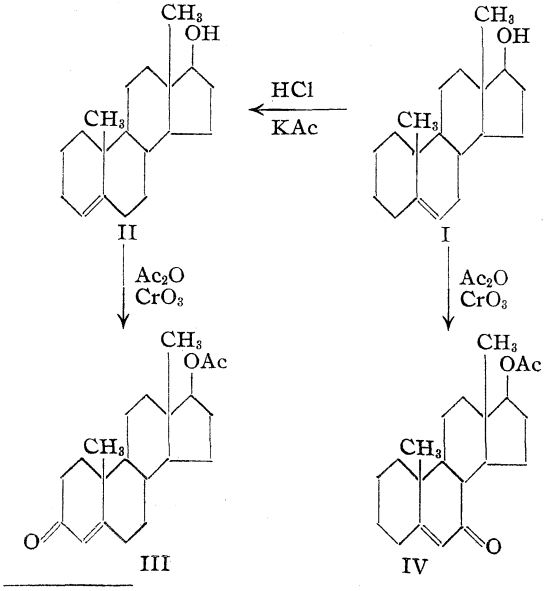
(1) Mauthner, *Monatsh.*, **28**, 1113 (1907); **30**, 635 (1909).

(2) Windaus, *Ann.*, **453**, 101 (1927).

(3) Schoenheimer and Evans, *J. Biol. Chem.*, **114**, 567 (1936).

pounds (I) and (II) do not. $\Delta^{4,5}$-Androstenone-17 was prepared from desoxotestosterone (II) by oxidation of the hydroxyl group to a carbonyl group while protecting the double bond with bromine. It was also prepared by isomerization of the double bond of $\Delta^{5,6}$-androstenone-17 with hydrogen chloride but the resulting mixture of isomers was difficult to separate by crystallization due to the low melting point and greater solubility. These isomeric carbonyl compounds are similar to the acetates in showing a depression in melting point when mixed.

While a double bond such as in neo-cholestene ($\Delta^{2,3}$-cholestene) is completely split into a dibasic acid by chromic acid oxidation, a more highly substituted bond as in cholesteryl acetate is attacked at the α-methylene position to give 7-keto compounds.[4] Thus $\Delta^{4,5}$-cholestene can be converted to cholestenone on oxidation.[5] An analogous oxidation was carried out with desoxotestosterone (II) after acetylation of the hydroxyl group and gave a mixture from which testosterone could be isolated readily. In a repetition of this oxidation, using $\Delta^{4,5}$-androstenol-17 acetate contaminated with some $\Delta^{5,6}$-androstenol-17 acetate, a small amount of an isomer of testosterone acetate was also obtained. The position of the carbonyl group was not definitely known but the compound was regarded as a 6 or 7 keto-androstenol-17 acetate. Since this work was completed an abstract appeared[6] in which 7-keto-$\Delta^{5,6}$-androstenol-17 acetate (IV) was prepared from $\Delta^{5,6}$-androstenol-17 acetate by an oxidation similar to those of the present work. The melting points recorded for 7-keto-$\Delta^{5,6}$-androstenol-17 and the acetate are identical with those of the compound obtained in this work and thus identify it as the 7-keto compound (IV). An oxidation of desoxotestosterone without the protection of the hydroxyl group, or of $\Delta^{4,5}$-androstenone-17, yielded androstenedione in an analogous manner.



(4) Mauthner and Suido, *Monatsh.*, **17**, 593 (1896).
(5) Grasshof, *Z. physiol. Chem.*, **223**, 249 (1934).
(6) Kuwada and Tutihasi, *C. A.*, **33**, 8209 (1939).

Experimental

The Oxidation of $\Delta^{5,6}$-Cholestene Dibromide.—In a 12-liter flask was placed 230 g. of cholestene dibromide and 500 cc. of carbon tetrachloride. When solution was completed, 8 liters of glacial acetic acid was added and the solution was warmed to 45° with stirring. To this stirred solution at 48–50° was added dropwise a stirred solution of 320 g. of chromic anhydride in 350 cc. of water and 800 cc. of acetic acid, over a period of four to five hours. The solution was stirred at 50° for six hours and then cooled with cold water or ice to 30°. Ethyl alcohol (250 cc.) was then added slowly to this stirred solution in about one-half hour and the acetic acid was then removed under reduced pressure until the volume of the solution had been reduced about one-half. During the evaporation the temperature of the solution was kept at 40–45°. The solution was cooled slightly and the unchanged dibromide was filtered off and dried. The filtrate was then further concentrated under reduced pressure at 40° until only a small quantity of acetic acid remained. This residue was diluted with 4 l. of water and 2.5 l. of ether and stirred until all the material was in solution; the water layer was then separated and extracted with 2.5 l. of ether. The combined ether solutions were washed well with 2 l. of water, 3 l. of water containing 300 cc. of concd. hydrochloric acid, and twice with 1.5 l. of salt water, sufficient salt to cause rapid separation of the layers. The ether solution was evaporated to dryness, the last ether being taken off cautiously to avoid undue heat and one liter of acetic acid was then added to the residue with 5 g. of powdered zinc dust. The solution was stirred vigorously and heated to 95° on the steam-bath, when 45 g. of zinc was added to this stirred solution in small portions over a period of forty-five minutes. The solution now was filtered from the caked zinc and this was washed well with acetic acid; the acetic filtrate was evaporated to dryness on the steam-bath and the residue dissolved in two liters of ether. The ether solution was washed twice with water and the acid fraction extracted with 5% sodium hydroxide solution, until all acids were removed. The ether was evaporated to dryness and the residue steam distilled to remove the volatile products. The product was redissolved in ether and the water separated. The ether was evaporated to dryness and the residue dissolved in 200 cc. of 95% ethyl alcohol; 5 g. of semicarbazide hydrochloride and 6 g. of sodium acetate were added, the solution was refluxed on the steam-bath for four hours, and the alcohol concentrated to one-half volume. The

solution was cooled and diluted with 500 cc. of ether. After shaking the suspension for about one-half hour with cooling, 200 cc. of water was added, the solution was shaken and cooled in a salt-ice-bath and filtered with suction. The white solid was washed well with water and then ether. It was refluxed with 50 cc. of alcohol for one hour, cooled, filtered and air dried, yielding 5 g. of white, powdered semicarbazone, m. p. 285–287°.

Anal. Calcd. for $C_{20}H_{31}N_3O$: C, 72.8; H, 9.5. Found: C, 73.0; H, 9.6.

$\Delta^{5,6}$-Androstenone-17.—A solution of 6.7 g. of $\Delta^{5,6}$-androstenone-17 semicarbazone, m. p. 280–285°, in 500 cc. of 95% ethyl alcohol, 35 cc. of concentrated sulfuric acid and 35 cc. of water was refluxed for two and one-half hours on the steam-bath. The solution was diluted with water and the organic product was extracted with ether. The ether solution was washed well with water and sodium bicarbonate until alkaline and evaporated to dryness. The residue was purified by distillation at 80° in a molecular still and crystallization from dilute alcohol to yield 3 g. of $\Delta^{5,6}$-androstenone-17, m. p. 100–105°. This on further purification had m. p. 105–107°.

Anal. Calcd. for $C_{19}H_{28}O$: C, 83.7; H, 10.4. Found: C, 83.5; H, 10.4.

$\Delta^{5,6}$-Androstenol-17.—A solution of 1.7 g. of $\Delta^{5,6}$-androstenone-17 in 26 cc. of refluxing *n*-propyl alcohol was treated with 2.5 g. of sodium in small portions for one-half hour. The solution was poured into water and the white solid was filtered off. This was crystallized from methyl alcohol to yield 1.4 g. of $\Delta^{5,6}$-androstenol-17, m. p. 163–165°.

Anal. Calcd. for $C_{19}H_{30}O$: C, 83.1; H, 11.0. Found: C, 83.0; H, 11.3.

$\Delta^{5,6}$-Androstenol-17 Acetate.—$\Delta^{5,6}$-Androstenol-17 was refluxed for one hour with excess acetic anhydride and then the solution was evaporated to dryness under reduced pressure. The residue was dissolved in hot methyl alcohol and allowed to crystallize, m. p. 133–135°.

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.7; H, 10.4. Found: C, 80.0; H, 10.5.

Hydrolysis of this acetate gave the original hydroxy compound.

$\Delta^{4,5}$-Androstenol-17 Acetate.—A stream of dry hydrogen chloride was bubbled through a solution of 1 g. of $\Delta^{5,6}$-androstenol-17 in chloroform, cooled to 0°, for several hours. The cold solution was allowed to stand for several hours and then carefully evaporated to dryness under reduced pressure. The white solid hydrochloride was dissolved in ethyl alcohol and refluxed for six hours with 4 g. of fused potassium acetate. The solution was poured into water and the hydroxy compound was filtered off and dried. This product consisted of a mixture of $\Delta^{4,5}$- and $\Delta^{5,6}$-androstenols, m. p. 150–155°, which could not be separated by crystallization. The total product was converted to the acetate by refluxing it with acetic anhydride for two hours. Crystallization of the acetate effected a separation into a small amount of the less soluble $\Delta^{5,6}$-androstenol-17 acetate, m. p. 133–135°, and a larger amount of the $\Delta^{4,5}$-androstenol-17 acetate, m. p. 97–100°.

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.7; H, 10.4. Found: C, 79.2; H, 10.1.

A mixture of these two acetates gave a depression in melting points, 72–82°.

$\Delta^{4,5}$-Androstenol-17.—A solution of 500 mg. of $\Delta^{4,5}$-androstenol-17 acetate, m. p. 97–100°, in 25 cc. of methyl alcohol was refluxed for one-half hour with a solution of 1 g. of potassium hydroxide in 10 cc. of 50% methanol. The solution was then diluted with water and the product extracted with ether. The ether solution was washed with water and evaporated to dryness. The hydroxy compound was purified by crystallization from methanol, m. p. 146–149°.

Anal. Calcd. for $C_{19}H_{30}O$: C, 83.1; H, 11.0. Found: C, 83.0; H, 11.0.

This product gave no depression in melting point with the $\Delta^{5,6}$-androstenol-17, m. p. 163–165°, but a melting range between the two melting points.

$\Delta^{4,5}$-Androstenone-17.—A solution of 200 mg. of $\Delta^{4,5}$-androstenol-17 in 100 cc. of acetic acid was treated with bromine in acetic acid until saturated and then a solution of 300 mg. of chromic anhydride in 20 cc. of 90% acetic acid was added with shaking. The solution was allowed to stand at room temperature for one hour and then treated with 5 g. of zinc dust on the steam-bath. The solution was filtered, poured into water and the product extracted with ether. The ether solution was washed well with water and dilute alkali and evaporated to dryness. The residue was distilled in a molecular still under reduced pressure and then crystallized from dilute methyl alcohol, m. p. 78–80°.

Anal. Calcd. for $C_{19}H_{28}O$: C, 83.7; H, 10.4. Found: C, 83.4; H, 10.7.

This ketone gave a depression in melting point, 60–65°, when mixed with $\Delta^{5,6}$-androstenone-17.

Testosterone.—To a solution of 2 g. of $\Delta^{4,5}$-androstenol-17 acetate in 75 cc. of glacial acetic acid at 50° was added a solution of 2 g. of chromic anhydride in 25 cc. of 90% acetic acid over a period of one hour. The solution was poured into water and the product was extracted with ether. The ether solution was washed well with water and dilute sodium carbonate solution and then evaporated to dryness. The remaining oil, which showed a high androgenic activity, was treated with Girard's reagent to separate the ketonic fraction. The crude ketones were treated with warm alcoholic hydrochloric acid to remove the acetate radical and then distilled in a molecular still at 0.01 mm. pressure. Crystallization of the product so obtained from ether–pentane or dilute methyl alcohol gave testosterone, m. p. 148–150°, which gave no depression in melting point with the known product.

7-Keto-$\Delta^{5,6}$-androstenol-17 Acetate.—From the neutral product of an oxidation similar to that above using $\Delta^{4,5}$-androstenol-17 acetate contaminated with some $\Delta^{5,6}$-androstenol-17 acetate a small amount of a second crystalline acetate was obtained. It was purified by crystallization from methyl alcohol, in which it is not very soluble, m. p. 215–217°.

Anal. Calcd. for $C_{21}H_{30}O_3$: C, 76.29; H, 9.17. Found: C, 76.30; H, 9.31.

Hydrolysis of this acetate with alcoholic hydrogen

chloride at 80° for several hours yielded the corresponding hydroxy compound, m. p. 141.5–142.5°.

Anal. Calcd. for $C_{19}H_{28}O_2$: C, 79.2; H, 9.68. Found: C, 79.7; H, 9.89.

This hydroxy ketone was further characterized by the orange colored 2,4-dinitrophenylhydrazone, m. p. 230–232°, which it formed.

Anal. Calcd. for $C_{25}H_{32}N_4O_5$: C, 64.0; H, 6.89. Found: C, 63.2; H, 6.99.

Androstenedione.—To a solution of 2.5 g. of $\Delta^{4,5}$-androstenol-17 in 200 cc. of acetic acid was added at 35–45° and with stirring a solution of 3 g. of chromic acid in 50 cc. of 90% acetic acid. The addition required one-half hour and the solution was then kept at 45° for one-half hour. The solution was poured into water and the product was extracted with ether. The ether solution was washed well with sodium carbonate solution and water and concentrated to a small volume. On cooling this solution for some time crystals formed and were filtered. They were recrystallized from ether to yield androstenedione, m. p. 168–170°, identical with the known product.

Summary

Cholestene dibromide was oxidized to $\Delta^{5,6}$-androstenone-17 which was converted to desoxotestosterone acetate and $\Delta^{4,5}$-androstenone-17. These new compounds on oxidation were converted to testosterone acetate and androstenedione. An isomeric 7-keto-$\Delta^{5,6}$-androstenol-17 was also obtained.

STATE COLLEGE, PENNA.
DETROIT, MICH. RECEIVED DECEMBER 1, 1939

NOTES

An Attempted Synthesis of Morphenol

BY ALFRED BURGER AND S. AVAKIAN

A recent announcement by Gilman and Cheney[1] that these authors are studying the closure of a six-membered ring between positions 1 and 9 in dibenzofuran types prompts us to report unsuccessful attempts to synthesize methylmorphenol through 6-methoxy-9-hydroxy-phenanthrylene oxide and subsequent selective reduction of the 9-hydroxy group. 4-Methoxy-dibenzofuran-1-acetic acid was treated with (a) concentrated sulfuric acid, (b) 85% sulfuric acid, (c) anhydrous hydrogen fluoride at room temperature,[2] and (d) stannic chloride in the cold, and at the boiling point of the condensing agent. The acid chloride was treated with aluminum chloride in ice-cold benzene (e), and the acid bromide with aluminum chloride in nitrobenzene solution at room temperature (f), and with boiling stannic chloride (g), but none of these reactions yielded phenanthrene derivatives. It is possible that Gilman and his coworkers will achieve ring closure by using compounds containing strongly *para*-orienting groups in position 6 of the dibenzofuran system.[1]

Since the distance between sulfur and carbon atoms is greater than that between oxygen and carbon atoms, the positions 1 and 9 in dibenzothiophene should be closer to each other than in dibenzofuran, and ring closure should be easier in the dibenzothiophene series. In investigating the effect of substituting sulfur atoms for —CH=CH— groups in polycyclic aromatic systems we are now studying the intramolecular dehydration and decarboxylation of 1-carboxy-dibenzothiophene-9-acetic acid, which should lead to derivatives of 4,5-phenanthrylene sulfide, a possible isoester of pyrene.

Experimental

4-Methoxydibenzofuran-1-carboxylic acid[3] was converted into the chloride by the action of thionyl chloride. The acid chloride crystallized from benzene–ligroin as colorless needles, m. p. 162.5–163.5°. The yield was 93%.

Anal. Calcd. for $C_{14}H_9ClO_3$: C, 64.48; H, 3.48. Found: C, 64.22; H, 3.62.

The acid chloride was stirred with an ethereal solution of diazomethane for sixteen hours. The diazo ketone crystallized out. Recrystallization from benzene–petroleum ether rendered yellow crystals, m. p. 150–151° (dec.). The yield was 86%.

Anal. Calcd. for $C_{15}H_{11}N_2O_3$: C, 67.39; H, 4.15. Found: C, 67.50; H, 4.00.

The diazo ketone was treated with ammonium hydroxide in dioxane solution according to Arndt and Eistert.[3,4] 4-Methoxydibenzofuran-1-acetamide crystallized from ethanol as colorless needles, m. p. 203°. The yield was 75%.

Anal. Calcd. for $C_{15}H_{13}NO_3$: C, 70.56; H, 5.14. Found: C, 70.93; H, 5.34.

(1) Gilman and Cheney, THIS JOURNAL, **61**, 3149 (1939).
(2) Fieser and Hershberg, *ibid.*, **61**, 1272 (1939).
(3) Gilman, Parker, Bailie and Brown, *ibid.*, **61**, 2836 (1939).
(4) Arndt and Eistert, *Ber.*, **68**, 200 (1935).

The acid amide was boiled under reflux with thirty parts of a 20% alcoholic solution of potassium hydroxide for three hours. The alcohol was replaced by water and evaporated, and the 4-methoxydibenzofuran-1-acetic acid was precipitated from the filtered solution. It was recrystallized from ethanol and appeared as colorless needles, m. p. 223–224°. The yield was 90%.

Anal. Calcd. for $C_{15}H_{12}O_4$: C, 70.28; H, 4.73. Found: C, 70.31; H, 4.43.

UNIVERSITY, VIRGINIA RECEIVED NOVEMBER 21, 1939

The Preparation of Acetyl Bromide*

BY THEODORE M. BURTON WITH ED. F. DEGERING

Acetyl bromide was prepared as early as 1863 by distilling it as formed from a mixture of glacial acetic acid, bromine and phosphorus.[1]

Investigations have shown, however, that acetyl bromide undergoes substitution with bromine to form bromo-acetyl bromides with decrease in the yield of acetyl bromide. Further improvements designed to increase the yield of acetyl bromide have also resulted in increased bromination in the nucleus.[2]

By the elimination of free bromine it was thought possible to increase the yield of acetyl bromide according to the reaction

$$3CH_3CO_2H + PBr_3 \longrightarrow 3CH_3COBr + P(OH)_3$$

Phosphorus tribromide (b. p. 169–170° at 740 mm.) can be prepared readily in 99.5% yield by slowly adding dried bromine from a dropping funnel into a slight excess of freshly washed and dried red phosphorus placed in a round-bottomed flask equipped with a mechanical stirrer and a reflux condenser.

The acetyl bromide was prepared by adding slowly through the dropping funnel, with stirring, a slight excess of 99.5% glacial acetic acid (3.075 moles of CH_3COOH per mole of phosphorus tribromide) to the cold phosphorus tribromide. The mixture separated into two layers which were distilled separately into a common receiver packed in ice. The crude acetyl bromide was rectified in a modified Podbielniak column to produce a water-white fraction boiling from 73–76° at 740 mm. The yield varied from 71.4 to 73.4% of the theoretical.

In other experiments the phosphorus tribromide was purified before use, but yields were increased only by a slight amount to 74.9% of the theoretical. In an effort to test the effect of temperature, the acetyl bromide was distilled from the reaction mixture at room temperature under reduced pressure. The product was collected in a gas bottle immersed in a bath cooled with solid carbon dioxide. No change, however, was observed in the yield. In all cases large amounts of hydrogen bromide were liberated so that the reaction probably does not proceed as indicated in the above equation.

It was found possible to prepare acetyl bromide without the formation of hydrogen bromide by adding phosphorus tribromide slowly, with stirring, to an excess of boiling acetic anhydride. The boiling point dropped as acetyl bromide was formed and when the addition of phosphorus tribromide was completed, the acetyl bromide was distilled from the mixture and rectified as before. The yield was 81.7% of the theoretical.

By using the readily prepared phosphorus tribromide, instead of free bromine with glacial acetic acid, substitution reactions are avoided and the yield of acetyl bromide can be increased to about 80% of the theoretical.

CHEMICAL LABORATORY
PURDUE UNIVERSITY
WEST LAFAYETTE, INDIANA RECEIVED AUGUST 3, 1939

Hydrogen Bonds Involving the C–H Link. IX.[1] Nitriles and Dinitriles as Solvents for Hydrogen Containing Halogenated Methanes

BY M. J. COPLEY, G. F. ZELLHOEFER AND C. S. MARVEL

Nitriles should be capable of bonding with hydrogen in halogenated methanes of the CH_2X_2 and CHX_3 types and hence should be good solvents for these products. Work reported earlier[1] shows that valeronitrile and benzonitrile do dissolve methylene chloride and monochlorodifluoromethane in excess of the amount calculated from Raoult's law. It is interesting to find that the aliphatic dinitriles, succinonitrile and glutaronitrile, dissolve less than the calculated amounts of these two halogenated methanes. Adiponitrile dissolves almost the exact calculated amount and sebaconitrile takes up more than the calculated amount. These results are interesting when considered with the boiling points of the dinitriles.

*Presented before the Indiana Academy of Science at Terre Haute, Indiana, November, 1939.

(1) H. Gal, *Ann.*, **129**, 53 (1863); M. Hanriot, *Ann. chim. phys.*, [5] **17**, 83 (1879).

(2) H. Gal, *Compt. rend.*, **56**, 1258 (1863); F. Urech, *Ber.*, **13**, 1687 (1880); J. Volhard, *Ann.*, **242**, 144 (1887); C. Hell, *Ber.*, **21**, 1726 (1888); C. F. Ward, *J. Chem. Soc.*, **123**, 2207–2213 (1923); H. B. Watson, *ibid.*, **127**, 2067–2082 (1925); Bernard Gwynn and Ed. F. Degering, *Proc. Indiana Acad. Sci.*, 87 (1939).

(1) For the eighth communication in this series see THIS JOURNAL, **61**, 3550 (1939).

TABLE I

SOLUBILITY OF HALOGENATED METHANES IN NITRILES

Theoretical solubility	Formula	B. p., °C.	CH_2Cl_2 G./g.	CH_2Cl_2 M. F., 0.311	$CHCl_2F$ G./g.	$CHCl_2F$ M. F., 0.381
Caprylonitrile	$CH_3(CH_2)_6CN$	198–200	0.462	0.405	0.875	0.420
Benzonitrile	C_6H_5CN	190.7	.463	.359	See Ref. 1	
Succinonitrile	$CN(CH_2)_2CN$	265–267	.199	.158	.231	.152
Glutaronitrile	$CN(CH_2)_3CN$	285–287	.319	.261	.457	.294
Adiponitrile	$CN(CH_2)_4CN$	295	.364	.316	.560	.428
Sebaconitrile	$CN(CH_2)_8CN$	199–200 (15 mm.)	.425	.435	.730	.522

It is obvious that succinonitrile and glutaronitrile are associated to a considerable extent; this undoubtedly is due to bonding between hydrogens of the methylene groups and the nitrogen atom of the nitrile groups. In succinonitrile the $-CH_2-$ group is alpha to one nitrile residue and beta to another and the cumulative effect is sufficient to give labile hydrogen atoms. In glutaronitrile the further separation of the nitrile groups makes their cumulative effect less on each $-CH_2-$ group. In adiponitrile this effect is fairly well overcome by the distance between the nitrile groups. In sebaconitrile the solubility goes above the calculated value but not as much as might have been expected from the solubility of the mononitriles. This evidence for hydrogen bond association in the dinitriles is of interest in view of the recent estimation that hydrogen cyanide is similarly associated to the extent of 3% at the boiling point.[2]

The solubility determinations were made at 32.2° as described earlier[3] and are reported in the table.

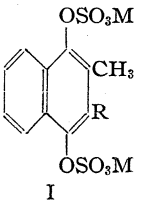
(2) Giauque and Ruehrwein, THIS JOURNAL, **61**, 2626 (1939).
(3) Zellhoefer, *Ind. Eng. Chem.*, **29**, 584 (1937).

NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS
URBANA, ILLINOIS
WILLIAMS OIL-O-MATIC HEATING CORPORATION, BLOOMINGTON, ILLINOIS RECEIVED DECEMBER 1, 1939

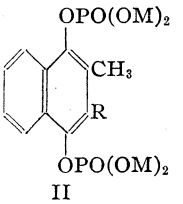
Water-Soluble Antihemorrhagic Esters

BY LOUIS F. FIESER AND EDWARD M. FRY

As a possible means of providing antihemorrhagic compounds which can be administered parenterally in a small volume of aqueous solution, we have prepared a series of water-soluble sulfuric and phosphoric acid ester derivatives of vitamin K_1 and of other quinones of established vitamin K activity. In chick assays conducted by Dr. W. L. Sampson potassium vitamin K_1 hydroquinone disulfate (I, R = phytyl, M = K) was found inactive at a dosage of 500 γ, an observation which perhaps finds a counterpart in the great loss of biological activity attending the conversion of oestrone into oestrone sulfate.[1] Similarly sodium 2,3-dimethyl-1,4-naphthohydroquinone disulfate was inactive at the same high dosage, in contrast to the corresponding quinone which is active at 50 γ. On the other hand, vitamin K_1 hydroquinone diphosphoric acid II (R = phytyl, M = H) shows activity at dosages down to 25 γ, but not at 10 γ, and thus does not fall greatly short of vitamin K_1, which gives a response at 1.5–2 γ by the same procedure. Still more potent is the sodium salt of 2-methyl-1,4-naphthohydroquinone disulfuric acid (I, R = H, M = Na), which shows antihemorrhagic activity at a level of 2 γ (assays at lower dosages are still to be made). The substance crystallizes as a dihydrate, and if the administered material undergoes hydrolysis it could give rise to only 52% of its weight of 2-methyl-1,4-naphthoquinone.



I



II

Of the water-soluble substances previously suggested for use in vitamin K therapy, phthiocol[2] suffers from being only weakly active, and free naphthohydroquinone and aminonaphthol derivatives[3] are highly sensitive to oxidation. The above active ester derivatives are colorless solids which are stable in aqueous solution and not sensitive to air or light. Furthermore, 2-methyl-3-phytyl-1,4-naphthohydroquinone diphosphoric acid can be described as a water-soluble form of vitamin K_1.

In a clinical trial conducted by Drs. H. A. Frank, A. Hurwitz and A. M. Seligman at the

(1) Butenandt and Hofstetter, *Z. physiol. Chem.*, **259**, 222 (1939).
(2) Almquist and Klose, THIS JOURNAL, **61**, 1923 (1939).
(3) Doisy, *et al.*, *ibid.*, **61**, 1932, 2563 (1939).

Beth Israel Hospital, Boston, sodium 2-methyl-1,4-naphthohydroquinone disulfate was given to a patient having a complete biliary fistula. A solution of 10 mg. of the salt in 10 cc. of 0.9% salt solution remained clear after autoclaving at 250°F. and when given intravenously reduced the prothrombin clotting time from 54 seconds to 28.5 seconds in four hours; the lowest level reached was 25 seconds in about twelve hours (normal, 15 seconds).

Experimental Part[4]

Potassium Vitamin K_1 Hydroquinone Disulfate.—A cooled suspension prepared by slowly adding 0.6 cc. of chlorosulfonic acid to 2 cc. of pyridine and 5 cc. of carbon tetrachloride was treated with 0.48 g. of vitamin K_1 hydroquinone. On manipulating the mixture with a stirring rod and boiling for ten minutes, the pyridine salt separated as a viscous mass which went to a sticky solid on cooling and diluting with ether. The liquor and washings afforded 0.17 g. of oil giving no color test with alcoholic alkali. The solid was treated while cooling with sufficient 10 *N* sodium hydroxide to produce a red color, ether was added to dissolve the liberated pyridine, and the sodium disulfate ester was separated by centrifugation as a dark red oil. This was stirred with excess 25% absolute alcoholic potassium hydroxide to effect conversion to the potassium salt, which separated as a light brown crystalline solid after dilution with absolute alcohol. Crystallization from 95% alcohol (Norite) gave colorless plates. The salt gives a clear solution in water. The sample was dried at 80° and 18 mm.

Anal. Calcd. for $C_{31}H_{46}O_8S_2K_2$: C, 54.04; H, 6.73; K, 11.35. Found: C, 54.54; H, 6.71; K, 10.67.

Sodium 2-Methyl-1,4-naphthohydroquinone Disulfate.—A mixture of 0.5 g. of 2-methyl-1,4-naphthohydroquinone with a cooled suspension from 1 cc. of pyridine, 10 cc. of carbon tetrachloride and 0.5 cc. of chlorosulfonic acid was heated for ten minutes on the steam-bath, cooled, and the solvent decanted from the oily yellow pyridine salt. This was treated with a slight excess of 10 *N* alkali, the mixture was extracted with ether, and the residual red oil taken up in a little hot water. Alcohol added in portions precipitated first inorganic material, which was removed, and then the ester salt as tan crystals (0.58 g., 0.27 g. more from the mother liquor). Crystallization from water gave 0.4 g. of colorless product free from inorganic salts, and this was further purified by dissolving it in water and adding alcohol. The air dried material proved to be a dihydrate.

Anal. Calcd. for $C_{11}H_8O_8S_2Na_2 \cdot 2H_2O$: C, 31.89; H, 2.92; Na, 11.10; H_2O, 8.70. Found: C, 31.82; H, 3.20; Na, 11.21; H_2O, 8.29.

Sodium 2,3-dimethyl-1,4-naphthohydroquinone disulfate was prepared as above from 0.5 g. of the hydroquinone. The pyridine salt was obtained on cooling as a highly hygroscopic solid. The sodium salt was crystallized once from water (0.8 g.) and then from water diluted with alcohol, giving colorless plates (air dried).

(4) Microanalyses by Lyon Southworth.

Anal. Calcd. for $C_{12}H_{10}O_8S_2Na_2 \cdot 2H_2O$: C, 33.64; H, 3.29; Na, 10.74; H_2O, 8.41. Found: C, 33.47; H, 3.49; Na, 10.97; H_2O, 9.00.

Sodium 2-Methyl-1,4-naphthohydroquinone Diphosphate (Normal Salt; II, M = Na).—A solution of 0.3 g. of the hydroquinone in 0.8 cc. of pyridine was added by drops with ice cooling to a suspension prepared by adding 0.5 cc. of phosphorus oxychloride with cooling to 1 cc. of pyridine. At the end the mixture was allowed to warm up until the exothermic reaction was over. The white suspension was then treated with 6 cc. of water, added cautiously at first with ice cooling and later heating to dissolve the product. Solid sodium carbonate was added until alkaline to litmus and the pyridine layer which separated was removed. The solution of sodium salts was stirred with absolute alcohol and the solvent decanted, leaving an aqueous solution of greatly diminished volume. The remainder of the water can be removed by stirring either with fresh portions of alcohol or with smaller portions of pyridine, leaving the sodium salt as a gum. Inorganic salts can be largely eliminated by dissolving in the least amount of hot water, cooling in ice, centrifuging and decanting from the crystallizate. Alternately, the gum is treated in the cold with methanol and enough water to bring the oily salt into solution; by adjusting the proportions inorganic salts are left undissolved and are removed by filtration. For crystallization of the product such a methanol–water filtrate was concentrated and cooled, oily salt was brought into solution with a little water, pyridine was added by drops until the solution became cloudy, and on warming on the steam-bath the sodium diphosphate separated as an oil which then crystallized (it is less soluble hot than cold). The colorless crystals were washed with methanol and dried; yield 0.68 g. The substance is very hygroscopic and liquefies on exposure to moist air. The sample for analysis was dried at 150° and 2 mm.

Anal. Calcd. for $C_{11}H_8O_8P_2Na_4 \cdot 2H_2O$: C, 28.83; H, 2.64. Found: C, 28.36; H, 2.21.

Vitamin K_1 Hydroquinone Diphosphoric Acid.—A solution of 0.48 g. of vitamin K_1 hydroquinone in 10 cc. of pyridine was cooled and added to an iced mixture of 1 cc. of phosphorus oxychloride and 5 cc. of pyridine (temperature rise to 15°). The solvent was largely removed in vacuum at 45° and the residue treated with 10 cc. of water and extracted with ether. The ethereal extract was shaken with a slight excess of 1 *N* sodium hydroxide and the alkaline layer separated and acidified with hydrochloric acid, when the diphosphoric acid precipitated. Collected by extraction with ether, the substance was obtained as a light tan amorphous solid (0.4 g.). Repetition of the process of purification by extraction from ether with alkali and precipitation with acid gave a somewhat waxy, nearly colorless solid. It gives a gel with a small amount of water and a clear solution with an adequate quantity. The sample was dried at 100° and 1 mm. (oil).

Anal. Calcd. for $C_{31}H_{50}O_8P_2$: C, 60.76; H, 8.23. Found: C, 60.92; H, 8.20.

CONVERSE MEMORIAL LABORATORY
HARVARD UNIVERSITY
CAMBRIDGE, MASS.

RECEIVED DECEMBER 18, 1939

The Preparation of Pure Stearic Acid

BY J. P. KASS AND L. S. KEYSER

The preparation of pure stearic acid is complicated by the difficulty of removing final traces of the contaminating palmitic acid, since the separation by physical means is tedious and never unquestionably complete. In a recent study, Guy and Smith[1] considered it necessary to subject "pure" stearic acid to twenty-four recrystallizations from various solvents and to three fractional distillations to obtain a 3.8% yield of final product, m. p. 69.62°, the homogeneity of which was still not beyond question. During the course of our investigations of the chemistry of the fatty acids, we have found it convenient to prepare pure stearic acid totally free from palmitic acid by the catalytic reduction of the readily purifiable octadecenoic acids. Elaidic acid,[2] and especially the α- or β-eleostearic acids,[3] are easily available and may be brought to a high state of purity by a few recrystallizations of the free acids, while pure linoleic acid[4] of theoretical iodine value may be obtained from the crystallizable α-tetrabromostearic acid.[5] Quantitative reduction was effected by shaking the acetic acid solutions of the unsaturated acids for three hours in an atmosphere of hydrogen at room temperature and 45 lb. (3 atm.) pressure in the presence of platinum oxide catalyst. One recrystallization of the product from acetic acid or 85% alcohol yielded a stearic acid melting in a capillary tube at 69.6–70.2° (corr.) and dissolving in concentrated sulfuric acid at 70° without discoloration. A similar procedure was used by Francis, Collins and Piper[6] for the preparation of behenic acid from erucic acid.

(1) Guy and Smith, *J. Chem. Soc.*, 616 (1939).
(2) Rankoff, *Ber.*, **64**, 619 (1931); Smith, *J. Chem. Soc.*, 976 (1939).
(3) Wan and Chen, THIS JOURNAL, **61**, 2283 (1939).
(4) Rollet, *Z. physiol. Chem.*, **62**, 410 (1909).
(5) McCutcheon, *Can. J. Research*, **16**, 158 (1938).
(6) Francis, Collins and Piper, *Proc. Roy. Soc.* (London), **A158**, 707 (1937).

HORMEL FOUNDATION
DEPARTMENTS OF BOTANY AND CHEMISTRY
UNIVERSITY OF MINNESOTA
MINNEAPOLIS, MINN. RECEIVED NOVEMBER 17, 1939

The Preparation of *m*-Halogenophenols

BY HERBERT H. HODGSON

The author's attention has been drawn to a recent paper by S. Natelson and S. P. Gottfried[1] in which the preparation of *m*-bromophenol is described in language which implies originality, *viz.*: "Since this paper[1] was written, Smith and Haller[2] have published a method for obtaining *m*-bromophenol in good yield .... Their over-all yield is not as good as that obtained from the procedure described herein[1] nor is their procedure as simple."

It is of interest to note that from January to May of this present year (1939) the preparation of *m*-bromophenol has been described no fewer than three times,[1,2,3] and in only one of them[3] has the work of the present writer been mentioned.

The method apparently claimed as new by Natelson and Gottfried[1] was patented by the author[4] in 1923, and C. F. Koelsch[3] has stated recently that this patent of seventeen years ago is substantially true and that yields of 75–80% may be obtained thereby. Similar confirmations of the patent claim, however, have already been made to the writer by numerous chemists during the past seventeen years, who have found yields of the order of 80–90%.

Yields of over 90% of *m*-chlorophenol from *m*-chloroaniline have been obtained by the patented method[4] in large scale (kilo.) preparations. Subsequent work proved that excellent yields of *m*-fluorophenol[5] could also be obtained from *m*-fluoroaniline, while even the non-steam volatile *m*-hydroxybenzaldehyde[6] was prepared in excellent yield by the process.

The patented method[4] is substantially the same in detail as that described at length by Koelsch,[3] and is probably the best process yet devised for the preparation of steam-volatile phenols, since it is of universal application.

(1) Natelson and Gottfried, THIS JOURNAL, **61**, 1001 (1939).
(2) Smith and Haller, *ibid.*, **61**, 143 (1939).
(3) C. F. Koelsch, *ibid.*, **61**, 969 (1939).
(4) H. H. Hodgson and The British Dyestuffs Corporation, English Patent 200,714 (1923); *B. C. A.*, [i] 1005 (1923).
(5) H. H. Hodgson and J. Nixon, *J. Chem. Soc.*, 1879 (1928).
(6) H. H. Hodgson and H. G. Beard, *J. Soc. Chem. Ind.*, **45**, 91T (1926).

DEPARTMENT OF CHEMISTRY
TECHNICAL COLLEGE
HUDDERSFIELD, ENGLAND RECEIVED JULY 29, 1939

The Freezing Points of Pure High Polymers

BY EDWIN L. LOVELL AND HAROLD HIBBERT

In a recent publication[1] it was shown that the setting points of the polymer-homologous series of polyoxyethylene glycols $HO(CH_2CH_2O)_pH$ followed very exactly the *empirical* equation

$$t_s = P/(a + bP) \qquad (1)$$

(1) Lovell and Hibbert, THIS JOURNAL, **61**, 1916 (1939).

where t_s is the setting point in °C., P the number of repeating units in the chain, and a and b constants. The experimental data covered molecules with from 54 to 558 atoms in the straight chain, a much wider range than has previously been available for pure compounds. At that time it was duly noted that this homologous series did *not* follow the logarithmic freezing point equation deduced from what might be termed "kinetic" considerations by Austin[2] but the authors could offer no explanation for the form of the equation actually obtained.

Very recently, however, a publication has appeared by Huggins[3] concerning the properties of long-chain compounds; it includes the derivation on purely thermodynamic grounds of a general law relating the freezing points in a polymer-homologous series to the number of atoms in the chain. This equation is

$$T_f = (A + Bn)/(C + Dn) \qquad (2)$$

where T_f is the absolute freezing point, n the number of atoms in the straight chain and the other symbols are constants. Inspection of the empirical relationship (1), and substituting for t_s its equivalent $T_f - 273$, reveals that this equation is identical in form with that of Huggins. This provides excellent support for the latter over a very wide range of chain lengths, many times greater than is possible in the n-alkane series, agreement for which (up to C_{70}) is shown by the previous work of Garner[4] and co-workers, who also have attempted to justify their results theoretically.[5] In both series the relation fails for chains of less than 20 atoms.

The agreement thus found between Huggins' thermodynamically derived freezing point equation and the freezing point data for the higher polyoxyethylene glycols is important additional evidence for the purity (uniformity of chain length) of this series of synthetic polymers.

(2) Austin, THIS JOURNAL, **52**, 1049 (1930).
(3) Huggins, *J. Phys. Chem.*, **43**, 1095 (1939).
(4) Garner, van Bibber and King, *J. Chem. Soc.*, 1533 (1931).
(5) Garner, Madden and Rushbrooke, *ibid.*, 2491 (1926).

McGILL UNIVERSITY
MONTREAL, CANADA RECEIVED NOVEMBER 21, 1939

The Conversion of Chlorophyll to Pheophytin

BY G. MACKINNEY AND M. A. JOSLYN

In a previous paper[1] we presented evidence showing the rate of conversion of chlorophyll to pheophytin in 90% acetone was of first order with respect to acid concentration (normality) and possibly of second order with respect to chlorophyll. It was necessary to consider the two chlorophylls as a single component because we did not have the individual components separated. Evidence favored the assumption that the reaction was chiefly a conversion of chlorophyll a to pheophytin a, because the reaction was rarely carried to more than 80% completion. We have now separated sufficient quantities of chlorophylls a and b[2] to repeat previous experiments. Measurements were made at 5350 Å. for chlorophyll a, at 5280 Å. for chlorophyll b, where the respective pheophytin maxima occur.

Results are condensed in Table I. The first and second order rate constants, k_1 and k_2, have been calculated, and each value represents the average of 8–13 determinations over periods of time varying from two minutes to seven hours. The temperature was 28 ± 0.5°. The column Δ indicates the mean deviation of the arithmetic mean of the individual determinations. The values of k/N, whether k_1 or k_2 is taken, clearly show the reaction is of first order with respect to acid concentration, confirming our earlier work.

TABLE I

RATE CONSTANTS FOR CHLOROPHYLL, IN 90% ACETONE, WITH OXALIC ACID

Normality	k_1	Δ	k_2	Δ
	Chlorophyll *a*			
0.002	0.211	0.046	0.0069	0.0010
.004	.539	.072	.0189	.0099
.007	.907	.088	.0332	.0114
.01	1.39	.170	.0562	.0301
	Chlorophyll *b*			
0.01	0.148	0.021	0.0040	0.0007
.02	.328	.126	.0088	.0022
.05	.804	.180	.0271	.0049
.10	1.69	.216	.0580	.0148

We were previously at some loss to decide the order with respect to chlorophyll, because in most cases there was an apparent falling off in the calculated constants with time. The k_2 constants for oxalic acid were reasonably constant which led us to suggest a second order for chlorophyll. We knew only that pheophytin b contributed to the absorption at 5350 Å., but we could not then evaluate the extent of its absorption. Because the a and b mixture used was not highly purified, extensive recalculations are not deemed profit-

(1) Mackinney and Joslyn, THIS JOURNAL, **60**, 1132 (1938).
(2) Details will be published shortly.

able. Assuming, however, that with 0.002 N oxalic acid, for periods up to five hours, there is no conversion of chlorophyll b, we have recalculated some values on the basis of a 25% inert ingredient, *i. e.*, the chlorophyll b. Under these conditions, the oxalic results fall in line with the others, and we are given little preference between k_1 and k_2 for chlorophyll.

A limitation must be remembered, that with the visual B and L spectrophotometer, we cannot vary our chlorophyll concentrations within a wider range than 3 to 5 times without loss of accuracy. Initial concentrations of chlorophyll in the present experiments were 0.5×10^{-4} M, and the acid varied from 0.01 to 0.002 N for chlorophyll a and from 0.10 to 0.01 N for chlorophyll b.

The present values show no falling off with time, indicating there may be an error inherent in our earlier calculations as there could be no accurate compensation for the effect of chlorophyll b. The k_1/N values are in both cases more constant than those for k_2/N, and in two of the acid levels for chlorophyll b, and in three for a, the deviations are smaller for k_1 than for k_2. Furthermore, there is very little trend in the k_1 values, while in some cases there is a definite upward trend for k_2. We are therefore inclined to believe that the reaction is of first order with respect to both chlorophyll components.

An explanation is required for the fact that with 0.01 N oxalic acid, k_1/N for chlorophyll a has a value of 139, for chlorophyll b, 14.8. If the reactions are correctly interpreted on the basis of first order in both cases, the question arises as to the cause of this difference. We hope to throw further light on this in studies on the removal of magnesium from allomerized components, phytol-free derivatives, and the heats of activation.

Conclusions.—For the pure a and b chlorophyll components, it is confirmed that the reaction involving loss of magnesium is of first order with respect to acid. It is probably of the same order with respect to chlorophyll. The two hydrogens replacing the magnesium must therefore enter at different rates, and in all probability the entrance of the first hydrogen is the rate-governing step. This would materially weaken the remaining magnesium–nitrogen bond, in which respect it would then no longer be equivalent to the initial condition, presumably highly covalent in character.

The chlorophyll a reacts from seven to nine times more rapidly than chlorophyll b.

FRUIT PRODUCTS DIVISION
UNIVERSITY OF CALIFORNIA
BERKELEY, CALIFORNIA RECEIVED OCTOBER 13, 1939

The Synthesis of Amino Acids from Benzoylaminomalonic Ester

BY E. P. PAINTER

The use of benzoylaminodiethyl malonate in the synthesis of amino acids as recently reported by Redemann and Dunn[1] has been found to be superior in many respects to the malonic ester and phthalimido malonic ester methods.[2]

The ester alkylates in absolute alcohol with all alkyl halides tried. The ester or derivatives is readily hydrolyzed with constant boiling hydrochloric or hydrobromic acid. Glycine can be isolated in 85% yields by hydrolyzing the free ester with concentrated hydrobromic acid. To the list of amino acids prepared in good yields by Redemann and Dunn by the use of this reagent may be added norleucine, α-amino-γ-phenoxy-*n*-butyric acid and the lactone of α-amino-γ-hydroxy-*n*-butyric acid. These have been isolated after hydrolysis of the ester alkylated with *n*-butyl bromide, β-bromoethyl phenyl ether and ethylene bromohydrin.

In an attempt to prepare β- and γ-halogen amino acids benzoylaminomalonic ester has been alkylated with methylene dibromide, ethylene bromide and ethylene chloride. The products formed contain some halogen but always less than the theoretical amount and the desired amino acids have not been isolated after hydrolysis.

The aminomalonic ester was prepared by the method of Cerchez,[3] excepting the reduction was carried out in alkaline solution with aluminum amalgam made from aluminum turnings and the amino ester benzoylated in a suspension of sodium carbonate in ether saturated with water. By carrying the reaction straight through to the benzoyl compound without isolating the intermediary products, 40–45% over-all yields may be expected. Redemann and Dunn were able to obtain slightly better yields of benzoylaminomalonic ester, but their procedure is more expensive and not as convenient for many laboratories.

The use of anhydrous reagents in alkylations should be emphasized.

(1) Redemann and Dunn, *J. Biol. Chem.*, **130**, 341–348 (1939).
(2) Painter, Ph.D. Thesis, U. of Minnesota, 1939.
(3) Cerchez, *Bull. soc. chim.*, [4] **47**, 1281 (1930).

From the author's experience and the paper by Redemann and Dunn it appears that benzoylaminomalonic ester should find general use in the synthesis of α-amino acids.

DIVISION OF AGRICULTURAL BIOCHEMISTRY
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UNIVERSITY OF MINNESOTA
ST. PAUL, MINNESOTA RECEIVED NOVEMBER 15, 1939

The 3-Nitrophthalates of the Mono Ethers of Ethylene and Diethylene Glycol

BY A. J. VERAGUTH[1] AND HARVEY DIEHL

The problem of identifying the monoethyl ether of ethylene glycol (Cellosolve) arose here recently and was successfully solved by the use of the 3-nitrophthalic anhydride reagent proposed by Nicolet and Sachs[2] for the identification of alcohols. The work has now been extended to the other commercially available monoethers of ethylene glycol ("Cellosolve" series), and of diethylene glycol ("Carbitol" series).

The ethers were obtained from the Carbide and Carbon Chemicals Corporation, and were purified by fractional distillation. A constant boiling fraction was taken, the boiling points and refractive indices checking with recorded values.

The procedure followed for the preparation of the acid 3-nitrophthalate esters of these ether alcohols was essentially that recommended by Nicolet and Sachs.

The anhydride was heated with an excess of the ether alcohol at the boiling point of the latter until all of the anhydride had dissolved and then for fifteen minutes longer. In the cases of those liquids having boiling points above 150°, toluene was added to avoid higher temperatures which cause decomposition of the esters formed; the toluene was then removed by distillation under reduced pressure. The oily layer of ester was then extracted with hot water to remove the unreacted reagents. It was then treated with a hot mixture of water and the least amount of ethyl alcohol necessary to effect complete solution. This solution was allowed to cool slowly with frequent scratching to induce crystallization. The initial crystallization was generally very slow, periods of standing for several days in a refrigerator sometimes being required. Recrystallization was continued until a constant melting point was obtained, generally three to five recrystallizations. Toluene was found to be a better solvent for recrystallization of the monophenyl ether of ethylene glycol than the water–alcohol mixtures.

Molecular weights of the derivatives were determined by titrating, with standard alkali, a solution containing 0.5 g. of the ester in 50% alcohol, using phenolphthalein as indicator. The melting points were taken with standard Anschütz thermometers in a mechanically stirred bath.

White crystalline derivatives were obtained from the monomethyl, monoethyl, monobutyl and monophenyl ethers of ethylene glycol and from the monomethyl ether of diethylene glycol but not from the monobenzyl ether of ethylene glycol or from the monoethyl or monobutyl ethers of diethylene glycol.

The 3-nitrophthalates obtained from the monoethyl ether of ethylene glycol and from the monomethyl ether of diethylene glycol crystallize with one molecule of water. Their water of crystallization was determined by drying a weighed amount of the ester in a vacuum at 100° over anhydrous magnesium perchlorate (Fischer drying pistol). The percentages of water found were 5.89 and 5.83, the calculated values being 5.98 and 5.43, respectively.

TABLE I

3-NITROPHTHALATES OF MONO ALKYL ETHERS OF ETHYLENE GLYCOL

Alkyl	3-Nitrophalates M. P., °C.	Mol. wt. Calcd.	Found
Methyl	128.4–129.0	269	268 ± 1
Ethyl	118.0–118.6	283	284 ± 3
Ethyl (monohydrate)	94.2–94.5	301	302 ± 4
Butyl	121.0–120.6	311	311 ± 1
Phenyl	112.0–113.0	331	330 ± 2

The 3-nitrophthalate monohydrate of the monomethyl ether of diethylene glycol was also a white crystalline solid and melted at 87–90°. The anhydrous 3-nitrophthalate melted at 91.4–92.2° and was found to have a molecular weight of 313 ± 1, as compared with the calculated value of 313. All attempts to induce the liquid reaction products from the monobenzyl ether of ethylene glycol ("Benzyl Cellosolve") and the monoethyl and monobutyl ethers of diethylene glycol ("Carbitol" and "Butyl Carbitol," respectively) to crystallize failed.

DEPARTMENT OF CHEMISTRY
PURDUE UNIVERSITY
LAFAYETTE, INDIANA RECEIVED OCTOBER 9, 1939

(1) Taken from a Thesis submitted to the Faculty of Purdue University by Mr. Veraguth in partial fulfilment of the requirements for the Degree of Master of Science.

(2) Nicolet and Sachs, THIS JOURNAL, **47**, 2348 (1925); see also the further work of Dickinson, Crosson and Copenhaver, *ibid.*, **59**, 1094 (1937).

COMMUNICATION TO THE EDITOR

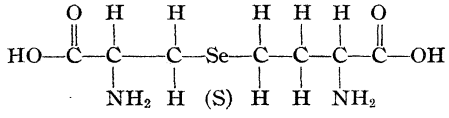
ISOLATION OF A CRYSTALLINE SELENIUM-CONTAINING ORGANIC COMPOUND FROM PLANT MATERIAL

Sir:

Horn, Nelson and Jones[1] and Franke and associates,[2,3] in connection with their study of the diseases of farm animals apparently caused by selenium in grain, have shown definitely that the selenium is present in an organic form intimately associated or combined with protein. It is important to ascertain the chemical nature of this organic selenium compound and to determine the manner in which it is tied up in the plant, and for several years we have been attempting to isolate it. We have now succeeded, after many failures, in obtaining a crystalline selenium compound having the properties of an amino acid. This substance has been obtained repeatedly from different lots of the same source material in the form of well-defined, elongated prisms. Analyses show it to have the percentage composition: C, 33.38; H, 5.83; N, 10.98; Se, 20.62; S, 4.20; O, 24.99 (by difference).

These analytical results correspond to the empirical formula $C_{21}H_{44}N_6Se_2SO_{12}$. The compound gives a strong ninhydrin reaction, and all of its nitrogen is in the amino form. Its equivalent weight is 130.5. It decomposes at 263–265°. It is insoluble in alcohol and organic solvents, and is difficultly soluble in water. The selenium in the compound is notably stable.

The fact that all the nitrogen is in the amino form suggests a compound of a simple type. By substituting selenium for sulfur, the simple formula, $C_7H_{14}N_2O_4Se$, is derived, which suggests that we may be dealing with an isomorphous combination of two compounds, $C_7H_{14}N_2O_4Se$ and $C_7H_{14}N_2O_4S$, in the ratio of 2 to 1, respectively. Such an assumption is in agreement with the structural formula



Whatever its structure, it appears that we are dealing with a naturally-occurring new type of amino acid of unusual scientific and economic interest.

This report is wholly preliminary. Further work is in progress and the results will be published later in greater detail.

PROTEIN AND NUTRITION RESEARCH DIVISION
BUREAU OF AGRICULTURAL CHEMISTRY AND ENGINEERING
UNITED STATES DEPARTMENT OF AGRICULTURE
WASHINGTON, D. C. M. J. HORN
D. BREESE JONES

RECEIVED DECEMBER 13, 1939

(1) M. J. Horn, E. M. Nelson and D. Breese Jones, *Cereal Chem.*, **13**, 126 (1936).
(2) K. W. Franke, *J. Nutrition*, **8**, 609 (1934).
(3) K. W. Franke and E. P. Painter, *ibid.*, **10**, 599 (1936).

NEW BOOKS

Calculations of Quantitative Analysis. By CARL A. ENGELDER, Ph.D., Professor of Analytical Chemistry, University of Pittsburgh. John Wiley and Sons, Inc., 440 Fourth Avenue, New York, N. Y., 1939. viii + 174 pp. 15.5 × 23.5 cm. Price, $2.00.

This book contains three hundred problems divided into fifteen groups of twenty problems each. The odd-numbered problems are provided with answers and are intended for home assignments. The even-numbered problems are without answers and are intended for class work, quizzes, or examinations. At the beginning of each section is a short discussion of theory, followed by several examples of typical problems and their solutions. At the end of the book are several tables useful to the student of analytical chemistry.

This book should find ready use in many courses where sufficient emphasis is placed on the solving of problems as a means of learning stoichiometry and other phases of analytical chemistry.

CHESTER M. ALTER

A History of Chemistry. By F. J. MOORE, Ph.D., Late Professor of Organic Chemistry in Massachusetts Institute of Technology. Revision prepared by WILLIAM T. HALL, Associate Professor of Analytical Chemistry in Massachusetts Institute of Technology. Third edition. McGraw-Hill Book Company, Inc., 330 West 42nd Street, New York, N. Y., 1939. xxi + 447 pp. Illustrated. 14.5 × 21 cm. Price, $3.00.

This latest edition of Professor Moore's book is a careful attempt to retain the general characteristics of the earlier editions and at the same time incorporate into the volume recent advances in chemistry, many more biographical notes and valuable additions to the older periods which had been somewhat neglected. In the main part of the book, there are one hundred and twenty more pages printed on thinner paper, giving no increased bulk to handle.

There are but few adverse criticisms. A number of corrections suggested by Professor Oesper in his review of the second edition unfortunately have not been made.[1] In a publication containing so many facts it is hard to avoid a few errors such as the date when Madam Curie was awarded the Nobel prize (p. 355) and the omission of Lomonosov in the index (p. 440). The biographical notes which have been inserted in the text occasionally make the account seem somewhat disconnected but they serve a purpose that is exceedingly important. The bibliographical material includes the more important recent books on history of chemistry, yet all but a few of the references in journals such as *Isis* and *The Journal of Chemical Education* are omitted.

The chapter headings are practically the same except that the concluding one is now a single long chapter combining the three preceding the last of the second edition. This is a wise move as the topics of inorganic chemistry, physical chemistry and radioactivity are inseparably connected. The scattering of the final chapter on Chemistry in the United States with many additions through the entire text where the information is pertinent, not only eliminates the former sense of isolation which was given to American Chemistry but also presents the history too often ignored by foreign writers. The introduction and history of the growth of organic chemistry is more logical and greatly improved. Numerous additions to the biographical material, including the brief life history and contributions of famous living chemists, particularly Nobel prize winners, are a distinct asset since the work of living chemists will be a background for the future. Few histories discuss the work of contemporary chemists. Therefore this book will remain up to date for a longer time. The author also indicates that it is increasingly difficult to keep up with all fields of chemistry so that this biographical material demonstrates that the science is progressing at a rate never before equalled.

There are quite a number of new illustrations and some of the former dubious and less important ones have been eliminated. Instead of feeling that the book is a trifle too brief to be used as an essential purchase by students of the history of chemistry, the new edition contains enough material to make the reviewer feel that it gives a splendid foundation from which to start toward further reading. Both the author and publisher are to be congratulated upon producing so fine a revision without increasing the price.

VIRGINIA BARTOW

(1) R. E. Oesper, *J. Chem. Education*, **8**, 2101–2102 (1931).

Semimicro Qualitative Analysis. By ARTHUR R. MIDDLETON, Ph.D., Professor of Inorganic Chemistry, Purdue University, and JOHN W. WILLARD, B.S. Prentice-Hall, Inc., 70 Fifth Avenue, New York, N. Y., 1939. xi + 446 pp. 7 figs. 16 × 23.5 cm. Price, $3.50.

The text outlines a course of qualitative analysis which can be covered in nine to six hours per week for one semester. The preliminary study of the behavior of the common ions, practice in the solution of solid materials and the removal of interfering ions, analysis of seven practice unknowns (not graded) and of eight unknowns require 32 laboratory periods. At Purdue, an additional 14 laboratory periods are devoted to the analysis of salt mixtures and alloys.

A special section gives a detailed description of the semimicro technique. The working directions are presented in detail and the methods have been tested with large classes. The separations are performed in centrifuge cones and the volumes of precipitates are made the basis for the estimation of quantities. An interesting rigid scheme of elimination is followed in the detection of anions. Only a few organic reagents are used.

The theoretical part, which occupies nearly half of the volume, contains much useful information. The sections on the use of units in chemical calculation and on the precipitation of metallic sulfides are of special interest, and the sharp distinction between homogeneous and heterogeneous equilibria is a commendable feature. While the advisability of the introduction of the definition of acid and base in accordance with the conceptions of Hantzsch may be questioned and the substitution of hydronium ion for hydrogen ion is objectionable as long as the state of hydration of the other ions is not indicated in the equations, the animated presentation recommends the book, which rates among the best of its kind.

A. A. BENEDETTI-PICHLER

Inorganic Syntheses. Volume I. By HAROLD SIMMONS BOOTH, Western Reserve University, Editor-in-Chief, and L. F. AUDRIETH, JOHN C. BAILAR, JR., W. CONARD FERNELIUS, WARREN C. JOHNSON and RAYMOND E. KIRK. McGraw-Hill Book Company, Inc., 330 West 42nd Street, New York, N. Y., 1939. xiii + 197 pp. 31 figs. 16 × 23.5 cm. Price, $3.00.

The dedication in the fly leaf of Volume I of Inorganic Syntheses reads as follows:

> To
>
> the countless unknown but valiant soldiers of science upon whose labors Inorganic Syntheses are based, this series of volumes is dedicated in the hope that it will ease the toil of future legions.

This dedication helps one to realize the amount of labor and enthusiasm which has preceded the compilation of this

book, and the unselfish devotion of the editors, the contributors, and those who have verified the procedures of the contributors.

In this first volume of the series appear sixty-six procedures for the preparation of a diverse assortment of inorganic substances. The arrangement is in Chapters I to VIII for the Groups of the Periodic Arrangement with Chapter IX reserved for materials or techniques of value to chemists. In this volume the only contribution to Chapter IX is No. 67, A Laboratory Cement. Potassium Fluoborate is placed in Chapter III, Mono-chloramine in Chapter V and Silicomolybdic Acid in Chapter VI.

The appearance of the contributions appears to follow their availability rather than any systematic plan arranged by the editors. Nevertheless, a good index makes it possible to quickly find if a desired procedure has appeared, and the necessarily unsystematic order of appearance is not really a serious disadvantage.

Some of the methods offered are new but many are improvements on older procedures. Where it is thought helpful a critical survey of known methods introduces the directions for the synthesis and a summary of the more common properties follows the directions. The most important references are given. It should be regarded as fortunate that exhaustive lists of references are avoided. The plan of checking all of the syntheses in independent laboratories and the critical editing of each synthesis by every editor helps greatly to ensure the reliability of the procedures, and it illustrates the degree of devotion shown by all who are engaged in this enterprise.

This series of volumes of Inorganic Syntheses which is so happily begun in this Volume I is destined to be one of the major contributions to chemistry.

ARTHUR A. BLANCHARD

The Merck Index. Fifth Edition. An Encyclopedia for the Chemist, Pharmacist, Physician, Dentist and Veterinarian. Compiled and published by Merck & Co., Inc., Rahway, N. J., 1940. 1060 pp. 17 × 23.5 cm. Flexible fabric. Price, $3.00.

This new edition of Merck's Index contains so much reference material of extreme value that a brief review cannot possibly do it justice. The list of chemicals and drugs that characterizes the series occupies 592 pages as compared with 570 pages in the Fourth Edition. The descriptions have been simplified, rewritten and rearranged. Many substances of recent importance are included, such as sulfapyridine and α-tocopherol. Structural formulas of many of the complex organic compounds are now given for the first time.

Following this section and not appearing in earlier editions are lists of coal tar colors and dyes used in foods, drugs and cosmetics, with descriptions (4 pages); indicators with properties, including adsorption, mixed, oxidation–reduction and universal indicators (5 pages); important minerals with characteristics, in tabular form (20 pages); and of special usefulness, 350 pages devoted to a list of chemical and clinico-chemical reactions, tests and reagents, listed by names of authors, covering and presumably amplifying the material previously found only in the rare German list "Merck's Reagenzien Verzeichnis." This is supplemented by an 18-page index arranged by names of substances tested for or employed.

In the remaining 70 pages are found descriptive lists of culture media, fixatives and staining solutions with formulas for their preparation, miscellaneous tables of units of measurement and their equivalents; thermometric equivalents, specific gravity comparisons, anti-freeze mixtures, cooling mixtures, constant humidity solutions, boiling and solidification temperatures of common, useful organic materials, refractive indexes and specific gravities of some important liquids and solids, weights per gallon of many organic liquids; and finally antidotes for poisons (12 pages).

The size of type generally used is smaller than that employed in *Chemical Abstracts*, but the arrangement of the vast amount of material collected into these 1060 pages is so clear, well spaced and uncomplicated as to make possible an almost immediate location of desired information. The labors of the compilers, Drs. Rosin, Addinall and Cone must have been great in preparing so comprehensive and essentially useful a volume.

WILLIS A. BOUGHTON

Chemische Gasreaktionen. (Chemical Reactions in the Gaseous Phase.) By H. J. SCHUMACHER, Director of the Physical Chemical Institute of the University of Frankfurt. Theodor Steinkopff, Residenzstrasse 32, Dresden-Blasewitz, Germany, 1938. xviii + 487 pp. 53 figs. 125 Tables. Price, RM. 32.25; bound, RM. 33.75.

This monograph is third in a series edited by Professor K. F. Bonhoeffer. The first two dealt with photochemistry and with solids. This is restricted to the kinetics of homogeneous thermal reactions in the gas phase.

The book is encyclopedic in its thoroughness. It contains over a thousand references and covers the fundamental theories and practically all the quantitative researches published in the field up to 1938. The conclusions of the various investigators are given accurately and fairly. Occasionally the author makes a critical comment or suggests a different interpretation but in general he merely abstracts the findings of the different researches.

The first 121 pages are concerned with the theories of chemical kinetics. The chapter headings show the wide variety of subjects covered: the laws of mechanical collisions, application of the classical Boltzmann statistics to the velocity and energy distribution in ideal gases, bimolecular collisions, derivation of thermodynamical quantities from statistical mechanics, transfer of energy in collisions, unimolecular reactions, theory of bimolecular reactions, three-body reactions, the quantum mechanical calculation of the absolute rate of reactions. These theories and their formulas are given clearly but the original papers, which are cited, must be consulted for details and proofs.

The second and larger part of the book describes the results of experimental researches. It may be read independently of the theoretical part, which it supplements and illustrates. The several chapters describe first, second and third order reactions, atomic reactions, free radicals,

tracer experiments with deuterium, ortho-para hydrogen conversion and homogeneous catalysis.

The treatment of chain reactions in the last sixty-eight pages is excellent though handicapped by the exclusion of photochemical reactions.

Free radicals and their part in gas kinetics are treated briefly.

The influence of pressure on the specific reaction rate and the observed change from first to second order at low pressures is reviewed. The theories of Lindemann, Hinshelwood, O. K. Rice, Ramsperger and Kassel are summarized and illustrated with over fifty different gas reactions. In the opinion of the reviewer many of these illustrations which depend on pressure measurements alone will need revision if future experimental work shows the reactions to be more complicated. In some cases at least it is likely that the changes appearing at low pressures may be explained by intermediate chemical steps and wall effects.

All the investigations which make up the kinetics of gas reactions have been treated impartially without nationalism or race prejudice. One wonders however if the author was not handicapped in giving adequate recognition for help in the theoretical part of the book, particularly on the wave mechanical calculation of absolute reaction velocities. The footnote to Chapters X and XI "ferner H. Epstein unveröffentlich" (besides H. Epstein unpublished) may be expressing one of the tragedies of science. With their heritage of internationalism scientists have a special responsibility in helping to bring about a new world order.

The book is clear, complete and well organized, a good example of the thorough German reference books which have done much to bring fundamental science to its present level. Unquestionably "Chemische Gasreaktionen" is the most complete and most up-to-date review of the literature on the kinetics of gas reactions.

FARRINGTON DANIELS

Thorpe's Dictionary of Applied Chemistry. Fourth edition, revised and enlarged, Vol. III. Chemical Calculations–Diffusion. By JOCELYN FIELD THORPE, C.B.E., D.Sc., F.R.S., F.I.C., and M. A. WHITELEY, O.B.E., D.Sc., F.I.C., Imperial College of Science and Technology. Longmans, Green and Company, 114 Fifth Avenue, New York, N. Y., 1939. 608 pp. Price, $25.00.

The first volume of the Fourth Edition of this Dictionary was reviewed in the November, 1937, number of THIS JOURNAL and the second volume in the January, 1939, number. The comments and commendations previously given apply equally well to this volume so that little more needs to be added. The 608 pages of this third volume cover the same part of the alphabet which required 352 pages in the third edition. This volume contains long articles, many of them entirely new, on chemical calculations, chemical warfare, chlorine, chlorophyll, chromium, cinchona alkaloids, colloids, colorimeters, condensers, copper, corrosion of metals, cyanides, deuterium, diazo-compounds, diffusion and many others. The list of about sixty contributors is a roster of distinguished British chemists.

GRINNELL JONES

Compositiones Variae. From Codex 490, Biblioteca Capitolare, Lucca, Italy. An Introductory Study. By ROZELLE PARKER JOHNSON. The University of Illinois Press, Urbana, Illinois, 1939. 116 pp. 18 × 27 cm. Price, $1.50.

The progress of civilization is dependent upon the transmission, to successive generations, of the accumulated knowledge of the past. We are familiar with the main route by which the transmission of chemical knowledge has taken place. The extensive empirical information accumulated by the highly civilized nations of antiquity—Egypt, Chaldea and India—between 3500 and 750 B. C., fertilized by the speculations of the Greek philosophers in the immediately succeeding centuries, found expression in the earliest works on chemistry, namely, those written by the Greek–Roman–Egyptian scientists of northern Egypt in the first, second and third centuries of our era. Most of these, tinged with the alchemical speculations of the period, were destroyed, either as a result of the decree of Emperor Diocletian in 296 against alchemical literature or in the burning of the Serapeum. Some, however, were translated from the Greek into Syrian, into Arabic, and thence finally, in the eleventh century, by scholars in Spain and Italy, into Latin.

There was, however, an alternative route by which the accumulated empirical knowledge of the ancients was transmitted to modern times. Skilled artisans, craftsmen and technicians from the earliest times possessed books of recipes and directions for the prosecution of their art, craft or technology. The earliest surviving example of such a handbook is the collection of Assyrian cuneiform tablets of the seventh century B. C. found in the library of King Assurbanipal at Sardanapalus dealing chiefly with the manufacture of glass and of various pigments. The next surviving example is the Leyden Papyrus X found near Thebes and dating from the third century of our era, composed of a large number of quantitative chemical and technological recipes. It contains little or no theoretical discussion and has distinctly the character of a laboratory manual.

The next representative of this tradition is the manuscript entitled "Compositiones Variae" described in the present book. This manuscript, dating from about 800 A. D., again is a collection of technical and chemical recipes made by the monks attached to the ancient monastery at Lucca in Tuscany. Its 135 recipes deal with dyeing, the preparation of dyes and of pigments, gilding, varnishing, soldering, gluing, the working of metals and their preparation, the manufacture of glass, parchment, etc. These recipes are unsystematic and are often unduly condensed, but the information given is precise and definite. The mysticism and symbolism so prevalent in later books on alchemy, are completely absent. From the nature of the material and the omissions it appears that they were intended chiefly as reminders for those already skilled in the practice of the various arts with which they dealt.

The chief contribution of the present work is to show that these recipes, on the one hand, can be traced back successively to similar recipes found in such antecedents as the Latin Papyrus X and the Assurbanipal Tablets and, on the other hand, are substantially identical with similar recipes published in succeeding centuries, thus demonstrat-

ing beyond question the reality and importance of this route via recipe book or laboratory manual for the transmission of the chemical knowledge of the ancients.

Anyone concerned with the history of chemistry will find this monograph interesting and illuminating and will wish success to the further studies in this connection which the author mentions. It is unfortunate that the parallel references are given only in the original Greek and Latin, as this considerably restricts their interest and usefulness to the general reader who retains but little of his knowledge of these languages.

ARTHUR B. LAMB

Kurzes Lehrbuch der Enzymologie. (Brief Textbook of Enzymology.) By Dr. phil. THEODOR BERSIN, Professor of Physiological Chemistry at the University of Marburg. Second edition. Akademische Verlagsgesellschaft m. b. H., Sternwartenstrasse 8, Leipzig C1, Germany, 1939. viii + 183 pp. 32 figs. 16 × 23.5 cm. Price, RM. 11; bound, RM. 12.80.

Dr. Bersin has expanded his interesting book with new material, which appeared in the literature since the publication of the first edition in 1938 (reviewed in THIS JOURNAL, **60**, 1274 (1938)). The new edition includes brief descriptions and microphotographs of the recently crystallized apozymase, catalase, papain and the several chymotrypsins.

While some references to the literature are given in the book, a more extensive bibliography would greatly improve its value.

HENRY TAUBER

BOOKS RECEIVED

November 10, 1939, to December 10, 1939

F. C. BAWDEN. "Plant Viruses and Virus Diseases." Chronica Botanica Co., P. O. Box 8, Leiden, Holland, and G. E. Stechert and Co., 31 East 10th St., New York, N. Y. 272 pp. Approx. $4.00 (7 Dutch guilders).

THEODOR BERSIN. "Kurzes Lehrbuch der Enzymologie." Second edition. Akademische Verlagsgesellschaft m. b. H., Leipzig, Germany. 183 pp. RM. 11; bound, RM. 12.80.

G. K. T. CONN. "The Nature of the Atom." Blackie and Son, Limited, 50 Old Bailey, London, England. Distributed in the United States by Chemical Publishing Co., Inc., 148 LaFayette Street, New York, N. Y. 115 pp. $1.50.

G. K. T. CONN. "The Wave Nature of the Electron." Blackie and Son, Limited, 50 Old Bailey, London, England. Distributed in the United States by Chemical Publishing Co., Inc., 148 LaFayette Street, New York, N. Y. 78 pp. $1.50.

P. J. DURRANT. "General and Inorganic Chemistry." Longmans, Green and Co., 114 Fifth Avenue, New York, N. Y. 547 pp. $2.75.

GERHARD HERZBERG. "Molecular Spectra and Molecular Structures. I. Diatomic Molecules." Translated by J. W. T. SPINKS. Prentice-Hall, Inc., 70 Fifth Avenue, New York, N. Y. 592 pp. $6.50.

ALBERT P. MATHEWS. "Physiological Chemistry." Sixth edition. The Williams and Wilkins Co., Baltimore, Maryland. 1488 pp. $8.00.

MARTIN MEHMEL. "Nomogramme zum Mineralbestimmen mit Röntgenstrahlen." Verlag der Deutschen Mineralogischen Gesellschaft, Berlin W 35, Germany. 13 pp.

ELMER S. MILLER. "Quantitative Biological Spectroscopy." Mimeoprinted by the Burgess Publishing Co., Minneapolis, Minnesota. 213 pp. $3.50.

S. SNIJDER. "Periodiek Systeem der Elementen met Toelichtingen." P. Noordhoff, N. V., Uitgerszaak, Gröningen, Holland. 1 p. Dutch fl, 0.75.

R. STREBINGER. "Praktikum der qualitativen chemischen Analyse. Einschliesslich Mikro- und Tüpfelreaktionen." Verlag Franz Deuticke, Vienna, Germany. 154 pp. RM. 6.

ARTHUR I. VOGEL. "A Textbook of Quantitative Inorganic Analysis, Theory and Practice." Longmans, Green and Co., 114 Fifth Avenue, New York, N. Y. 856 pp. $5.00.

A. G. WARD. "The Nature of Crystals." Blackie and Son, Limited, 50 Old Bailey, London, England. Distributed in the United States by Chemical Publishing Co., Inc., 148 LaFayette Street, New York, N. Y. 114 pp. $1.50.

"Abeggs Handbuch der anorganischen Chemie, Die Elemente der achten Gruppe des periodischen Systems. Vierter Teil. Nickel und seine Verbindungen." Verlag von S. Hirzel, Königstrasse 2, Leipzig C 1, Germany. 310 pp. RM. 40.

"Gmelins Handbuch der anorganischen Chemie." Edited by E. PIETSCH. 1 Ergänzungsband, Teil 2. "Aluminumlegierungen Patentsammlung." By G. APEL. Verlag Chemie, G. m. b. H., Berlin W 35, Germany. RM. 49.50.

"Vitamin E." Society of Chemical Industry, Clifton House, Easton Road, London, N. W. 1, England. 88 pp. 5 shillings.

JOURNAL OF THE
AMERICAN CHEMICAL SOCIETY

VOLUME 62 FEBRUARY 7, 1940 NUMBER 2

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STANFORD UNIVERSITY]

Studies of Solutions of Hydrocinnamic Acid and of Lauryl Sulfonic Acid with the Film Balance

BY JAMES W. MCBAIN AND WARREN V. SPENCER

In 1935 McBain and Wilson[1] and Doss[2] showed that the Pockels–Langmuir–Adam trough or film balance invented for insoluble films floating on water, gave highly interesting and unexpected results when applied to clean surfaces of ordinary solutions. The film balance does not measure surface tension of solutions. It has, however, uncovered the fact that while some solutions may have their surfaces enlarged by sweeping, or contracted by compressing with a movable barrier, without in any way affecting the balance or float, others are very sensitive to one or the other or both of these procedures. Often different behavior depends upon the range of concentration of one particular substance, and all the phenomena may go through maxima in intermediate concentration.

Two of the most striking phenomena are, first, the long times, almost infinitely long as compared with processes of diffusion, that are involved in some instances, and not in others or in other concentrations; and, second, the discovery of the formation of a semi-insoluble pellicle upon suitable compression of certain surfaces, exhibiting a well-defined "characteristic final pressure," at or above which only it will dissolve. A simple example of this behavior is normal caproic acid in aqueous solution, one of the most stable compounds of organic chemistry. McBain and Perry[1] ascribed this to orientation.

The phenomena are so novel and complicated that no satisfactory explanation embracing all of them has yet been forthcoming. They are not due to contamination, or to evaporation, for these have been painstakingly avoided, at least in the later work.

Doss considers that diffusion in the surface zone of a solution has to be activated and suggests that a potential barrier is formed by the diffuse double layer. He suggested that if the concentration is doubled the rate of accumulation in the surface should increase more than fourfold. However, we here find for solutions of lauryl sulfonic acid, proceeding from a concentration of 1.55 g./liter, that the velocity is increased either by concentration or by dilution.

To account for the special properties of the pellicle McBain and Perry suggest formation of polymolecular leaflets with the hydrophilic groups not exposed.

The present communication describes experiments upon several specimens of hydrocinnamic acid, cinnamic acid and, most carefully, dodecyl sulfonic acid, the latter being an example of the very large group of modern detergents with Type III curves of surface tension.[3] In these a mere trace lowers the surface tension of water by a large fraction. Upon further addition the sur-

(1) McBain and Wilson, THIS JOURNAL, **58**, 379 (1936); see also McBain and Perry, *Ind. Eng. Chem.*, **31**, 35 (1939).

(2) Doss, *Current Sci.*, **4**, 405 (1935); see also *ibid.*, **5**, 645 (1937); 6, 446 (1938); **7**, 182 (1939); *Proc. Indian Acad. Sci.*, **4**, 11, 97 (1936); *Kolloid Z.*, **84**, 138 (1938); **86**, 205; **87**, 272 (1939).

(3) McBain, Ford and Wilson, *Kolloid Z.*, **78**, 1 (1937); McBain, Vinograd and Wilson, THIS JOURNAL, **62**, 244 (1940).

face tension either remains constant or, as in this case, actually rises again. The most concentrated solution studied was only 5 g./liter and the minimum in the surface tension curve lies at 1.55 g./liter.

Apparatus and Method

A Cenco film balance was remodelled. The trough was coated with twenty-five superimposed layers of bakelite lacquer, each baked on for thirty minutes at 135–150°. The level of the liquid was fixed by a capillary tube attached to a suction pump near the end of the trough. The trough was 14 cm. wide and the barrier was always placed originally 40 cm. from the float. For solutions of lauryl sulfonic acid a thin coat of dicetyl was placed on the edges of the trough and the level of the solution kept low.

The float was a strip of platinum–iridium bent longitudinally to form an inverted V, the top of the fold coated with dicetyl and the bottom dipping deeply into the solution. Dicetyl was used with 0.0025 mm. gold foil to make the connection between float and trough. Before assembling, the float was heated to redness. The torsion wire was non-rusting 0.18 mm. phosphor–bronze used within its elastic limit. The barriers were of fused silica 1 cm. square and 26 cm. long, completely coated with bakelite lacquer, with some dicetyl where they touched the edges of the trough when using lauryl sulfonic acid.

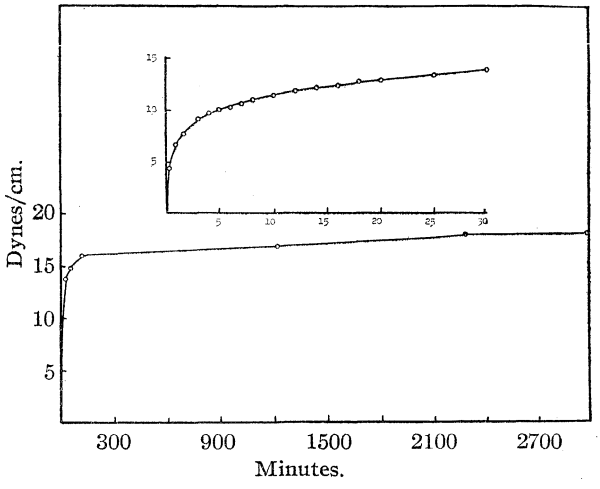


Fig. 1.—Laurylsulfonic acid 1.55 g. per liter, Procedure I.

To eliminate evaporation the entire trough was placed in a tight chamber thermostated at 25° using 42 ft. (12.8 meters) of $1/4''$ (6.4 mm.) copper tubing, through which thermostated water flowed. The bottom of the chamber was an open reservoir of thermostated water into which dipped cloth drapes to help keep the enclosed atmosphere saturated.

Invariably, before each experiment and procedure (except Procedure II), the surfaces on both sides of the float were swept several times by placing a barrier next to the float and sweeping it away. Each barrier in turn was left in place at the end of the trough until another had come back to it. The tests for contamination were described by McBain and Perry. Pure water was always studied for several days before using any solution. If clean, neither sweeping nor compression nor time affects the position of the float.

The routine of operations, abbreviated from the procedures of McBain and Perry is[1] sweeping both sides to begin with, and continuing to sweep the large side, the torsion necessary to keep the float in the zero position is noted. Having thus measured both the maximum pressure difference and the time required for its production, these are confirmed by Procedure II, by the simple expedient of stopping the sweeping and measuring the rate and time for the pressure to fall to zero.

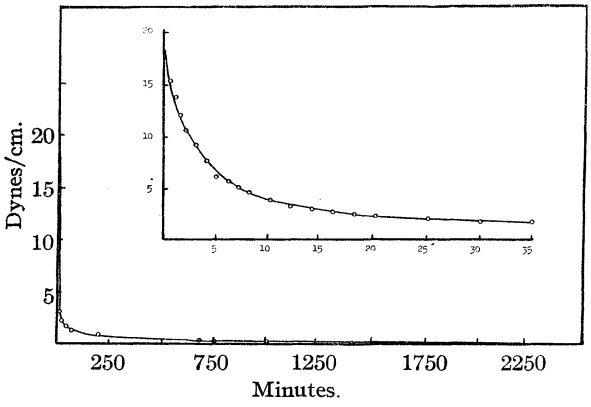


Fig. 2.—Laurylsulfonic acid, 1.55 g. per liter, Procedure II.

Again, both sides being swept and fully aged, the area on the large side is diminished by a definite percentage by moving the barrier toward the float and the initial and final pressure and the rate of change throughout are determined. Other procedures described by McBain and Perry occasionally were used.

Hydrocinnamic and Cinnamic Acids

Results with Eastman Hydrocinnamic Acid.—The hydrocinnamic acid was recrystallized from hot water and the principal results of McBain and Perry were repeated and confirmed. However, very much longer time effects were observed although the results show a close agreement with those of McBain and Perry for similar time intervals. For example, in Procedure I, after thirty minutes of aging, McBain and Perry found a pressure difference of 0.41 dyne per cm. while we now find 0.40, although in 4000 minutes this rises to 2.17 with a change of only 0.02 dyne during the last nineteen hours. In both Procedures I and II, the more rapid change has been accomplished within about five minutes. Classical diffusion phenomena would of course account for less than a second. These extremely slow adjustments are in accord with observations of surface tension of hydrocinnamic acid solutions communicated by McBain, Ford and Mills.[4]

Again, if the surface is compressed and then allowed to stand at constant area for a sufficiently long period, we obtain the same final characteristic pressure as McBain and Perry, namely, 0.42 dyne per cm. The first observable initial pressure occurs at 45% compression as was found by McBain and Perry.

(4) McBain, Ford and Mills, to be published.

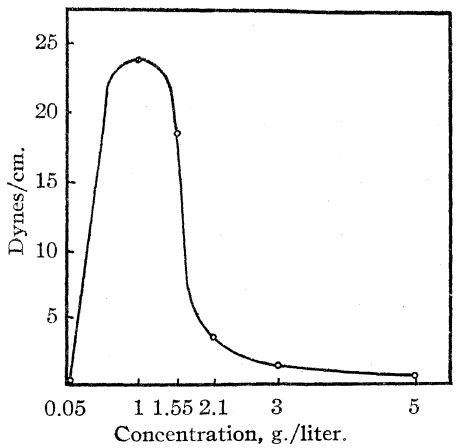


Fig. 3.—Laurylsulfonic acid, Procedure I. Maximum pressures produced on float by sweeping away from float.

Results with British Drug Houses Hydrocinnamic Acid.—The surface properties for all shorter times agreed with the foregoing, but for longer periods the values here were less. With 87.5% compression, the initial pressure for Eastman and British Drug Houses, respectively, was 2.4 and 2.5, falling in 30 min. to 1.18 and 1.15, and giving the final characteristic pressure after standing overnight 0.42 and 0.41.

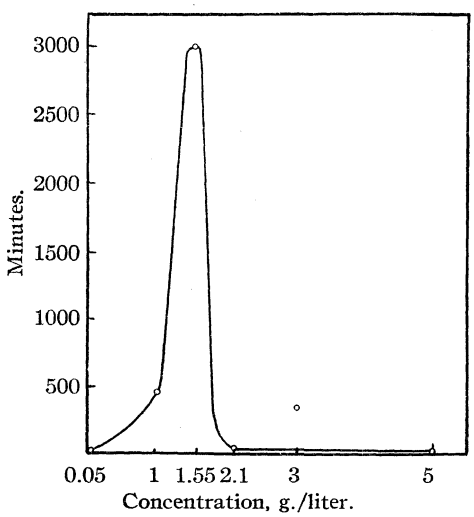


Fig. 4.—Laurylsulfonic acid, Procedure I. Time required for maximum pressure.

Experiments with Cinnamic Acid.—When 0.01 g. of cinnamic acid crystals was sprinkled on 560 sq. cm. of clean water, the spontaneous pressure after twenty minutes was 0.4 dynes/cm. falling off overnight to the final pressure of 0.19. Upon compression by 95%, the initial pressure became 1.03, but this fell to the 0.19 final value overnight.

Now when a solution of hydrocinnamic acid was similarly contaminated with cinnamic acid crystals, a maximum pressure of 2 was produced, which 87.5% compression raised to 3.33, falling to a final pressure overnight of 0.59 (= 0.41 + 0.18!). However, after thorough sweeping, apparently all cinnamic acid was eliminated, for on compressing surfaces aged thirty minutes by 87.5% the initial pressure was 2.5, falling in thirty minutes to 1.10 and giving the characteristic final pressure 0.40; all three values were thus identical with those quoted above for pure hydrocinnamic acid.

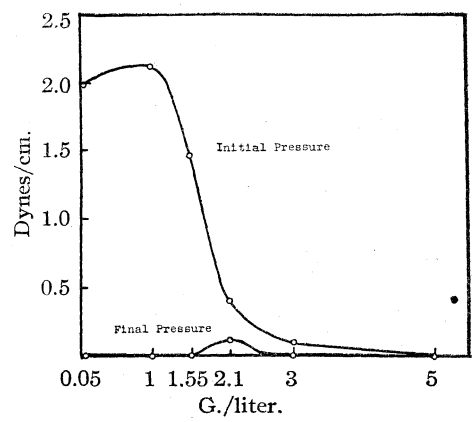


Fig. 5.—Laurylsulfonic acid, Procedure V, compressed 10%.

Spreading of Oil on Solutions of β-Phenylpropionic Acid.—Oil spreads upon a freshly swept solution extremely rapidly, just as on water,[5] and the oil spreads circularly about as fast as the eye can follow. However, when the surface is aged and compressed, the oil again spreads circularly but very slowly. Freshly swept surfaces of solutions of hydrocinnamic acid are quite mobile while the compressed surface shows rigidity.

Similar experiments with oxidized oil and oleic acid were attempted on a solution of lauryl sulfonic acid of minimum surface tension containing 1.55 g./liter. On a freshly swept surface the drop rapidly spreads circularly until several centimeters in diameter. Then islands appear in the oil film which gradually breaks up into a very large number of minute droplets. On compressing and expanding the surface rapidly, these expand and the larger ones again form islands. On a clean aged surface the

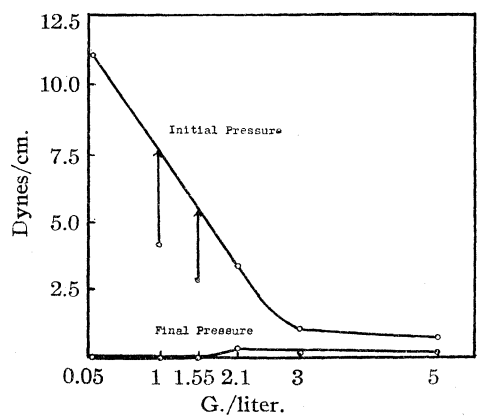


Fig. 6.—Laurylsulfonic acid, Procedure V, compressed 50%.

(5) T. F. Ford and D. A. Wilson, *J. Phys. Chem.*, **42**, 1051 (1938).

drops do not spread at all. Upon compression the surface moves as a whole, showing some elasticity.

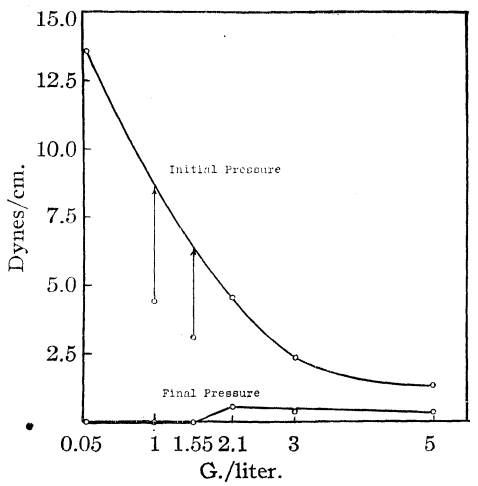


Fig. 7.—Laurylsulfonic acid, Procedure V, compressed 75%.

Dodecyl Sulfonic Acid

Study of Solutions of Dodecyl Sulfonic Acid. Five Grams per Liter.—Fifteen to twenty minutes are required before the effect of sweeping away from the float disappears and the maximum effect is 0.51 dyne per cm.

A pellicle is formed on sufficient compression. It is only after the surface has aged for the above-mentioned fifteen or twenty minutes that the final constant characteristic pressure of lauryl sulfonic acid of 0.51–0.52 dyne per cm. is exhibited upon compression and sufficient standing, then for 87.5% compression the initial pressure is 2.54, falling in about twenty min. to the 0.52 value. There is no initial pressure until compression amounts to 20% and no final pressure at all until the compression is 40%. The final pressure does not reach its characteristic constant value until the compression is 85% or more. The time effects of compression are interesting and unexpected. Both for small and for very high compressions the fall to the characteristic pressure is rapid. For moderately large compressions, the time passes through a high maximum. This is observed again with other dilutions.

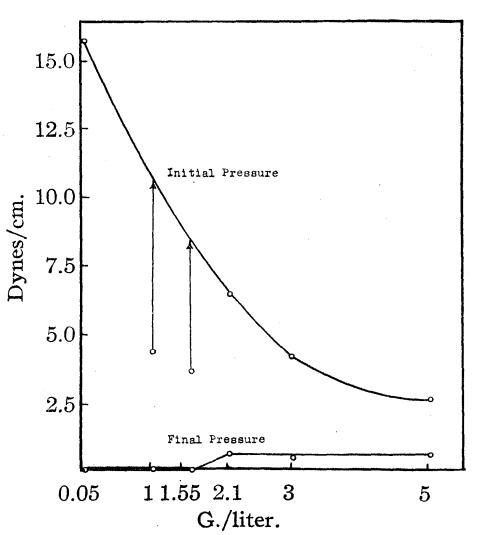


Fig. 8.—Laurylsulfonic acid, Procedure V, compressed 87½%.

Three Grams per Liter.—Instead of the fifteen to twenty minutes above, six hours is here necessary for this solution to recover after sweeping away from the float, and the maximum effect is raised from the 0.51 to 1.34 dynes per cm. Compression again produces a pellicle.

2.1 Grams per Liter.—Once more the effect of sweeping is greater and the pressure upon the float rises to 3.40. However, the solution recovers within thirty minutes. On the other hand, the outstanding observation is that upon compression the initial pressures are again greatly increased, being 7.08 for 92.5% compression. Nevertheless, the final characteristic pressure is 0.51–0.55 attained in about forty-five min.

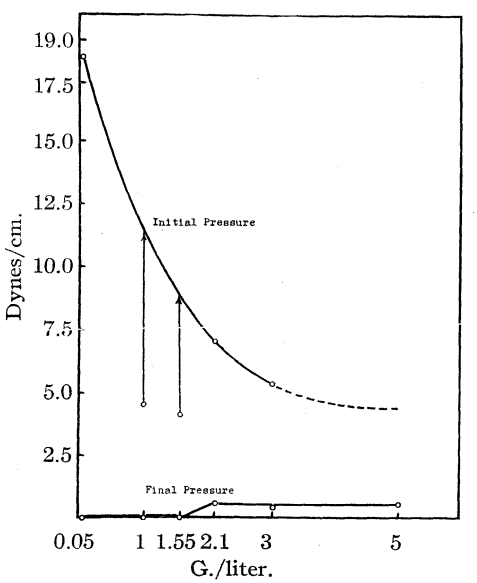


Fig. 9.—Laurylsulfonic acid, Procedure V, compressed 92½%.

1.55 Grams per Liter.—The effect of sweeping clean is relatively enormous, being now 18.02 dynes per cm., and requiring several thousand minutes for recovery. This is illustrated in Figs. 1 and 2.

The most important single observation is the fact that no final pressures are obtained upon compression, however great. Curiously, the time required for the initial pressure produced by compression to disappear rises with amount of compression until a sharp maximum is reached, after which it is very short. As an example, at 10% compression it required only six minutes to drop to zero, whereas at 87.5% compression it required 950 minutes, while at 96.5% compression it dropped to zero in only twelve minutes.

One Gram per Liter.—Now that the minimum surface tension has been passed, the great increases in time required to restore the surface after sweeping clean are no longer observed as in the foregoing series of higher concentrations, but drop again from a few thousand to a few

hundred minutes. However, the initial effect of sweeping is far greater, being 23.54 dynes.

Upon compression there is again no permanent pellicle, but the initial pressures are still greater than with the 1.55 g. concentration. Once more the time for the initial pressure to disappear increases with compression but suddenly falls after 75 to 87.5%.

One-half Gram per Liter.—This very dilute solution still gives definite pressures. Sweeping produces only a slight pressure difference, which disappears in fifteen minutes. However, compression produces enormous initial pressures, up to 18 dynes per cm., much higher than those for the less dilute solutions but they disappear within a few seconds for 10% compression, three minutes for 75% compression and about thirty sec. for 92.5% compression.

Discussion

Considerations of space prohibit reproduction in full of the varied and numerous data[6] (62 tables and 44 graphs). Instead, we can merely supplement the information already given by a series of summary tables and graphs showing how the results depend upon concentration for lauryl sulfonic acid solutions. These should be compared with those given by McBain and Perry for hydrocinnamic acid.

TABLE I

Procedure I. Dodecyl Sulfonic Acid Solution		
Concn., g./liter	Max. press. diff., dynes/cm.	Time interval, min.
5	0.51	15
3	1.34	(340)[a]
2.1	3.40	30
1.55	18.02	3000
1	23.54	450
0.05	0.40	15

[a] Result uncertain owing to drift of the zero point.

TABLE II

Concn., g./liter	Initial pressure, dynes/cm.	Final pressure, dynes/cm.	Time interval
	Procedure V. 10% Compression		
5	0	0	..
3	0.10	0	..
2.1	0.40	0.12	<30 min.
1.55	1.47	0	6
1	2.13	0	20
0.05	1.99	0	20 sec.
	Procedure V. 50% Compression		
5	0.72	0.20	...
3	1.02	0.13	60 min.
2.1	3.36	0.33	60
1.55	2.84[a]	0	400
1	4.15[a]	0	50
0.05	11.09	0	3
	Procedure V. 75% Compression		
5	1.28	0.31	...
3	2.28	0.36	60 min.
2.1	4.60	0.54	40
1.55	3.10[b]	0	360
1	4.45[b]	0	1435
0.05	13.62	0	3
	Procedure V. 87.5% Compression		
5	2.56	0.52	17 min.
3	4.16	0.37	60
2.1	6.40	0.54	45
1.55	3.60[c]	0	950
1	4.32[c]	0	90
0.05	15.72	0	1
	Procedure V. 92.5% Compression		
5	...	0.52	...
3	5.30	0.36	115 min.
2.1	7.08	0.55	60
1.55	4.06[d]	0	...
1	4.57[d]	0	40
0.05	18.30	0	40 sec.

[a] These concentrations were compressed from 10 to 50%, instead of from 0 to 50%.

[b] These concentrations were compressed from 50 to 75%, instead of from 0 to 75%.

[c] These concentrations were compressed from 75 to 87.5%, instead of from 0 to 87.5%.

[d] These concentrations were compressed from 87.5 to 92.5%, instead of from 0 to 92.5%.

To sum up, it is evident that but little is known of the properties of the surface layers of solutions. The assumption current during the past twenty years that clean solutions may be regarded as uniform solution right up to a bounding monomolecular film is untenable; and the common interpretations of their hypothetical monomolecular film as gaseous, etc., become very doubtful. This is in complete contrast to the well-established and beautifully simple behavior of oil films on water or insoluble contaminations upon solutions.

Summary

The film balance when applied to ordinary solutions yields a complex series of novel results which bear but little relation to previous conceptions derived from analogy with insoluble monomolecular films floating on water; and thus a new field is open to investigation.

Particularly striking is the fact that the various phenomena of surface pressure and of time frequently pass through a high maximum in an intermediate range of dilute solution. Again, whether a pellicle forms or not depends both upon the concentration and the degree of compression

(6) Stanford University theses are being made available in bibliofilm, U. S. Dept. of Agriculture.

of the surface. Some substances apparently never form it. When it is formed and sufficiently compressed, the final pressure is characteristic only of the substance. On the other hand, the initial pressure may be greatest where the final pressure vanishes.

STANFORD UNIVERSITY, CALIFORNIA
RECEIVED OCTOBER 3, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STANFORD UNIVERSITY]

Observations of Surface Tension in the PLAWM[1] Trough

BY J. W. McBAIN, J. R. VINOGRAD[2] AND D. A. WILSON

In recent years attention has been drawn to the long time effects observed in the surface tensions of solutions. The time effects are of a much higher order of magnitude than can be accounted for by ordinary diffusion. Likewise great interest attaches to solutions whose surface tensions are of Type III. In these, a trace of solute lowers the surface tension to a fraction of that of the solvent, whereupon further addition leaves the surface tension constant or may cause it to pass through a minimum in very dilute solution. In either case, application of the Gibbs theorem, where the slope of surface tension against concentration is zero, would seem to predict zero adsorption, just where the surface tension is most greatly lowered and where adsorption is actually pronounced.[3] About one hundred such cases have been reported.[4]

In attempting to verify the existence of these reported effects it is highly desirable to find a method of measuring surface tension which shall fulfil the requirements that (a) the surface is static and undisturbed, (b) that it is swept free from contamination, (c) that it is observed for an adequate period and (d) that evaporation is avoided. None of the previously existing methods fulfilled all of the first three requirements and every method had been criticized by other authors.[5] For these reasons the PLAWM trough was devised. In this, the superficial floating barrier of the Pockels–Langmuir–Adam surface film trough is replaced by one which is water-tight and yet flexible. This was done by cementing to the bottom and walls of the trough with dicetyl a sheet of vulcanized dipped latex rubber 0.004″ (0.1 mm.) thick of density 1.02 especially made for us by the Miller Rubber Company, Inc., Akron, Ohio. This delicate rubber partition was also fastened to a float in the line of the surface. Thus, the trough is separated into two compartments, one of which may contain water, the other solution; both have plane surfaces which can be swept. If hydrostatic effects are equalized, the only force acting upon the float is the difference of surface tension on the two sides.

Although the PLAWM trough is simple in principle, it is very exacting in practice. However, it here serves its purpose of demonstrating beyond question the existence of Type III curves and it is of much interest to compare the results obtained by this method with those from a number of other current methods.

The Apparatus

As the basis, we used a trough made for us through the courtesy of Dr. N. K. Adam. It consisted of a brass tray 50 × 14 × 2 cm. carrying a compound torsion balance. The tray was given 18 superimposed coats of Bakelite lacquer, each baked on at 150°. The same treatment was given to all other metal parts which might come in contact with liquid, with the exception of the float which consisted of a 12-cm. strip of platinum–iridium folded longitudinally. The rubber membrane was first attached with dicetyl to a U-shaped frame and then at the height of the meniscus to the float; the whole frame was then fitted water-tight into the trough with dicetyl. Two strands of 0.04 mm. silver wire connected the float to the torsion mechanism and mirror.

In the original experiments of Wilson, which are here referred to only briefly, the rubber membrane was made with folds so voluminous that it was found experimentally that the hydrostatic pressure on both sides was equalized within fifteen to forty-five minutes, after addition of more water or solution, as was shown by the float returning to the original zero point. In the present experiments only about 1 cm. extra of rubber was allowed on both sides and under the float, but the two compartments of the trough were connected by a siphon of 2 cm. bore which could be closed with stopcocks.

All the measurements were made in an atmosphere which was practically saturated with water vapor. The case

(1) Pockels–Langmuir–Adam–Wilson–McBain; see McBain, Ford and Wilson, *Kolloid Z.*, **78**, 1–9 (1937).

(2) Bristol-Myers Company Research Fellow.

(3) J. W. McBain and L. A. Wood, communicated to the Royal Society, 1939.

(4) For references, see J. W. McBain and G. F. Mills, Reports on Progress in Physics, Vol. 5, p. 30, 1939, published by the Physical Society, Cambridge University Press, England.

(5) See also for example Bartell, Culbertson and Miller, *J. Phys. Chem.*, **40**, 885 (1936).

surrounding the trough had been made water-tight by coating with paraffin, and water was allowed to stand on the floor to a depth of a few centimeters. Streamers of cheesecloth dipped into this pool of water and extended to the top of the case. A hygrometer always read 100% relative humidity. Access to the instrument was made by means of small sliding doors.

Experimental Technique

To begin each run the trough was rinsed repeatedly with distilled water which was drawn out through the top of the siphon. Conductivity water from a Barnstead still was then added to both sides, and the surfaces were swept at least five times. Three Bakelited quartz sweeps were manipulated so that two were always in position near the immersed ends of the siphon but on the side toward the float. The stopcocks of the Pyrex siphon were not closed until the light beam of the optical indicator came to rest. After closing the stopcocks the surfaces were again swept and the light beam was observed over a time interval similar to one considered in the measurement. The experiment was begun only if the position of the optical indicator and thus that of the float did not change.

A sweep was placed within 3 mm. of the platinum–iridium float and a measured amount of solid was added to the water in the large compartment outside this sweep. In the case of the slowly soluble hydrocinnamic acid the solid was finely ground and then sprinkled on the surface through a platinum gauze. This considerably enhanced the rate of solution which otherwise for concentrated solutions might require days. The solution was then stirred until it was homogeneous, using a quartz rod cleaned by heating to redness. The experiment was begun by drawing the sweep over the large surface from the float position to a position near the end of the trough. The moment of sweeping was considered the beginning of the experiment.

For the period of observation the light beam and thus also the float were maintained at a fixed position by adjusting the torsion wire. The experiment was in some cases repeated by sweeping the solution surface a second time. The observation of each solution was continuous for some hours, with the object of ascertaining when the value became constant. At the conclusion of the surface tension readings, the solutions were analyzed, the hydrocinnamic acid by the Zeiss interferometric refractometer and the lauryl sulfonic acid by titration with potassium hydroxide.

Experimental Tests

In the actual experiments the siphon was kept closed after the initial equalization of hydrostatic pressure. However, preliminary observations were made as follows.

With the siphon open the displacement of the float due to the addition of 5 cc. of water is nullified in one minute.

With the siphon closed when 5 cc. of water was removed the original position of the light beam was reëstablished when the water was replaced in the trough.

The float returned to the original position after stirring as soon as the violent disturbance died down.

The addition of water to one side gave a definite effect proportional to the amount of water added, 1.02 dynes/cm./g. of water. An increment of 0.60 dyne/cm./g. was observed when varying amounts of sucrose up to 10 g. were added. The effect of the maximum amount of sucrose used on the surface tension of water is 0.05 dyne/cm. and this was below the sensitivity of the apparatus. While the addition of pure water influences the float only through the effect of increased depth upon hydrostatic pressure, the addition of soluble solids influences it partly through the change produced in depth but also through the change in density of the solution and these effects may reinforce or partly neutralize each other depending upon the actual volume effects for the particular case. The results obtained were corrected for this hydrostatic effect.

The apparatus was calibrated frequently by hanging weights on the lever arm of the torsion balance. With the 0.18 mm. phosphor-bronze torsion wire used in experiments on hydrocinnamic acid the conversion factor was 0.136 dyne/cm. per degree torsion. In view of the large surface tension lowering of lauryl sulfonic acid, 0.25 mm. phosphor–bronze wire was used. The corresponding factor was 0.648 dyne/cm. per degree torsion. Since torsions could be read to 0.1 degree the uncertainty in the readings for lauryl sulfonic acid solutions corresponds to 0.25 dyne/cm.

Materials

The potassium laurate was a special preparation made by Kahlbaum mentioned in previous communications. The hydrocinnamic acid was made by Eastman Kodak Co. and was purified in the usual manner by cooling an aqueous solution saturated under 50° (18 g./liter) toward room temperature, rejecting the crystals separating but taking those formed on further cooling to 0°. Sodium butylbenzene sulfonate was prepared by the method of Neville and Jeanson.[6] The lauryl sulfonic acid was a specially pure specimen prepared by M. E. Synerholm under the direction of Dr. C. R. Noller.

Preliminary Results

In the experiments of Wilson in 1936 a Lloyd and Scarth ring tensiometer was also incorporated in the PLAWM trough. The surface tensions so measured were in agreement with those yielded by the PLAWM trough.

Of much interest was the observation that whereas soap solutions commonly exhibit a pronounced minimum in their surface tension curves,[7] and the potassium laurate behaved likewise, addition of 0.0116 *N* potassium hydroxide, added with the intention of suppressing hydrolysis, eliminated this sharp minimum occurring at about 1 g./liter by causing all the higher concentrations to remain at this low value.

The results with sodium butylbenzene sulfonate are given in Fig. 1, both trough and tensiometer exhibiting a minimum similar to that described by Neville and Jeanson.[6] Here the minimum occurs in much less dilution and it remains to be

(6) Neville and Jeanson, *J. Phys. Chem.*, **37**, 1001 (1933).

(7) "International Critical Tables," Vol. V, McGraw-Hill Book Co., Inc., New York, N. Y., 1929, p. 449–450.

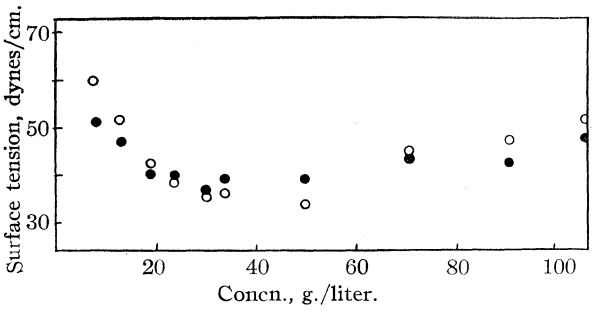


Fig. 1.—Graph showing minimum in surface tension of aqueous sodium butylbenzene sulfonate corroborating Neville and Jeanson[6]; ○, PLAWM; ●, ring method.

proved whether further purification (hydrolysis is of course impossible) might flatten out the minimum. However, Wood[3] found a very definite minimum in more dilute solution with moderately pure butylbenzene sulfonic acid.

Results with Solutions of Hydrocinnamic Acid

These solutions of β-phenylpropionic acid exhibit a surface tension which changes over long periods of time. Whereas until recently it has always been taken for granted that the surface tension of ordinary dilute solutions would change from the perfect dynamic or instantaneous value, almost equal to that of the solvent, down to the final or equilibrium value as fast as the concentration of the surface zones could be adjusted by classical processes of diffusion, a matter of a small fraction of a second, we here have another clear case like that of Adam and Shute[8] showing that the surface tension is not fully lowered until after enormously greater periods of time.

It is equally difficult to measure the perfect dynamic surface tension of a solution and its perfect final static or equilibrium surface tension. All existing measurements probably fall between the two. Drop number and drop weight and maximum bubble pressure upon which many investigators have relied prove to be semi-dynamic. The ring methods are better in that the surface may be aged for days before the ring is pulled through the surface, but this latter process is accompanied by stretching and formation of new surface.

We are fortunate in being able to present in Fig. 2 data obtained by Dr. Donald Purdie of Cambridge, England, with a Sugden maximum bubble pressure equipment, together with the data of Professor E. A. Hauser of Massachusetts Institute of Technology with his pendant drop method, the measurements of Drs. R. C. Swain and C. R. Bacon with the drop weight method, those of Dr. G. F. Mills with the ring method of Harkins and Jordan, together with our own results

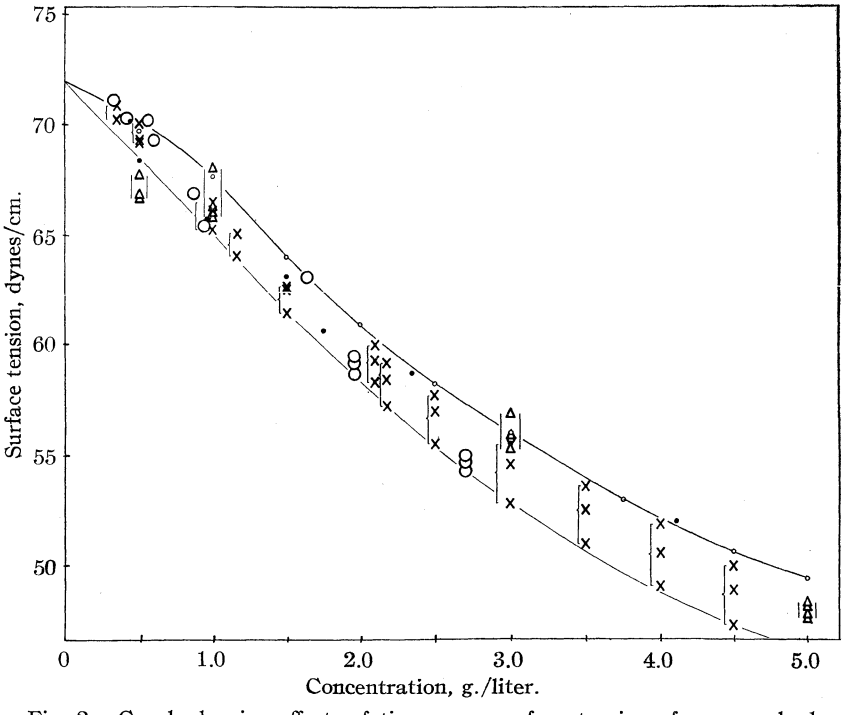


Fig. 2.—Graph showing effects of time upon surface tension of aqueous hydrocinnamic acid as studied by many methods: ×, ring method, uppermost point at age of surface 5 min., next point below at 1 hr., lowest point 9 hrs.; ○, drop weight at 30 sec.; ●, maximum bubble pressure for releasing bubbles; Δ, pendant drop method, uppermost at 15 sec., followed in order by 60, 120 and 300 sec.; ◯, PLAWM trough, for 2 and 2.7 g./liter at 15 min., 60 min. and 120 min. in order, but for the more dilute solutions only one determination between 30 to 60 min.

using the PLAWM trough. It is abundantly clear that the surface tension of any one solution is a function of time over long periods and that no method of measuring surface tension measures either the true initial or the true final value.

With the sessile bubble, etc., the surface is small in comparison with the bulk of the solution

(8) Adam and Shute, *Trans. Faraday Soc.*, **34**, 758 (1938).

and impurities may concentrate therein without possibility of sweeping. With the PLAWM trough there is a large area (560 sq. cm.) whose surface tension is found to be but little affected by stirring or by disturbing a small portion of it. It may be swept an indefinite number of times to eliminate surface contamination. These latter points may and should be adopted in the ring method, which then would become with the precautions indicated by Mills perhaps the most informative and trustworthy method of measuring surface tension.

In Fig. 2 we have drawn the uppermost curve through the data for drop weight obtained with drops thirty seconds old. The bottom curve is that for the surface tensions by the ring method at the ostensible age of nine hours. Between these two arbitrary curves all the other data are bracketed. The methods that are capable of showing change with time show it. In plotting the data, all measurements were arbitrarily corrected to 25° by adding the difference in surface tension of pure water at 25° and the temperature of measurement. Only the pendant drop and the PLAWM trough were used at 25°. The drop weight and the ring were at 22–23°, and the bubble pressure at 21.5°, so that the data may be easily reconverted.

Results with Lauryl Sulfonic Acid.—Again we are fortunate in being able to present Fig. 3 which critically establishes the existence of Type III curves of surface tension with a minimum in extremely dilute solution. The data given are those of Dr. H. B. Bull of Northwestern Medical School using the Wilhelmy method, those of Dr. L. A. Wood with the ring method (using swept carefully protected surfaces), after periods up to forty-eight hours, those for the PLAWM trough, and two measurements for extremely dilute solutions by Professor Grinnell Jones and Dr. W. A. Ray of Harvard with their precision capillary method which gave for 0.0285 and 0.2225 g./liter, respectively, 0.9936 and 0.9141 times that of water for 25°.

Once more the surface tension is a function of time over very long periods, but for the present purpose we are only interested in the proof that the equilibrium surface tension curve is of this form.

Differential Results with Lauryl Sulfonic Acid.—Since it has been shown that observed surface tensions of solutions are somewhat arbitary values dependent upon time and the method of measurement, a new approach was made to establish that in the very dilute solutions containing between 1.5 and 2 g./liter the surface tension does actually increase with concentration. For this purpose the surface tension in the PLAWM trough was first measured for a solution containing about 1.55 g./liter and the establishment and reëstablishment of a surface tension of 30 dynes/cm. eighty minutes after each sweeping was observed. As is shown in Fig. 4 the surface tension fell 7 dynes between the first and eightieth minutes.

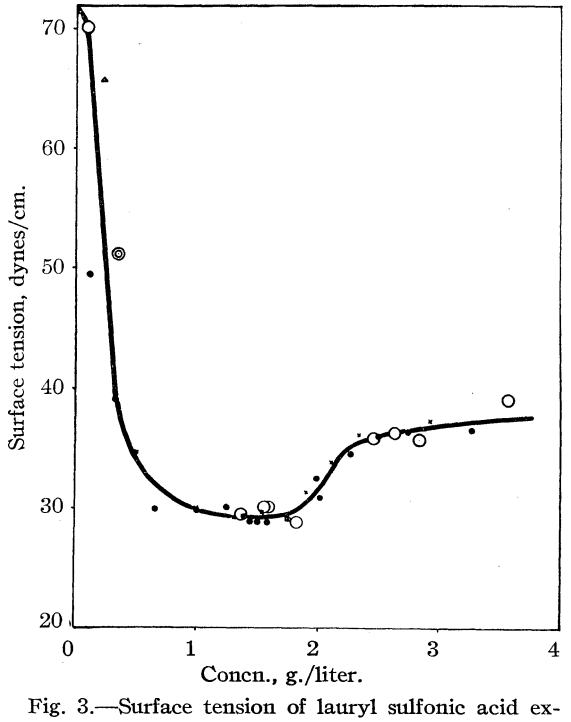


Fig. 3.—Surface tension of lauryl sulfonic acid exhibiting Type III curve with minimum at 1.55 g./liter. The values shown represent the final lowering of surface tension at the times stated: ○, PLAWM trough at 60 min.; ◎, PLAWM trough at 10 hrs.; ×, Wilhelmy method at at least 45 min.; ●, ring method at 1 to 2 days; △, capillary rise method, time not stated.

Thereupon, additional lauryl sulfonic acid was put in to bring the concentration to about 2.5 g./liter. Figure 4 shows that now the surface tension was 36 dynes/cm., almost independent of age or sweeping. This differential method which upon repetition yielded the same results proves critically the existence of the minimum in the surface tension curve which has led to the unsolved contradiction between the thoroughly established[8] actual positive adsorption and the zero

and negative adsorptions apparently demanded by the Gibbs theorem.

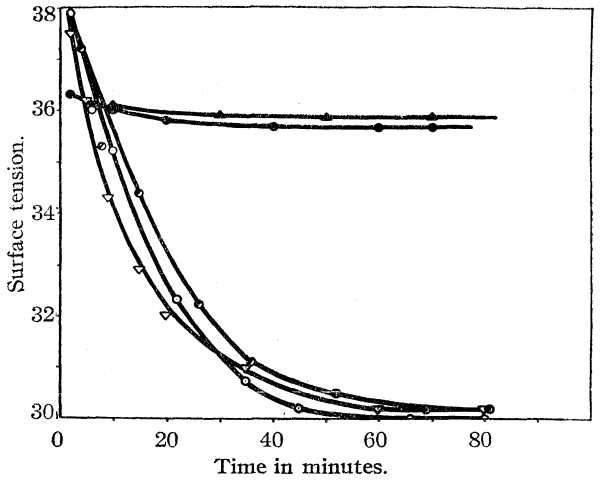


Fig. 4.—Differential method with PLAWM trough to establish existence of minimum in surface tension of aqueous lauryl sulfonic acid: ○, ▽, ◐, surface tension observed after first, second and third sweepings, respectively, for 1.575 g./liter, showing surface tension falling from 38 to 30 dynes/cm. in 80 min.; thereupon for 2.460 g./liter showing surface tension raised to and remaining at 36 dynes for 80 min., and also up to 260 min., ●, for first sweeping; ▲, after second sweeping.

Tartar and Cadle reported at the Sixteenth National Colloid Symposium, 1939, even more striking minima in their surface tension curves for the sodium straight chain alkyl sulfonates. Likewise, Adam and Shute[9] find definite minima for aqueous cetyltrimethylammonium bromide at 0.045% and for sodium dodecyl sulfate at 0.01 *N;* their time effects are similar to ours. It is of interest to note that, owing to the long time required for dilute solutions of lauryl sulfonic acid to exhibit full lowering of surface tension as compared with the almost immediate attainment of it in solutions containing over 2.5 g./liter, Wood found for very short times a Type I curve rapidly sagging down into the position shown by our Type III curve in Fig. 3. Naturally the thermodynamic theorem of Gibbs refers only to the final equilibrium value and not to any arbitrary value between that and the initial instantaneous dynamic surface tension.

Other Uses of the PLAWM Trough.—Since it has been abundantly shown[9] that the ordinary film balance strikingly fails to measure surface tension of solutions and that complicated time effects reach their maximum in an intermediate range of dilute solution, it becomes of great interest to carry out similar experiments with the PLAWM trough which of necessity measures the actual surface tension and the influence thereon of such procedures as sweeping and compression. Indeed, this will be necessary in order to interpret the results obtained with the film balance. However, the latter is sufficient to show that the effect of sweeping the surface of a solution of lauryl sulfonic acid, while negligible in infinite dilution and again at solutions containing 2.5 g./liter, is so great in a solution containing 1.5 g./liter that an error of over 2 dynes remains if the surface tension is measured as soon as one hour after sweeping.

(9) McBain and Perry, *Ind. Eng. Chem.*, **31**, 35 (1939); McBain and Spencer, This Journal, **62**, 239 (1940); also references to Doss quoted therein.

Summary

The PLAWM trough, consisting of a film balance divided into two compartments by a watertight flexible float, has been applied to solutions of hydrocinnamic acid, potassium laurate, sodium butylbenzene sulfonate and lauryl sulfonic acid.

In conformity with data by other recognized methods kindly supplied us by other workers, it has been shown that the surface tension of solutions of hydrocinnamic acid is not fully established until after periods of time enormously greater than those expected from classical diffusion processes.

The existence of Type III curves with a minimum has been critically established. In these a trace of solute reduces the surface tension of the solvent to a fraction of its value, whereupon further small addition raises the surface tension again to a still low maximum or constant value. This has been shown for lauryl sulfonic acid (and also for sodium butylbenzene sulfonate), again in conformity with data kindly supplied us by other workers. With potassium laurate addition of alkali appears to lower the flat maximum to the value of the minimum.

It is pointed out that the PLAWM trough will be invaluable in repeating and interpreting the surprising results obtained with clean solutions of soluble substances with the Pockels–Langmuir–Adam film balance.

Stanford University, Calif.

Received October 17, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, SOUTH DAKOTA STATE COLLEGE, AND THE SCHOOL OF CHEMISTRY OF THE INSTITUTE OF TECHNOLOGY, UNIVERSITY OF MINNESOTA]

Ionization Constants of Acid–Base Indicators in Ethanol

BY L. S. GUSS AND I. M. KOLTHOFF

In a buffer system containing the acid–base system, A and B and the indicator system I_a and I_b, we define a concentration equilibrium constant by the equation:

$$K = \frac{c_{I_b}\, c_A}{c_{I_a}\, c_B} \qquad (1)$$

and a thermodynamic constant, K', by a similar equation using activities in place of concentrations

$$K' = \frac{a_{I_b}\, a_A}{a_{I_a}\, a_B} = K\frac{f_{I_b} f_A}{f_{I_a} f_B} \qquad (2)$$

According to the limiting Debye–Hückel expression

$$-\log f_{ion} = \alpha z^2\sqrt{\mu} \qquad (3)$$

From equations (2) and (3), it follows that

$$pK = pK' + 2\alpha(z_{I_a} - z_A)\sqrt{\mu} \qquad (4)$$

where z refers to the charges on the respective molecules. The value of α in water at 25° is 0.5, in methanol, 2.0, and in ethanol, 2.9. Hence, any variation between pK values and ionic strength in water will be magnified by four times in methanol and almost six times in ethanol.

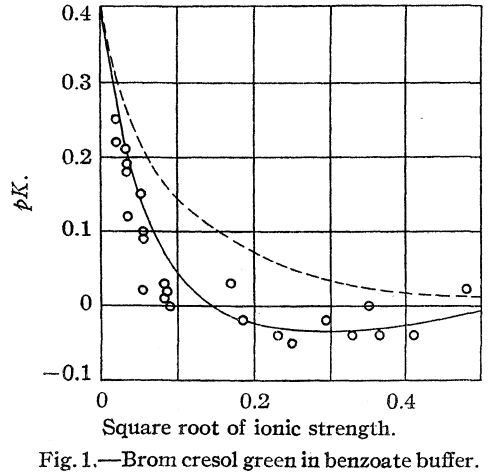


Fig. 1.—Brom cresol green in benzoate buffer. Broken line illustrates corresponding data in methanol.

In a previous study[1] it was shown that equation (4) accounts quantitatively for the change with the ionic strength as long as the latter is small. In his study of indicators in ethanol, Kolthoff[2] hardly found a change of the color equilibrium of sulfonephthaleins in buffers composed of an uncharged acid and a univalent anion base upon dilution from an ionic strength of 0.1 to 0.01. Erroneously, he concluded that dissociation constants remain unchanged on going from infinite dilution to finite concentrations. It is the purpose of this investigation to correct these data in the light of the above discussion and to consider the effect of varying ionic strength on some indicator–buffer equilibria.

(1) I. M. Kolthoff and L. S. Guss, THIS JOURNAL, **60**, 2516 (1938).
(2) I. M. Kolthoff, *J. Phys. Chem.*, **35**, 2732 (1931).

Experimental

Reagents.—A good grade of synthetic ethanol, free of aldehydes, was dehydrated by the method of Lund and Bjerrum,[3] followed by distillation over sulfanilic acid. As in the case of methanol, final purity was checked by density measurements with a 100-ml. pycnometer. All alcohol used contained less than 0.05% water. As

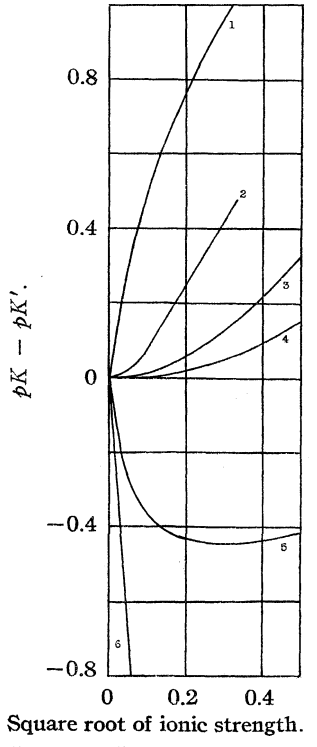


Fig. 2.—Indicator–buffer systems in ethanol: (1) methyl yellow, methyl red, and thymolbenzein in trichloroacetate, neutral red in salicylate; (2) thymolbenzein in veronalate; (3) methyl orange in trichloroacetate; (4) methyl red in benzoate; (5) sulfonphthaleins in uncharged acid buffers; (6) brom cresol green in ammonium.

(3) H. Lund and J. Bjerrum, *Ber.*, **64B**, 210 (1931).

pointed out before,[1] the presence of a trace of water will have no effect on these buffered solutions.

Indicators and acids were purified by methods already described. Ionic strength was controlled by the addition of lithium chloride, precipitated from methanol solution by the addition of hydrogen chloride and fused in platinum in an atmosphere of hydrogen chloride. Sodium ethoxide was prepared by dropping pure sodium into ethanol, the solutions showing no discoloration.

Method.—The general method was that used in the solvent methanol.[1] Values of pK for a given buffer-indicating system were determined over an ionic strength range from about 5×10^{-4} to 0.1. Ionic strengths of 0.01 and less are due to the salt in the buffer, a greater ionic strength being obtained by the addition of lithium chloride. The values of pK were plotted against the square root of the ionic strength and the curve extrapolated to infinite dilution, the final slopes of the curves agreeing with equation (4).

TABLE I

VALUES OF pK IN VARIOUS INDICATOR–BUFFER SYSTEMS IN ETHANOL

Indicator	Buffer	Ionic strengths 0.0	0.002	0.005	0.01	0.02	0.05	0.1
Brom phenol blue	Salicylate	0.8	0.55	0.45	0.45	0.45	0.4	0.4
Brom phenol blue	*o*-Nitrobenzoate	1.0	.75	.6	.6	.55	.55	.55
Brom phenol blue	*m*-Nitrobenzoate	0.4	.15	.1	.1	.15	.15	.15
Brom phenol blue	*p*-Nitrobenzoate	.5	.25	.2	.15	.1	.1	.1
Brom phenol blue	Benzoate	− .85	−1.05	−1.05	−1.1	−1.1	−1.1	−1.1
Brom cresol green	Benzoate	.4	0.15	0.05	0.05	0.05	0.05	
Brom cresol green	Acetate	.15	− .1	− .15	− .2	− .2	− .2	
Brom cresol green	Ammonium	.05	− .5	− .65				
Brom cresol purple	Benzoate	1.8	1.55	1.5	1.45			
Brom cresol purple	Veronalate	−1.05	−1.3	−1.4	−1.45	−1.45	−1.45	−1.4
Brom thymol blue	Veronalate	0.1	−0.05	−0.15	−0.2	−0.2	−0.2	−0.2
Phenol red	Veronalate	.45	.2	.25	.1	.1	.1	.1
Thymol blue	Veronalate	2.1	1.85	1.8	1.8	1.75		
Thymol blue	Trichloroacetate	−0.4	−0.4	−0.4	−0.4	−0.35	−0.3	− .025
Methyl orange	Trichloroacetate	−2.4	−2.4	−2.35	−2.35	−2.3	−2.2	
Methyl red	Benzoate	0.2	0.2	0.2	0.2	0.2	0.25	0.35
Methyl red	Trichloroacetate	−2.25	−2.1	−1.95	−1.85	−1.7	−1.4	
Methyl yellow	Trichloroacetate	−2.7	−2.5	−2.4	−2.3	−2.15	−1.8	−1.5
Neutral red	Salicylate	−0.5	−0.25	−0.05	0.1	0.35		
Thymolbenzein	Trichloroacetate	−2.5	−2.25	−2.1	−2.05	−1.95	−1.7	−1.5
Thymolbenzein	Veronalate	0.8	0.8	0.85	0.9	1.0		

TABLE II

IONIZATION CONSTANTS OF INDICATORS IN ETHANOL

Indicator	Buffer	pK_A	pK'	$pK_{I(EtOH)}$	$pK_{I(MeOH)}$	$pK_{I(H_2O)}$
Tropeoline 00	Hydrogen chloride			2.3	2.2	2.0
Brom phenol blue	Salicylate	8.7[a]	0.8	9.5	8.9	4.1
Brom phenol blue	*o*-Nitrobenzoate	8.6[b]	1.0	9.6		
Brom phenol blue	*m*-Nitrobenzoate	9.2[b]	0.4	9.6		
Brom phenol blue	*p*-Nitrobenzoate	9.1[b]	.5	9.6		
Brom phenol blue	Benzoate	10.25[a]	− .85	9.4		
Brom cresol green	Benzoate	10.25	.4	10.65	9.8	4.9
Brom cresol green	Acetate	10.6[a]	.15	10.75		
Brom cresol green	Ammonium	10.5[a]	.05	10.55		
Brom cresol purple	Benzoate	10.25	1.8	12.05	11.3	6.4
Brom thymol blue	Veronalate	13.1	0.1	13.2	12.4	7.3
Phenol red	Veronalate	13.1	.45	13.55	12.8	8.0
Thymol blue(1)	Trichloroacetate	5.8[a]	− .4	5.35	4.7	1.65
Thymol blue(2)	Veronalate	13.1	2.1	15.2	14.0	9.2
Methyl orange	Trichloroacetate	5.8	−2.4	3.4	3.8	3.45
Methyl red(1)	Trichloroacetate	5.8	−2.25	3.55	4.1	2.3
Methyl red(2)	Benzoate	10.25	0.2	10.45	9.2	5.0
Methyl yellow	Trichloroacetate	5.8	−2.25	3.55	3.4	3.25
Neutral red	Salicylate	8.7	−0.5	8.2	8.2	7.4
Thymolbenzein(1)	Trichloroacetate	5.8	−2.5	3.3	3.5	
Thymolbenzein(2)	Veronalate	13.1	0.8	13.9	13.15	

[a] Dissociation constant of acid has been obtained from I. M. Kolthoff, *J. Phys. Chem.*, **35**, 2732 (1931). [b] Dissociation constant of acid has been obtained from H. Goldschmidt, *Z. physik. Chem.*, **99**, 116 (1921).

Results.—As an example, the data obtained in an investigation of brom cresol green in benzoate buffer are shown by the solid curve in Fig. 1. From the graph, a value of $pK' = 0.4$ is obtained. Knowing that, for benzoic acid, $pK_A = 10.25$[2], we find pK_I of brom cresol green to be 10.65.

In Table I is given a summary of pK values of indicator–buffer systems at various ionic strengths, as well as the values at infinite dilution. The behavior of indicator–buffer systems is more clearly seen in Fig. 2, where it is found that the systems studied fall into a few well-defined groups.

Discussion

The behavior of acid–base indicators in ethanol is much the same as in methanol. At infinite dilutions, the curves approach the slope of 5.8, required by the Debye–Hückel limiting law. At higher salt concentrations, the ionic diameter and individual molecular characteristics bring about variations that can be expected.

The behavior of sulfonephthaleins in ethanol is in agreement with the extension of the concept of Bjerrum[4] as discussed in a previous paper.[1] This is indicated in Fig. 1, in which the system of brom cresol green in benzoate is compared in methanol and ethanol. Although the general shapes of the curves are the same, the ethanol curve is compressed toward the zero-concentration axis. In other words, the individual effects of the separate charges on a zwitterion become apparent at much lower salt concentrations than in methanol. As a result, although the limiting slope is greater in ethanol, the limiting value of pK above the horizontal portion of the curve is about the same in the two solvents.

The same comparison seems applicable in cases of the other zwitterion indicators, *i. e.*, thymolbenzein, thymol blue in trichloroacetate and methyl orange. The behaviors of the basic indicators, methyl yellow and neutral red, are in accord with present concepts. Methyl red behaves as if the intermediate form (Red II) is a true amino acid and not a zwitterion, in agreement with results found in methanol. In trichloroacetate, it behaves as a cation acid; in benzoate as an uncharged acid.

In Table II is given a summary of the true ionization constants of the indicators studied. These are calculated from the pK' values obtained in this study and accepted values of pK_A found in the literature. The pK_A of veronal was found to be 13.1, from a study of the brom cresol purple–veronalate system. For comparison, the values in methanol and water are also listed. The value for tropeoline 00 was determined in dilute hydrogen chloride.

Summary

1. A study has been made of the dissociation of acid–base indicators in ethanol, especial attention being paid to the effect of ionic strength.

2. Values of thermodynamic ionization constants of these indicators have been measured.

BROOKINGS, SOUTH DAKOTA
MINNEAPOLIS, MINNESOTA

RECEIVED SEPTEMBER 28, 1939

(4) N. Bjerrum, *Z. physik. Chem.*, **104**, 147 (1923).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, IOWA STATE COLLEGE]

The Conductance of Solutions of Organosubstituted Ammonium Chlorides in Liquid Hydrogen Sulfide

BY E. E. LINEKEN[1,2] AND J. A. WILKINSON

I. Introduction

Organic ammonium salts were found to form conducting solutions in the liquid hydrides of phosphorus, sulfur, and the halogens by McIntosh and Steele,[3] and in the liquid hydrides of the halogens and sulfur by Steele, McIntosh and Archibald.[4] Antony and Magri[5] have reported that solutions of tetramethylammonium iodide, in liquid hydrogen sulfide, conduct. Quam and Wilkinson[6] have reported the conductances of solutions of methylammonium, dimethylammonium, and triethylammonium chlorides at a number of different concentrations in liquid hydrogen sulfide. Their work shows distinctly the

(1) From a portion of a thesis submitted by E. E. Lineken in partial fulfilment of the requirements for the degree of Doctor of Philosophy at Iowa State College in March, 1939.

(2) Present address: Department of Chemistry, University of Vermont, Burlington, Vermont.

(3) D. McIntosh and B. D. Steele, *Proc. Roy. Soc.* (London), **A73**, 450–463 (1904).

(4) B. D. Steele, D. McIntosh and E. H. Archibald, *Phil. Trans. Roy. Soc.* (London), **A205**, 99–167 (1906).

(5) U. Antony and G. Magri, *Gazz. chim. ital.*, **35**, 206–226 (1905).

(6) G. N. Quam and J. A. Wilkinson, THIS JOURNAL, **47**, 989–994 (1925).

increased conductance of solutions of substituted ammonium chlorides as the number of substituents increases. Their report indicates also an increased molecular conductance with increasing concentration. The present investigation was undertaken to repeat earlier measurements using modern bridge technique, to extend the concentration range for these solutions and to make measurements on solutions of other organosubstituted ammonium chlorides in order to be able to compare the conductances of several series of compounds. The compounds selected were mono-, di-, tri-, and tetramethylammonium chlorides and the corresponding ethyl and *n*-propyl compounds.

The conductances of all solutions in liquid hydrogen sulfide are much lower than those of similar solutions in water. This might be expected on comparison of their viscosities and dielectric constants at somewhat similar temperatures. The conductances of the hydrogen sulfide solutions were determined at −78.5°, which is the equilibrium temperature of the mixture of solid carbon dioxide and ether. At this temperature the dielectric constant of liquid hydrogen sulfide is 9.05 compared to 81.5 for water at 16.3°. The viscosity for hydrogen sulfide at the same temperature is 4.12 millipoises compared to 17.94 for water at 0°.

II. Apparatus, Chemicals and Method

1. Shielded, Alternating Current Wheatstone Bridge.—The shielded bridge was constructed in general according to that described by Shedlovsky.[7] The twin (double) variable air condenser which Shedlovsky used was replaced in this work by two 500 mmf. variable air condensers, one shunting the conductance cell and the other shunting the measuring resistance. The ratio arms were of 5000 ohms each and were a unit from a General Radio Company Type 216 capacitance bridge. No provision was made for reversing the ratio arms. The earthing circuit was made of two 5000-ohm coils similar to those described above, a 20-ohm variable rheostat, and two 500 mmf. variable air condensers. Each instrument comprising the bridge was mounted in a separate covered compartment of a galvanized iron box. The box served for a shield and every precaution was taken to ensure symmetrical shielding. While making a measurement, covers were removed from those compartments containing the balancing resistance, the condenser shunting the balancing resistance, and the detector switch. The conductance cell was not shielded. Terminals leading to the oscillator, the amplifier, and the conductance cell were mounted on the side of the box with adequate bakelite insulation. Wires leading to the oscillator and amplifier were shielded. All connections between shields were soldered and grounded at one point. Connections between parts of the bridge were made through rather large holes cut in the walls of the various compartments of the galvanized iron box.

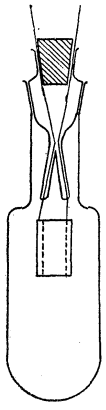


Fig. 1.

The balancing resistance consisted of a Leeds and Northrup decade box, 1–9,999 ohms, and calibrated International Resistance Company Type WW-1 precision wire resistors totaling 1.49 × 10^6 ohms. Resistances larger than 1.5 × 10^6 ohms were determined by shunting the conductance cell with a 5 × 10^5-ohm resistor, measuring the combined parallel resistance, and calculating that of the solution in the cell. During the latter part of the investigation a 1.5 × 10^6-ohm Shallcross resistor was added, permitting a direct balance up to 3 × 10^6 ohms. The use of Shallcross wire wound resistors has been described by Cox, Kraus and Fuoss.[8] When measuring resistances lower than 5 × 10^2 ohms, the 5000 ohm ratio arms were replaced with a Leeds and Northrup Kohlrausch slide wire. The slide wire was used at its midpoint, or at a point not more than five of its one thousand divisions from the midpoint, when measuring resistances between 115 and 500 ohms. Only when measuring resistances less than 115 ohms was it not used at the midpoint. This includes but seven determinations, the highest four of the tetrapropyl, the highest of tetraethyl, and the highest two of the tetramethyl compounds.

2. The Oscillator and Amplifier.—The oscillator was designed according to that described by Jones and Josephs.[9] The two-stage amplifier was constructed according to the design described by Bickford.[10]

3. Conductance Cells.—The cell used for all measurements excepting those for the monosubstituted ammonium chlorides contained electrodes in the form of two concentric cylinders of platinum separated at a distance of about one millimeter by glass bead-like separators. The leads of platinum wire were sealed into glass tubes which protruded downward from the ground-glass stopper of the electrode vessel. The leads were brought out through the top of the cell stopper and were held apart by a rubber stopper. This arrangement is shown in Fig. 1. The rubber stopper served also to prevent moisture from condensing in the tubes supporting the electrodes, thereby short-circuiting the electrodes. The electrode vessel had a volume of approximately 100 ml. The constant of the cell was approximately 0.01. Because of its removable electrodes, this cell had to be restandardized at frequent intervals. No more than four runs were made without restandardizing the cell, and usually less than this. Only twice were four runs made based on one standardization

The cell used in measuring the monosubstituted compounds contained three concentric platinum cylinders 80 mm. long and 17, 19 and 21 mm. in diameter.[8] The electrodes were separated by glass beads as before. The leads were of heavy platinum wire and were brought out

(7) Shedlovsky, THIS JOURNAL, **52**, 1793–1805 (1930).

(8) N. L. Cox, C. A. Kraus and R. M. Fuoss, *Trans. Faraday Soc.*, **31**, 749–761 (1935).

(9) G. Jones and R. C. Josephs, THIS JOURNAL, **50**, 1049–1092 (1928).

(10) W. G. Bickford, Thesis, Library, Iowa State College, Ames, Iowa, 1935.

through the cell walls on opposite sides of the cell where the constriction takes place. The leads then passed into glass tubes which extended far enough above the stopper so that they would be at about room temperature to minimize condensation of moisture. The glass tubes were sealed into small mercury cups. The stopper was of glass ground into the electrode vessel. The heavy platinum leads supported the electrodes and the possibility of more than a very slight movement of the electrodes as a unit was obviated by a number of tips of glass projecting inward from the walls of the vessel. The constant of this cell was 0.001.

The cell having the higher cell constant was standardized directly against a 0.01 demal solution of potassium chloride at 25.0° according to the data of Parker and Parker.[11] The cell having the lower constant was standardized by comparing the resistance of conductivity water in it and in the first cell.

4. Preparation of Liquid Hydrogen Sulfide.—Figure 2 shows the arrangement of apparatus for the preparation, purification, and liquefaction of hydrogen sulfide. Concentrated hydrochloric acid was added from the dropping funnel B to powdered calcium sulfide in the three-liter distilling flask A. Accumulations of calcium chloride solution could be removed by applying suction to the bottle C and opening the cock D to the atmosphere. The hydrogen sulfide was washed with water in bottles E and F which removed most of the hydrogen chloride. Bottle G was charged with a saturated solution of barium hydroxide and this after being converted to barium hydrosulfide would react with any hydrogen chloride remaining in the gas stream. Towers H and I contained calcium chloride for drying. J contained aluminum sulfide which further dried the gas, liberating at the same time an equivalent amount of hydrogen sulfide, and reacting with any small amount of hydrogen chloride set free from the calcium chloride.[12] K and L contained phosphorus pentoxide. Much of the liquefaction took place in M and was completed in the electrode vessel in N. M and N were cooled with a mixture of solid carbon dioxide and ether. O contained phosphorus pentoxide to prevent condensation in the electrode vessel of water vapor from the air in the form of ice. O was used only infrequently as sufficient hydrogen sulfide escaped liquefaction to prevent the entrance of air into the exit tube.

The average specific conductance of twenty-three samples of liquid hydrogen sulfide prepared as described above was 3.08×10^{-10} mho. This agrees well with the value reported by Bickford,[13] 3.1×10^{-10}. The conductances of these twenty-three samples range from 0.9×10^{-10} to 8.7×10^{-10} mho.

Four other samples, prepared with a smaller and older sample of aluminum sulfide in bottle J showed specific conductances ranging from 9×10^{-10} to 44.41×10^{-10} mho. These values are cited as evidence that aluminum sulfide plays an important part in purifying the gas.

5. The Substituted Ammonium Chlorides.—These were prepared or purified carefully. The final drying of each compound was accomplished (after careful washing with absolute ether) by drawing dry air at reduced pressure slowly through the finely ground salt for a number of days. Immediately before use, the compound was transferred to a dry weighing bottle. These salts are hygroscopic but, providing the compounds were very dry to start with and were transferred to the weighing bottle and to the liquid hydrogen sulfide rapidly and only on days when the absolute humidity of the air was low, no detectable absorption of water occurred. The analyses of the compounds are shown in Table I.

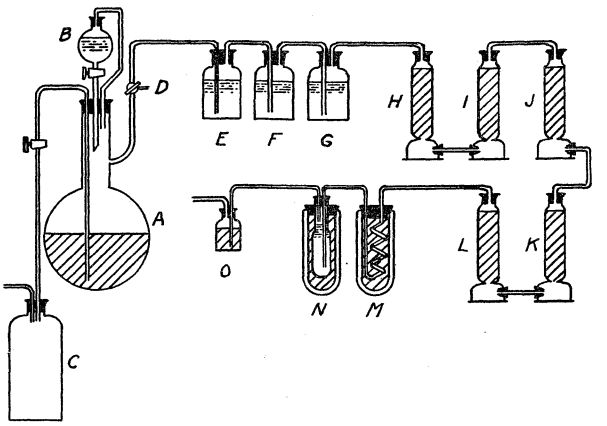


Fig. 2.

TABLE I

ANALYSES OF THE SUBSTITUTED AMMONIUM CHLORIDES

Compound, chloride	Chlorine, % Calcd. from formulas	Found by anal.
Methylammonium[a]	52.52	53.14 53.11[c]
Dimethylammonium[a]	43.49	43.42 43.50
Trimethylammonium[a]	37.10	37.06 37.04
Tetramethylammonium[b]	32.35	32.34 32.20
Ethylammonium[a]	43.49	43.48 43.66
Diethylammonium[a]	32.35	32.28 32.34 32.39
Triethylammonium[b]	25.76	25.89 25.69
Tetraethylammonium[b]	21.36	21.53 21.18
Propylammonium[b]	37.10	37.10 37.13
Dipropylammonium[b]	25.76	25.74 25.76
Tripropylammonium[b]	19.72	19.94 19.80
Tetrapropylammonium[b]	15.99	16.08 16.19

[a] Eastman Kodak Co. products, purified in this Laboratory. [b] Prepared and purified in this Laboratory. [c] Methylammonium chloride proved to be non-conducting in liquid hydrogen sulfide and was not further purified.

6. Procedure.—After measuring the resistance of the liquid hydrogen sulfide at the temperature of the cooling bath of solid carbon dioxide and ether (−78.5°),[14] a sample of the finely powdered, dry organosubstituted ammonium chloride was added from a weighing tube. After solution was complete, the resistance of the solution was measured, and the cell was lifted out of its freezing mixture only far enough to permit measuring the distance between a selected point at the top of the cell and the meniscus. The volume of solution in the cell was determined from a calibration

(11) H. C. and E. W. Parker, THIS JOURNAL, **46**, 312–335 (1924).
(12) J. A. Wilkinson, *Chem. Reviews*, **8**, 237–250 (1931).
(13) W. G. Bickford, *Iowa State Coll. J. Sci.*, **11**, 35–38 (1936).
(14) A. Theil and E. Schulte, *Z. physik. Chem.*, **96**, 312 (1920).

curve comparing distances from the top of the cell to the menisci for known volumes of water at room temperature. The contraction of the glass in cooling from room temperature to that of the freezing mixture is small and was neglected. After completing these measurements for one solution, another weight of salt was added, and the measurements were continued. Sorption effects at the electrodes were assumed to be negligible. They have been shown to be negligible at concentrations above 10^{-5} normal for solutions in several non-aqueous solvents at 25°.[8]

III. Results

The results are shown in Table II where C is the concentration in moles per liter and Λ is the molecular conductance. K_s indicates the conductance of solvent and K that of the solute.

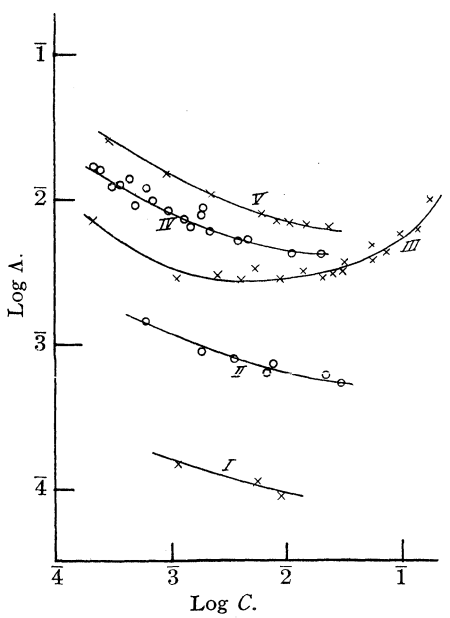


Fig. 3.—Conductance curves for substituted ammonium chlorides in hydrogen sulfide at −78.5°: I, $C_2H_5NH_3Cl$; II, $C_3H_7NH_3Cl$; III, $(CH_3)_2NH_2Cl$; IV, $(C_2H_5)_2NH_2Cl$; V, $(C_3H_7)_2NH_2Cl$.

The specific conductances of the monomethyl and monoethyl compounds are not much greater than that of pure liquid hydrogen sulfide, and those for the propyl compound are about twice that of the pure solvent. With corrections as large as these, the results are not accurate and are given merely to indicate their order of magnitude.

The conductance of the solvent was significant (at greatest, 11% of that of the solution) in measuring the more dilute solutions of the di- and trisubstituted salts. For the tetrasubstituted compounds, the correction was never greater than one part in one thousand, and for most solutions it was negligible.

Figures 3 and 4 show the plots for the data of Table II.

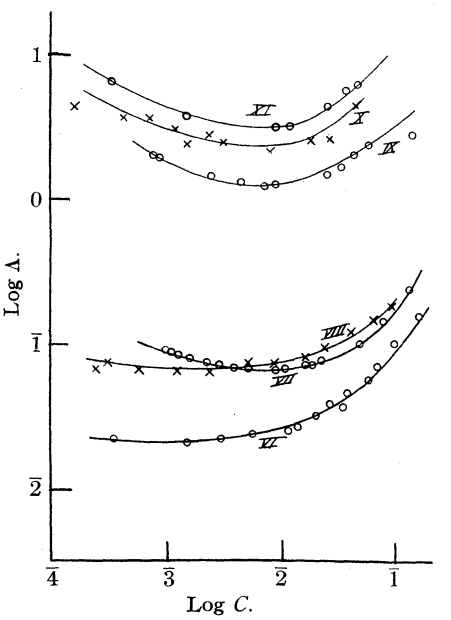


Fig. 4.—Conductance curves for substituted ammonium chlorides in hydrogen sulfide at −78.5°: VI, $(CH_3)_3NHCl$; VII, $(C_2H_5)_3NHCl$; VIII, $(C_3H_7)_3NHCl$; IX, $(CH_3)_4NCl$; X, $(C_2H_5)_4NCl$; XI, $(C_3H_7)_4NCl$.

IV. Discussion of Results

The greater the number of groups substituted in the ammonium radical the greater the conductance becomes. The mono substituted compounds are poor conductors and very little evidence of conductance with the monomethyl compound was observed. This may be due to the fact that the solubility of the compound in liquid hydrogen sulfide is almost nil.

In general the higher the molecular weight of the substituted group, the higher is the value of the conductance. The only exception to this is that the triethyl compound shows higher conductance than the tripropyl ammonium chloride at low concentrations.

The conductance is not greatly altered by changing the substituent from methyl to ethyl to propyl groups. Changing the number of the substituted groups has a greater effect on the magnitude of the conductance, the greatest increase occurring when going from the tri- to the tetrasubstituted compounds.

The compounds in general show an increasing

TABLE II

CONDUCTANCE OF SUBSTITUTED AMMONIUM CHLORIDES IN LIQUID HYDROGEN SULFIDE

Ethylammonium Chloride

C	$K_s \times 10^9$	$K \times 10^9$	$\Lambda \times 10^4$
0.001073	1.450	0.167	1.56
.004993	1.450	.561	1.12
.008965	1.450	.663	0.740

Diethylammonium Chloride

C	$K_s \times 10^8$	$K \times 10^8$	$\Lambda \times 10^3$
0.0002032	0.0340	0.3920	19.3
.0002193	.01207	.4226	19.3
.0002674	.0208	.3751	14.0
.0003154	.0102	.5700	18.1
.0003830	.00964	.4901	12.8
.0005182	.0184	.4605	8.89
.0005879	.01207	.6706	11.4
.0007231	.0340	.8703	12.0
.0007305	.00964	.6842	9.37
.0008505	.0184	.7660	9.01
.001465	.0208	1.017	6.94
.001726	.00964	1.135	6.58
.002023	.0208	1.221	6.04
.002156	.03559	1.469	6.81
.002680	.00972	1.492	5.57
.003718	.0208	1.803	4.85
.004399	.0151	2.149	4.89
.01127	.0151	4.406	3.91
.01996	.0151	7.700	3.86

Triethylammonium Chloride

C	$K_s \times 10^8$	$K \times 10^8$	$\Lambda \times 10^2$
0.0001556	0.058	1.964	12.6
.0009717	.036	8.282	8.52
.001115	.013	8.973	8.05
.001272	.013	9.886	7.77
.001516	.058	11.33	7.47
.002082	.013	14.43	6.93
.002617	.013	17.04	6.51
.004863	.058	28.55	5.87
.008706	.013	47.19	5.42
.009710	.036	53.91	5.55
.01566	.036	91.50	5.84
.01658	.036	97.45	5.88
.01748	.036	104.4	5.97
.01890	.036	114.2	6.04
.02222	.058	144.1	6.49
.04727	.058	458.8	9.71
.07513	.058	1117	14.87
.1211	.058	3242	26.8

Tetrapropylammonium Chloride

C	$K_s \times 10^6$	$K \times 10^6$	Λ
0.0003434	0.0002	2.505	7.29
.001556	.0002	6.244	4.01
.009210	.0002	29.19	3.17
.01086	.0002	35.06	3.23
.02573	.0002	120.7	4.69
.03373	.0002	183	5.43
.04414	.0002	288	6.52
.07463	.0002	645	8.64

Propylammonium Chloride

C	$K_s \times 10^9$	$K \times 10^9$	$\Lambda \times 10^4$
0.0005862	0.87	0.87	14.8
.001623	0.87	1.37	8.44
.003587	3.01	2.45	6.83
.006953	0.87	3.57	5.13
.008380	3.01	5.02	5.99
.02116	3.01	10.27	4.85
.02763	3.01	12.56	4.55

Dipropylammonium Chloride

C	$K_s \times 10^8$	$K \times 10^8$	$\Lambda \times 10^3$
0.0003255	0.0381	0.6619	20.3
.0009289	.0381	1.229	13.2
.001769	.0381	1.827	10.3
.005979	.0381	4.000	6.69
.008129	.0381	5.068	6.23
.01083	.0381	6.276	5.80
.01514	.0381	8.213	5.42
.02564	.0381	13.07	5.10

Tripropylammonium Chloride

C	$K_s \times 10^7$	$K \times 10^7$	$\Lambda \times 10^2$
0.0002381	0.0044	0.1676	7.04
.0003102	.0039	.2344	7.56
.0005608	.0039	.3797	6.77
.0007806	.0039	.5103	6.54
.001269	.0039	.8051	6.34
.001520	.0044	.9398	6.18
.002273	.0044	1.405	6.18
.003483	.0044	2.192	6.29
.005288	.0044	3.450	6.52
.007892	.0044	5.417	6.86
.009991	.0044	7.115	7.12
.01513	.0044	11.90	7.87
.02129	.0044	18.70	8.78
.02928	.0044	29.43	10.1
.04021	.0044	48.15	12.0
.06305	.0044	105.2	16.7
.08876	.0044	205.9	23.1

Tetraethylammonium Chloride

C	$K_s \times 10^6$	$K \times 10^6$	Λ
0.0004173	0.00014	1.969	4.72
.0004547	.00028	1.792	3.94
.0007197	.00014	2.694	3.74
.001308	.00014	3.936	3.01
.001437	.00028	3.595	2.50
.002140	.00014	5.477	2.56
.002145	.00014	5.516	2.57
.003155	.00014	7.367	2.34
.007832	.00028	14.69	1.88
.01698	.00014	42.90	2.53
.02375	.00028	63.16	2.66
.05606	.00028	27.5	4.91

Dimethylammonium Chloride

C	$K_s \times 10^8$	$K \times 10^8$	$\Lambda \times 10^3$
0.0002132	0.0189	0.1521	7.13
.001212	.0189	.3616	2.98
.002195	.0189	.5469	2.49
.002798	.0189	.6530	2.33
.004253	.0189	.9111	2.14
.005074	.0162	1.282	2.53
.009098	.0189	1.815	1.99
.01523	.0162	3.736	2.45
.02308	.0162	6.138	2.66
.02848	.0162	8.040	2.82
.03576	.0189	9.005	2.52
.03623	.0162	11.19	3.09
.05262	.0162	19.22	3.65
.06000	.0189	19.32	3.22
.07593	.0162	34.24	4.51
.08115	.0189	32.01	3.94
.1055	.0162	60.97	5.78
.1244	.0189	70.05	5.63
.1480	.0189	99.56	6.73
.2086	.0189	217.3	10.42

Trimethylammonium Chloride

C	$K_s \times 10^8$	$K \times 10^8$	$\Lambda \times 10^2$
0.0003321	0.0548	0.4471	1.35
.001668	.0548	2.229	1.34
.002945	.0334	4.744	1.61
.005205	.0334	8.773	1.69
.0103	.0334	19.87	1.93
.01166	.0548	20.20	1.73
.01856	.0334	43.66	2.35
.02581	.0548	63.32	2.45
.03534	.0548	107.3	3.04
.04003	.0548	134.8	3.37
.05801	.0548	277.8	4.79
.07639	.0548	500.3	6.55
.1002	.0548	945.3	9.43
.1498	.0548	2636	17.6

Tetramethylammonium Chloride

C	$K_s \times 10^6$	$K \times 10^6$	Λ
0.0008370	0.0003	1.855	2.22
.0009173	.0009	1.960	2.14
.002499	.004	3.665	1.47
.004377	.0009	5.839	1.33
.007264	.0009	9.009	1.24
.008985	.004	10.89	1.21
.02556	.004	37.6	1.47
.03219	.0009	47.12	1.46
.04276	.0009	89.88	2.10
.05786	.0009	149	2.58
.07994	.0009	251	3.14

molecular conductance both in more dilute and in more concentrated solutions. A conductance minimum is characteristic of electrolytes dissolved in solvents having low dielectric constants.[15] Those

(15) R. M. Fuoss and C. A. Kraus, THIS JOURNAL, **55**, 2387–2399 (1933).

which do not show this, the monosubstituted salts and dipropyl- and diethylammonium chlorides, would be expected to have increasing conductance in more concentrated solutions. Additional measurements were made extending concentrations to higher values than those reported for dipropyl and diethylammonium chlorides but no increase in conductance with increasing molecular concentration was noticed with these two salts.

Acknowledgments.—The authors are indebted to Dr. W. G. Bickford for help and suggestions while constructing the conductance bridge and its auxiliaries. A substantial part of the experimental work was done in the Chemistry Laboratories of the University of Vermont.

V. Summary

The conductances of solutions of mono-, di-, tri- and tetrasubstituted methyl-, ethyl- and *n*-propylammonium chlorides in liquid hydrogen sulfide have been measured. These show that the molecular conductance increases both with the number and the size of the substituted groups, the number having a greater effect than the size.

The conductance concentration curves show a minimum which is characteristic of solutions of electrolytes in solvents of low dielectric constant.

AMES, IOWA RECEIVED AUGUST 16, 1939

[CONTRIBUTION FROM THE LABORATORY OF CHEMISTRY, UNIVERSITY OF WISCONSIN]

Chemical Activation by Isomeric Radioactive Transition; the Reaction of Br^{80} (18 min. half-life) with Carbon Tetrachloride

BY JOHN E. WILLARD

Investigations in this Laboratory utilizing radioactive bromine have shown that it undergoes a reaction with carbon tetrachloride. This reaction is not activated by either heat or light but must be accounted for on the basis of chemical activation resulting from the radioactive transition of Br^{80} (4.4 hr. half-life) to Br^{80} (18 min. half-life).

Freshly prepared radioactive bromine contains a mixture of Br^{80} (4.4 hr. half-life), Br^{80} (18 min. half-life) and Br^{82} (34 hr. half-life), all of which may be formed from the common isotopes Br^{79} and Br^{81} by neutron capture. Br^{80} (4.4 hr.) and Br^{80} (18 min.) are radioactive isomers[1,2,3,4] the first of which changes into the second as a result of a loss in nuclear energy. In somewhat less than 70% of the transitions[5] this energy appears as a gamma ray while in the remaining transitions it serves to eject a conversion electron from one of the electron shells of the atom.

It has been shown that the change from Br^{80} (4.4 hr.) to Br^{80} (18 min.) is capable of activating the hydrolysis of *t*-butyl bromide,[2] the rupture of bromate ion,[3] and the decomposition of ethylene dibromide.[6] These reactions result in the preferential splitting out of Br^{80} (18 min.) atoms from the parent molecule. The activation of these processes has been attributed to the recoil energy imparted to the Br^{80} (18 min.) by the ejection of a gamma ray or conversion electron, but in view of a subsequent determination[7] of the energy of the conversion electrons involved, this explanation is not tenable.

In agreement with the work cited above, it has been found that Br^{80} (18 min.) is the reactive bromine species in mixtures of bromine isotopes with carbon tetrachloride. Calculations discussed below indicate that only those transitions of Br^{80} (4.4 hr.) to Br^{80} (18 min.) which occur with the emission of a conversion electron result in reaction with the carbon tetrachloride. The electronic rearrangements which follow such emission afford ample energy to account for the activation.

The results which have been obtained emphasize the fact that special precautions must be exercised in the use of certain radioactive elements as isotopic tracers if erroneous conclusions are to be avoided. It is to be noted, however, that Br^{82} (34 hr.) may be used as an isotopic tracer without danger of ambiguity. This isotope may be obtained by allowing mixtures of isotopes to stand until the relatively short-lived Br^{80} isomers have decayed.

(1) Snell, *Phys. Rev.*, **52**, 1007 (1937).
(2) Segre, Halford and Seaborg, *ibid.*, **55**, 321 (1939).
(3) DeVault and Libby, *ibid.*, **55**, 322 (1939).
(4) Roussinow and Yusephovich, *ibid.*, **55**, 979 (1939).
(5) Siday, *Nature*, **143**, 681 (1939).
(6) Le Roux, Lu and Sugden, *ibid.*, **143**, 518 (1939).
(7) (a) Valley and McCreary, *Phys. Rev.*, **55**, 666 (1939); (b) **55**, 863 (1939).

It might be expected that reactions caused by the beta rays in solutions of the type under consideration would mask reactions, such as those observed, which preferentially separate one period of activity. This, however, does not occur because the proportion of radioactive bromine to normal bromine is extremely small.

Experimental Procedure

Radioactive Bromine.—Radioactive bromine was produced by irradiating 3 liters of ethyl bromide with neutrons from a Ra (200 mg.)–Be source for twenty-four hours. Following irradiation the ethyl bromide was extracted with 150 cc. of water containing about 0.05 g. of sodium bromide. The water solution was then evaporated to about 0.5 cc. and pipetted into the reaction tube (A) of Fig. 1, together with a small amount of potassium bromate and sulfuric acid. The reagents were frozen with liquid air to prevent reaction until (A) had been sealed shut. The bromine which was liberated in (A) with gentle warming was condensed in (B) with an ice–salt mixture. The reaction tube (A) was then sealed off from the system, the gas-escape (D) was sealed, and the bromine was frozen with liquid air. The system was then evacuated through the tube (H) with the aid of a mercury vapor pump and the bromine was distilled onto phosphorus pentoxide in the trap (C), where it was kept until it was admitted to the carbon tetrachloride in the tubes (F).

Carbon Tetrachloride.—Mallinckrodt "Low Sulfur" carbon tetrachloride was strongly illuminated while saturated with chlorine and chlorine dioxide,[8] washed with sodium hydroxide and with water, and dried over phosphorus pentoxide. It was then distilled into an all-glass reservoir (G) equipped with glass taps which could be opened by a magnetically operated hammer. It was degassed by several repetitions of the process of freezing–evacuating–melting. Samples were taken from the reservoir as desired by distilling into evacuated reaction tubes (F). After a sample was obtained the reservoir was sealed off while the carbon tetrachloride was frozen. About 1 cc. was collected in each tube.

Reaction Mixture.—The bromine which was collected in the trap (C) was transferred to the tubes (F), containing the carbon tetrachloride, by cooling the latter with liquid air and opening the stopcock or glass tap at (E). (Stopcocks were greased with Apiezon grease.) The tubes (F) were then sealed from the system as a unit; their contents were melted, mixed and refrozen, and they were sealed off from one another. Their bromine concentration was about 0.05 *M*.

Analysis.—After the reaction tubes had been allowed to stand for the desired length of time, they were opened and the contents washed three times with 5-cc. portions of 20% potassium iodide to give a colorless carbon tetrachloride layer containing the reaction products. This layer showed no radioactivity if the extraction was made immediately after the bromine was added to the carbon tetrachloride.

The relative radioactivity of samples was determined by means of a Geiger–Müller counter tube the end of which consisted of a thin glass bulb which could be lowered into a cup of the solution to be tested. Counts were made on unextracted carbon tetrachloride–bromine solutions, carbon tetrachloride from which the bromine had been extracted, and on the extraction liquid. Frequent determinations of the background count showed it to be very constant at a value of 10 ± 2 per min. The activities which were measured ranged from several thousand counts per min. down to the value of the background.

(8) Dickinson and Jeffreys, THIS JOURNAL, **52**, 4289 (1930).

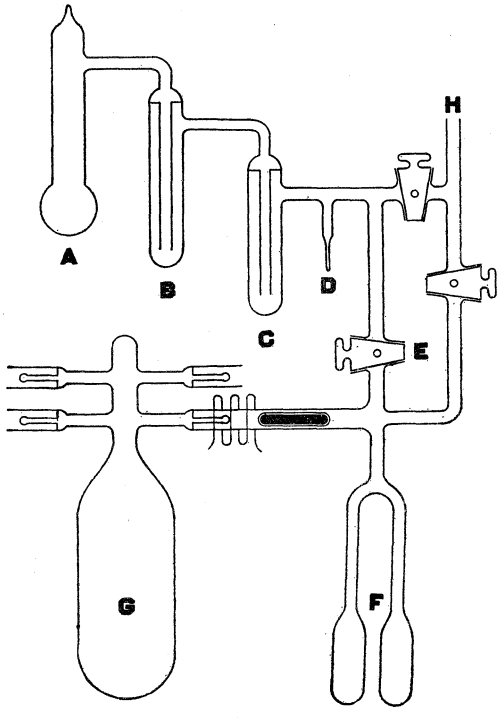


Fig. 1.

Results

Activity Entering Carbon Tetrachloride.—When bromine containing an equilibrium mixture of Br^{80} (4.4 hr.) and Br^{80} (18 min.), some Br^{82} (34 hr.), and a large proportion of non-radioactive bromine is allowed to stand for two hours or more with carbon tetrachloride, between 30 and 40% of the activity measured by the counter described above is found to enter the carbon tetrachloride. This activity is, within the limits of resolution of the apparatus, solely 18 min. activity. A typical decay curve for such a solution is shown in (A) of Fig. 2. The circles represent the experimental data; the line is a calculated curve for the decay of activity with an 18 min. half-life.

Growth of Activity in Carbon Tetrachloride.—If bromine enters the carbon tetrachloride molecule as a result of activation accompanying the transition of Br^{80} (4.4 hr.) to Br^{80} (18 min.) it

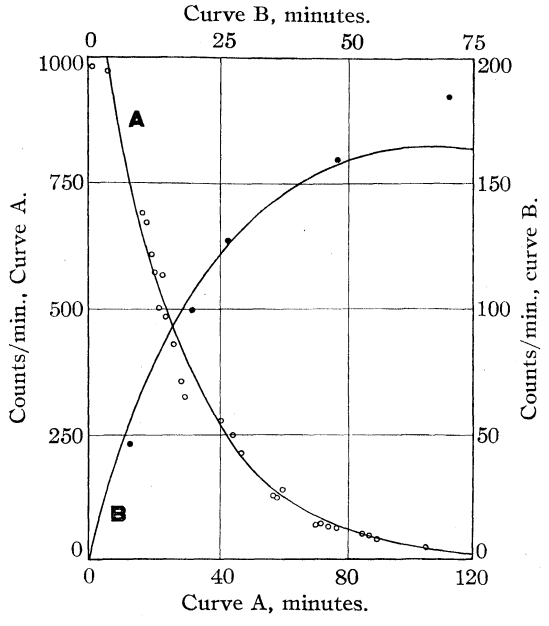


Fig. 2.—Curve A: circles show decay of radioactive bromine which has reacted with carbon tetrachloride. Solid line is calculated decay curve for species with 18 min. half-life. Curve B: points show growth of activity in carbon tetrachloride reacting with radioactive bromine. Solid line shows calculated growth of 18 min. activity from 4.4 hr. activity.

would be expected that a plot of activity entering the carbon tetrachloride against time of contact of the carbon tetrachloride with the bromine would show a growth curve typical of the build-up of 18 min. activity from a relatively long-lived parent. Such a curve is shown in Fig. 2(B). The points were obtained from counts on five samples of the same solution which had been allowed to react for different lengths of time before extraction. The counts have been corrected for the decay which occurred between the start of extraction and the time of taking the counts. The solid line is a theoretical growth curve for the production of 18 min. activity from 4.4 hr. activity.

Activity in Extraction Solution.—The circles of Fig. 3 show the experimentally determined values (less the 34 hr. activity) for the activity of bromine at different times after extraction from a carbon tetrachloride solution in which it had stood for two hours. The activity increases immediately after extraction, passes through a maximum, and finally falls off with a 4.4 hr. decay period. This behavior would be expected if the freshly extracted bromine contained less than the equilibrium amount of Br^{80} (18 min.), that is, if some of the latter had reacted with the carbon tetrachloride.

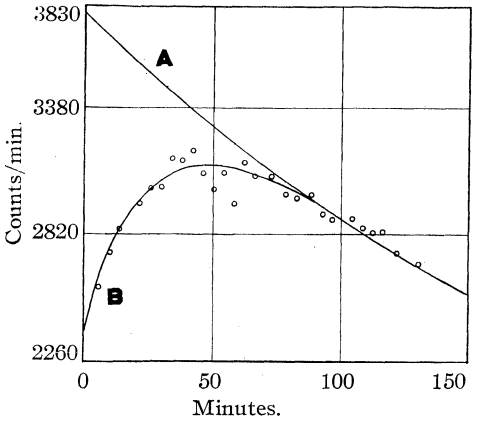


Fig. 3.—Circles show activity of radioactive bromine extracted from carbon tetrachloride solution after standing in the latter for two hours. Curve A: calculated decay of equilibrium mixture of Br^{80} (4.4 hr.) and Br^{80} (18 min.). Curve B: calculated change in radioactivity of extraction solution assuming that 37% of Br^{80} (18 min.) has been removed by reaction with carbon tetrachloride and that radiations from Br^{80} (4.4 hr.) do not register on the counter.

The intersection of the line (A) of Fig. 3 with the zero time ordinate gives the counts per min. which would have been obtained from the extraction solution at the time of extraction if none of the 18 min. activity had reacted with the carbon tetrachloride. It is calculated from the 4.4 hr. decay curve given by the experimental points for times after equilibrium was reëstablished.

Reaction Efficiency.—If the relative efficiency with which the radiations from Br^{80} (4.4 hr.) and Br^{80} (18 min.) affect the Geiger–Müller counter is known, the fraction of the Br^{80} (18 min.) atoms which react with carbon tetrachloride can be obtained readily from the value for the count in the extraction solution at the time of extraction and the value of the intercept of curve (A), Fig. 3, with the zero ordinate.

The 4.4 hr. radiations consist of conversion electrons with energies of 23.6, 35.5, and 47.2 kev., and gamma rays with energies of 48.9 and either 37.1 or 25.3 kev.[7] Calculations show that the fraction of such gamma rays which are absorbed by the counter used in this work is so slight that the number of counts which they produce is negligible. The conversion electrons are also

ineffective in counting because they are almost completely absorbed by the walls of the counter tube before entering the counting chamber.

Therefore it may be concluded that the total count produced by mixtures of Br^{80} (4.4 hr.) and Br^{80} (18 min.) is due to the β rays ejected in the change from Br^{80} (18 min.) to Kr^{80}. These have been found to have a maximum energy of 2 mev.[9]

This conclusion is in agreement with the results of DeVault and Libby[3] and LeRoux, Lu and Sugden,[6] whose data indicate that less than 25 and 10%, respectively, and possibly no part of the total count from radioactive bromine in their counters is due to the 4.4 hr. isomer.

With the knowledge that the radiations from Br^{80} (4.4 hr.) do not affect the counter, it may be determined from the data of Fig. 3 that 0.37 of the Br^{80} (18 min.) atoms formed from Br^{80} 4.4 hr. react with the carbon tetrachloride. This value is in agreement with values of 0.3 to 0.4 obtained by measuring both the activity in the carbon tetrachloride layer and that in the extraction solution immediately after extraction of solutions of radioactive bromine in carbon tetrachloride.

Effect of Temperature and Phase.—If the energy which is made available to a bromine atom by the change from the 4.4 hr. to the 18 min. species is greatly in excess of the activation energy required for a given chemical reaction of the bromine, it is to be expected that the reaction will be independent of temperature. To test this point the maximum fraction of the activity which will enter the carbon tetrachloride has been determined at room temperature, at $-10°$ where the reaction mixture is a liquid, at $-50°$ where it is a solid, and at liquid air temperatures. The results are given in Table I. The values given in the table have been corrected for the background count and for the decay which occurred between the start of extraction and the time of taking the count.

TABLE I

T, °C.	Total counts/min.	CCl_4 counts/min.	% in CCl_4
25	1061	361	34
− 10	518	155	30
− 50	566	45	8
−190	1190	145	12

Different determinations at a single temperature varied as much as 20% from the average, probably due in a large part to the fact that the counter tube was not designed for exactly reproducible comparisons of different samples. The accuracy is adequate, however, to show qualitatively that temperature has little or no direct effect upon the reaction but that the reaction efficiency is reduced to about one-third of its liquid phase value when the reaction system is frozen.

It is to be noted in the table that the reaction does occur even in the solid phase at liquid air temperatures. The amount of reaction at $-10°$ where the mixture is liquid is equivalent to that at 25°. The amount of reaction at $-50°$ where the mixture is a solid is equivalent to that at $-190°$. The change in going from -10 to $-50°$ evidently is due to the change in phase.

If the reaction were a chain reaction with secondary steps for which thermal activation energy was required, it would be dependent on temperature. However, this would not be apparent from the measurements made in this work since they show only the final disposition of Br^{80} (18 min.).

Mechanism of Activation.—It has been suggested[2] that chemical activation by the isomeric transition of Br^{80} is due to the recoil energy which the newly formed Br^{80} (18 min.) atoms acquire as the result of the ejection of a gamma ray or conversion electron when they are formed from Br^{80} (4.4 hr.). Since the publication of this suggestion Valley and McCreary[7] have determined the upper energy of the conversion electrons emitted in this transition to be 47.2 kev. and have concluded from their data that the upper energy of the gamma rays is 48.9 kev.

The recoil energy acquired by a bromine molecule as the result of the ejection of a 47.2 kev. electron is about 3.7 kcal. per mole and the recoil energy made available by the emission of a 48.9 kev. gamma ray is about 0.2 kcal. per mole. These energies are not adequate to account for the observed reaction of bromine and carbon tetrachloride, which are normally very inert to one another.

A larger source of activation energy is, however, available. In emitting a conversion electron a bromine atom initiates an electronic rearrangement of which evidence is given by X-rays[4] and Auger electrons.[5] Such a rearrangement readily can produce highly reactive states of the bromine molecule, atom or ion. A knowledge of the exact nature of the state which leads to the reaction of Br^{80} (18 min.) with carbon tetrachloride is not

(9) Livingston and Bethe, *Rev. Mod. Phys.*, **9**, 245 (1937).

necessary for the purposes of this paper. However, a number of possibilities may be suggested. The molecular ion, formed when a conversion electron, followed by an X-ray, is emitted from a bromine molecule, may have an electronic configuration which makes it capable of reacting directly with a carbon tetrachloride molecule. Alternatively the electronic state may be such as to lead to the dissociation of the molecular ion into a neutral atom and an atomic ion. If this latter process occurs the fragments may part with sufficient kinetic energy to cause them to react with carbon tetrachloride molecules, or the reaction may be accounted for by the electronically excited state of the atomic ion formed. Another possibility is that the reaction is due to a reactive excited state produced when the ion regains an electron.

Whatever the exact mechanism of the activation is, it is necessary to conclude that only those isomeric transitions which occur with the emission of a conversion electron, and consequent electronic rearrangements, can produce reaction.

Siday[5] has found that the fraction of the Br^{80} (4.4 hr.)$\longrightarrow$$Br^{80}$ (18 min.) transitions which emit a conversion electron is slightly more than 0.3. This value sets an upper limit for the fraction of the Br^{80} (18 min.) atoms which can react with carbon tetrachloride, if reaction occurs only following the ejection of an electron. This upper limit is in close agreement with the experimentally determined reaction efficiency discussed above. Therefore it may be concluded that essentially all of those Br^{80} (18 min.) atoms which are formed with the emission of a conversion electron react.

Since the decomposition of radioactive bromate ion[3] and of radioactive ethylene dibromide[6] occur for at least 75 and 90%, respectively, of the Br^{80} (4.4 hr.)$\longrightarrow$$Br^{80}$ (18 min.) transitions and since, according to Siday, a much smaller fraction of these transitions involve the loss of a conversion electron, it appears that some explanation not dependent on the emission of a conversion electron must account for at least part of the observed reaction in these cases. The recoil energy from the transition gamma rays (0.2 kcal.) is insufficient to do so. Therefore, if the observed values for the reaction efficiencies, for the conversion coefficient, and for the energies of the conversion electrons, are valid, some explanation which is not yet apparent must be sought.

Reaction Due to Beta Rays.—Since each beta ray and conversion electron shot out from the radioactive atoms in solution probably disrupts or ionizes several thousand carbon tetrachloride molecules, there must be many reactive fragments capable of combining with bromine in the solution. If more than a very small fraction of the bromine were radioactive, experiments would therefore show a considerable proportion of the 4.4 hr. Br atoms as well as of the 18 min. atoms entering the carbon tetrachloride. However, the proportion of radioactive to non-radioactive bromine atoms in the solution is probably less then $1:1 \times 10^{12}$, so the effect in question is not observable in the measurements of activity.

Neutron–Bromine Reaction.—Incidental to the preparation of radioactive bromine, determinations were made of the rate of decay of the activity of ethyl bromide samples which had just been removed from the Ra–Be source after twenty-four hour exposures. In all cases plots of the logarithm of the activity against time showed the initial decay to have a half-life of the order of twenty minutes, which changed to a half-life of about four and one-half hours after the ethyl bromide had been away from the neutron source for a little over an hour. This indicates that Br^{80} (18 min.) may be formed directly by neutron bombardment, since if all of the 18 min. activity were produced as daughter activity of the 4.4 hr. isomer, the decay curves would be of the 4.4 hr. type from the start.

The author wishes to express his appreciation to Mr. William Van Horne and Mr. Hugh Hulburt for the loan of the counting apparatus used in the foregoing work, to Dr. Joseph O. Hirschfelder for helpful discussions, and to the Wisconsin Alumni Research Foundation for the use of the Ra–Be neutron source.

Summary

1. It has been found that the radioactive transition from Br^{80} (4.4 hr.) to Br^{80} (18 min.) activates bromine in such a way as to enable it to react with carbon tetrachloride.

2. Decay and growth curves of the activities involved give consistent proof of the existence of the reaction.

3. Experiments over a wide temperature range show the reaction to be independent of temperature and to have an efficiency about one-third as great in the solid phase as in the liquid phase.

4. The evidence indicates that only those

Br^{80} (18 min.) atoms react which are produced as the result of the emission of a conversion electron.

5. In the light of new data, the recoil energies previously thought to account for chemical activation by the isomeric radioactive transition of bromine, are found to be too small to do so.

MADISON, WIS. RECEIVED SEPTEMBER 2, 1939

[CONTRIBUTION FROM THE NEW YORK STATE AGRICULTURAL EXPERIMENT STATION, NO. 345]

Partial Vapor Pressures from Nicotine Solutions at 25°*

BY L. B. NORTON, C. R. BIGELOW AND W. B. VINCENT

Little information is available on the loss of nicotine by evaporation and the concentration of nicotine vapor which can be built up when a dilute solution of nicotine is applied to foliage as an insecticide. A knowledge of the partial vapor pressures of both water and nicotine through the complete range of their solutions is therefore of great practical importance from that standpoint, and of theoretical interest in showing the thermodynamic behavior of a highly non-ideal solution.

The published values of the vapor pressure of pure nicotine at ordinary temperatures are in very poor agreement. The values at 25° range from 0.02 mm., determined experimentally by Harlan and Hixon,[1] to 0.17 mm. calculated from the equation found by Gorbachev[2] to be valid from 100 to 250°. A similar equation obtained by Young and Nelson[3] gives 0.12 mm. as the vapor pressure at 25°. No data are available on the evaporation of nicotine from solutions, except some approximate determinations by McDonnell and Young[4] of the final concentration and the loss of nicotine from a dilute solution exposed to the air for a long period at room temperature.

Experimental

Materials.—The nicotine was prepared by purifying the commercial 95% alkaloid, furnished by the Tobacco By-products and Chemical Corporation of Louisville, Ky., according to the method of Ratz,[5] and distilling it *in vacuo*. The product boiled at 125° at 17 mm. pressure, was water-white, and had a specific rotation $[\alpha]^{20}D$ −168.90°. Different samples which were purified at intervals during the investigation varied from this rotation not more than 0.2°. Ordinary distilled water was used as the other component.

Apparatus.—The dynamic gas-saturation method was used for the measurements because of the extremely low vapor pressure of the nicotine. The apparatus was arranged as in Fig. 1. Nitrogen, which was used instead

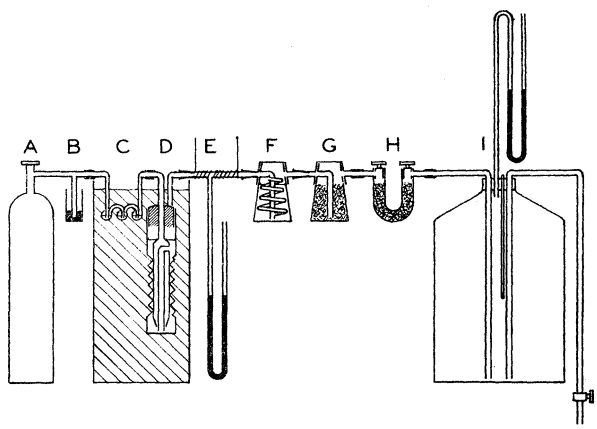


Fig. 1.—Apparatus for vapor pressure measurements.

of air to eliminate slow oxidation of the nicotine, was passed from the cylinder A over the mercury trap B, which served as a safety valve and pressure regulator, and into the vaporizers C and D. C was a series of three small bulbs charged with the solution to be measured, which saturated the gas partially, thus preventing appreciable changes in the concentration of the solution in the main vaporizer D by evaporation losses. D was the main vaporizer, consisting of a Friedrichs spiral gas-washing tower containing 200 cc. of the solution under investigation. The upper part of the tower was packed with glass wool saturated with the same solution to stop any spray and to ensure complete saturation of the nitrogen passing out. Both vaporizers were completely immersed in a water-bath maintained at 25 ± 0.02°. The outlet tube E was heated electrically by a winding of resistance wire to prevent condensation of vapor and was connected with a manometer. The nicotine was absorbed in the modified Turner absorption bulb F, which was filled with dilute sulfuric acid. The second absorption bulb G was filled with anhydrous magnesium perchlorate "Anhydrone" to absorb the water vapor coming from the vaporizer and the first absorber. The U-tube H also contained Anhydrone to absorb any water vapor coming back from the aspirator The aspirator bottle I had a capacity of 40 liters and was fitted with a manometer, thermometer, and siphon tube.

(*) Approved by the Director of the New York State Agricultural Experiment Station for publication as Journal Paper No. 345, October 30, 1939.

(1) Harlan and Hixon, *Ind. Eng. Chem.*, **20**, 723 (1928).

(2) Gorbachev, *J. Applied Chem. (U. S. S. R.)*, **7**, 388 (1934).

(3) Young and Nelson, *Ind. Eng. Chem.*, **21**, 321 (1929).

(4) McDonnell and Young, *U. S. Dept. Agr. Bull.*, No. 1312 (1925).

(5) Ratz, *Monatsh.*, **26**, 1241 (1905).

All connections from the vaporizer to the last absorber were made with ground glass joints, since rubber has been shown to take up appreciable quantities of nicotine under these conditions. The joints were lubricated only on their outer parts, and the lubricant was kept away from the inlet hole in the nicotine absorber in order to avoid possible absorption of nicotine by the grease.

Procedure.—The nitrogen was bubbled through the vaporizers for thirty minutes before the absorbers were connected to ensure complete thermal and vapor equilibrium. The rest of the apparatus was then assembled, and the units turned on in order, the absence of leaks being indicated by the lack of bubbles through the vaporizers, all of the nitrogen escaping through the trap B. The outlet from the aspirator was opened last, and the outflow adjusted to 8–10 liters per hour. The tube in the mercury trap B was quickly adjusted to such a height that the saturated gas coming from the vaporizer was at atmospheric pressure, as indicated by the manometer at E. The run was continued, with only occasional slight adjustments necessary, until 15 to 35 liters had passed through.

The barometric pressure was read at the beginning and the end of each run. The manometer and the thermometer in the aspirator were read at the end of the run, and the manometer at E, as mentioned before, was maintained continuously at zero pressure difference. Both of the filled absorbers were weighed before and after the run, any lubricant on the joints being removed with benzene. The water displaced from the aspirator was weighed to 5 g. on a large solution balance. The solution from absorber F and a sample of the solution from the vaporizer D were analyzed for nicotine.

Analysis.—Most of the original solutions were analyzed by polarimetric measurements, which were found to be superior to chemical analyses for the concentrated solutions. The rotation was determined by means of a Schmidt and Haensch triple field polarimeter with a sodium vapor lamp, using a 2-dm. jacketed tube through which water at 20° was circulated. The nicotine content was read from a curve of concentration plotted against angular rotation, based on the data of Jephcott.[6] The solutions containing less than 5% of nicotine and the absorber solutions were analyzed by precipitation of the nicotine with silicotungstic acid.[7]

Calculation.—The method of calculation was similar to that of Young and Nelson[3] with the addition of a correction for the vapor pressure of the water in the aspirator and for the difference in pressure between the aspirator and the atmosphere, and the extension of the formula to two different vapors. The calculation corresponded to the formulas

$$\text{V. P. (nicotine)} = 760nPT/(273P'V + 760T(n + w))$$
$$\text{V. P. (water)} = 760wPT/(273P'V + 760T(n + w))$$

where P is the barometric pressure as read; P' the barometric pressure corrected for water vapor and the manometer reading; T the absolute temperature of the aspirator; V the gross volume of nitrogen passed through, as measured by the weight of water displaced from the aspirator; n the volume at standard conditions of the vaporized nicotine (g. absorbed nicotine × 22,400/162); and w the corresponding volume of water vapor (g. absorbed water × 22,400/18). The weight of the absorbed water is taken as the net gain in weight of the two absorbers less the weight of absorbed nicotine found by analysis.

Errors.—The estimated random errors from the experimental measurements were as follows: pressure, 0.2%; temperature, 1%; weights, 0.1%. The errors from analysis varied from less than 1% to 5% in different parts of the range.

A systematic error of less than 0.1% was incurred in the calculation by the assumption of the validity of the ideal gas laws. The most serious systematic errors probably came from incomplete vaporization or absorption of the vapors, giving consistently low results, or contamination of the heated outlet tube from spray or other sources, giving high results. The apparatus was tested for such errors by determining the vapor pressure of pure water. The average value found by several runs was 23.57 mm., as compared with the accepted value of 23.75 mm., indicating the absence of sources of serious consistent errors. Complete vaporization of nicotine was demonstrated by a series of determinations on a dilute solution of nicotine, in which the same value of the vapor pressure was obtained, within the expected error, when different solutions, including pure nicotine, were used in the bulbs preceding the main vaporizer. A second nicotine absorber following the first yielded no test for nicotine, showing complete absorption in the first. It was concluded therefore that subsequent determinations would include only accidental errors of this type, limited to single runs.

Results and Discussion

Pure Nicotine.—Because of the uncertainty of the previously determined values at low temperatures, the vapor pressure of pure nicotine was measured as accurately as possible. Ten determinations were made, including five different samples of nicotine, yielding a value of 0.0425 ± 0.0003 mm. for the vapor pressure at 25°. This result indicates considerable error in the values of Harlan and Hixon[1] which, however, were only intended to be approximate, as well as those calculated from the equations of Gorbachev[2] and Nelson and Young,[3] which are somewhat uncertain at 25° because of the long distance of the extrapolation from the experimental points considered.

The complete series of partial vapor pressure measurements are presented in Table I, and the vapor pressures are plotted against the mole fractions in Fig. 2. It will be noted that the vapor pressures of the two components are plotted on different scales in Fig. 2 since they are of a quite different order of magnitude.

(6) Jephcott, *J. Chem. Soc.*, **115**, 104 (1919).
(7) "Assoc. Official Agr. Chem., Official Methods," 61 (1935).

TABLE I

VAPOR PRESSURES OF NICOTINE AND WATER FROM SOLUTIONS AT 25°

Nicotine, %	V. P. nicotine, mm.	V. P. water, mm.	Nicotine, %	V. P. nicotine, mm.	V. P. water, mm.
0.000	0.00000	23.57	80.50	0.0196	19.55
.108	.00035	...	82.10	.0217	19.50
.186	.00045	...	82.40	.0221	19.33
.281	.00049	...	84.30	.0207	18.27
.648	.00100	...	85.55	.0247	18.36
1.318	.00227	...	87.80	.0245	17.80
2.00	.00341	...	89.16	.0267	17.16
4.00	.00442	...	91.95	.0309	15.30
5.00	.0057	23.61	92.19	.0317	15.39
9.80	.0081	23.32	92.70	.0282	14.41
12.60	.0088	23.10	94.80	.0314	12.72
26.65	.0097	22.86	95.60	.0330	13.04
33.28	.0093	23.12	96.20	.0311	11.73
40.30	.0105	23.02	96.90	.0330	11.42
47.95	.0112	22.88	97.50	.0336	10.27
55.90	.0125	22.63	98.07	.0382	8.38
61.55	.0138	22.25	98.82	.0375	5.71
65.23	.0154	22.00	99.22	.0405	4.39
68.89	.0163	21.69	99.60	.0402	3.09
79.45	.0214	20.30	100.00	.0425	0.00

Raoult's Law.—The dotted lines in Fig. 2 represent the ideal curves to be expected if both components followed Raoult's law. The close approach of the upper ends of both experimental curves to these ideal curves shows that either nicotine or water follows Raoult's law reasonably well over a limited range of dilute solutions of the other. Throughout the rest of the range both components show abnormally high vapor pressures. At the lower ends of the curves the very dilute components approximately follow Henry's law over an appreciable range, although the deviations from Raoult's law are very large. Of particular interest is the very abrupt rise in the vapor pressure of nicotine in dilute solutions. Zawidzki[8] obtained a pair of curves from water and pyridine almost identical in form with these.

The Duhem Equation.—The Duhem equation, $d \ln P_1/d \ln x = d \ln P_2/d \ln (1 - x)$, permits the calculation of the partial vapor pressures of the nicotine from those of the water. Following Zawidzki's procedure,[8] we derived the following empirical equation for the partial vapor pressures of the water, neglecting the points at the extreme ends of the curve

$$\text{Log } P_1 = 1.3714 + 1.50 \log x + 0.643(1 - x) - 0.709(1 - x)^2 + 1.23(1 - x)^3$$

where x represents the mole fraction of the water.

From this empirical equation and the equation of Duhem, the corresponding equation for the partial vapor pressures of nicotine is

$$\text{Log } P_2 = -1.3716 + 0.02 \log(1 - x) - 0.643x + 1.14x^2 - 1.23x^3$$

A comparison of the calculated with the observed values is given in Table II.

TABLE II

COMPARISON OF OBSERVED AND CALCULATED VAPOR PRESSURES

Mole fraction nicotine	V. P. water Obsd.	V. P. water Calcd.	V. P. nicotine Obsd.	V. P. nicotine Calcd.
0.98	1.3	0.9	0.0415	0.0413
.95	3.2	2.8	.0403	.0397
.90	6.0	5.9	.0384	.0374
.80	10.3	10.3	.0350	.0342
.70	12.8	12.9	.0321	.0318
.60	14.9	14.8	.0292	.0296
.50	16.7	16.5	.0267	.0271
.40	18.3	18.3	.0238	.0240
.30	20.0	20.0	.0203	.0202
.20	21.6	21.7	.0164	.0158
.10	22.7	23.0	.0123	.0114
.05	23.0	23.4	.0100	.0093
.02	23.2	23.5	.0082	.0078

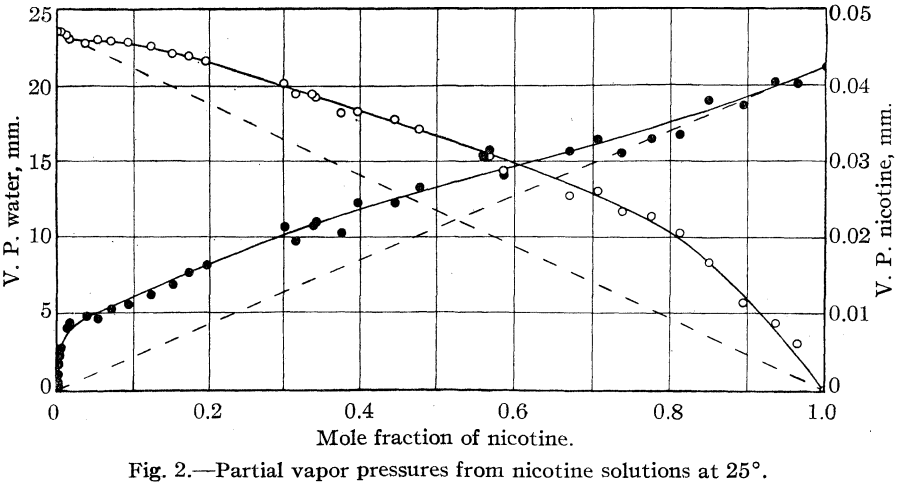


Fig. 2.—Partial vapor pressures from nicotine solutions at 25°.

The agreement of the calculated with the observed values for water shows the faithfulness of the empirical equation. The simultaneous agreement of the corresponding values for nicotine shows that the Duhem equation is valid for this system. The equations are, however, not suitable

(8) Zawidzki, *Z. physik. Chem.*, **35**, 129 (1900).

for calculations at very low or very high concentrations.

Activity.—In view of the extreme abnormality of the lower end of the nicotine vapor pressure curve, it is of interest to calculate the corresponding change in the activity of the nicotine with concentration in this region. The ratio of vapor pressure to mole fraction appears to approach a value of approximately 1.6 in very dilute solutions. The region where $P = 1.6x$ was therefore chosen as the standard state, and the relative activity coefficients calculated as the ratios $P/1.6x$ for solutions up to 0.1 mole fraction, using a large-scale plot of this section of the curve for interpolation of the vapor pressure values. The resulting activity coefficients are shown in Table III.

TABLE III

ACTIVITY COEFFICIENTS OF NICOTINE IN DILUTE SOLUTIONS

Mole fraction nicotine	γ nicotine
0.001	0.90
.005	.63
.010	.45
.020	.26
.030	.19
.040	.15
.050	.13
.100	.08

The activity coefficients decrease extremely rapidly at first with increasing concentration, then show a slow decrease in more concentrated solutions. These values are in satisfactory agreement with the activity coefficients calculated from freezing point data to be published later. It will be noted that the standard state for the nicotine in dilute solution yields an extrapolated value of 1.6 mm. for the ideal vapor pressure of pure nicotine widely different from the actual value of 0.0425 mm.

Rate of Evaporation.—From a practical standpoint the most desirable information is the relative speed of evaporation of the components as a function of the percentage composition. It can be assumed that the rate of evaporation in the open air at low humidity will be roughly proportional to the vapor pressure. The large difference in molecular weight between the components introduces two factors altering the curves in Fig. 2. First, with equal vapor pressures of the two, the evaporation of the nicotine by weight will be nearly ten times as great; second, the lower part of the curves will be greatly lengthened and the higher greatly compressed in changing from mole fractions to percentage composition. Accordingly, after the first rapid rise in the vapor pressure of nicotine at low concentrations, neither the water nor the nicotine changes greatly from 10 to 70%. Even at 90% nicotine, both vapor pressures are about half those of the pure components. The relative losses by evaporation through most of the range will be of the order of 200 of water to 1 of nicotine by weight.

Under actual conditions the ratio will be somewhat less, because of the presence of water vapor already in the air, which will have the effect of subtracting a definite pressure from the effective vapor pressure of the water. The final concentration of any nicotine solution exposed to the air can be determined from the curves as that concentration at which the vapor pressure of the water is equal to the partial pressure of water vapor in the air.

Summary

The partial vapor pressures of nicotine and water in all their binary solutions at 25° have been determined by the dynamic method.

The deviations from Raoult's law are found to be very large and in the direction of higher vapor pressures for both components.

The results are shown to agree with the Duhem equation.

The activity coefficients of nicotine in dilute solutions are found to decrease very rapidly with increasing concentration.

With increasing percentages of nicotine the loss of nicotine relative to that of the water first increases rapidly, then remains nearly constant over a long range, and finally increases very rapidly during free evaporation.

GENEVA, NEW YORK RECEIVED NOVEMBER 1, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, NEW YORK UNIVERSITY]

Free Radicals in the Pyrolysis of Acetaldehyde

BY MILTON BURTON, JOHN E. RICCI AND THOMAS W. DAVIS

Leighton and Mortensen[1] have described experiments in which they detected the formation of free alkyl radicals by the transport of radioactivity (due to Ra-D) from a Paneth radio-lead mirror over which the radicals were passed.[2] We have modified their method in regard to the collection of the transported Ra-D and have been successful in this way in establishing the formation of free radicals in the pyrolysis of acetaldehyde at 500°.

Experimental

The apparatus used in this investigation was essentially as shown in Fig. 1.

Eastman Kodak Co. acetaldehyde was distilled into reservoir A immersed in dry-ice from a reservoir cooled with ice and subsequently freed from air by repeated alternate warming and evacuation at dry-ice temperatures. In this way the extensive polymerization caused by freezing in liquid air[3] was largely avoided. Of two samples so prepared, one, used in runs 17 to 25, had a v. p. of ~335.6 mm., and the other, used in runs 26 to 34, had a v. p. of ~334.6 mm. at 0°. Comparison of these values with that of 337 mm. given by Emeleus[4] would indicate that the presence of the polymer, which could be readily discerned as acetaldehyde was removed, decreased the vapor pressure.

Pellets of natural radio-lead (Pb) prepared from spent radon tubes[5] in a manner already described[6] were introduced into the system (beyond the graded seal G) at a fracture at C which was thereafter sealed. The section of tubing extending to the right of the furnace had an internal diameter of ~5 mm. Heavy mirrors, ~5–6 mm. long in runs 16 to 25 and ~1 cm. long in runs 26 to 34 were deposited at B at a distance ≤ 4 cm. from the end of an electrically heated quartz furnace Q. Because of the presence of radioactive materials it was necessary to modify the usual methods of deposition.[2] Before each deposition any remnant of old mirror was removed by external heating with a gas flame while a stream of acetaldehyde vapor passed through the tube via stopcocks 2, 3 and 4. A fresh mirror was then driven ahead of a gas flame toward the furnace in the usual way and deposited instead of the old. This was removed in the manner just described and a new mirror was deposited for the run. In order to remove the last trace of any volatile radioactive compound the system was now pumped out for several hours before the actual commencement of the run. It is known that delay in the use of lead mirrors decreases their sensitivity to free radicals. It is our opinion that, because of the delay, the mirrors so prepared had both variable and limited active surface. As a result, the figures we list in Table I can be compared only qualitatively with one another. Consequently any temperature coefficients derived from them would be without significance.

During runs, with the exception of the blanks 17, 19 and 22, the mirror was heated externally by steam.[7]

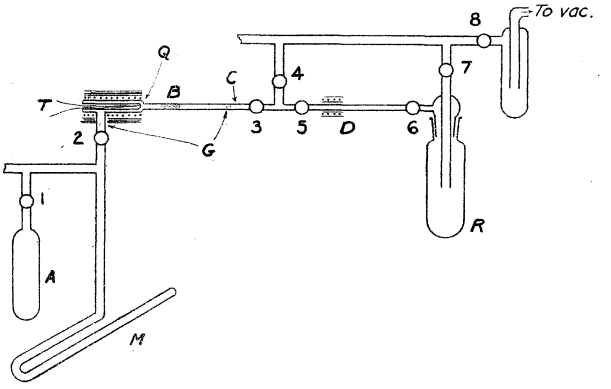


Fig. 1.—Set-up of apparatus.

The temperature of the furnace Q (which was ~10 cm. in length and ~1.2 cm. in internal diameter, and whose well was ~0.8 cm. in outer diameter) was measured with a thermocouple T extending to the tip of the well. Observations, not here recorded, showed a temperature variation along the well with a maximum somewhat higher than at the tip. In the experiments at higher temperature (*i. e.*, ~650°) the maximum was ~50° greater than the observed value while in the lower temperature experiments it was probably no more than 40° above the observed.

During runs, the pressure of acetaldehyde vapor at the stopcock 2, measured on the sloping manometer M, was ~4 mm. The lead tetramethyl presumably formed at the mirror (together with polonium alkyls) was carried by the vapor through stopcocks 3 and 5 to a section of glass tubing heated by the movable heater D to a temperature of 400–500°. Since $Pb(CH_3)_4$ is unstable at such temperatures,[2] free Pb deposited in the tubing near the ends of the "cracking furnace." At the end of a run, stopcocks 1, 3, 5 and 6 were closed, stopcock 4 was opened and the segment of tubing containing the deposited lead was cut out. The lead was dissolved in hot dilute nitric acid and the solution was evaporated to dryness. The radioactivity of the lead nitrate so produced was determined by noting its effect on the rate of discharge of a Lind electroscope into which it was introduced. The net activity (expressed in reciprocal minutes) was in each case corrected for the apparent activity of the empty dish.

(1) P. A. Leighton and R. A. Mortensen, THIS JOURNAL, **58**, 448 (1936).

(2) *Cf.* F. O. Rice and K. K. Rice, "The Aliphatic Free Radicals," The Johns Hopkins Press, Baltimore, Md., 1935.

(3) *Cf.* M. W. Travers, *Trans. Faraday Soc.*, **32**, 246 (1936).

(4) H. J. Emeleus, *J. Chem. Soc.*, **1733** (1929).

(5) We are indebted to Dr. Otto Glasser of the Cleveland Clinic, Cleveland, O., and to Dr. Roscoe W. Teahan of the Jeanes Hospital, Philadelphia, Pa., for the gift of these tubes.

(6) J. E. Ricci and M. Burton, THIS JOURNAL, **60**, 727 (1938).

(7) *Cf.* T. G. Pearson and R. H. Purcell, *J. Chem. Soc.*, 1151 (1935).

In order to check the possibility that a substantial amount of Pb might actually be passing the "cracking furnace" D without deposition, a second such heater was installed to the right of the first and both heated segments of tubing were examined for radioactivity after the runs. In every positive case tested the activity of the right-hand sample was $<1/4$ that of the left-hand sample.

The results of the experiments are summarized in Table I. Each of the runs reported lasted approximately forty-eight minutes. All the pertinent data of the investigation are included in the table; the runs prior to those listed were used in developing the technique of the method. After run 34 the whole system became so seriously contaminated with radio-lead, when the latter was through error introduced into the furnace, that the work had to be abandoned.

TABLE I

TRANSPORT OF RADIO-LEAD IN THE PYROLYSIS OF ACETALDEHYDE

Run	CH_3CHO press., mm.	Furnace temp., °C.	Distance of mirror from furnace, cm.	Net activity, min.$^{-1}$
17[a]	4.0	Room	3.5–4	0.0038
18	4.0	550–560	3.5–4	.38
19[a]	4.0	Room	3.5–4	.027
20	4.0	550–560	3.5–4	.060
21	4.0	550–560	3.5–4	.23
22[a]	4.0	Room	3.5–4	.0018
23	4.0	650	3.5–4	.18
24	0	660	3.5–4	.0054
25	4.0	650–660	3.5–4	.22
26	0	660	3.5–4	.044
27	0	650	3.5–4	.013
28	4.1	460–465	4	.11
29	4.0	460	4	.16
30	4.2	663	2.8	.70
31	4.2	660–670	3.5	.28
32	4.0	352	3	.017
33	0	660	3	.026
34	4.0	375	2.7	.007

[a] The Pb* mirror was cold in experiments 17, 19 and 22.

Discussion

Runs 17, 19 and 22 were blanks in which both furnace and mirror were at room temperature with acetaldehyde flowing through the system. Runs 24, 26, 27 and 33 were blanks in which the furnace and mirror were both heated (the latter with steam) and no acetaldehyde was flowing. These experiments clearly showed that a negligible quantity of radio-lead was transported either by free flow of vapor or by possible volatilization of Pb* at steam temperature. In runs 32 and 34, with the furnace heated to 352 and 375°, respectively, a negligible transfer occurred, thus demonstrating that only acetaldehyde heated to a sufficiently high temperature, that is, the decomposed substance, was effective in transporting Pb*.

The low net activity in run 20 is perhaps to be attributed to a chance preparation of an insensitive mirror. The average activity, in min.$^{-1}$, observed for the other actual tests (18, 21, 23, 25, 28, 29, 30, 31) is 0.28, with limits 0.11 to 0.70. The average activity for the blank experiments (17, 19, 22, 24, 26, 27, 33) is 0.016, with limits 0.0018 to 0.044. In our opinion the difference is real, and on this basis the results of experiments 32 and 34 can be called negative. The lowest temperature (of the tip of the thermocouple) at which transfer was clearly established was 460°, corresponding to a maximum temperature in the furnace of ~500°.

The lowest temperature at which the pyrolysis of acetaldehyde appears to have been studied is 430°[8] but the more detailed work has been done at slightly higher temperatures (~475°).[9] Staveley and Hinshelwood[10] have stated that "the photochemical production of free radicals, which might in any case be expected, from what we know of other catalysts, to have a catalytic action on the decomposition of acetaldehyde, does not prove their occurrence in the thermal reaction." Neither, it may be said, does the decomposition induced[11] by azomethane. The lowest temperature at which the actual detection of free radicals has been reported hitherto in the pyrolysis of acetaldehyde is 743°.[12] The results here presented, however, seem clearly to demonstrate the existence of free radicals in the products of the pyrolysis at ~500° and it seems probable, therefore, that they exist in the products of the pyrolysis at the lowest temperatures studied, as indicated by the Rice–Herzfeld mechanism.[13]

The data of Table I are sufficient for decision as to the existence or non-existence of free radicals under a particular set of conditions but are not satisfactory for quantitative estimation of numbers or of relative numbers of free radicals formed. Work of a more quantitative nature is being continued with artificial radio-antimony, with which substance complications caused by the existence

(8) C. N. Hinshelwood and W. K. Hutchison, *Proc. Roy. Soc.* (London), **A111**, 380 (1926).

(9) *Cf.* M. Letort, *Compt. rend.*, **199**, 351 (1934); *ibid.*, **200**, 312 (1935).

(10) L. A. K. Staveley and C. N. Hinshelwood, *J. Chem. Soc.*, 812 (1936).

(11) D. V. Sickman and A. O. Allen, THIS JOURNAL, **56**, 1251 (1934).

(12) F. O. Rice and W. R. Johnston, *ibid.*, **56**, 214 (1934).

(13) F. O. Rice and K. F. Herzfeld, *ibid.*, **56**, 284 (1934); *cf.* H. A. Taylor and M. Burton, *J. Chem. Phys.*, **7**, 414 (1939); T. W Davis and M. Burton, *ibid.*, **7**, 1075 (1939).

of radioactive recoil particles, as from the radiodecomposition of Pb*, can be avoided.

Summary

The method of Leighton and Mortensen employing natural radio-lead in Paneth mirrors has been modified and used for the detection of low concentrations of free radicals.

In this way the existence of free radicals in the pyrolysis of acetaldehyde at 500° has been detected.

NEW YORK, N. Y. RECEIVED NOVEMBER 7, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF DUKE UNIVERSITY]

The Action of Elementary Fluorine upon Organic Compounds. VII. The Vapor Phase Fluorination of Ethyl Chloride

BY JOHN D. CALFEE, NOBUKAZU FUKUHARA, DEWALT S. YOUNG AND LUCIUS A. BIGELOW

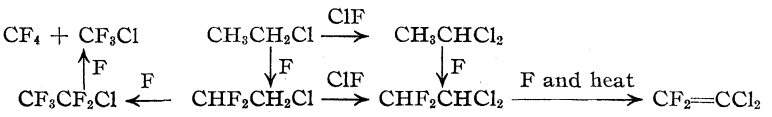
In the third paper of this series,[1] we discussed the vapor phase fluorination of hexachloroethane over copper gauze, which resulted in the substitution of chlorine by fluorine, and yielded *sym*-difluorotetrachloroethane. Since then we have developed an improved technique for the fluorination of organic gases,[2] and this paper deals with the interesting results obtained by applying it to ethyl chloride. Fluorination and chlorination took place simultaneously during the reaction.

Results and Discussion

The ethyl chloride was fluorinated smoothly in a metal apparatus, over copper gauze, under conditions described fully before.[2] The products were condensed by liquid air, transferred to a Booth–Podbielniak low temperature fractionating unit, separated, rectified and analyzed. There were formed carbon tetrafluoride, trifluorochloromethane, CF_3Cl, b. p. −80° (−80°)[3]; pentafluorochloroethane, CF_3CF_2Cl, b. p. −38° (−38°)[4] m. p. −106°; 1,1,2,2-difluorodichloroethylene, $CF_2{=}CCl_2$, b. p. 0° (15°?),[4] m. p. −116°; 1,1,2-difluorochloroethane, CHF_2CH_2Cl, b. p. 35° (35°)[5]; and other products. The observed molecular weights agreed well with the calculated values. The last of these compounds was washed with dilute alkali, dried and distilled in the ordinary way, and the ethylene derivative was passed through a 5% sodium hydroxide solution before analysis. The difluoro- and pentafluoroethyl chloride, as well as the difluorodichloroethylene, have not been obtained before by direct fluorination.

Henne and Renoll[5] gave the boiling point of $CF_2{=}CCl_2$ as 15°, whereas we have found it to be 0°. However, they did not report any molecular weight or analysis, while the values given in Table II leave no doubt as to the composition of the sample which we have examined. The only possible isomer of this compound, CFCl=CFCl, boils at 20.9° according to Booth and collaborators.[6]

In addition to the compounds which were isolated, several others were produced in lesser quantities. A small fraction boiling near 60° was observed repeatedly, and when a larger portion containing this material was distilled at reduced pressure, two small samples were obtained, one of which had a molecular weight of 135, and the other of 98. Now the compound CHF_2CHCl_2 (mol. wt. 135) boils at 60°,[7] and ethylidene chloride CH_3CHCl_2 (mol. wt. 99), distils at 57°. It therefore seemed likely that the two last-named compounds were formed during the reaction. Granting this, a partial mechanism for the fluorination of ethyl chloride may be represented tentatively as



This mechanism involves the substitution of chlorine by fluorine, RCl + 2F ⟶ RF + ClF, and chlorination by chlorine fluoride, RH + ClF ⟶ RCl + HF. The reaction RCl + HF ⟶ RF + HCl may occur, but this seems doubtful.

(1) Miller, Calfee and Bigelow, THIS JOURNAL, **59**, 198 (1937).

(2) Calfee and Bigelow, *ibid.*, **59**, 2072 (1937); Calfee, Fukuhara and Bigelow, *ibid.*, **61**, 3552 (1939).

(3) Ruff and Keim, *Z. anorg. allgem. Chem.*, **201**, 245 (1931).

(4) Locke, Brode and Henne, THIS JOURNAL, **56**, 1726 (1934).

(5) Henne and Renoll, *ibid.*, **58**, 889 (1936).

(6) Booth, Burchfield, Bixby and McKelvey, THIS JOURNAL, **55**, 2231 (1933).

(7) M. Swartz, *Bull. soc. chim.*, **35**, 1557 (1924).

Several fluorinations were run, using different gas volume ratios of fluorine to ethyl chloride, and in one case the fluorine was diluted with nitrogen. The copper gauze was protected at all times from air and moisture, which decreased its efficiency greatly. This effect was not observed when ethane was fluorinated.[2] Table I shows the proportions in which the more important products were formed expressed in liquid volume per cent. of the total condensate, as has been done previously. The figures have been rounded off to the nearest 5% and are significant.

TABLE I

THE FLUORINATION OF ETHYL CHLORIDE

Liquid volume % of:	Gas volume ratios of $F/C_2H_5Cl/N$ 2/2/0	3/2/0	4/2/0	4/2/4
CF_4	10	10	10	trace
CF_3Cl	5	10	15	trace
CF_3CF_2Cl	trace	5	10	5
$CF_2{=}CCl_2$	0	5	5	trace
CH_3CH_2Cl	70	40	10	20
Residue b. p. > 12°	5	15	20	40
Transition fractions	15	20	30	40

The total volumes of liquid condensate in the four runs were 50, 32, 21 and 26 ml., respectively, calculated on a ten-hour operating basis. The results were in general consistent, since the more highly fluorinated products increased in quantity as the ratio of F/C_2H_5Cl increased, and decreased sharply when the fluorine was diluted. The material boiling above 12° was collected together and subsequently redistilled.

Method of Analysis

We believe that the development of a precise, convenient procedure for the quantitative analysis of stable low boiling organic fluoro-chloro gases for both halogens is a matter of importance, and have devoted considerable time to this problem, which is not as simple as might at first appear. The procedure finally adopted was based on the one described by Hubbard and Henne,[8] but differs from it in several important respects, the most significant of which is that our gas samples were weighed. In the older method, gas volumes were measured, which admittedly involved the question of how closely the sample behaved as a perfect gas.

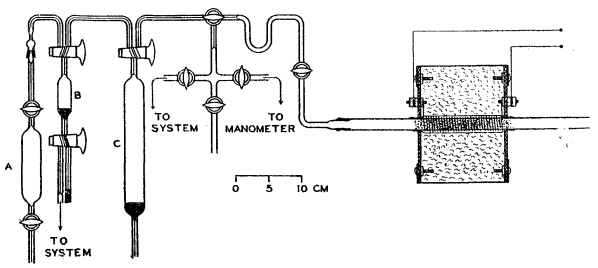


Fig. 1.—Analytical apparatus.

The combustions were run on a semi-micro scale, but the samples were conveniently weighed on an ordinary analytical balance, which necessitated the taking of gas aliquots. The complete apparatus is illustrated to approximate scale in Fig. 1. It was mounted on the same frame as the Booth–Podbielniak unit, and connected directly to that system. The furnace consisted of a 46-cm. length of clear silica tubing with a 13 mm. bore, which was wrapped with asbestos paper, wound directly with no. 24 Chromel wire over about 13 cm. of its length and surrounded by an insulating unit made of aluminum sheet and filled with powdered asbestos. This combustion tube was packed with ground silica, about 20 mesh, held in place at the ends by larger pieces of the same material. It was sealed to the system and also to the absorption apparatus by means of de Khotinsky cement. The maximum temperature in the furnace was maintained at approximately 900° by a calibrated rheostat. The volumes of container A (about 60 ml.) together with the connecting line, and B (about 12 ml.) were determined accurately by calibration with mercury.

The operating procedure was as follows: The container A was exhausted and the sample allowed to expand into it, through B, up to atmospheric pressure, after which it was detached and the gain in weight noted (0.2–0.3 g.). Then B was exhausted and the sample allowed to expand into it, giving a known quantity of material, about one-fifth of the original amount. This gas was next conducted into C, where it was mixed with 100 ml. of oxygen, and then pushed slowly through the furnace during a period of 50 min., and into the absorption vessel. This consisted of a U-tube with a half dozen bulbs, similar to that described before,[8] and contained 10 ml. of 1.0 *N* sodium hydroxide solution and 1 ml. of superoxol. The sample was followed successively by 200 ml. of oxygen, 100 ml. of nitrogen, 200 ml. of hydrogen and finally by nitrogen directly from the tank for one and one-half hours, all at the rate of approximately 200 ml. per hour. The excess of oxygen was necessary to prevent back diffusion of the sample into the nitrogen, with subsequent failure to burn, and the hydrogen was used to reduce silicon oxychloride.[8] Also it was necessary to remove any accumulation of silica deposited in the entrance arm of the absorption apparatus during a combustion, since it tended to retain halogen. Finally, the alkaline solution was washed out, 1 ml. of superoxol added and the mixture heated to boiling. Then it was made up to 200 ml., and aliquot portions of 25 and 50 ml. taken for the determination of fluoride and chloride ions, respectively.

The fluoride ion was titrated with approximately 0.01 *N* thorium nitrate solution, according to the well-known Hoskins and Ferris[9] procedure. Approximately 180 ml. was collected in the distillation, which was made up to 200 ml., and the average value obtained by titrating four or five 25-ml. aliquot portions of this was taken as the correct one. It was found desirable to use a small light box with a blue bulb for constant illumination at the end-point, but care should be taken on account of the heat effect. The chloride ion was titrated with standard silver

(8) Hubbard and Henne, THIS JOURNAL, **56**, 1078 (1934).

(9) Hoskins and Ferris, *Ind. Eng. Chem., Anal. Ed.*, **8**, 6 (1936).

nitrate solution using a dichlorofluorescein adsorption indicator according to Kolthoff and collaborators.[10] This method is applicable in the presence of silica, and has proved very efficient. We have not found the Volhard procedure to be satisfactory in this work.

Finally the several products obtained by the fluorination of the ethyl chloride were analyzed and results are summarized in Table II.

TABLE II

ANALYTICAL VALUES

Compd.	Calcd. F	Calcd. Cl	Found F		Found Cl	
CF_2Cl_2[a]	31.4	58.7	31.4	...	58.7	...
CF_3Cl	54.5	34.0	54.6	54.3	34.0	34.0
CF_3CF_2Cl	61.5	23.0	61.4	61.5	23.1	23.1
$CF_2{=}CCl_2$	28.6	53.4	28.6	28.6	53.3	53.6
CHF_2CH_2Cl[b]	37.8	35.3	37.8	38.0	35.2	...

[a] Analysis of purified Freon, to test the procedure. [b] Decomposed in a Parr bomb.

(10) Kolthoff, Lauer and Sunde, THIS JOURNAL, 51, 3273 (1929).

These results leave no doubt as to the composition of the compounds which were isolated in this work.

Summary

Ethyl chloride was fluorinated in the vapor phase over copper gauze under varying conditions, and the relative amounts of the more important products determined.

The compounds CF_4, CF_3Cl, CF_3CF_2Cl, $CF_2{=}CCl_2$ and CHF_2CH_2Cl were isolated from the reaction mixture. The last three of these have not been obtained before by the action of elementary fluorine on an organic compound.

A precise analytical procedure for determining fluorine and chlorine in stable organic gases has been described.

DURHAM, NORTH CAROLINA RECEIVED AUGUST 4, 1939

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY OF THE UNIVERSITY OF CHICAGO]

The Electrostatic Influence of Substituents on Reactions Rates. I

BY F. H. WESTHEIMER AND MARTIN W. SHOOKHOFF

Ingold has postulated that the effect of a polar substituent on the rate of saponification of an aliphatic ester, like the effect of such a substituent on the ionization constant of an acid, is largely electrostatic. In 1930[1] he employed Bjerrum's quantitative electrostatic formulation[2] to compute, from the ratios of the rates of saponification of the first and second ester groups, the separation of the carbalkoxy groups in a series of esters of dibasic acids. Ingold's evidence went far toward establishing his hypothesis in those cases in which the molecule is long and the substituent can be regarded as a negative charge.

Kirkwood and Westheimer[3] have recently refined Bjerrum's approximate computations of the electrostatic free energy involved in a chemical reaction; the success of the new equations, while general, has been most conspicuous in the considerations of the ionization constants of short dibasic and of dipole substituted acids,[4] cases for which the older formulation is inadequate. The shortcomings of Ingold's modified equation[5] have been presented previously.

The present paper deals with the rate of alkaline hydrolysis of esters and amides in cases in which the substituent is a negative charge, a positive charge and a dipole, all placed close to the seat of the reaction. When the substituent is close to the ester or amide bond that is broken, the rates of hydrolysis of the substituted and unsubstituted compounds differ by a factor of a hundred or more. Since the measurements were made by conductivity, very slow and very fast reactions were excluded: the former because of action of alkali on the glass of the cell, the latter because of the time required to attain thermal equilibrium. These considerations necessitated a careful selection of the pairs of compounds employed.

To illustrate the effect of a negative charge as substituent, the rate of alkaline hydrolysis of the sodium salt of oxamic acid was compared with the rate for oxamide; to illustrate the effect of a positive charge, the rate of saponification of the chloride of the tertiary butyl ester of betaine was compared with the rate for the tertiary butyl ester of dimethylglycine; and to illustrate the

(1) Ingold, *J. Chem. Soc.*, 1375 (1930), 2170 (1931); Ingold and Mohrhenn, *ibid.*, 1482 (1935).

(2) Bjerrum, *Z. physik. Chem.*, **106**, 219 (1923).

(3) Kirkwood and Westheimer, *J. Chem. Phys.*, **6**, 506 (1938); Westheimer and Kirkwood, *ibid.*, **6**, 513 (1938).

(4) Westheimer and Shookhoff, THIS JOURNAL, **61**, 555 (1939); Westheimer, *ibid.*, **61**, 1977 (1939); *cf.* Eucken, *Z. angew. Chem.*, **45**, 203 (1932).

(5) Ingold, *J. Chem. Soc.*, 2179 (1931).

effect of a dipole, the rate of saponification of the tertiary butyl ester of chloroacetic acid was compared with the rate for the tertiary butyl ester of acetic acid.

The equations of Kirkwood and Westheimer apply accurately only to spheres and to prolate ellipsoids in which substituents and charges are at the foci. Due to the experimental limitations mentioned above, some sacrifice in the shape of the molecule was unavoidable.

Theoretical

Ingold treated the reaction velocity problem by means of Christiansen's theory,[6] that is, as a case in which the local concentration of hydroxide ions differs, due to the presence in the molecule of a polar substituent, from that in the remainder of the solution. The assumptions involved can be more conveniently stated, however, when the problem is formulated in Brönsted's terms.[7]

Brönsted postulated a rapid equilibrium between the reactants and an activated complex, followed by a slow decomposition of the activated complex to form the reaction products. In order to apply the electrostatic theory, it is further necessary to assume that the rates of decomposition will be the same for activated complexes formed from two closely similar molecules.[8] Stated mathematically

$$k_{\text{obsd.}} = kK \text{ and } k'_{\text{obsd.}} = k'K'$$

$k_{\text{obsd.}}$ and $k'_{\text{obsd.}}$ are the observed velocity constants, corrected to infinite dilution, for the bimolecular reactions, and K and K' are the equilibrium constants for the formation of the two activated complexes. If k and k', the rate constants for the decomposition of the activated complexes, are assumed equal, then

$$k_{\text{obsd.}}/k'_{\text{obsd.}} = K/K'$$

In other words, to compute the ratio of the velocity constants at infinite dilution, it is only necessary to compute the ratio of the equilibrium constants for the formation of the critical complexes.

The rest of the argument exactly parallels that given by Kirkwood and Westheimer[3] for the case of the ionization constants of acids with and without polar substituents. $\boldsymbol{k}''T \log_e K - \boldsymbol{k}''T \log_e K'$ is equal to $\Delta w'$, where $\boldsymbol{k}''$ is Boltzmann's constant, T the absolute temperature, and $\Delta w'$ is the average reversible work expended in the transfer of a hydroxide ion from the unsubstituted activated complex to the substituted ester, infinitely separated in the solvent. Part of $\Delta w'$ is an entropy term, arising from differences in molecular symmetry. The electrostatic part of $\Delta w'$, called Δw, is that which can be computed. The part of $\Delta w'$ connected with the intrinsic structure of the molecules is by no means to be overlooked, but it is assumed that, as a first approximation, it will vanish because of cancellations between the substituted and unsubstituted compounds.

It follows, therefore, that

$$\Delta w = \boldsymbol{k}''T \log_e K/\sigma K' = \boldsymbol{k}''T \log_e k/\sigma k' = 2.303\ \boldsymbol{k}''T\ \Delta \log k$$

where $\boldsymbol{k}''$ is the Boltzmann constant, σ is a statistical factor (equal to two in the saponification of esters or amides of dibasic acids) and the equation serves to define $\Delta \log k$.

From the equations of Kirkwood and Westheimer and from the experimental values of $\Delta \log k$, it is possible to compute the distance between the negative charge in the activated complexes, and the positive charge in the chloride of tertiary butyl betaine, the center of the dipole in tertiary butyl chloroacetate, and a positive charge in oxamide, located approximately in the position of the ionizable proton in oxamic acid. These distances are then compared with those obtained from an independent source.

Experimental

Apparatus.—Conductivity was measured with a calibrated Leeds and Northrup bridge, using a slide wire of the Kohlrausch type, and a Clough–Brengle audio frequency oscillator as the source of current. The apparatus was slightly modified[9] from the standard Washburn type, and was capable of measuring resistances with a precision of 0.01%.

The design of the conductivity cells was dictated primarily by the experimental observation that the percentage time rate of change of conductivity due to the solution of the glass in alkali increases with temperature, dilution, and the ratio of surface to volume, as shown in Table I. Cell A, used at alkali concentrations of 0.0003 to 0.003 was spherical, of one liter capacity, and had bright electrodes, 1.8 cm. in diameter and 2 cm. apart. Due to the large size of this cell, at least an hour was necessary to attain temperature equilibrium; it was not, then, very satisfactory for the more rapid reactions. For the concentration range 0.003 to 0.05, cell B was used. It was cylindrical in shape, 3 cm. in diameter and 11 cm.

(6) Christiansen, *Z. physik. Chem.*, **113**, 35 (1924).

(7) Brönsted, *Chem. Rev.*, **5**, 231 (1928).

(8) The application of electrostatic theory to the problem of the change of rate with solvent involves a more limited assumption (Scatchard, *J. Chem. Phys.*, **7**, 657 (1939)). Since the transmission coefficient is usually in the neighborhood of unity, a broader assumption is involved in Eyring's theory (*ibid.*, **3**, 107 (1935)).

(9) Jones and Josephs, THIS JOURNAL, **50**, 1049 (1928).

long, with lightly platinized electrodes 1 cm. in diameter and 8 cm. apart. Cell C was 8 cm. longer than cell B, and the electrodes were 8 cm. further apart; the cells were otherwise identical. Cell D was designed according to Jones and Bollinger.[10] The electrodes were unplatinized and their area and the distance between them were approximately the same as for cell A.

An oil thermostat controlled the temperature to 0.01°.

TABLE I

RATE OF CHANGE OF CONDUCTIVITY OF SODIUM HYDROXIDE SOLUTIONS DUE TO SOLUTION OF GLASS

Cell	Alkali concn., *N*	Change in % per hr., at 30°	at 35°
A	0.002	0.022	
B	.005	.064	
B	.008		0.10
B	.030	.022	
C	.015	.030	.050
C	.050	.012	

Materials.—Tertiary butyl acetate was prepared according to Skrabal and Hugetz,[11] oxamide according to Liebig[12] and oxamic acid according to Oelkers.[13] Dimethylglycine was synthesized by the method of Michaelis and Schubert[14] and the chloride of betaine amide by the method of Renshaw and Hotchkiss.[15] To determine its purity, each was analyzed before use.

Tertiary Butyl Chloroacetate.—While the tertiary butyl chloroacetate used in the velocity determinations was prepared by direct esterification, a more convenient method of preparation follows: 60 cc. of chloroacetyl chloride was placed in a three-necked flask equipped with thermometer, stirrer, dropping funnel and an outlet protected by a calcium chloride tube. A mixture of 100 cc. of dimethylaniline and 75 cc. of tertiary butyl alcohol (m. p. 23°) was added dropwise during the course of an hour, maintaining the temperature at 0° by means of an ice-bath. At the end of this time, the ice-bath was removed and the mixture allowed to stand overnight. Water was then added, and the heavy ester layer separated, washed with water, dilute hydrochloric acid, sodium bicarbonate solution, and water again. The oil was dried over calcium chloride and vacuum distilled: yield, 72 g., or 60%, of the ester. The product is a colorless liquid, slightly heavier than water, boiling at atmospheric pressure at 155° with some decomposition and at 60.2° at 15 mm., $n^{20}D$ 1.4230.

Anal. Calcd. for $C_6H_{11}O_2Cl$: C, 47.8; H, 7.37; Cl, 23.56; sapon. equiv., 150.5. Found: C, 47.6; H, 7.33; Cl, 23.63; sapon. equiv., 150.6.

The material actually used in the velocity determinations had been carefully fractionated at reduced pressure, and was of analytical purity.

An acidified portion of completely saponified ester gave no precipitate with silver nitrate, showing that there is no appreciable hydrolysis of the chlorine during saponification. Another portion of the ester was hydrolyzed, the tertiary butyl alcohol isolated, dried, and identified by melting point and the melting point of a mixture with an authentic sample.

Tertiary Butyl Betainium Chloride.—Twenty grams of tertiary butyl chloroacetate and 62 cc. of a 2.5 molar solution of trimethylamine in dry benzene were mixed with cooling. Although crystals formed in a few minutes, it proved advisable to allow the mixture to stand for twenty-four hours; yield, 18 g. The crude material can be crystallized from acetone or dioxane to which a small amount of water has been added. The product is a white crystalline powder, which, when dry, melts with decomposition around 220°, the exact temperature depending somewhat on the rate of heating.

Anal. Calcd. for $C_9H_{20}O_2NCl$: Cl, 16.91; N, 6.68. Found: Cl, 16.89; N, 6.79.

The material used in the rate determinations had been recrystallized several times, and was of analytical purity.

Tertiary Butyl Dimethylglycinate.—Twenty grams of tertiary butyl chloroacetate and 43 cc. of a 4 molar solution of dimethylamine in dry benzene were mixed, with cooling, and allowed to stand at room temperature for twenty-four hours. The resultant material was extracted with 1:1 hydrochloric acid, and the extract washed once with ether. The aqueous layer was then saturated with potassium carbonate and extracted with ether. The ether extract was dried with potassium carbonate, the ether removed by distillation, and the residue fractionated at reduced pressure. The yield of colorless oil, having a slight ammoniacal odor, was 12 g. The hydrochloride was prepared by adding a slight excess of hydrogen chloride in methanol, and evaporating to dryness under reduced pressure. The residue can be recrystallized from a 10% solution of tertiary butyl alcohol in benzene. The white twice recrystallized material which was used in the velocity determinations melted about 150°, the exact temperature depending somewhat on the rate of heating.

Anal. Calcd. for $C_8H_{18}O_2NCl$: Cl, 18.13; N, 7.16. Found: Cl, 18.08; N, 7.12.

Conductivity water and carbonate free alkali were used throughout. Chemicals other than those recorded here were of reagent grade.

Method.—The usual procedure in the determination of reaction velocity by conductivity is to determine the initial and final conductivities of the solution and to calculate the rate on the assumption that the conductivity of the solution is a linear function of the extent of reaction. In the determinations here described, since it was inconvenient in most cases to measure the initial and final conductivity, each velocity determination was standardized by measuring the conductivity of solutions corresponding in ionic composition to that present at several different times during the reaction.[16] Since the concentrations of the various ions in the standardizing-solution could not conveniently be made exact

(10) Jones and Bollinger, THIS JOURNAL, **53**, 411 (1931).

(11) Skrabal and Hugetz, *Monatsh.*, **47**, 17 (1926).

(12) Liebig, *Ann.*, **9**, 1 (1834); see "Beilstein," IV ed., Vol. II, p. 546.

(13) Oelkers, *Ber.*, **22**, 1566 (1889).

(14) Michaelis and Schubert, *J. Biol. Chem.*, **115**, 221 (1938).

(15) Renshaw and Hotchkiss, THIS JOURNAL, **48**, 2698 (1926).

(16) A similar standardization procedure has been described by Crocker and Lowe, *J. Chem. Soc.*, **91**, 952 (1907).

duplicates of those at any point during the reaction, a small correction had to be added to the conductivity of each standardizing solution. In order to estimate this correction, it was only necessary to know the ratios of the conductivities of all the ions present to that of hydroxide ion.

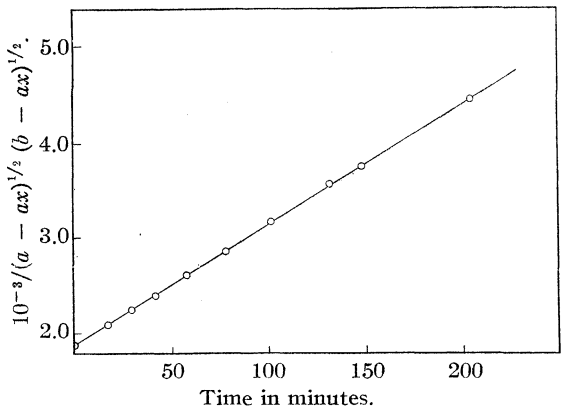


Fig. 1.

The values of the conductances are given in Table II, arbitrarily assigning to hydroxide ion a value of 100 at every temperature. The values in the upper part of the table were calculated from existing data,[17] those in the lower part of the table were measured. Since the correction was in all cases small, comparatively large errors in the relative conductivities of the ions do not affect the final result appreciably. The measurements were made in an ionic environment similar to that in the actual reaction mixtures, except in the case of tertiary butyl betainium chloride, which was measured in a solution containing only the pure compound.

TABLE II

RELATIVE CONDUCTIVITIES OF THE IONS

Ion	Temperature 6.5°	10°	30°
Hydroxide	100.0	100.0	100.0
Chloride	39.0	38.7	
Acetate	20.6		
Oxalate			70.3
Sodium	24.7	24.7	24.7
Ammonium			35.6
Chloroacetate	16.6		
Oxamate			18.7
Dimethylglycinate	12.5		
Betaine amide	19.8		
t-Butylbetainium	17.8		

In some cases there was a slow reaction between the ions of the standardizing solutions. Since the extent of the reaction was always quite small, it was not difficult to extrapolate accurately back to the time when the solution was prepared. The procedure could not be used for tertiary butyl betainium chloride, because of the rapid reaction of the positive ion with alkali; therefore the corresponding amide was used in place of the ester. After determining the relative conductivities of the ester and amide ions, it was possible to estimate the conductivities of the solutions used in the reaction velocity determinations. While the error in this case is probably greater than in any other, it cannot be large, since only 10% of the total conductivity is contributed by the positive ion.

(17) Landolt–Börnstein, "Physikalisch-chemische Tabellen," Erg. IIIc.

Results

The data for a typical velocity determination, the saponification of tertiary butyl chloroacetate, are given in Table III. Here a is the initial concentration of sodium hydroxide in moles per liter, b the initial concentration of the ester, and x the fraction of the alkali consumed in time, t. The rate constants were obtained graphically by plotting time against $\log(1 - x)/(b - ax)$, or, when the initial concentrations of the two reactants were nearly equal, against $1/(a - ax)^{1/2}(b - ax)^{1/2}$. Figure 1 is a graph of the data in Table III.

TABLE III

DATA FOR THE SAPONIFICATION OF TERTIARY BUTYL CHLOROACETATE

a = 0.000782 Time in min.	b = 0.000835 Conductivity	x
0.0	4462	0.346
17.4	4165	.420
29.1	4000	.461
41.4	3851	.498
57.3	3683	.540
77.3	3510	.583
101.2	3334	.627
131.6	3170	.667
147.7	3094	.686
203.8	2887	.738
262.9	2727	.778

Conductivity in this case is a linear function of the extent of reaction. When $x = 0.010$ the conductivity is 5813 and when $x = 0.660$ the conductivity is 3197. The conductivities are all in arbitrary units.

The solution of glass in alkali changes both the conductivity and the hydroxide-ion concentration. In correcting for the former effect, it was assumed that the percentage time rate of change of conductivity due to reaction with the

TABLE IV

SUMMARY OF THE VELOCITY DETERMINATIONS

Organic reactant	Cell	a	b	μ	T	k in min.$^{-1}$ (mols/l.)$^{-1}$
Oxamide	B	0.004669	0.003207	0.00467	30.1°	1.36
	A	.002076	.001301	.00208		1.40
						Av. 1.38
Sodium oxamate	C	.05504	.05492	.110	30.1°	0.0158
	B	.03209	.02676	.0589		.0143
	B	.02732	.01738	.0447		.0138
	C	.01424	.01197	.0262		.0132
				Value for infinite dilution		.0101
t-Butyl dimethylglycinate	B	.01408	.01618	.0303	10.2°	.0220
	B	.00731	.00866	.0160		.0228
						Av. .0224
t-Butyl betainium chloride	D	.002143	.002112	.00426	10.2°	23.5
	D	.000849	.00776	.00163		23.8
	D	.000841	.00835	.00168		21.0
	A	.000596	.000593	.00119		(18.9)
	D	.0005042	.0004880	.000992		20.7
	A	.0005042	.0004880	.000992		20.8
	D	.0004354	.0004288	.000864		23.2
						Av. 22.2
t-Butyl acetate	B	.03181	.01981	.0318	6.6°	0.0247
	B	.01421	.04087	.0142		.0254
	A	.002269	.01421	.00227		.0244
						Av. .0248
t-Butyl chloroacetate	D	.000782	.000835	.000782	6.6°	11.9
	A	.000629	.000587	.000629		(14.4)
	D	.000582	.000570	.000582		21.1
	A	.000582	.000570	.000582		12.5
	D	.0004362	.0004405	.000436		12.4
						Av. 12.2

glass is constant during a given experiment. In correcting the latter, the hydroxide-ion concentration at each point was reduced by a factor of $1 - pt$, where p is the percentage time rate of change of hydroxide ion and t the time. It was assumed that the change in hydroxide-ion concentration was 1.6 times the change in conductivity given in Table I. While neither of these computations is exact, the total correction is so small that the methods used will cause no serious errors.

In the case of the saponification of the ester of dimethylglycine, the base formed, dimethylglycinate ion, contributes to the hydroxide-ion concentration. So does the ammonia formed in the hydrolysis of sodium oxamate and of oxamide. Furthermore, in this latter case, the hydrolysis of the second amide group will be a complicating factor. However, these corrections are so small that the values of the velocity constants obtained using a standard bimolecular form are not significantly different from those obtained by more complicated equations in which these corrections are, at least to a first approximation, embodied.[18]

The constants for all the velocity determinations are collected in Table IV. Here μ is the initial ionic strength, k the rate constants in inverse minutes and inverse moles per liter. The initial concentrations were varied at least twofold; the constants usually deviate less than 5% from the average. The values in parentheses were not used in averaging.

The observed rate constants for the hydrolysis of sodium oxamate increase with increasing ionic

(18) For the hydrolysis of sodium oxamate and the tertiary butyl ester of dimethylglycine, for example, the following equation takes into account the ionization of the base.

$$kt + C = \frac{1}{[a(a-b)^2 + a^2K_B]}\left\{ -a(a - b + K_B)\log_e(b - ax) + \frac{a(a - b + K_B)}{2}\log_e[a(1-x)^2 + K_B] + b\sqrt{aK_B}\tan^{-1}\frac{ax - a}{\sqrt{aK_B}}\right\}$$

Here a is the initial concentration of sodium hydroxide, b that of the ester, k is the rate constant, K_B the ionization constant of the base, and x the fraction of the sodium hydroxide that has been consumed at time, t. C is a constant of integration. When the second stage hydrolysis of oxamide is taken into account, the equation is even more complex.

strength. Since the reaction is one between two negative ions, Brönsted's theory[7] predicts a positive primary salt effect. However, at the ionic strengths at which the measurements were made, the observed salt effect is less than the theory predicts. Extrapolation of the plot of log $k_{obsd.}$ against the square root of the ionic strength gives a value of 0.0111 for the rate constant; extrapolation of the lowest point using the theoretical limiting slope gives a value of 0.0091. These are an upper and lower value, respectively, for the true value at infinite dilution. For the purposes of the present paper, the mean value, 0.0101, is sufficiently precise. Since the saponification of tertiary butyl betainium chloride was carried out at very low ionic strength, and since the accuracy of these measurements is not very great, extrapolation to infinite dilution does not seem warranted.

The ion $(CH_3)_2N^+HCH_2CO_2C(CH_3)_3$ would be expected to saponify at a rate several hundred times greater than that of the free base. However, an estimate of the base strength of the ester (from the base strength of glycine ethyl ester[19]) indicates that, in solutions of the alkalinity employed in the velocity determinations, no significant part of the rate can be due to hydrolysis of this ion.

The logarithms of the ratios of the rates, corrected for statistical factor, for substituted and unsubstituted compounds ($\Delta \log k$) are assembled in Table V. It is at once obvious that errors of the magnitude indicated for the velocity constants will have no significant effect upon these logarithms.

Discussion of Results

From the data given in Table V and Kirkwood's and Westheimer's equations, it is possible to compute the separation of the polar substituent and the negative charge contributed by the hydroxide ion to the activated complex. In order to carry out these calculations, the volumes of the molecules have been estimated, as usual, by using Traube's rule.[20]

TABLE V

SEPARATION OF CHARGE AND SUBSTITUENT, COMPUTED FROM VELOCITY DATA

Organic reactants	$\Delta \log k$	Separation in Å. R	R_D	R_B
Oxamide Sodium oxamate	1.84	4.15	3.85	1.71
t-Butyl betainium chloride	3.02	4.85	4.05 (glycine)	1.02
t-Butyl ester of dimethylglycine			4.25 (betaine)	
t-Butyl chloroacetate *t*-Butyl acetate	2.70	3.15	3.00	0.48

(19) Edsall and Blanchard, THIS JOURNAL, **55**, 2337 (1933).

The computations for oxamide were made on the basis of a spherical model, with the charges on a diameter. The distance between a positive charge placed approximately as the proton in oxamic acid, and the negative charge of the activated complex, is given to the nearest 0.05 Å. by R; it is compared with R_D, the separation of the protons in oxalic acid computed in a similar manner from dissociation constant measurements.

The calculations for tertiary butyl chloroacetate are more complicated. The difference between the carbon–chlorine dipole moment and the carbon–hydrogen moment was taken as 1.86 Debye units.[21] The negative charge of the activated complex was placed arbitrarily on the extension of that carbon to carbon bond nearest the ester linkage in the acid portion of the molecule. The computations were made on the basis of two different assumptions. First, the charge and dipole were placed equidistant from the center on a diameter, and, second, the charge was placed at the center of the molecule.[22] The two methods led to values of R differing by 0.4 Å.; the average is given in Table V. The value of R_D is that obtained from computations based on the ratio of the ionizations constants of chloroacetic and acetic acids.

The computations for the chloride of the tertiary butyl ester of betaine were made both on the basis of an ellipsoid with the charges at the foci, and on the basis of a sphere, with the charges on a diameter, but the positive charge twice as far from the center of the sphere as the negative charge.[23] Again the two methods give values

(20) Traube, *Saml. Chem. Chem.-tech. Vortr.*, **4**, 255 (1899).

(21) Smyth, *J. Phys. Chem.*, **41**, 209 (1937).

(22) In this case, the equation for the electrostatic work reduces to the form

$$\Delta \log k = \frac{eM \cos \zeta}{2.303\, k'' T R^2 D_i}$$

where e is the electronic charge, M the dipole moment of the substituent, ζ the angle between the dipole and the line joining it to the center. D_i the "internal dielectric constant," has been assigned the value of 2.00, as previously.

(23) In this case the appropriate value of the "effective dielectric constant" is given by the equation

$$1/D_E = \frac{1}{D_i}\left[1 - \frac{x_1 + x_2}{1 + x_1x_2}\right] + \frac{1}{D}\left[\frac{2(x_1 + x_2)}{1 + x_1x_2} - \frac{x_1 + x_2}{x_1x_2} \log_e (1 + x_1x_2)\right]$$

where $x_1 = r_1/b$ and $x_2 = r_2/b$. r_1 and r_2 are the distances of the first and second charges from the center, b the radius of the sphere,

differing by about 0.3 Å.; the average appears in the table.

There is no value of R_D obtained from ionization constant data which is strictly comparable with this value of R. For, while the ionization constant of betainium chloride is known, the ionization constant of dimethylglycine, due to its zwitterionic structure, cannot be considered that of the corresponding unsubstituted acid. However, the strength of betainium chloride was compared with that of trimethylacetic acid,[17] the "isosteric" structure,[24] in which a carbon atom rather than a nitrogen atom holds the three methyl groups. Neuberger's data show that this is a fair approximation.[25] The length given in Table V is the average of one in which the molecule is regarded as an ellipsoid with charges at the foci, and one in which the molecule is regarded as a sphere with the charges equidistant from the center on radii separated by the tetrahedral angle. Fortunately, these two values of R_D differ by only 0.3 Å. The value of R_D for glycine is placed alongside the approximate one for betaine.

The values of R_B were computed using Bjerrum's[2] and Eucken's[4] equations. In the case of the chloroester, the fully extended model was used in determining the value of R_B.

Inspection of Table V reveals that, despite the approximations made in assigning simple shapes to these esters and amides, the values of R obtained from velocity data are in good agreement with R_D, computed from dissociation constants. It must be stressed that these latter values have previously been shown in all cases to be of reasonable magnitude. The values of R_B, obtained from the Bjerrum equation, are, however, much too small. Since R appears as the square in the equation for the potential of a dipole, the inadequacy of the simple equation in the case of the chloroester, serious as it appears, is actually even more significant.

The retardation caused by a negative charge, the acceleration caused by a positive charge and a dipole in saponification, are not only qualitatively but quantitatively in accord with predictions made on the basis of the electrostatic effect of the substituents.

(24) Schwarzenbach, *Z. physik. Chem.*, **A176**, 133 (1936).

(25) Neuberger, *Proc. Roy. Soc.* (London), **A158**, 68 (1937).

Summary

1. The electrostatic theory has been applied to the problem of the effect of polar substituents on reaction velocities.

2. The rates of alkaline hydrolysis of the following pairs of compounds have been measured: oxamide and sodium oxamate, tertiary butyl acetate and tertiary butyl chloroacetate, the tertiary butyl ester of dimethylglycine and the chloride of the tertiary butyl ester of betaine.

3. By means of the equations previously developed by Kirkwood and Westheimer, it has been shown that the ratio of the rates for each pair is quantitatively in accord with the hypothesis that the effect of a polar substituent on the velocity of these hydrolyses is primarily electrostatic in origin.

CHICAGO, ILLINOIS RECEIVED NOVEMBER 22, 1939

[CONTRIBUTION FROM THE ESSO LABORATORIES OF THE STANDARD OIL DEVELOPMENT COMPANY, CHEMICAL DIVISION, AND THE I. G. FARBENINDUSTRIE AKTIENGESELLSCHAFT]

Preparation and Structure of High Molecular Weight Polybutenes

BY R. M. THOMAS,* W. J. SPARKS,* AND PER K. FROLICH*

M. OTTO† AND M. MUELLER-CUNRADI†

The polymerization of isobutene at low temperatures[1,2] with catalysts of acidic nature[3,4,5,6] takes place with almost explosive violence, and is among the most rapidly completed of organic reactions. Under suitable conditions, it is possible to obtain an almost quantitative yield of rubber-like solid from liquid isobutene within a fraction of a second. This transformation is of particular interest in that it is characterized by the absence of any apparent decrease in rate of reaction with lowering of temperature, and also by the fact that polymers of the highest molecular weight as determined by the Staudinger viscosity method[7] are obtainable at the lowest temperatures.

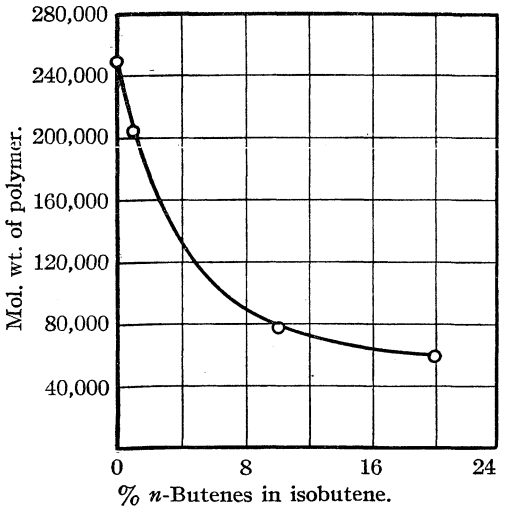


Fig. 1.—Effect of *n*-butenes on the molecular weight of polyisobutenes produced at −95° using BF_3 catalyst.

For example, a sample of isobutene maintained at its boiling point and treated with a slow stream of BF_3 will show a considerable induction period followed by a vigorous reaction to produce an oil, whereas a similar sample precooled to −80° will react immediately on introduction of the BF_3 gas to produce a polymer of much higher molecular weight.

This marked difference in reaction behavior and in the character of the products is indicative of a difference in mechanism between low temperature polymerization and the more common reactions which characterize tertiary olefins. Other important factors in the polymerization of isobutene at low temperature are discussed below.

Purity of Raw Materials.—Under particular test conditions that have been used by the writers, certain compounds have been observed to act as poisons for the reaction. These materials in isobutene reaction mixtures result in a decided lowering of the molecular weight of the polymer product,[8,9] or, in extreme cases, interfere even more seriously with the course of the reaction.

It is of particular interest to note the behavior of pure isobutene intentionally contaminated with other hydrocarbon olefins. Lower olefins such as ethylene and propylene are apparently inert. Normal butenes are more reactive but they differ greatly from isobutene as regards their polymerization characteristics.[10,11] However, they are capable of reacting with isobutene under the low temperature conditions of reaction. This results in a lowering of the molecular weight of the polymer product as shown in Fig. 1.

Similarly, higher olefins may exhibit a depressing effect on the molecular weight of the polymer. For example, very small quantities of diisobutene will greatly decrease both the yield and molecular weight of the polyisobutene. This observation is of special interest since it shows that, although the polymerization must pass through successive stages of chain formation, the possible intermediate stage represented by molecular dimer as obtained by conventional polymerization

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(1) M. Otto and M. Mueller-Cunradi, U. S. Patent 2,084,501 (1937).

(2) F. A. Howard, U. S. Patent 2,049,062 (1936).

(3) P. K. Frolich, U. S. Patent 2,109,772 (1938).

(4) Schering, German Patent 278,486 (1914).

(5) J. C. Zimmer and E. W. Carlson, U. S. Patent 2,074,093 (1937).

(6) H. G. Schneider, U. S. Patent 2,131,196 (1938).

(7) Staudinger, "Die hochmolekularen organischen Verbindungen," Verlag Julius Springer, Berlin, 1932.

(8) E. L. Baldeschwieler, U. S. Patent 2,131,342 (1938).

(9) R. T. Haslam, U. S. Patent 2,145,350 (1939).

(10) British Patent 467,932 (1936).

(11) L. W. Lebedev and E. P. Filanenko, *Ber.*, **58**, 163–168 (1925)

methods cannot be present in appreciable quantity during or preceding the polymerization step in the preparation of high polymers. Triisobutene has a similar effect.

In this connection it is also of interest to point out that while dimers or trimers of isobutene are capable of slow polymerization at room temperature to give oily products, when using the low temperature technique discussed here, high polymers have not been obtained.

Other poisons are sulfur compounds such as hydrogen sulfide or mercaptans, and hydrogen halides such as anhydrous hydrogen fluoride or hydrogen chloride. The latter have a marked depressing effect on the molecular weight of the polymer in spite of their well-known promoter action in certain metallic halide catalyzed alkylation[12] or dimerization reactions. At elevated temperatures, the use of hydro-halogen acids has been found beneficial for the polymerization of olefins with boron fluoride.[13]

This difference in behavior of halogen acids in polymerization and in alkylation reactions appears to support the view that the formation of high polymers and the well-known dimerization reactions result from different types of activation. The poisoning effect of hydrogen chloride may therefore result from the formation of diisobutene which is known to be a polymerization depressor in the formation of polyisobutene at low temperatures. The negative action of halogen acids observed here has also been found in the case of the polymerization of styrene by stannic chloride.[14]

Catalysts.—A variety of catalysts for the polymerization of isobutene has been reported.[15] The effectiveness of these depends upon the conditions employed for carrying out the reaction, but good results are generally obtained with such materials as titanium tetrachloride,[16] boron fluoride, and aluminum chloride.

In general, the suitability of a catalyst for the low temperature polymerization of isobutene cannot be predicted. Double compounds of the Friedel–Crafts type catalysts with various polar solvents have been found effective in polymerizing olefins at temperatures in the neighborhood of 0°,[17] but appear to be inactive at considerably lower temperatures.

Temperature.—Temperature control is of great importance in the polymerization process since the reaction is rapid and exothermic. Experimentally, the heat of reaction is somewhat difficult to measure accurately, but it has been established to be in the neighborhood of 10,000 calories per mole at about −78°. Higher values would be expected on the basis of theoretical calculations.

The general effect of temperature upon the molecular weight of isobutene polymers produced under otherwise constant conditions is shown in Fig. 2 for one type of catalyst.[18]

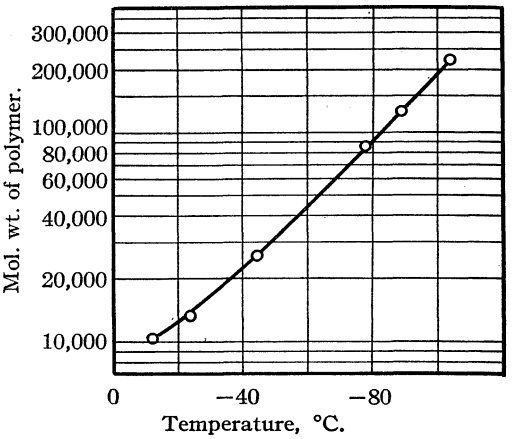


Fig. 2.—General effect of reaction temperature on the molecular weight of polymers produced from isobutene.

Diluents.—Diluents are employed in the polymerization to moderate the violence of the reaction and thereby make for better temperature control, so that products of uniformly high molecular weight can be obtained.[19]

The important role played by diluents in the preparation of polyisobutene is clearly indicated by the data presented in Fig. 3, where, under a given set of experimental conditions, the molecular weights of products obtained are plotted against corresponding amounts of an inert diluent in the reaction mixture. It will be noted from these results that the molecular weight of the product increases acording to an exponential func-

(12) V. N. Ipatieff and A. V. Grosse, *Ind. Eng. Chem.*, **28**, 461 (1936).

(13) F. Hofman, M. Otto and W. Stegemann, German Patent 504,730.

(14) G. Williams, *J. Chem. Soc.*, 1046 (1938).

(15) British Patent 483,563 (1936).

(16) R. P. Russell, U. S. Patent 2,139,038 (1938).

(17) British Patent 358,068 (1931).

(18) It may be mentioned here that the molecular weights cited throughout this paper, while comparable insofar as the one variable under consideration is concerned, are not necessarily the maximum values obtainable. By proper manipulation of the different reaction variables, it is possible to extend considerably the molecular weight range of the polymers in a number of cases.

(19) P. J. Wiezevich, U. S. Patent 2,138,895 (1938).

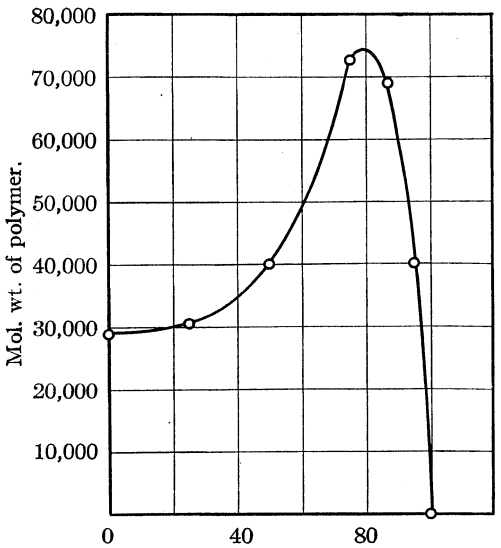


Fig. 3.—General effect of diluent concentration on the molecular weight of polymers produced from isobutene.

tion with increasing proportions of diluent until a limiting concentration of approximately 80% by volume is reached, at which point there occurs a precipitous drop in the molecular weight. Closely similar curves are obtained using different diluents. In some instances, the actual values for molecular weight may be somewhat shifted by as much as 10,000 due to the difficulty in controlling other variables. In all cases, however, the general shape of the curve remains the same.

Catalyst Concentration.—With regard to the concentrations in which catalysts are employed, several interesting effects have been observed. In one specific case, it has been demonstrated that a critical concentration of catalyst (approximately 0.03%) has to be exceeded for the production of polymer. Some idea of the actual quantity of polymer which may be obtained from a given amount of an aluminum chloride catalyst is shown in Figs. 4 and 5, the latter being constructed from the limiting slopes of Fig. 4. The catalyst efficiency is noted to be highest at the greatest dilutions, presumably because of a lower loss due to mechanical occlusion of unreacted catalyst in the polymer. Figure 5 is of interest in giving an extrapolated ratio of about three moles of polymer per mole of aluminum chloride at an infinitely low concentration. However, this should not be taken as definite proof that one molecule of aluminum chloride produces three molecules of polymer, for the data may be subject

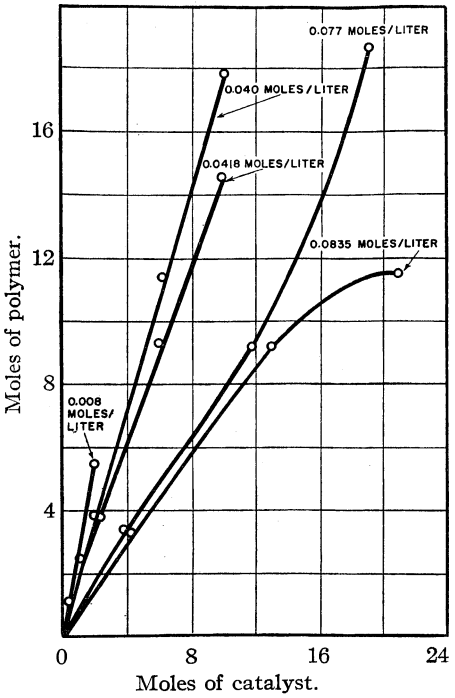


Fig. 4.—Moles of isobutene polymer produced vs. moles of $AlCl_3$ catalyst added for different catalyst concentrations.

to some question because of possible uncertainties involved in the determination of exact molecular weights by viscosity methods.

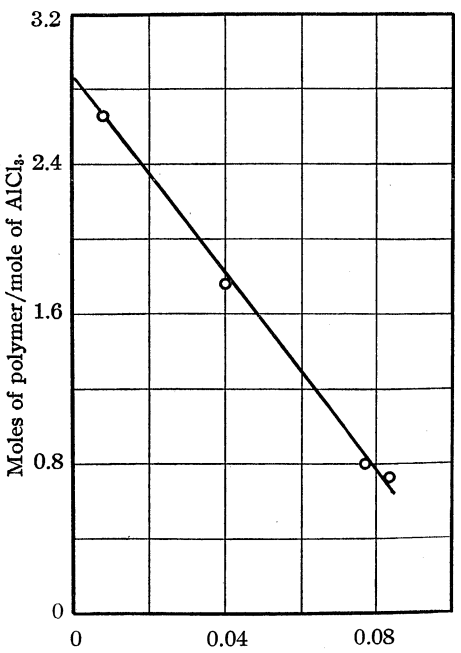


Fig. 5.—Efficiency of catalyst in polymerizing isobutene at −78° as a function of catalyst concentration.

Yield.—The polymerization of isobutene to high molecular weight products can be carried out with yields of 90% or better. Within reasonable limits, the yield to which the reaction is carried has not been found to influence the average molecular weight of the products.

Structure of Polybutene.—A discussion of the low temperature polymerization of isobutene quite naturally raises the question of the structure of the polymers produced by that technique.

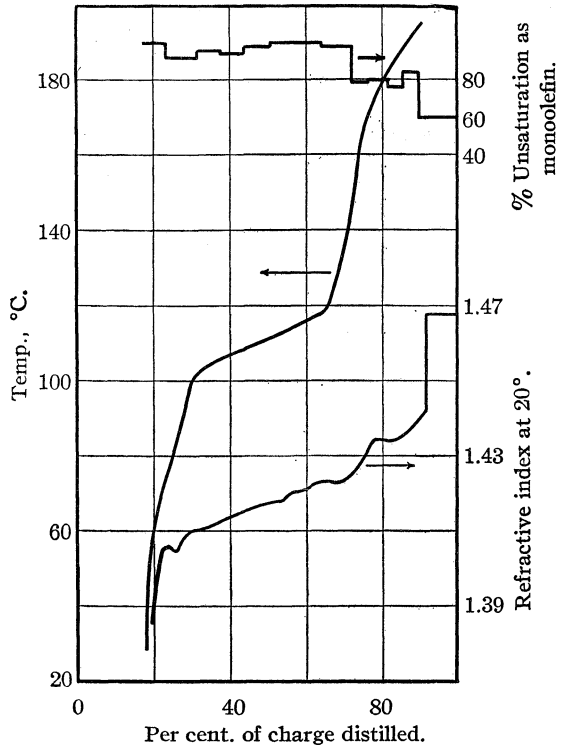
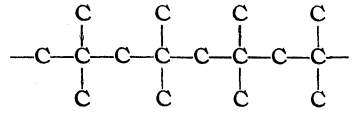


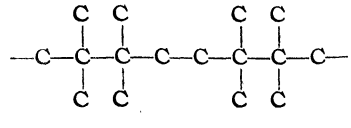
Fig. 6.—Analytical distillation of C_4 to C_{12} hydrocarbons from the thermal decomposition of polyisobutene in an iron still at 350°.

On the basis of numerous observations which would lead too far to be included in a condensed report, it is the writers' belief that the polymers are linear, and that therefore there are only four structural possibilities to consider, namely

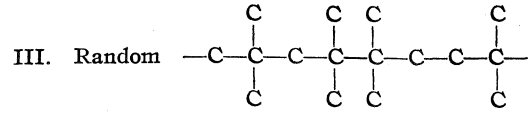
I. Head to Tail



II. Head to Head



III. Random



IV. Mixture of Type I, II or III molecules.

It is assumed that all of these structures include one residual terminal double bond, which seems to be borne out by determination of unsaturation of the product as related to average molecular weight.

Of these various structures, type I is most probable for the polyisobutene molecule. Its decomposition would be expected to give the ordinary diisobutenes, 2,4,4-trimethyl-1-pentene and its -2-isomer. It is a fact that an isobutene polymer of about 20,000 molecular weight on decomposition at 350° gave degradation products, an analytical distillation of which is shown in Fig. 6. The polymer gave about 50% of monomer and about 20% hydrocarbons boiling in the octene range. Figure 7 shows the result of a refractionation of the dimer cut. A portion of fraction 1 reacted with phenol to give a 65% yield of the characteristic tetramethylbutylphenol, m. p. and mixed m. p. 84°.

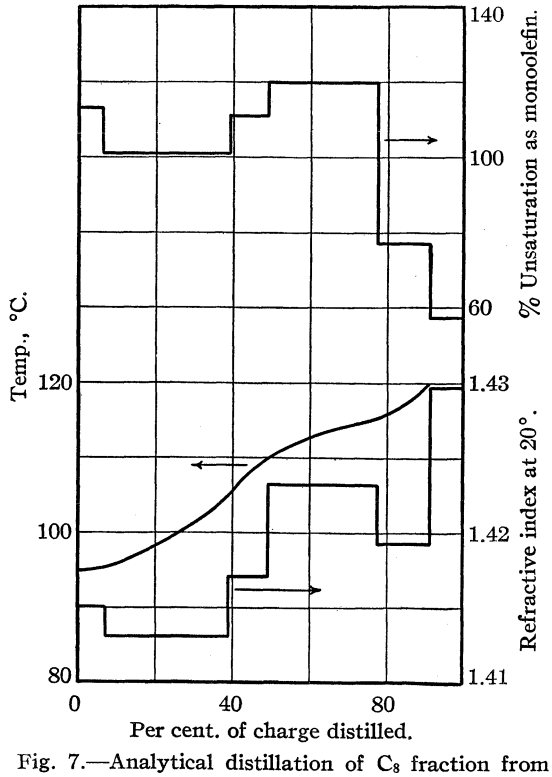


Fig. 7.—Analytical distillation of C_8 fraction from the thermal decomposition of polyisobutene in a glass still at a controlled temperature of 350°.

The occurrence of the higher boiling octenes

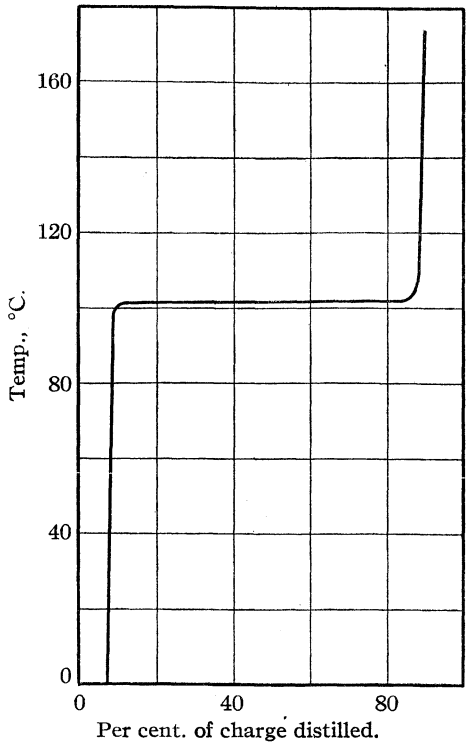


Fig. 8.—Fractionation of 2,4,4-trimethylpentene-1 subjected to a temperature of 350° for one hour.

may be due either to isomerization during the pyrolysis or to the possibility of some random structure (III) in the polymer. The material boiling at 110–115° on ozonization or chromic acid oxidation gave acetone, acetic acid and an odor of fatty acids. This may indicate the presence of 2,5-dimethyl-2-hexene.

The possibility of isomerization of the octenes after their liberation from the polymer was tested by heating diisobutene (b. p. 101.5–101.9°) at 350° for an hour. As shown in Fig. 8, cracking and polymerization took place but there was no noticeable degree of isomerization.

Acknowledgment.—The writers wish to acknowledge the active participation of many of their associates in obtaining the large amount of information from which this paper is abstracted.

Summary

The catalytic polymerization of isobutene at low temperatures to form a homologous series of polymers ranging to very high molecular weights is discussed in detail.

The structure of the polymers is partially established.

ELIZABETH, NEW JERSEY RECEIVED AUGUST 18, 1939

[CONTRIBUTION FROM THE UNIVERSITY OF MISSOURI]

The Action of Aluminum Chloride on Aromatic Hydrocarbons. II. The 1,3-Dimethyl-4-propylbenzenes

BY DOROTHY NIGHTINGALE AND BENOIST CARTON, JR.[1]

When the 1,3-dimethyl-4-butylbenzenes are warmed with aluminum chloride, the butyl group migrates to the 5 position.[2] During the rearrangement, the *n*- and *s*-butyl radicals are isomerized to *s*- and *t*-butyl radicals, respectively.

We have now completed a similar study of the 1,3 - dimethyl - 4 - propylbenzenes. The results, showing that both the 4-*n*-propyl and the 4-isopropyl hydrocarbon rearrange to yield 1,3-dimethyl-5-isopropylbenzene, should be compared with those of Baddeley and Kenner,[3] who reported that 1,3,4-tri-*n*-propylbenzene when heated to 100° with aluminum chloride yielded 1,3,5-tri-*n*-propylbenzene. These authors, however, gave no evidence to support their statement that the migrating propyl group did not isomerize to an isopropyl group and, in view of our results, their conclusion is questionable. Similarly, Heise and Tohl's[4] conclusions that *n*-propylbenzene and aluminum chloride yielded *m*- and *p*-di-*n*-propylbenzene are also doubtful.

The present investigation has shown that the *n*-propyl radical in 1,3-dimethyl-4-*n*-propylbenzene does not readily shift to the 5 position but that its migration is accompanied by isomerization. At 55° the rearrangement is far from complete; at 85 and 100° the product appeared to consist largely of 1,3-dimethyl-5-isopropylbenzene along with some of the starting material.

Rearrangement of 1,3 - dimethyl - 4 - isopropyl-

(1) Abstract of a dissertation to be presented by Benoist Carton, Jr., in partial fulfilment of the requirement for the degree of Master of Arts at the University of Missouri.

(2) Nightingale and Smith, THIS JOURNAL, **61**, 101 (1939).

(3) Baddeley and Kenner, *J. Chem. Soc.*, 303 (1935).

(4) Heise and Tohl, *Ann.*, **270**, 155 (1892).

benzene to the 1,3,5 isomer took place more readily and was nearly complete at 55°.

In order to be certain of the structure of the rearrangement products, both 1,3-dimethyl-5-isopropylbenzene and 1,3-dimethyl-5-*n*-propylbenzene were synthesized. All of the synthetic hydrocarbons and the rearrangement products were identified by means of their diacetamino derivatives, and by oxidation to a tricarboxylic acid.

Smith and Perry[5] have suggested that during the alkylation of *m*-xylene in the presence of aluminum chloride, a 1,3,4-hydrocarbon is formed initially and is subsequently rearranged to yield finally a 1,3,5-hydrocarbon. If this is true, any alkylation in the presence of aluminum chloride which will lead to the formation of *n*-propylbenzene would be expected to yield a 1,3-dimethyl-5-isopropylbenzene when benzene is replaced by *m*-xylene. If the 1,3-dimethyl-5-propylbenzene is formed directly, such a procedure should yield a product containing a *n*-propyl radical in the 5 position.

There are two alkylating agents which yield *n*-propylbenzene with aluminum chloride as the catalyst: *n*-propyl formate[6] and cyclopropane.[7] *n*-Propyl formate and *m*-xylene yielded 1,3-dimethyl-5-*i*-propylbenzene. Cyclopropane and *m*-xylene yielded 1,3-dimethyl-4-*n*-propylbenzene. Both of these reactions may be interpreted as supporting the above view. It should be noted that the maximum temperatures during these alkylations were 60 and 15°, respectively, and with entirely different alkylating agents. There is considerable evidence in the literature to indicate that the temperature of the reaction as well as the size and type of alkyl group may be an important factor in governing the configuration of the polyalkylbenzenes formed.

Acknowledgments.—The authors wish to express their thanks to E. I. du Pont de Nemours and Company through Dr. Miles A. Dahlen for the *m*-xylene used in this investigation, and to the University Research Council for funds to purchase other necessary chemicals and apparatus to continue the study.

Experimental[8]

1,3-Dimethyl-4-*n*-propylbenzene.—The 4-propionyl-*m*-xylene was prepared by the usual Friedel–Crafts procedure from 60 g. of *m*-xylene, 46 g. of propionyl chloride, 66 g. of aluminum chloride, and 200 cc. of carbon disulfide. The yield of pure ketone was 57 g. (80%), b. p. 112° (10 mm.). The hydrocarbon was prepared from the ketone (50 g.) by the Clemmensen reduction in 50% yield; b. p. 95° (23 mm.); $n^{25}D$ 1.4995.

Anal. Calcd. for $C_{11}H_{16}$: C, 89.12; H, 10.88. Found: C, 88.95; H, 10.95.

The hydrocarbon also was obtained from *m*-xylene, cyclopropane, and aluminum chloride by the procedure of Grosse and Ipatieff[7] for the preparation of *n*-propylbenzene from benzene and cyclopropane.[9] The cyclopropane (22 g.) was bubbled slowly through 120 g. of *m*-xylene and 4.4 g. of aluminum chloride at 0 to 5°. About half of the cyclopropane was absorbed during four and one-half hours. The temperature was allowed to rise to 15°, at which temperature the remainder of the cyclopropane was absorbed rapidly during thirty minutes while the flask was again cooled with ice. The product was decomposed in the usual manner, and distilled under reduced pressure; yield: 28 g. (40%); b. p. 95° (23 mm.).

The diacetamino derivative of this hydrocarbon melted at 284° and did not depress the melting point of the diacetamino derivative of the hydrocarbon prepared from 4-propionyl *m*-xylene. Oxidation of the hydrocarbon yielded trimellitic acid, m. p. 216°.

1,3-Dimethyl-4-isopropylbenzene.—The *m*-xylene (375 cc.) and isopropyl alcohol (47 cc.) were mixed and the flask placed in water cooled with ice. A mixture of 500 cc. of concd. sulfuric acid and 110 cc. of water was added during two hours while the solution was stirred mechanically. The stirring was continued at room temperature for fourteen hours. The xylene layer was separated and washed with dilute alkali and water, dried and vacuum distilled; yield 70 g. (75%), b. p. 77° (13 mm.); $n^{25}D$ 1.4998.

Anal. Calcd. for $C_{11}H_{16}$: C, 89.12; H, 10.88. Found: C, 89.34; H, 11.12.

1,3-Dimethyl-5-isopropylbenzene.—This hydrocarbon is the principal product from three different alkylating agents: isopropyl chloride, *n*-propyl chloride, and *n*-propyl formate.

A mixture of 53 g. of *m*-xylene and 15 g. of aluminum chloride was stirred mechanically while 20 g. of isopropyl chloride was added during an hour. The stirring was continued for an additional three hours. The mixture was decomposed in the usual way, washed, dried and distilled: yield 19 g. (48%), b. p. 83–85° (17 mm.); $n^{25}D$ 1.4930.

Anal. Calcd. for $C_{11}H_{16}$: C, 89.12; H, 10.88. Found: C, 88.91; H, 10.95.

Oxidation of this hydrocarbon yielded trimesic acid, m. p. 365°, and its diacetamino derivative melted at 295°.

The alkylation was repeated, using *n*-propyl chloride in place of the isopropyl chloride: yield of hydrocarbon, 17 g. (46%), b. p. 83–85° (17 mm.); $n^{25}D$ 1.4935. The diacetamino derivative of this product melted at 276° and when mixed with the diacetamino derivative of the hydrocarbon from isopropyl chloride, the melting point was 283°. The trimesic acid formed by oxidation melted at

(5) Smith and Perry, THIS JOURNAL, **61**, 1411 (1939).

(6) Bowden, *ibid.*, **60**, 645 (1938).

(7) Grosse and Ipatieff, *J. Org. Chem.*, **2**, 447 (1939).

(8) Semimicroanalyses for C and H by B. Carton; for nitrogen by R. G. Taylor.

(9) The cyclopropane was obtained from Mallinckrodt Chemical Works, St. Louis, Mo.

355°. These melting points would indicate that the hydrocarbon was largely 1,3-dimethyl-5-isopropylbenzene, containing perhaps some 1,3,4-isomer.

The procedure of Bowden[6] for the preparation of *n*-propylbenzene from benzene and *n*-propyl formate was followed in detail, with 320 cc. of *m*-xylene in place of benzene: yield of hydrocarbon from 22 g. of ester, 18 g. (50%), b. p. 90° (23 mm.); $n^{25}D$ 1.4930.

Oxidation of this product yielded trimesic acid, m. p. 360°. Its diacetamino derivative melted at 295° and did not depress the melting point of the diacetamino derivative of the hydrocarbon from isopropyl chloride.

1,3-Dimethyl-5-*n*-propylbenzene.—This hydrocarbon was obtained from the reaction of methyl *n*-propyl ketone and acetone in the presence of concd. sulfuric acid, following the procedure for the preparation of mesitylene from acetone and sulfuric acid.[10]

The sulfuric acid (1363 cc.) was added to 1060 cc. of methyl *n*-propyl ketone (tech.) and 1406 cc. of acetone at 0–10°. The material distilling at 150–240° was purified by treatment with sodium, and fractionated at 20 mm.: (I) 50 g. 67–92°; (II) 35 g. 92–94°; (III) 10 g. 94–96°; (IV) 16 g. above 96°. Fraction II was carefully refractionated to yield finally 19 g. of hydrocarbon, b. p. 90–91° (18 mm.); $n^{25}D$ 1.4913.

This product, when oxidized, yielded trimesic acid, m. p. 360°, and its diacetamino derivative melted at 239°.

The procedure of Morton and Fallwell[11] for the preparation of ethylbenzene from benzyl sodium and methyl iodide was followed in detail, substituting 80 cc. of mesitylene for 75 cc. of toluene, and with 78 g. of ethyl iodide. The yield of trialkylbenzene was 5.5 g., b. p. 92–93° (18 mm.); $n^{25}D$ 1.4900.

The diacetamino derivative of this hydrocarbon melted at 239° and did not depress the melting point of the derivative of the hydrocarbon from the ketone synthesis.

The diacetamino derivatives of the hydrocarbons were prepared by the procedure of Ipatieff and Schmerling[12] from 1 cc. of hydrocarbon. Purification was tedious, and the yield of pure product was small.

TABLE I

	Hydrocarbon 1,3-Dimethyl-	M. p., °C.[c]	Diacetamino derivative[a] % nitrogen found
A	4-*n*-Propylbenzene	284	10.81
B	4-Isopropylbenzene	292	10.96
C	5-Isopropylbenzene (isopropyl chloride)	295	10.76[b]
D	5-*n*-Propylbenzene (ketones)	239	10.78
E	5-*n*-Propylbenzene (organo alkali)	239	

[a] Calcd. for $C_{11}H_{22}N_2O_2$: C, 68.70; H, 8.39; N, 10.68. [b] Found: C, 68.80; H, 8.21. [c] Mixed melting points: A + B, 263°; B + C, 255°; A + C, 250°.

Rearrangements with Aluminum Chloride.—The aluminum chloride was added directly to the hydrocarbon, and the mixture warmed in a water-bath. A thermometer was placed in the reaction mixture and during the heating the flask was shaken frequently. After heating, the mixture was poured onto ice, extracted with ether, washed, dried and vacuum distilled. Fraction I contained some *m*-xylene and fraction II the trialkylbenzenes.

1,3-Dimethyl-4-isopropylbenzene.—The hydrocarbon (32 g.) was warmed with aluminum chloride (7 g.) at 55–60° for three hours. The reaction products were distilled at 20 mm. and yielded only two fractions: (I) 1.4 g. up to 85°; (II) 29 g. 85–86°. The boiling point of II was unchanged on redistillation. The diacetamino derivative of II melted at 295°, and did not depress the melting point of the derivative of 1,3-dimethyl-5-isopropylbenzene. This rearrangement product is therefore 1,3-dimethyl-5-isopropylbenzene.

1,3-Dimethyl-4-*n*-propylbenzene.—The hydrocarbon (35 g.) was warmed with aluminum chloride (8 g.) for three hours at 55°. The reaction products were fractionated at 30 mm.; (I) 3.6 g. 45–95°; (II) 14.9 g. 95–105°; (III) 6 g. 132°; residue 2 g.

Fraction II on slow distillation came over at 105° (38 mm.). The diacetamino derivative of this fraction melted at 279° and did not depress the melting point of the derivative of 1,3-dimethyl-4-*n*-propylbenzene. This fraction is therefore mainly unchanged 4-*n*-propyl hydrocarbon.

The reaction was repeated with 28 g. of hydrocarbon and 7 g. of aluminum chloride at 85–90° for four hours. The following fractions were obtained at 15 mm.: (I) 8.7 g. 45–89°; (II) 7.2 g. 89–94°; (III) 5.1 g. 105–110°.

Fraction II formed a diacetamino derivative which melted at 240–250°, and depressed the melting point of the derivatives of both the 4-*n*-propyl and 5-isopropyl hydrocarbons some 20°. The fraction is probably a mixture of unchanged 4-*n*-propyl hydrocarbon and 5-isopropyl hydrocarbon.

To determine whether or not longer heating and a higher temperature would improve the yield and quality of the trialkyl fraction, the rearrangement was carried out with the same amounts of materials at a temperature of 100° for four hours. These are the experimental conditions of Baddeley and Kenner[3] for 1,3,4-tri-*n*-propylbenzene.

The following fractions were obtained at 15 mm.: (I) 6.8 g. 45–92°; (II) 6.7 g. 89–92°; (III) 3 g. 95–97°; (IV) 2.6 g. 97–110°.

The diacetamino derivative of II melted at 280–285°. Mixed with the derivative of the 4-*n*-propyl hydrocarbon, the melting point was 260–265°, and with the derivative of the 5-isopropyl hydrocarbon the melting point was 285°. The trimesic acid obtained from the oxidation of II melted at 330°.

These data indicate that the 1,3-dimethyl-4-*n*-propylbenzene is largely rearranged to 1,3-dimethyl-5-isopropylbenzene and other hydrocarbons in the presence of aluminum chloride at 100°.

Summary

The 1,3-dimethyl-4-isopropylbenzene undergoes rearrangement on warming with aluminum chloride at 55° for three hours to yield 1,3-dimethyl-5-isopropylbenzene as the principal trialkylbenzene.

(10) "Organic Syntheses," Coll. Vol. I, p. 334.
(11) Morton and Fallwell, THIS JOURNAL, **60**, 1429 (1938).
(12) Ipatieff and Schmerling, *ibid.*, **60**, 1476 (1938).

The 1,3-dimethyl-4-*n*-propylbenzene is largely rearranged by aluminum chloride at 100° for four hours to yield 1,3-dimethyl-5-isopropylbenzene. After heating at 85–90°, the trialkyl fraction is a mixture, and at 55° the trialkyl fraction is mainly unchanged 1,3,4 hydrocarbon.

The 1,3-dimethyl-4-*n*-propylbenzene was prepared from *m*-xylene and cyclopropane with aluminum chloride as the catalyst, and by the reduction of 4-propionyl-*m*-xylene.

The 1,3-dimethyl-5-isopropylbenzene was obtained from *m*-xylene and isopropyl chloride, *n*-propyl formate, and *n*-propyl chloride with aluminum chloride as the catalyst.

The formation of the 4-*n*-propyl hydrocarbon from *m*-xylene and cyclopropane and the 5-isopropyl hydrocarbon from *m*-xylene and *n*-propyl formate support the view of Smith and Perry that a 1,3,4 hydrocarbon is the initial product of the reaction when *m*-xylene is alkylated in the presence of aluminum chloride.

COLUMBIA, MISSOURI RECEIVED OCTOBER 5, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING OF THE UNIVERSITY OF PENNSYLVANIA]

The Hydrogenation of Coumarin and Related Compounds

BY PETER L. DE BENNEVILLE AND RALPH CONNOR

γ-Valerolactone at 250° and 100–200 atmospheres of hydrogen over a copper chromite catalyst has been reported[1] to give pentanediol-1,4, the product expected from an ester under these conditions, and a small amount of hydrogenolysis product, pentanol-1. Over nickel, however, γ-butyrolactone and γ-valerolactone gave[2] 9% of tetrahydrofuran and 17% of α-methyltetrahydrofuran, respectively. These seem to be the only known examples, except in cases where other functional groups complicate the reactions, of the formation of ethers and also of the attack of an ester group in the presence of a nickel catalyst. Apparently no other γ-lactones and no δ-lactones have been investigated under these conditions.

The products obtained by the hydrogenation of coumarin and certain related compounds are shown in the flow sheet (Table I). Over copper chromite, the behavior of coumarin was like that of any α,β-unsaturated ester. The formation of dihydrocoumarin (II) at 140–160° was shown by the pressure drop but the hydrogenation was not interrupted to permit its isolation. At 250° there was obtained a good yield of the product expected from a normal ester hydrogenation, γ-(*o*-hydroxyphenyl)-propyl alcohol (V).

Dihydrocoumarin (II) was isolated from the hydrogenation of coumarin over Raney nickel at 100°. In hydrogenations at higher temperatures dihydrocoumarin was not isolated but was formed quantitatively, as shown by the hydrogen absorption, before any subsequent reaction occurred. At 200–250° the main reactions which occurred over Raney nickel were saturation of the benzenoid ring, giving octahydrocoumarin (III), and conversion of the lactone to the cyclic ether, hexahydrochroman (IV). Pure octahydrocoumarin was obtained in 50–55% yields by carrying out the hydrogenation at 200° and interrupting the reaction before the absorption of hydrogen had ceased.[3] Under these conditions 10–15% of hexahydrochroman was formed. Higher yields (up to 35%) of the latter product were obtained by using a relatively long reaction period at 250°.

Since the formation of ethers from esters over nickel is by no means a common reaction, it is of some interest to determine the intermediates in the formation of hexahydrochroman from coumarin. Three possible mechanisms are shown by broken lines in Table I and none of these may be definitely eliminated on the basis of the facts now available. Path (c) agrees with the observation that IV is the sole product obtained by the hydrogenation of III under these conditions. This also agrees with the results previously mentioned with γ-butyrolactone and γ-valerolactone except that the yield of ether from coumarin was

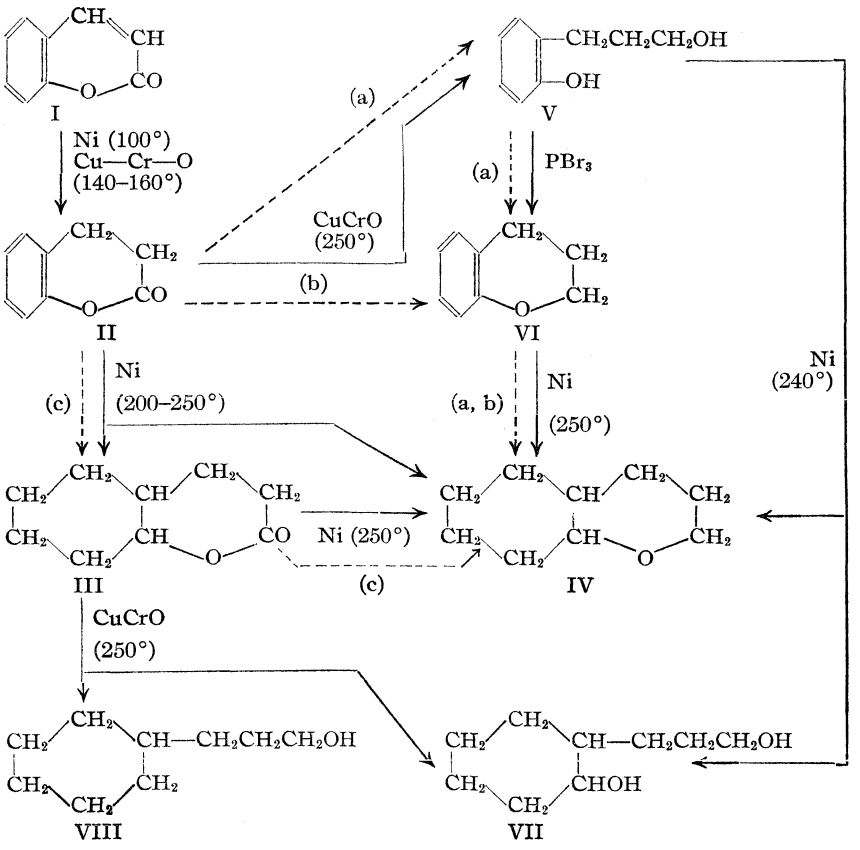
(1) Adkins, "Reactions of Hydrogen, etc.," University of Wisconsin Press, Madison, Wisconsin, 1937, p. 105.

(2) Ref. 1, p. 77.

(3) A plot of time against pressure showed a definite change in slope which seemed to mark the best time to interrupt the reaction. At 250° this point was not observed readily and, while good yields (60–70%) of the octahydrocoumarin fraction were obtained, the refractive index of the product showed that it contained unreacted dihydrocoumarin.

TABLE I

PRODUCTS FROM THE HYDROGENATION OF COUMARIN AND RELATED COMPOUNDS[a]



[a] Full lines refer to reactions described in Table II and the experimental part and broken lines to the possible mechanism for the formation of IV from II over nickel.

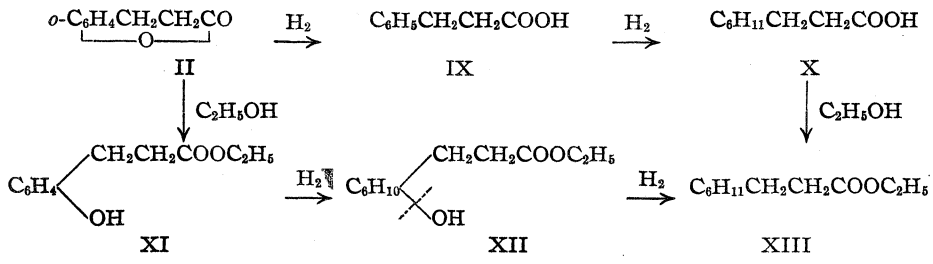
TABLE II

HYDROGENATION DATA[a]

Compd.	Moles	Time, hrs.	Solvent	Catalyst, g. Ni	Cu-Cr	Temp., °C.	% Products (see Table I) II	III	IV	V	VII	VIII	XIII	Polymer
I	0.2	8	C_2H_5OH	5	..	200	..	32	31	..	..	..	7	27
I	.2	4	C_2H_5OH	5	..	250	..	41	27	..	..	..	13	6
I	.2	3	C_7H_{14}	5	..	205	..	53	13	..	..	..	..	10
I	.2	0.3	C_7H_{14}	5	..	250	..	58[b]	9	..	..	..	..	11
I	.2	13.5	C_7H_{14}	5	..	250	..	19[c]	35	..	..	..	..	27
I	.2	0.5	$(C_2H_5)_2O$	5	..	100	90	..	..	..	..	..	..	..
I	.5	0.7	C_2H_5OH	..	5	250	..	..	..	90	..	..	..	..
I	.7	1.5	...	..	10	250	..	..	..	83	..	..	..	..
III	.08	6	C_7H_{14}	5	..	250	..	..	57[d]	..	..	..	..	..
III	.06	4.5	C_7H_{14}	..	3	250	..	..	..	..	50[d]	11	..	..
V	.13	2	C_2H_5OH	4	..	240	..	..	40	..	37	..	..	..
VI	.05	6	C_2H_5OH	2.5	..	250	..	..	41[d]	..	..	..	..	..
$C_6H_5(CH_2)_3OH$	.11	2	C_2H_5OH	3.3	..	220	..	..	..	..	..	86	..	..

[a] The reactions were carried out under a hydrogen pressure of 100–200 atm. [b] According to the refractive index ($n^{25}D$ 1.5025) this fraction probably contained some dihydrocoumarin ($n^{25}D$ 1.5541). [c] According to the refractive index ($n^{25}D$ 1.4728) this fraction probably contained some β-cyclohexylpropionic acid ($n^{20}D$ 1.4634). [d] Apparently the starting materials were converted completely to the products named but recovery was low because of the high mechanical loss in distilling small amounts of material.

considerably higher than from the γ-lactones. Path (b) seems the least probable of the three in view of the fact[4] that the structure $-\overset{\overset{O}{\|}}{C}-O-Aryl$ is not converted to $-CH_2O-Aryl$ under these conditions. Mechanism (a) represents the attack of the ester group over nickel proceeding according to that over copper chromite. The fact that IV was formed by the hydrogenation of pure V and of pure VI agrees with this mechanism. The formation of IV from V is, however, of some interest since it appears to be the first case of ring closure by dehydration under these conditions. It is noteworthy that nickel apparently catalyzes the ring closure, since no ethers were formed from γ-(*o*-hydroxyphenyl)-propyl alcohol and γ-(2-hydroxycyclohexyl)-propyl alcohol under conditions that were similar except that the catalyst was copper chromite.



The results of typical hydrogenations are reported in Table II. Certain by-products mentioned may require explanation. According to the behavior of esters of phenol,[4] it would be expected that dihydrocoumarin would give some β-phenylpropionic acid (IX) and that β-cyclohexylpropionic acid (X) would be the final product from this reaction. Indications of the presence of the acid were obtained (Table II) in prolonged hydrogenations in the complete absence of alcohol. However, this acid and the saturated lactone (III) have boiling points so close that they could not be separated by distillation and the use of alkali was futile because of the pseudo acid character of III. Additional evidence for the formation of X was obtained by the identification of its more readily isolable ethyl ester (XIII) when alcohol was present.[5] It should be pointed out, however, that except for the analogy to the behavior of aryl esters,[4] there is no evidence to exclude the possibility that XIII was formed by the alcoholysis of dihydrocoumarin, followed by hydrogenation and hydrogenolysis of the hydroxy esters (XI and XII).

The material designated as "polymer" in Table II was formed in larger amounts at 250° and as the time of the hydrogenation was prolonged. It was a thick, slow-flowing, non-distillable material which did not crystallize[6] but remained as the residue from the distillations. The yields of this material reported (Table II) were calculated from the total weight of the distillation residue and include the octahydrocoumarin which was present because of the hold-up of the fractionating column.

Since hexahydrochroman had not been made previously and since it had no reactive functions to facilitate a confirmation of its structure, it seemed necessary to prepare a sample of the material by a more orthodox method. This was done by the hydrogenation of chroman over nickel and the comparison of the physical properties of the two products to show that they were identical (Table III). The methods already described for the synthesis of chroman were not particularly satisfactory and as a matter of convenience a simple synthesis using coumarin as the starting material was devised. This method involved the hydrogenation of coumarin over copper chromite and treatment of the phenolic alcohol (V) with phosphorus tribromide.[7] The yields in these two steps were 90% and 87%, respectively.

These results show that coumarin may be converted to octahydrocoumarin, chroman or hexahydrochroman, depending on the conditions used. Because of the current interest in various natural products related to chromans and coumarins, the

(4) This statement is based upon unpublished data of Wm. R. McClellan and will be described in detail in a forth-coming communication.

(5) Aside from the formation of this ester, no differences were noted in comparison of alcohol and methylcyclohexane as solvents.

(6) Treatment of III with sodium ethoxide gave a thick, sticky product which was presumably a polymeric ester. It seems likely that the high-boiling material formed during the hydrogenations was also composed of polymeric esters. A closer examination of this product wil lbe made.

(7) Semmler[8] prepared chroman from V by treatment with alcoholic hydrogen chloride in a sealed tube.

(8) Semmler, *Ber.*, **39**, 2856 (1906).

TABLE III

PHYSICAL CONSTANTS AND ANALYSES OF PRODUCTS

Compound	B. p. (obsd.), °C.	Mm.	nt_D	t	dt_4	MR_D Calcd.	MR_D Found
Octahydrocoumarin (III)[a]	144–146	16	1.4970	24°	1.0999	41.02	40.98
Hexahydrochroman (IV) (from coumarin)[b]	186–187	760	1.4714	22°	0.9536	41.00	41.07
Hexahydrochroman (IV) (from chroman)[b]	186–187	760	1.4718	22°	0.9533	41.00	41.25
Chroman (VI)	210–214	760	1.5462	23°	1.0575	39.52	40.13[c]
γ-(2-Hydroxycyclohexyl)-propyl alcohol (VII)[d]	185–186	35	1.4867	25°	1.0294	44.61	44.24
Ethyl β-cyclohexylpropionate (XIII)	105–113[e]	17	1.4480[e]	22°	....	...	...
γ-(o-Hydroxyphenyl)-propyl alcohol (V)	159–161[f]	5	Benzoate, m. p. 98.5–99.5°[f]				
γ-Cyclohexylpropyl alcohol (VIII)	105–106[g]	10	α-Naphthylurethan, m. p. 82–83°[g]				

[a] Saponification number: Calcd., 155; found, 154. Octahydrocoumarin was prepared by another method by Cook and Lawrence,[11] who reported that it boiled at 145° (10 mm.). Since they gave no other physical properties the identity of our product was confirmed by analysis for carbon and hydrogen. [b] The properties of hexahydrochroman from both sources are given, since their similarity serves as a confirmation of the structure assigned to these products. *Anal.* Calcd. for $C_9H_{16}O$: C, 77.07; H, 11.5. Found: C, 76.9, 76.7; H, 11.6, 11.7. [c] The molecular refraction (40.03) of chroman calculated from the results of Semmler[8] is also slightly above theoretical. [d] *Anal.* Calcd. for $C_9H_{18}O_2$: C, 68.4; H, 11.6. Found: C, 68.2, 68.2; H, 11.6, 11.6. [e] Saponification number: Calcd., 184; found, 182. Sabatier and Murat[12] had previously prepared this compound, b. p. 231° (760 mm.), $n^{17}D$ 1.452. The identity of our product was confirmed by comparison of the physical properties with a sample prepared by another method.[4] [f] Semmler[8] reported the boiling point of V as 177–178° (8 mm.) and the melting point of the benzoate as 99–100°. [g] A sample of γ-cyclohexylpropyl alcohol (VIII) was prepared by the hydrogenation of γ-phenylpropyl alcohol (Table II). The product (b. p. 116° (20 mm.), 218° (760 mm.)) gave an α-naphthyl urethan, m. p. 83–84°. A mixed melting point showed that this was identical with the derivative of the hydrogenolysis product reported above. *Anal.* Calcd. for $C_{20}H_{25}O_2N$: N, 4.49. Found, N, 4.31. Waser[13] reported the boiling point of VIII as 110–111° (11 mm.).

reactions described here are being extended to more complex derivatives.

Experimental Part

The coumarin used was purified by recrystallization from a mixture of benzene and ligroin (b. p. 70–90°). Certain samples of coumarin, presumably of natural origin, were hydrogenated to dihydrocoumarin over nickel but gave no further reaction at 200° and very slow reaction at 250°. Recrystallization removed the impurity responsible for this behavior and the results given in Table II were readily duplicated. For hydrogenation over copper chromite, Merck coumarin was used without recrystallization.

Hydrogenations.—The apparatus was similar to those already described[9] and was used in conjunction with a potentiometer-controller temperature-recorder. In the hydrogenations in which alcohol was the solvent, the commercial absolute grade was used. Raney nickel and copper chromite catalysts were made by the conventional methods.[10] The nickel catalyst was stored under alcohol but in the experiments in which it was desired to avoid the effects of alcohol, the catalyst was washed several times with ether and finally with methylcyclohexane. The hydrogenation products were dried over magnesium sulfate and distilled under reduced pressure through a 10-cm. Vigreux column or a Widmer column containing a spiral 11 cm. long. The results of the hydrogenations are given in Table II. Since most of the products did not contain reactive functions and could not be converted to solid derivatives, physical properties and analyses were important factors in identification. Fortunately, these were satisfactory for the elimination of any likely alternative structures. The data obtained are reported in Table III.

Chroman (VI).—A solution of 30.4 g. (0.2 mole) of γ-(o-hydroxyphenyl)-propyl alcohol (V) in 100 ml. of dry benzene was placed in a 500-ml. three-necked, round-bottomed flask fitted with a mechanical stirrer, a dropping funnel and a reflux condenser connected to a trap to dispose of hydrogen bromide. The solution was cooled in a water-bath at 5°, about 2 ml. of phosphorus tribromide added, and the mixture stirred until it had become warm enough for reaction to begin. The reaction flask was kept in the bath of cool water and the remainder of the phosphorus tribromide added slowly enough to avoid a violent reaction. A total of 40.7 g. (0.15 mole) of phosphorus tribromide was used and about one-half hour was required for its addition. The reaction mixture was stirred for an additional two hours, allowed to stand overnight and on the next morning refluxed for one-half hour on the steam-bath. After cooling, the flask was immersed in cold water and a solution of 24 g. (0.6 mole) of sodium hydroxide in 100 ml. of water added cautiously with stirring. This mixture was refluxed on the steam-bath with stirring for three hours and the layers separated. The aqueous layer was washed once with an equal volume of benzene and the combined benzene extracts washed with an equal volume of water. The benzene solution was dried over calcium chloride and distilled. The yield of chroman (VI) was 23.3 g. (87%), b. p. 125–130° (70 mm.). The product was a colorless liquid which contained traces of halogen,[14]

(9) Ref. 1, p. 39.
(10) Ref. 1, pp. 13, 20.
(11) Cook and Lawrence, *J. Chem. Soc.*, 817 (1937).
(12) Sabatier and Murat, *Compt. rend.*, **156**, 752 (1913).
(13) Waser, *Helv. Chim. Acta*, **8**, 123 (1925).

(14) In this state the product was not hydrogenated over nickel but this treatment removed the impurity and the recovered chroman was readily hydrogenated by a second treatment over nickel (Table II).

and turned a straw color on standing. The physical properties of the product are given in Table III and exclude the possibility that it is the isomeric 2-methylcoumaran. The following properties have been reported for chroman[8] and 2-methylcoumaran,[15] respectively: b. p. 93.5° (8 mm.), 208–212°; n_D 1.54437 (20°), 1.5302 (25°); *d*, 1.0587 (20°), 1.028 (25°).

Omission of the treatment with alkali described above reduced the yields of chroman to 70–75%. None of the expected bromide was isolated but the chroman fraction contained large amounts of halogen. However, treatment of γ-(*o*-hydroxyphenyl)-propyl alcohol (V) with hydrobromic acid–sulfuric acid mixture as described[16] for lauryl bromide gave a 50% yield of chroman and 10% of what was probably γ-(*o*-hydroxyphenyl)-propyl bromide, b. p. 165° (23 mm.). The latter could not be purified, since hydrogen bromide was evolved slowly during distillation.

(15) Niederl and Storch, THIS JOURNAL, **55**, 4554 (1933).

(16) Gilman, "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., 440 Fourth Avenue, New York, N. Y., 1932, p. 27.

Summary

Products obtained by the hydrogenation of coumarin, or from its hydrogenation products, include dihydrocoumarin, octahydrocoumarin, chroman, hexahydrochroman and a substance believed to be a polymeric ester. Of especial interest is the conversion of δ-lactones and of a 1,5-glycol to cyclic ethers over Raney nickel.

PHILADELPHIA, PENNA. RECEIVED SEPTEMBER 15, 1939

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF YENCHING UNIVERSITY]

Ephedrine. III. Di-(α-hydroxyl-β-methylaminopropyl)-benzenes

BY STANLEY D. WILSON AND CHEN-TA CHANG

Although a large number of derivatives and homologs of ephedrine have been reported by numerous investigators, we can find no record of such derivatives with two α-hydroxyl-β-methylaminopropyl side chains. This paper reports the preparation of the meta and para compounds of this type. These compounds were prepared from the 1,3- and 1,4-dipropionylbenzenes, respectively, which we made from the corresponding phthalyl chlorides by modifications of Mixin's[1] method. According to this method the phthalyl chlorides were first converted into the diethyldiamides by treatment with diethylamine. These diethyl acid amides were then treated with ethylmagnesium bromide, which converted them into the desired dipropionyl compounds. In the first step Mixin employed ether as a solvent with the para compound but used benzene with the meta compound. The substitution of ether for the benzene in the case of the meta compound resulted in better yields and much greater ease in purification of the product. Mixin reports a yield of 25–30% in the second step from the Grignard reaction when he refluxed for four hours. We obtained yields of 35–40% by refluxing for nine hours.

The dipropionylbenzenes were next treated with bromine, which converted them into two new derivatives: 1,3- and 1,4-di-(α-bromopropionyl)-benzenes. When the bromo compounds were treated with methylamine they were converted into the corresponding di-(α-methylaminopropionyl)-benzenes which also have not been described previously. These amino compounds were then reduced by hydrogen in the presence of platinum to give the desired new ephedrines. The last three reactions have been employed in the preparation of the more normal types of ephedrine homologs by Späth and Göhring,[2] Hyde, Browing and Adams,[3] Wilson and Sun[4] and others.

The free base of the new para ephedrine was a thick oil but that of the meta compound was an amorphous solid. The salts of the para compound crystallized well and had high melting points, while the hydrochloride, sulfate, oxalate, and phosphate of the meta derivative were thick liquids, but the picrate was a somewhat gummy amorphous solid. This agrees with Koller's[5] finding, that salts of *p*-methoxyephedrine were crystalline and had melting points while the salts of *m*-methoxy-*p*-hydroxyephedrine were liquids. These compounds contain four asymmetrical carbons and their resolution into their optical isomers would be an interesting problem.

Experimental Part

Preparation of 1,4-Di-(α-bromopropionyl)-benzene.—8.41 g. of bromine was added gradually to 5 g. of 1,4-

(1) Mixin, *Ann. Chim.*, **9**, 55 (1928).

(2) Späth and Göhring, *Monatsh.*, **41**, 319 (1920).

(3) Hyde, Browing and Adams, THIS JOURNAL, **50**, 2287 (1928).

(4) Wilson and Sun, *J. Chinese Chem. Soc.*, **2**, 243 (1934).

(5) Koller, *Monatsh.*, **47**, 397 (1926).

dipropionylbenzene dissolved in 100 cc. of glacial acetic acid while the solution was heated on the water-bath under a reflux condenser. After the hydrogen bromide was nearly all expelled, the solution was cooled in an ice-bath. The bromo compound separated in colorless plates, which were recrystallized from alcohol, yield 95%, m. p. 109–110°. The compound is insoluble in water, moderately soluble in alcohol and very soluble in benzene and ether.

Anal. Calcd. for $C_{12}H_{12}O_2Br_2$: Br, 45.93. Found: Br, 45.97.

Preparation of 1,4-Di-(α-methylaminopropionyl)-benzene Hydrogen Chloride.—Seven grams of the 1,4-di-(α-bromopropionyl)-benzene dissolved in 200 cc. of benzene was added drop by drop to 3 g. of methylamine in 200 cc. of benzene. The reaction mixture was allowed to stand at room temperature for one hundred hours. Crystals of methylamine hydrobromide separated and were filtered off. A portion of the benzene and the excess of the methylamine were removed by distillation. The residual solution was then treated with a current of dry hydrogen chloride at room temperature. The 1,4-di-(α-methylaminopropionyl)-benzene hydrochloride which separated out was recrystallized from methyl alcohol and ether to give fine colorless plates, which did not melt but decomposed above 320°. The product is slightly soluble in ether, moderately soluble in alcohol and very soluble in water. The yield was 3 g. or 62%.

Anal. Calcd. for $C_{14}H_{22}N_2O_2Cl_2$: C, 52.32; H, 6.91; Cl, 22.08. Found: C, 52.50; H, 6.70; Cl, 21.64.

Preparation of 1,4-Di-(α-hydroxyl-β-methylaminopropyl)-benzene Hydrochloride.—Two grams of the 1,4-di-(α-methylaminopropionyl)-benzene hydrochloride dissolved in 100 cc. of 95% alcohol was reduced by hydrogen in the presence of platinum catalyst. The catalyst was removed by filtration and the solution concentrated by evaporation of a portion of the ethyl alcohol. Upon addition of ether, the new compound separated in a yield of 1.8 g. On recrystallization from methyl alcohol and ether it formed rosets, m. p. 285–287°. The product was insoluble in benzene and ether, moderately soluble in alcohol and very soluble in water.

Anal. Calcd. for $C_{14}H_{26}N_2O_2Cl_2$: C, 51.67; H, 8.06. Found: C, 51.65; H, 8.03.

Preparation of the Free Base.—It was difficult to separate and purify the free base when it was set free from the hydrochloride by addition of potassium hydroxide. On the other hand, the free base of the corresponding ketone was easily obtained by the same treatment and gave the corresponding ephedrine on catalytic reduction. Both bases were slightly brownish, somewhat gummy amorphous substances which decomposed on heating. The sulfate (decomposed above 320°), mandelate (m. p. 214°), and tartrate (m. p. 167–168°), of the ephedrine were prepared easily by treating an alcoholic solution of the base with an alcoholic solution of the corresponding acids. They were recrystallized from mixtures of alcohol and ether. All were white nicely crystallized products.

Preparation of 1,3-Di-(α-hydroxyl-β-methylaminopropionyl)-benzene Hydrochloride.—This compound was prepared from the corresponding 1,3-dipropionylbenzene by an analogous series of reactions. It was found more satisfactory to substitute carbon tetrachloride as a solvent during the bromination of the dipropionyl compound. The bromo compound, the hydrochloride of the amino ketone and the hydrochloride of the ephedrine were all liquids which did not solidify even at −20°. The solubilities were very similar to those of the corresponding 1,4-derivatives.

Anal. Calcd. for $C_{14}H_{26}N_2O_2Cl_2$: C, 51.67; H, 8.06; Cl, 21.81. Found: C, 51.38; H, 7.61; Cl, 22.94.

The Free Base.—In this case the free base was prepared by treating a water solution of the hydrochloride of the ephedrine with potassium hydroxide. It proved to be an amorphous solid which decomposed on heating. This product is soluble in alcohol and benzene but insoluble in water. Treatment of saturated alcoholic solutions of the base with alcoholic oxalic, sulfuric and phosphoric acids gave only liquid products which did not solidify even at −20°. The picrate was an amorphous solid which decomposed on heating.

We wish to thank The China Foundation for the Promotion of Education and Culture for a grant which defrayed the expense of this investigation.

Summary

1. Two new ephedrine homologs, 1,3- and 1,4-di-(α-hydroxyl-β-methylaminopropyl)-benzene, have been prepared.

2. Four new intermediate compounds were obtained: the 1,3- and 1,4-di-(α-bromopropionyl)-benzenes and the 1,3- and 1,4-di-(α-methylaminopropionyl)-benzenes.

PEIPING, CHINA RECEIVED NOVEMBER 29, 1939

[CONTRIBUTION FROM THE PHYSICO-CHEMICAL LABORATORY OF THE NEW YORK STATE EXPERIMENT STATION]

Splitting the CONH Linkage by Means of Ultraviolet Light[1]

BY D. C. CARPENTER

Any method which would enable us to break selectively the peptide (CONH) linkage between certain of the various amino acids of a protein, should bring forth a certain amount of information on the arrangement of the individual amino acids within the molecule. Inasmuch as the specific properties of proteins such as insulin probably depend on the presence of a certain sequence of grouping of amino acids in the molecule, a method bearing on the finding of these groupings is of considerable interest and importance. From recent results it appears that ultraviolet light may be a useful tool for opening up the protein molecule in such work.

Rideal and Mitchell[2] showed that stearic anilide $C_{17}H_{35}CONHC_6H_5$ when irradiated as a monolayer with light of wave length 2350–2400 and 2483 Å. was decomposed into stearic acid and aniline. In this experiment the benzene ring functioned as the chromophore group. Inasmuch as the bond energy of the C–N linkage (48.6 kcal./mole)[3] is the weakest linkage in the compound, it is not surprising that breakage occurs at this point. It might be concluded that Rideal and Mitchell's experiment applied directly to the breakage of peptides in a similar manner. However, in the peptides and proteins the benzene ring or other light absorbing group is contained in a side chain and situated several atoms away from the point of splitting. To be of any use in splitting peptides or the main peptide chain in proteins, the matter arises as to whether light energy absorbed by the chromophore group can pass through several CH_2 groups and still cause splitting of the CONH linkage. Norrish and Appleyard[4] irradiated methyl butyl ketone, CH_3CH_2-CH_2CH_2—CO—CH_3, at 2200–3000 Å., where the CO group is the chromophore, and found that $CH_3CH{=}CH_2$ and CH_3—CO—CH_3 were produced. This showed that energy is able to travel along a chain and cause breakage of a molecule at a distant point. How far energy may travel in this way has not been established.

In the present paper[5] we have confirmed the observations of Rideal and Mitchell with respect to the photolysis of stearic anilide. In addition to this we have prepared benzylstearylamine ($C_{17}H_{35}CONHCH_2C_6H_5$) and β-phenylethylstearylamine ($C_{17}H_{35}CONH(CH_2)_2C_6H_5$) and examined the photolysis of these compounds containing one and two CH_2 groups, respectively, interposed between the chromophore and the keto-imino linkage. We have found that both of these latter compounds undergo photolysis at 2537 Å. and therefore it may be expected that peptides and proteins having side chains bearing chromophore groups will behave similarly, and the CONH groups adjacent to the side chain undergo photolysis and the light absorbing amino acid is liberated from the peptide or protein molecule. This behavior would conform to observations that the free amino groups in proteins are increased by irradiation.[6]

Experimental

Preparation of Materials

Stearic Anilide.—This compound was prepared by converting pure stearic acid m. p. 69.3° (cor.) into the acid chloride by adding small portions dissolved in anhydrous chloroform to thionyl chloride and refluxing over a steam-bath for one-half hour. The thionyl chloride was used in 35% excess of the calculated amount. The excess thionyl chloride and chloroform were removed by distillation *in vacuo* over a water-bath.

Stearyl chloride (8.2 g.) was treated with 2.5 g. of aniline dissolved in 30 cc. of dry benzene and warmed on the steam-bath for two to three minutes. The benzene solution was decanted into a separatory funnel and washed successively with water, 5% hydrochloric acid solution, 5% sodium hydroxide solution and finally with water. The benzene was evaporated and the stearic anilide recrystallized several times from petroleum ether, alcohol and finally twice from acetone; 9.0 g. of stearic anilide in white needles m. p. 94° (cor.) was obtained.

Benzylstearylamine.—This compound was prepared in analogous fashion from benzylamine b. p. 184° (cor.) and stearyl chloride, and after recrystallizing as above was obtained as white flakes, m. p. 98.6° (cor.).

β - Phenylethylstearylamine.—β - Phenylethylamine of b. p. 194.5–196° (cor.) prepared by the method of Ladenburg[7] was condensed with stearyl chloride as above and

(1) Approved by the Director of the New York State Experiment Station for publication as Journal Paper No. 348.

(2) Rideal and Mitchell, *Proc. Roy. Soc.* (London), **159A**, 206 (1937).

(3) Pauling and Niemann, THIS JOURNAL, **61**, 1862 (1939).

(4) Norrish and Appleyard, *J. Chem. Soc.*, 874 (1934).

(5) Carpenter, *Science*, **89**, 251 (1939).

(6) Fort and Lloyd, *J. Soc. Dyers and Colourists*, **30**, 73 (1914); Fort, *ibid.*, **32**, 184 (1917).

(7) Ladenburg, *Ber.*, **19**, 782 (1886).

after several recrystallizations was obtained as white needles, m. p. 91.8° (cor.).

Absorption Spectrum.—The absorption spectrum of each of the compounds was determined in anhydrous ethyl alcohol as solvent by means of a Bausch and Lomb ultraviolet sectorphotometer, suitable dilutions being employed to cover the absorption range. The absorption spectra are shown in Fig. 1. Comparison of our data for stearic anilide with the results of Rideal and Mitchell shows good general agreement for the maximal absorption region, but the latter's results show somewhat greater absorption throughout the entire range. The band is fairly flat between 2360 and 2500 Å. with a maximum close to 2420 Å.

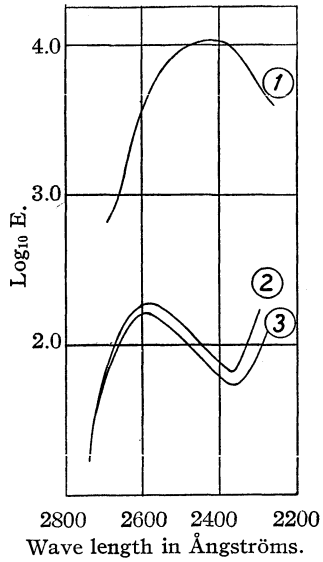


Fig. 1.—Absorption spectra; 1, stearic anilide; 2, benzylstearylamine; 3, β-phenylethylstearylamine.

The absorption spectra for benzylstearylamine and β-phenylethylstearylamine are close together and considerably less than for stearic anilide, the introduction of the first CH_2 group between the ring and the fatty acid residue accounting for most of the decreased absorption and the shift of the maximum toward the visible range. Both of these compounds have an absorption maximum close to 2580 Å.

Irradiation Experiments.—Rideal and Mitchell employed a large quartz monochromator for obtaining monochromatic light. A monochromator of sufficient size to be useful was not available to us, consequently as a source of light in our experiments we have used a quartz-mercury lamp with a combination of light filtering solutions[8] in quartz containers. Rideal and Mitchell record that in the photolysis of stearic anilide no reaction can be detected at 2537 Å. while reactions occur at 2483 Å. They put the threshold for the photochemical reaction near 2500 Å. With the system of light filters we have used, both the 2483 and 2537 Å. lines are transmitted, so we are unable to say definitely whether the photochemical effects we have observed are due to the 2483 or the much more intense 2537 Å. line. We have not observed any effects when using the 2650 and 2700 Å. lines, which are both transmitted when employing a different combination of filter solutions.

(8) Bowen, *J. Chem. Soc.*, 76 (1935).

In our experiments, mono-layers of the substances have been formed by spreading dilute benzene solutions onto normal or tenth normal hydrochloric acid solutions contained in a Pyrex glass trough. The collapse areas of the films have been measured and the theoretical molecular areas calculated. These results are contained in Table I and show that the respective molecules

TABLE I

MOLECULAR AREAS OF SUBSTANCES

	Molecular area, sq. Å. Found	Calcd.
Stearic anilide	23.9	23.7
Benzylstearylamine	30.7	30.4
β-Phenylethylstearylamine	28.6	28.1

are oriented as shown in Fig. 2. In the latter figure the benzene ring is shown with dotted lines but the plane of the ring actually lies at right angles to the plane of the paper as is shown by the solid line. Calculation of the molecular area of

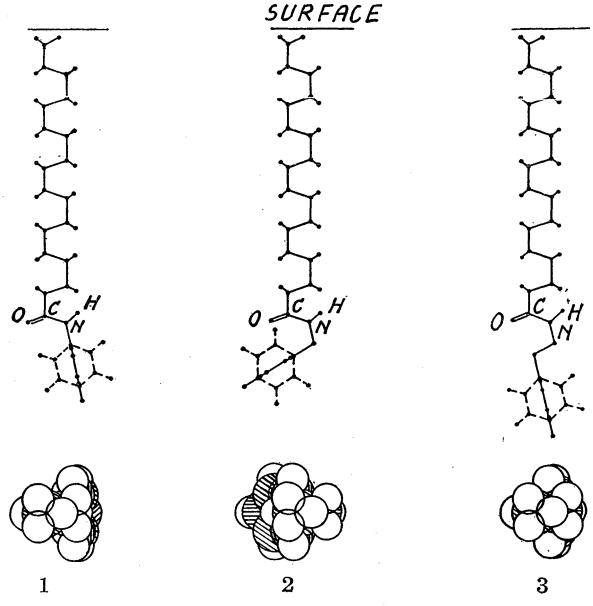


Fig. 2.—Monolayers on 0.1 *n* hydrochloric acid; 1, stearic anilide; 2, benzylstearylamine; 3, β-phenylethylstearylamine.

benzylstearylamine assuming the ring swung out to the right (free rotation about the N–C bond) and as distant as possible from the oxygen atom of the CO group, leads to an area of 36.8 sq. Å., which is altogether too high to agree with the experimental value and we may safely conclude that in a compressed film the ring lies on the same side

as the oxygen atom. The calculated molecular areas agree within 1–2% with the experimental values and this is about as good agreement as can be expected.

The film potential was measured[9] at intervals as the irradiation proceeded and the maximum ΔV values eventually came to around 550 mv. Rideal and Mitchell record a ΔV value for stearic acid of 545 mv. This indicates that the decomposition product remaining in the mono-layer is stearic acid in all cases.

The amines resulting from the photolysis remain in the hydrochloric acid solution substrate, as may be expected. Aniline was identified colorimetrically in the hydrochloric acid solution after irradiation for as short a period as ten minutes by the red color produced by diazotizing and coupling with β-naphthol. Benzylamine and β-phenylethylamine were identified as picrates, m. p. 195° (cor.)[10] and 168° (cor.),[11] respectively, after prolonged irradiation and frequent renewal of the mono-layer. Mixed melting points of each of these were done with the respective pure picrates prepared from the pure amines and confirmed the identity of the photolysis products. Between 4 and 5 mg. of the respective picrates was actually crystallized after about twenty-four hours of irradiation. That the reaction with stearic anilide is a photolysis and not hydrolysis in the presence of hydrochloric acid was definitely proved by inserting a glass filter in the optical system which excluded wave lengths below 3000 Å. Under these conditions no aniline was detected after thirty minutes exposure.

(9) Schulman and Rideal, *Proc. Roy. Soc.* (London), **130A**, 259 (1931).

(10) Moureu and Lazennec, *Bull. soc. chim.*, [3] **35**, 1183 (1906); Jerusalem, *J. Chem. Soc.*, 1283 (1909).

(11) Michaelis and Linow, *Ber.*, **26**, 2167 (1893); Weinhagen, *Biochem. J.*, **11**, 275 (1917).

Acknowledgment is made to Mr. B. E. Babcock and the American Philosophical Society for grants-in-aid and to the Bausch and Lomb Optical Company for the use of the ultraviolet sector-photometer for the absorption spectrum studies.

Summary

The absorption spectra of stearic anilide, benzylstearylamine and β-phenylethylstearylamine have been determined and the molecular areas when spread on hydrochloric acid solution have been measured. These substances as monolayers have been irradiated at 2483 and 2537 Å. and found to undergo photolysis at the CONH linkage. The products of the reaction have been identified by film potential measurements (stearic acid) and colorimetric tests (aniline) and as crystalline picrates (benzylamine and β-phenylethylamine).

It seems reasonable to expect that peptides and proteins containing amino acids with light-absorbing side chains may undergo breakage of the adjacent CONH linkages in an analogous manner.

GENEVA, N. Y. RECEIVED NOVEMBER 7, 1939

[COMMUNICATION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF MANITOBA]

The Heats of Solution, Heats of Formation, Specific Heats and Equilibrium Diagrams of Certain Molecular Compounds

BY A. N. CAMPBELL AND A. J. R. CAMPBELL

A very great number of studies of the freezing point (or melting point) diagrams of binary organic systems has been made.[1] As a result of these studies it appears that a molecular compound frequently is formed. In this connection the question of the relative stability of these numerous compounds has arisen. This question can only be answered with complete precision when the free energy of formation is known and this cannot be obtained readily for the systems under consideration, since the calculation requires a knowledge of the behavior of the specific heats from absolute zero upward. It is known, however, that in condensed systems the heat of formation very often approximates to the free energy of formation. It was thought that determinations of the heats of formation via the heats of solution of some of these organic molecular compounds would give at least the order of magnitude of the free energy change involved. Furthermore, if the specific heats, at room temperature, of reactants and products are known, an approximate calcula-

(1) *Cf.*, for instance, Kremann, *Monatsh.*, **25**, 1215 (1904), and following volumes to 1930.

tion can be made by means of the Kirchhoff equation of the heat of formation at absolute zero, assuming that the difference of molar heats of reactants and products remains constant down to absolute zero. At absolute zero the heats of formation are strictly a measure of the free energy change involved, since at that temperature

$$\Delta H = \Delta F$$

The experimental data required for the evaluation of the above relationships are the heat of formation and the specific heats of reactant and product. In most cases these data were unknown, and we have had to determine them, developing for the purpose methods which are to some extent new, or at least modifications of existing methods, to deal with organic substances, which are for the most part bad thermal conductors.

As this investigation was essentially one of relative stability, using that term in not too precise a sense, we investigated the equilibrium diagrams with a suitable solvent, in certain cases. The effect of this is to extend the information obtained from the freezing curve to a lower temperature. It answers the question of whether or not the compound continues to exist at the lower temperature. In addition it is usually considered that the extent of that portion of the curve, in both cases, along which compound is the stable solid, is a qualitative indication of the stability of the compound, that is, of its distance from a transition temperature. The systems studied were:[2] (1) phenol–urea: compound of 2 phenol:1 urea, congruent melting point, sharp maximum; (2) urea–*p*-toluidine: compound of 1 urea:1 *p*-toluidine, congruent melting point, sharp maximum; (3) β-naphthylamine–*p*-nitrosodimethylaniline: compound of 2 β-naphthylamine:3 *p*-nitrosodimethylaniline, congruent melting point, very flat maximum; (4) salicylic acid–acetamide: compound of 1 salicylic acid:1 acetamide, incongruent melting point, transition temp. 63–65°.

Experimental

Heats of Formation.—Attempts were first made to determine the heats of formation from the heats of combustion, but these were soon abandoned when it was realized that, owing to the large molecular heats of combustion, the difference figure was hopelessly inaccurate. A property of much smaller numerical value per mole was sought and found in the heat of solution, and the heats of formation were determined throughout from this quantity. As all the heats of solution were negative (heat absorbed), the method used was essentially that in which solute and solvent are mixed and the temperature then restored to its original value by electrical heating. The beauty of this method is that a knowledge of the water equivalent is not required. The electrical energy consumed was measured potentiometrically as the fall in potential across a standard ohm in series and across the heating coil of the calorimeter. The energy consumed is then $H = E_1E_2t$, where t is time in seconds and E_1 and E_2 the respective voltage drops. Minor precautions consisted in having large capacity lead accumulators as source of energy, using heavy copper leads, and packing the standard ohm in ice, in case of heating. Currents used were about 0.7 and 1.4 amp., with 2- and 4-volt circuits, respectively. The accuracy of the electrical measurement is said to be 1 in 10,000, certainly 1 in 1000, and therefore much in excess of the accuracy of the thermal measurement, which is 1 in 100 at best. As usual the calorimeter consisted of a dewar flask with beckmann thermometer, but it was found indispensable to immerse the calorimeter in a thermostat at 20°; otherwise radiation losses were appreciable, even through the wall of a silvered vacuum flask. In general, if the temperature of the contents of the dewar fell more than one degree below that of the environment, radiation losses were appreciable. As this was liable to occur when the heavier charges of solute were first introduced, the device was adopted of immediately switching in the 4-volt circuit whereby the temperature was brought to a few tenths below the equilibrium temperature in a few minutes (say, five minutes). The temperature was then restored exactly to its original value by means of the 2-volt circuit (energy input one quarter of the preceding). The energy input in each phase, each of about five minutes duration, was separately determined. A difficulty was encountered in stirring. Blank experiments showed that all kinds of mechanical stirrers raised the temperature several hundredths of a degree during the course of a run. The difficulty was overcome by using as stirring agent a fine stream of air injected through a coarse capillary. The air current passed first through a metal coil and then through a bubbler containing the solvent used in the calorimeter, both coil and bubbler being immersed in the thermostat. The variation of temperature produced by this means was not more than 0.01° during a run. The powdered solute was immersed in the thermostat for some time before its introduction to the calorimeter. In order to allow for any possible existence of a molecular compound in solution, the heats of solution were determined, not only in pure solvent, but also in solvent containing an equivalent amount of the other component.

Preparation of Molecular Compounds.—The lower melting component was melted completely, the calculated quantity of the second component added, the whole stirred until clear, if necessary with further heating, and then allowed to crystallize very slowly. The freezing point, in comparison with the literature, showed the purity of each compound. The molecular compound of *p*-

(2) Literature relating to equilibrium diagrams: (1) Kremann and Rodinis, *Monatsh.*, **27**, 138 (1906); J. C. Philip, *J. Chem. Soc.*, **83**, 823 (1903); H. Rheinboldt, *J. prakt. Chem.*, (2), **111**, 242 (1925). (2) Philip, *J. Chem. Soc.*, **83**, 821 (1903). (3) Kremann, *Monatsh.*, **25**, 1322 (1904); H. Rheinboldt, *loc. cit.* (4) Kremann and Auer, *Monatsh.*, **39**, 466 (1918); Rheinboldt, *loc. cit.*

toluidine and urea is stated to exist in two forms. The form used by us was the high melting and therefore stable form (m. p. 31.1°). This stable form is readily obtained by powdering the samples before use; even mere scratching with a glass rod appears to produce a change in crystalline structure.

Preparation of Materials.—Phenol was distilled repeatedly. One distillation is insufficient and, even then, for specific heat determinations, distillation must be carried out directly into the container, since the slightest trace of water lowers the melting point very abruptly.

Urea was recrystallized from alcohol.

p-Toluidine, taken as pure, m. p. 44.2°.

β-Naphthylamine was recrystallized from benzene.

p-Nitrosodimethylaniline was prepared from dimethylamine, crude product extracted with ether and first crystals separated.

Salicylic acid was recrystallized from water.

Acetamide was distilled several times and protected from access of moist air. The specific heat sample was distilled straight into its container.

Specific Heats.—Perhaps the best method of determining specific heats is to heat the substance electrically in an evacuated container determining the rise of temperature from the increase in resistance of the heating coil. We attempted something similar to this, using, however, a beckmann thermometer and solidifying a large block of substance around the bulb and heating coil, but we found our attempts defeated by the poor thermal conductivity of the materials. If the bulb of the thermometer was near the coil, the thermometer rose rapidly to a high value, and then, when current was cut off, fell to an uncertain final value. If the bulb were far removed from the coil, it commenced to rise only after a considerable interval of time, during which radiation was perhaps considerable and certainly unknown. Determination of temperature from the resistance of the coil would only have made matters worse. This uncertainty in the final temperature led us to adopt the following method, which is a modification of the method of mixtures. From 50 to 100 g. of substance sealed in a bulb of hard glass was placed in a metal container, packed in melting ice and left overnight. The same electrical circuit as was used in the determination of heats of solution was employed, and the same calorimeter, which contained 150 cc. of water, together with the same stirring device. The cooled sample was rapidly introduced into the calorimeter and the 4-volt circuit immediately switched on. The temperature was thus brought to about 0.1° below that of the thermostat, and then brought exactly to the equilibrium value by means of the 2-volt circuit. As the heat of the calorimeter penetrated the badly conducting organic material the temperature again fell but it was not allowed to fall more than 0.1° before the 2-volt circuit was again switched in. In this way radiation loss was reduced practically to zero, despite the comparatively long duration of the experiment (about half an hour). Completion of the experiment was clearly marked by the temperature not dropping, or even rising a little, after the heating current was cut off. In common with all applications of the method of mixtures, this method can only give the specific heat over a range, in this case from 20 to 0°, but, at temperatures so far removed from the absolute zero, the variation of specific heat with temperature will not be great.

Numerical Results.—All measurements were made in a thermostat at 20°.

1. Phenol-Urea

Heats of Solution in Water:

TABLE I

Solvent		Diln. in l. per mole	Heat of soln. in kj. per mole Our value	Lit. value[a]
Phenol	Water	1.79	−11.9	
		2.15	−11.82	
		2.29	−11.26	
		2.02	−11.30 (mean of 12 detns.)	
		∞	...	−10.9
Urea	Water	7.16	−13.81	
	contg.	3.07	−14.0	
	equiv.	1.85	−13.7	
	phenol	4.03	−13.8 (mean of 12)	
Urea	Pure water	1.63	−14.65	
		∞	...	−15.1
2 Phenol:1 Urea		5.30	−49.5	
	Water	4.07	−46.75	
		3.90	−46.8	
		4.10	−46.2	
		4.03	−46.58 (mean of 12)	

[a] From "International Critical Tables."

Results

While the heats of solution of phenol and of urea appear to be only slightly dependent on dilution, that of the compound is appreciably greater at the higher dilutions. This is due to the increased dissociation of the compound which is not complete, as can be seen from a comparison of the heat of solution of urea in water containing equivalent phenol and in pure water. Taking the heat of formation of the compound as 10.18 kj. per mole (*cf.* below), the percentage of double compound remaining undissociated at a dilution of about 4 liters per mole is calculated from the difference in the heats of solution of urea in equiva-

lent phenol and in pure water (= 0.85 kj. per mole) as 8.35%. This point was checked by determining the molecular conductivities in water of phenol, of urea, and of the compound. These were:

	μ, mho	Diln. in l./mole
Phenol	0.00921	1.84
Urea	.0464	3.69
Compound	.0578	3.69

Hence, 2 phenol + 1 urea = 0.0648, and the percentage of compound, undissociated, results as 10.8, assuming what is obviously incorrect, that the compound molecules are non-conducting.

Heat of Formation.—Taking mean values for corresponding dilutions, we have

2 phenol + 1 urea = 1 compound + x kj.
$2(-11.3) + (-13.8) = -46.58 + x$ kj.
x = 10.18 kj. = 2.43 kcal./mole

Specific Heats.—

	Sp. ht. in cal./g. Obsd.	Lit. value	Molar heat obsd. in cal./mole
Phenol	0.239	0.561 (liquid)[3]	22.45
Urea	.274	.321[3]	16.4
2 Phenol:1 Urea	.240	...	59.8

Heat of Formation of 2 Phenol:1 Urea, at Absolute Zero (Approximate).—Equation used: $(\Delta H_T - \Delta H_0)/T = C_{products} - C_{reactants}$.

2 Molar heat phenol + molar ht. urea = 61.3
Molar heat compound = 59.8
$C_{products} - C_{reactants}$ = −1.5
T = 293°A.
Hence, ΔH_0 = 1990 cal. = 1.99 kcal.

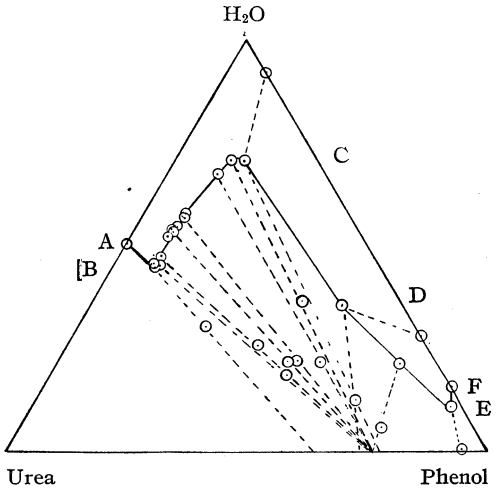


Fig. 1.—AB, urea, solution; B, urea, compound, solution; BC, compound, solution; CD, two liquids, compound; DE, compound, solution; E, compound, phenol, solution; EF, phenol solution.

(3) Magie, *Phys. Rev.*, **16**, 381 (1903), specific heats determined by introducing a weighed portion into one of the cups of the Pfaundler calorimeter.

Equilibrium Diagram.—The complete equilibrium diagram of the system phenol–urea–water was outlined at 20°. Urea was determined by the Kjeldahl method; phenol by the method of Redman, Weith and Brock.[4] The end-point of the latter method was greatly improved by filtering off the precipitated tribromophenol through glass wool, prior to titration. The results are contained in Table II and are expressed graphically in Fig. 1. The diagram has been rendered more complete by the incorporation of the results of Hill and Malisoff[5] for the mutual solubility of phenol/water at 20°.

TABLE II

	Solution % Compn. Phenol	Urea	Wet Solid % Compn. Phenol	Urea	Nature of equil. solid phase
1	...	49.8	...	...	Urea
2	7.85	46.8	Not analyzed		Urea (?)
3	8.5	46.9	26.6	43.7	Urea + compd., invariant pt.
4	9.3	45.3	48.8	32.7	Compound
5	8.7	44.0	39.3	35.1	Compound
6	7.7	40.2	Not analyzed		Compound
7	8.0	38.3	47.4	30.5	Compound
8	7.5	38.2	Not analyzed		Compound
9	8.2	37.0	Not analyzed		Compound
10	7.9	34.6	49.6	28.7	Compound
11	8.2	33.7	Not analyzed		Compound
12	10.15	22.2	54.1	24.1	Compound
13	11.6	17.8	43.2	20.9	Compound
14a	14.35	15.15	66.3	21.2	Two liquid layers +
14b	51.9	12.8	66.3	21.2	compd.
15	70.7	7.95	74.8	19.6	Compound
16	86.8	2.5	94.7	5.1	Compd. + phenol, invariant pt.
17	84.5	0.0	...	...	Phenol

If, in Fig. 1, a line is drawn joining the apex (H_2O) to the composition of the compound, it is apparent that on treatment with water the compound gives rise to two liquid layers; this is, indeed, visibly the case whenever the compound is treated with water.

2. Phenol-*p*-Toluidine

Heats of Solution in Alcohol.—For the determination of heats of solution commercial alcohol was used as solvent. This had d^{20}_4 0.8147, corresponding to 95.5% alcohol by weight.

From the approximate coincidence of the heats of solution of *p*-toluidine in alcohol only and in alcohol containing equivalent phenol, it appears that the compound is completely dissociated in solution.

(4) Thorpe and Whiteley, "Manual of Organic Chemical Analysis," 1925, p. 161.

(5) Hill and Malisoff, THIS JOURNAL, **48**, 918 (1926).

TABLE III

Compound	Solvent	Diln. in l. per mole	Heat of soln. in kj. per mole
Phenol	95.5% EtOH	7.47	− 4.00
		2.18	− 4.25
		1.14	− 4.20
		0.96	− 4.00
p-Toluidine	EtOH	21.0	−14.0
	containing	2.91	−13.4
	equiv.	1.40	−12.85
	phenol	1.00	−12.6
	Alcohol only	1.10	−12.45
Compound:	Alcohol	29.7	−26.1
1 Phenol:		12.85	−23.2
1 *p*-Toluidine		5.2	−22.8
		2.38	−21.9
		1.155	−21.6

Heat of Formation.—Taking the values for the highest concentrations, where the experimental error is least, we have

1 phenol + 1 *p*-toluidine = 1 compound + x kj.
$-4.00 + (-12.6) = -21.6 + x$
$x = 5.0$ kj. = 1.195 kcal.

Specific Heats.—

	Sp. ht. in cal./g. Obsd.	Lit. value	Molar heat obsd. in cal./mole
p-Toluidine	0.277	0.387[a]	29.7
		.232[a]	
Compound: 1 Phenol: 1 *p*-toluidine	.258	....	51.8

[a] "Int. Crit. Tables."

Heat of Formation of Phenol:*p*-Toluidine, at Absolute Zero.—

Molar heat phenol + molar heat *p*-toluidine = 52.1
Molar heat compound = 51.8
$C_{products} - C_{reactants}$ = −0.3
$\Delta H_0 = 1.195 - 0.3(293)/1000$ = 1.11 kcal.

Equilibrium Diagram.—Analytical difficulties rendered the exact working out of the equilibrium diagram (in water) difficult. The results, however, were sufficient to show that the greater part of the diagram is occupied by the equilibrium of two liquid layers: invariance is produced with *p*-toluidine, not compound, as the solid phase.

3. β-Naphthylamine : *p*-Nitrosodimethylaniline

Heats of Solution (in Acetone).—

TABLE IV

Compd.	Solvent	Diln. in l. per mole	Heat of soln. in kj. per mole
β-Naphthyl-amine	Acetone	13.65	−12.0
		4.33	−12.35
		2.86	−11.35
	Acetone contg. equiv. *p*-nitroso-dimethylaniline	4.10	−11.9
p-Nitroso-dimethyl-aniline	Acetone	6.70	−10.9
		3.67	−10.25
		2.77	−11.6
Compound: 2 β-naphthylamine 3 *p*-nitrosodi-methylaniline	Acetone	56.0	−66.3
		24.5	−62.6

The compound is completely dissociated in acetone solution, as an inspection of the heats of solution shows.

Heat of Formation.—The accuracy of the determinations of heat of solution is not good, owing to the slow rate of solution, even in acetone, which was the best solvent found. Mean values are therefore taken for the calculation, despite the fact that in strictness only values for the same dilution should be used; in other words, we assume that the heats of solution do not vary with dilution, and that the observed variations are errors of experiment. The calculation gives

2 β-Naphthylamine + 3 *p*-nitrosodimethylaniline = compound + x kj.
$2(-11.9) + 3(-10.9) = -64.6 + x$
$x = 8.1$ kj./mole = 1.94 kcal./mole

Specific Heats.—

	Sp. ht. in cal./g. obsd.	Molar heat in cal./mole
β-Naphthylamine	0.210	30.1
p-Nitrosodimethylaniline	.329	49.4
Compound	.279	205.0

Heat of Formation of 2 β-Naphthylamine: 3 *p*-Nitrosodimethylaniline at Absolute Zero.—

2 Molar heat naphthylamine + 3 molar heat nitrosodimethylaniline = 208.4
Molar heat compound = 205.0
$C_{products} - C_{reactants}$ = −3.4
$\Delta H_0 = 1.94 - 3.4(293)/1000$ = 0.94 kcal.

Equilibrium Diagram.—Analytical difficulties made the study of the equilibrium diagram impossible. There were, however, indications that the molecular compound lies within the transition interval at 20°.

4. Salicylic Acid–Acetamide

Heats of Solution (in 95.5% alcohol).—

TABLE V

	Solvent	Diln. in l. per mole	Heat of soln. in kj. per mole
Salicylic acid	Alcohol	3.68	−13.0
		1.78	−13.2
		1.17	−13.65
Acetamide	Alc. contg.	3.92	−11.4
	equivalent	1.74	−10.15
	sal. acid	1.04	−10.3
	Alcohol	1.9	−10.6

TABLE V (*Concluded*)

Compound:	Solvent	Diln. in l. per mole	Heat of soln. in kj. per mole
	Alcohol	17.9	−24.3
1 Sali-		6.45	−23.2
cylic		2.79	−23.3
acid		1.87	−24.0
1 acet-		1.41	−24.9
amide		1.13	−24.1

The compound is almost completely dissociated in alcohol solution.

Heat of Formation.—If the assumption is made that the variation in the heats of solution are errors of measurement and the means taken for the calculation, the heat of formation results as +0.1 kj./mole. In view of the smallness of this heat of formation, it was thought better to graph the results for salicylic acid (decreasing with dilution) and for acetamide (increasing with dilution) and to apply the interpolated values to each experimental value for the heat of solution of the compound. In this way the following results were obtained.

Diln.	Heat of formation, kj. per mole
17.9	+1.5
6.45	+0.2
2.79	−0.1
1.87	+0.4
1.41	+1.1
1.13	+0.7

Mean = +0.63 kj. = 0.15 kcal.

Specific Heats.—

	Sp. heat in cal./g.	Molar heat in cal./mole
Salicylic acid	0.1809	24.9
Acetamide	.270	15.9
Compound	.2055	40.5

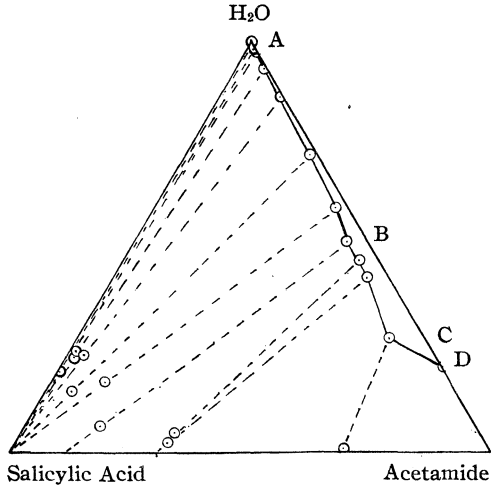


Fig. 2.—AB, Salicylic acid, solution; B, salicylic acid, compound, solution; BC, compound, solution; C, compound, acetamide, solution; CD, acetamide, solution.

Heat of Formation of Salicylic Acid : Acetamide at Absolute Zero.—

Molar heat salicylic acid + molar heat acetamide	=	40.8
Molar heat compound	=	40.5
$C_{products} - C_{reactants}$	=	−0.3
$\Delta H_0 = 0.15 - 0.3(293)/1000$	=	0.06 kcal.

Equilibrium Diagram.—The complete equilibrium diagram for salicylic acid–acetamide–water at 20° was readily determined, the salicylic acid being estimated by titration and the acetamide by distillation with sodium hydroxide. The results are contained in Table VI and expressed graphically in Fig. 2.

TABLE VI

	Solution, % compn.		Wet solid, % compn.		
	Salicylic acid	Acetamide	Salicylic acid	Acetamide	Nature of equil. solid phase
1	0.19	...			Salicylic acid
2	.225	0.4	86.5	0.1	Salicylic acid
3	.28	1.6	79.7	0.6	Salicylic acid
4	.26	2.0	73.4	1.3	Salicylic acid
5	.375	6.2	74.8	1.9	Salicylic acid
6	.53	12.85	72.4	3.5	Salicylic acid
7	1.30	25.9	79.7	5.1	Salicylic acid
8	2.71	37.8	71.7	11.0	Salicylic acid
9	4.13	44.3	78.0	15.3	Sal. acid + compd. invariant pt.
10	4.24	48.9	63.7	31.2	Compound
11	4.91	52.4	66.7	31.2	Compound
12	7.53	64.5	30.4	68.3	Compound + acetamide, invariant pt.
13	..	79.3	..	..	Acetamide

The molecular compound lies within the transition interval.

Numerical Values Obtained.—In work of this kind the possible sources of error are so many that it is difficult to assess the final error with any degree of certainty, but we would represent the results for heat of formation as follows

	System number			
	1	2	3	4
ΔH, in kj.	10.18 ∓ 0.03	5.0 ∓ 0.3	8.1 ∓ 2.4	0.63 ∓ 0.53

The high uncertainty in 3 is due, as mentioned above, to a slow rate of solution in this system.

The only error in the specific heats that we can assess is that of reproducibility in different determinations, which we put at ∓0.01 calorie per gram. The specific heats are all mean values applying to the range 0–20°.

Discussion of Results

It is apparent that the heats of formation of all these double compounds are small, though not

always as small as might be expected from the feebleness of chemical union usually attributed to such compounds. If the rather gross assumption is made that the difference of molar heats of reactants and products remains constant down to absolute zero, then the resulting heats of formation at absolute zero are also the free energies of formation at that temperature. These quantities stand in the relation: 33 : 19 : 16 : 1 for the compounds in the order treated. In agreement with this order, it is found that the compound phenol: urea is by no means completely dissociated in aqueous solution, while salicylic acid: acetamide is. On the other hand the compounds of phenol and *p*-toluidine and of β-naphthylamine and *p*-nitrosodimethylaniline are also completely dissociated in solution. Dissociation in solution, however, is governed by other factors than free energy of formation; neither is it certain that the order of the free energies of formation at absolute zero remains quantitatively or even qualitatively the same at room temperature. The assumption also that the difference $C_{\text{products}} - C_{\text{reactants}}$ remains constant down to the neighborhood of absolute zero is certainly incorrect, so that the values obtained can only be considered crude approximations. Exact calculations can be made by means of the Nernst heat theorem, but this requires an exact knowledge of the behavior of the specific heats between absolute zero and room temperature.

The determination of equilibrium diagrams in the presence of a solvent was only experimentally possible for the systems phenol–urea–water, and salicylic acid–acetamide–water. In the former case the equilibrium solid phase over a large portion of the diagram is the double compound, while in the latter the double compound is still the stable solid phase over a fairly extensive branch of the diagram. Here, again, there is no direct connection between the heat of formation, or free energy of formation, and the portion of the diagram occupied by double compound, other factors, such as solubility, entering in.

Summary

1. The object of this paper is to obtain some measure of the energy change involved in the formation of organic addition compounds.

2. Using the systems phenol–urea, phenol–*p*-toluidine, β-naphthylamine–*p*-nitrosodimethylaniline, and salicylic acid–acetamide, experimental determinations have been made, both for reactants and products, of heat of solution, specific heat, and solubility diagram (in the case of two systems only).

3. The heats of formation at room temperature and at absolute zero, have been calculated, the latter approximately only.

4. The equilibrium diagrams for the systems phenol–urea–water and salicylic acid–acetamide–water at 20°, have been outlined. In both cases the molecular compound is stable at room temperature.

WINNIPEG, MANITOBA RECEIVED JULY 31, 1939

[CONTRIBUTION FROM WILLIAM G. KERCKHOFF LABORATORIES OF THE BIOLOGICAL SCIENCES, CALIFORNIA INSTITUTE OF TECHNOLOGY]

Thermal Data XI. The Heat Capacities and Entropies of Guanidine Carbonate, Glutamic Acid Hydrochloride, Ornithine Dihydrochloride, *d*-Lactic Acid and *l*-Lactic Acid

BY HUGH M. HUFFMAN, EMORY L. ELLIS AND HENRY BORSOOK

In this paper we present the low temperature heat capacity data for the salts of three nitrogen containing organic compounds and the two optically active forms of lactic acid. These data have been utilized in conjunction with an empirical extrapolation formula to calculate the entropies of these compounds at 298.1°K.

Experimental

In principle the method of Nernst was employed with an aneroid calorimeter to determine the "true" specific heat. The details of the method have been described elsewhere[1] so that only a brief account need be given. In brief it consists of supplying, electrically, a measured amount of energy to the gold calorimeter containing the substance under investigation. To ensure rapid attainment of thermal equilibrium, the substance is pressed into dense pellets, about 2 mm. thick, and spaced along the centrally located thermocouple well by means of thin gold disks which are in good thermal contact with the walls of the calorimeter. The electrical measurements of current and voltage are made on a "White" double potentiometer

(1) Parks, THIS JOURNAL, **47**, 338 (1925).

by the proper use of accurately calibrated resistances. Time measurements are made by means of a calibrated stop watch. The temperature measurements are made by means of the White potentiometer in conjunction with a single-junction copper–constantan thermocouple. This couple is periodically standardized against one of the couples calibrated in the investigation of Giauque, Johnston and Kelley.[2]

The guanidine carbonate was an Eastman Kodak Co. product and was used without further purification. Titrations indicated that it was better than 99.8% pure. The ash content was less than 0.1%.

The *d*-glutamic acid hydrochloride was prepared from the glutamic acid used in the investigation of Huffman and Borsook.[3] Titrations indicated that it was better than 99.8% converted to the hydrochloride.

The ornithine dihydrochloride was a commercial product obtained from Hoffman–LaRoche and used without further purification. The stability of the hydrochloride was tested by placing a weighed sample *in vacuo* over phosphorus pentoxide and calcium oxide. The loss observed in twenty-four hours under the above conditions was about 0.01%. The chlorine content, determined volumetrically, was 99.7% of the theoretical. Microkjeldahl nitrogen determinations gave 98.8% of the theoretical.

The lactic acids were prepared from commercial lactic acid sirups according to the method of Borsook, Huffman and Liu.[4] Titrations showed that these preparations were better than 99.7% pure.

Discussion

The results of the heat capacity measurements in terms of the defined conventional calorie appear in Table I. In view of the purity of the compounds and the accuracy of the measurements involved, we estimate the absolute error as less than 1% except in the case of ornithine dihydrochloride.

The data for all of these compounds with the exception of those for ornithine dihydrochloride lie on smooth curves. The curve for this substance shows two humps which correspond to the melting and boiling points of hydrochloric acid and hence may indicate that a small amount of free hydrochloric acid was present. If this is the case we have estimated, from the curve, that 0.04% of hydrochloric acid would account for the humps.

We have determined the entropies of these compounds between 90 and 298.1°K. by graphical integration of a plot of C_p against ln T. In the case of ornithine dihydrochloride we have drawn a smooth curve between 140 and 200°K. The entropy between the experimental curve and the smooth curve was found to be 0.15 entropy unit per mole. If the humps are not characteristic of the substance, we estimate that the total error should not exceed 0.3 entropy unit per mole. The entropy at 90° was obtained by use of the extrapolation formula of Parks, Kelley and Huffman[5] for aliphatic substances (class I). The

TABLE I

SPECIFIC HEAT PER GRAM OF SUBSTANCE

T, °K.	C_p	T, °K.	C_p	T, °K.	C_p
Guanidine carbonate, crystals					
85.6	0.1381	180.0	0.2290	262.4	0.3073
89.5	.1438	200.2	.2488	266.8	.3113
94.1	.1477	220.2	.2679	274.3	.3187
99.9	.1532	240.2	.2866	275.3	.3208
110.0	.1633	244.3	.2905	276.2	.3213
120.0	.1732	250.0	.2962	279.4	.3256
135.6	.1871	255.9	.3015	284.9	.3306
150.2	.2007	259.8	.3050	291.4	.3378
165.5	.2153	261.1	.3067	298.1	.3434
d-Glutamic acid hydrochloride, crystals					
85.1	0.1165	151.0	0.1720	275.7	0.2572
90.5	.1215	170.5	.1856	282.7	.2620
97.3	.1282	190.4	.1998	289.8	.2671
109.3	.1390	210.9	.2134	296.8	.2714
120.0	.1480	231.0	.2262		
134.8	.1595	252.5	.2408		
Ornithine dihydrochloride, crystals					
85.3	0.1223	130.5	0.1700	187.9	0.2313
86.2	.1234	139.7	.1784	191.8	.2181
89.2	.1273	145.2	.1836	195.2	.2162
90.8	.1296	149.3	.1874	200.2	.2176
96.0	.1345	153.5	.1921	200.3	.2177
101.2	.1410	159.6	.1985	220.0	.2284
101.5	.1412	164.8	.2007	241.4	.2418
107.0	.1467	170.1	.2053	260.3	.2542
107.3	.1463	174.6	.2103	275.1	.2653
112.9	.1525	179.7	.2179	276.2	.2661
117.7	.1572	179.8	.2184	279.6	.2686
119.8	.1595	184.0	.2250	286.0	.2727
				292.8	.2778
d(*l*+)-Lactic acid, crystals					
84.2	0.1334	167.7	0.2168	275.7	0.3145
89.6	.1400	180.2	.2279	283.0	.3219
96.0	.1471	193.9	.2405	290.0	.3294
103.5	.1547	206.7	.2523	290.1	.3292
112.6	.1646	219.6	.2642	297.7	.3379
123.5	.1756	231.4	.2747	298.2	.3387
136.3	.1878	243.4	.2854	304.9	.3490
148.0	.1985	254.8	.2958	311.2	.3607
157.2	.2073	266.2	.3061		
l(*d*-)-Lactic acid, crystals					
84.1	0.1328	149.5	0.1997	277.2	0.3152
89.6	.1390	179.5	.2262	282.9	.3217
96.2	.1460	201.7	.2459	290.2	.3307
110.6	.1621	230.1	.2719	297.9	.3411
129.8	.1808	259.5	.2988		

(2) Giauque, Johnston and Kelley, THIS JOURNAL, **49**, 2367 (1927).
(3) Huffman and Borsook, *ibid.*, **54**, 4297 (1932).
(4) Borsook, Huffman and Liu, *J. Biol. Chem.*, **102**, 449 (1933).
(5) Parks, Kelley and Huffman, *J. Phys. Chem.*, **33**, 1802 (1929).

entropies thus calculated are given in Table II. Here we estimate that the uncertainty in the experimentally determined part should in all cases be less than 1%. For the extrapolated portion of the entropy it is impossible to make a reliable estimate of the uncertainty, especially in the case of the salts.

In addition to the data given above, we have made one determination of the heat of fusion of *d*(*l*+)-lactic acid. As is well known, this compound is not stable, showing a decided tendency to form a lactone and an anhydride with the elimination of water. For this reason the fusion was not very sharp; furthermore, having once been fused it was impossible, in the calorimeter, to obtain it again in the completely crystalline state. Nevertheless we believe it to be of some interest to present this preliminary value of the heat of fusion, which was found to be 4030 calories per mole.

TABLE II

ENTROPIES OF THE COMPOUNDS PER MOLE IN CAL. DEGREE^{-1} MOLE^{-1}

Substance	S_{90}	$\Delta S_{90-298.1}$	$S_{298.1}$
Guanidine carbonate	22.31	48.28	70.59
Glutamic acid hydrochloride	18.39	40.94	59.33
Ornithine dihydrochloride	21.31	48.94	70.25
d(*l*+)-Lactic acid	10.43	23.87	34.30
l(*d*−)-Lactic acid	10.26	23.75	34.00

Summary

1. The heat capacity data between 90 and 298.1°K. for five organic compounds have been presented.

2. The entropies of these five compounds at 298.1°K. have been calculated.

3. A preliminary value for the heat of fusion of *d*(*l*+)-lactic acid has been given.

PASADENA, CALIFORNIA RECEIVED DECEMBER 4, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF METALLURGY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

The Equilibrium FeO + H_2 = Fe + H_2O at Temperatures up to the Melting Point of Iron

BY JOHN CHIPMAN AND SHADBURN MARSHALL

Equilibria of iron and its lowest oxide with a gas phase containing steam and hydrogen or carbon dioxide and monoxide have been of interest in connection with the reduction of iron ore, the scaling of steel at high temperatures, the behavior of iron catalysts, and the establishment of the water gas equilibrium. Several careful researches on these equilibria have established the free energy of the lowest oxide in the form which occurs in equilibrium with solid iron at temperatures up to about 1360°. Reviews of the literature on this field were included in the papers of Emmett and Shultz[1] and of Chipman and Murphy[2] and need not be repeated here. One noteworthy paper has appeared more recently in which Britzke, Kapustinsky and Schaschkina[3] report measurements extending up to 1225°.

On account of the importance of ferrous oxide in many metallurgical reactions, a determination of its free energy at higher temperatures was undertaken. The plan of this investigation was to establish the equilibrium conditions involving steam, hydrogen, solid iron and liquid oxide over a sufficient range to permit extrapolation to the melting point of iron. At the same time a redetermination below the melting point of the oxide served as a useful check on existing data.

Experimental Method

A weight change method was adopted for the important reason that it permitted a minimum contact of the iron specimen with its support and hence a minimum contamination of either the metallic or non-metallic phase. It proved admirably suited to the problem at high temperatures where the reaction rate was rapid. As shown in Fig. 1 the specimen K was suspended from a balance A mounted directly over the tubular furnace. Commercial hydrogen was passed over platinized asbestos E at 400°, thence through a water saturator C maintained at a controlled temperature in a well-stirred oil-bath and the steam–hydrogen mixture was delivered to the bottom of the furnace. With the furnace at constant temperature, the saturator temperature was adjusted to create a gain or loss in the weight of the specimen, which, when both phases were present in the specimen, indicated respectively oxidizing and reducing conditions. When the saturator temperature was changed slowly and uniformly, it was

(1) Emmett and Shultz, THIS JOURNAL, **52**, 4268 (1930); **54**, 3780 (1932).

(2) Chipman and Murphy, *Ind. Eng. Chem.*, **25**, 319 (1933).

(3) Britzke, Kapustinsky and Schaschkina, *Z. anorg. allgem. Chem.*, **219**, 287 (1934).

possible to observe the change from gain to loss of specimen weight or *vice versa* within a very narrow temperature range. The mid-point of this range was taken as the equilibrium point and the constant was computed from the total pressure (barometric) and the known properties of steam.

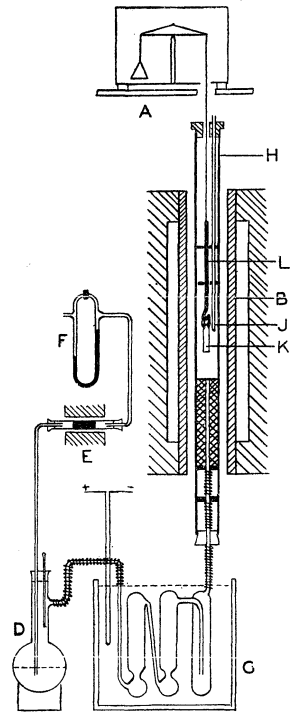


Fig. 1.—Arrangement of apparatus: A, balance; B, globar heating element; C, saturator; D, preliminary saturator; E, platinized asbestos; F, flow meter; H, impervious alumina tube; J, thermocouple protection tube; K, specimen; L, alundum rod.

The iron employed in this study was obtained in the form of rolled carbonyl iron sheet 1.2 mm. thick. This material was cut into strips 3 cm. wide and annealed in dry hydrogen inside a previously annealed Armco iron tube at 1200° for one hundred hours. After this treatment it was found to contain 0.002% oxygen; the annealing was therefore repeated after which the oxygen content was below 0.001%. The strips were cold rolled to 0.27 mm. thickness. Specimens were sheared to the desired size and cleaned in hot hydrochloric acid before use. Several pieces of the annealed strip were analyzed and the following results were the highest that were found: C below 0.005%; S below 0.004%; Si below 0.008%; Mn below 0.003%; Cu, 0.004%; P, 0.002%; Ni, 0.031; O, 0.001; N, nil.

The heating element B, Fig. 1, was a silicon carbide (Globar) tube 5 cm. inside diameter and 55 cm. long. Power was supplied by a motor generator controlled by a variable resistance in the field circuit. By hand regulation it was possible to maintain temperatures constant within ±2° up to 1600°.

Inside the heating element was placed a slightly longer tube H of impervious alumina (Alfrax 2 B). The platinum–platinum–10% rhodium thermocouple was mounted inside a small porcelain tube J (McDanel) which was inserted from the top. Cemented to this tube were two alumina disks which acted as radiation shields. For the same purpose the lower part of the tube was filled with a refractory insulating brick (K-30) the topmost piece of which extended well into the zone of uniform temperature. Between brick and disk was a distance of some 15 cm. within which no temperature differences could be detected by movement of the thermocouple. As further evidence of uniformity it was found in observations through the top of the furnace using blue furnace glasses that objects within this zone could not be distinguished. Specimens of iron 5 cm. long used in melting point determinations showed incipient melting uniformly over their entire length.

Before the first experiment the thermocouple was calibrated at the melting points of copper and nickel by an immersion method and at that of palladium (1555°) by the wire method. After expt. 4 and again after expt. 8 it was checked at the copper and palladium points. Finally, after use at the highest temperature and after several determinations of the melting point of iron, it was rechecked at the palladium point and again after the last run at the nickel and palladium points. In all of these tests the couple agreed with the standard tables within 1° and accordingly all temperatures were read from the table without correction.

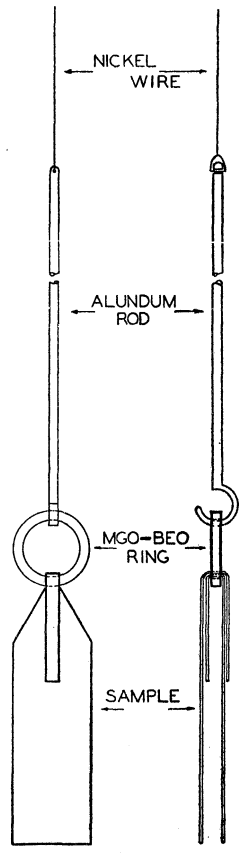


Fig. 2.—Method of suspending sample.

The saturator C was of a type which previously had been used in several investigations and had been found by thorough tests to give complete saturation of the gas. As indicated in Fig. 1, the hydrogen was given a preliminary wetting in a simple bubbler D which was held at approximately the temperature of the saturator. The latter consisted of two towers filled with glass beads and distilled water and a third empty tower which was used as a safeguard against entrainment of spray. The three towers, which were sealed together in an all-glass unit, were immersed in a well-stirred oil-bath whose temperature was controlled by hand regulation of bare wire heating coils. Temperatures were read to 0.01° by means of a four-junction copper–constantan thermocouple which was calibrated over the range used by comparison with a standard resistance thermometer. The e. m. f. of this couple and of that used in the furnace were read with an L. and N. "portable precision" potentiometer.

Several methods of mounting the specimen were tried but that shown in Fig. 2 was the only one that could be used at the highest temperatures. A thin alundum rod ground to the desired size from a larger piece extended from the hot zone to a point near the top of the furnace where it hung from the nickel wire which was suspended from the balance arm. The lower end of the rod was fashioned into a hook which supported a ring of magnesia or beryllia. The iron specimen was cut to such a shape that one end of it could be inserted through the ring and bent downward in an inverted U. Two such pieces were inserted from opposite sides and provided a total surface area of 28 sq. cm. and a weight of 3 g.

In carrying out a series of determinations the specimen was brought to a desired temperature under reducing conditions and the ratio of water vapor to hydrogen was then increased until oxidation began. It was found that the point at which a weight increase was first noted corresponded to a gas composition distinctly on the oxidizing side of equilibrium. The tendency of the metal to exhibit this passivity was quite variable and showed no definite relation to the previous preparation of the surface. In some cases oxidation began promptly and proceeded slowly and in some of the earlier runs this was confused with the equilibrium point. In one extreme case the specimen was exposed to a slightly oxidizing atmosphere at 1360° for thirty-two minutes before oxidation began. When it started suddenly, the specimen gained 0.35 g. in weight in ten minutes.

After an oxide coating had been obtained the saturation temperature was decreased until reduction was noted, then alternately increased and decreased so as to approach equilibrium slowly from each side. The record of one such determination is reproduced in Table I. Here the atmosphere has been changed from oxidizing to reducing and back to oxidizing, passing twice through the equilibrium which must correpond quite closely to the two observations indicated.

In illustration of the method of computation, the average of the two points of Table I will be used, namely, 1510° and a saturator temperature of 77.49°. The barometric pressure was 756.3 mm. (cor.) and the water vapor pressure 320.6 mm., from which P_{H_2O}/P_{H_2} is 0.734. This is the ratio at the saturator temperature which must be corrected for the deviation of water vapor from ideal gas behavior. This correction, which amounts to only 0.8 to 1.0%, was computed from the specific volume of saturated water vapor[4] and was applied to all data. The value of K corresponding to the ratio above is 0.742.

TABLE I

RECORD OF EXPERIMENT 13e

Time	Furnace temp., °C.	Saturator temp., m. v.	Oxygen, g.	Observations
4:31	1509			
4:32		12.749	0.265	Oxidizing
4:33		.753	.267	Oxidizing
4:34		.756	.268	Oxidizing
4:35	1509	.753	.270	Oxidizing
4:36		.746	.271	Oxidizing
4:37		.745[a]	.272	Oxidizing
4:38	1509	.738	.271	Reducing
4:39		.735	.271	Reducing
4:40		.734	.270	Reducing
4:41		.732	.269	Reducing
4:42	1510	.735	.268	Reducing
4:43		.736	.267	Reducing
4:44	1511	.742[a]	.267	Constant
4:45		.746	.267	Constant
4:46	1510	.750	.268	Oxidizing
4:47		.756	.269	Oxidizing

[a] Observations nearest equilibrium.

Results

A summary of all experiments is contained in Table II. The fifth column gives the approximate increase in weight of the specimen at the time of the equilibrium measurement. The last column indicates the manner in which the equilibrium gas composition was estimated, RO signifying that it was during a change from reducing to oxidizing conditions. It will be noted that many of the points constitute duplicate determinations in which the approach has been from both sides.

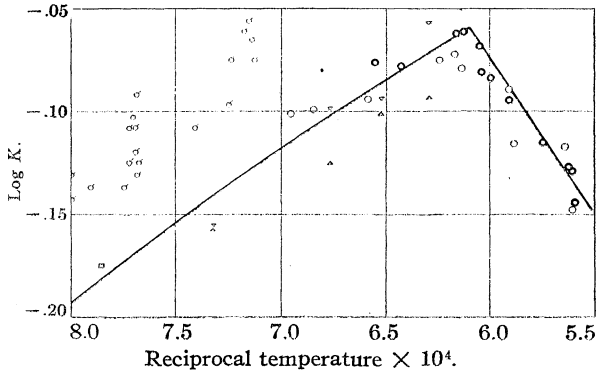


Fig. 3.—Experimental values of log (P_{H_2O}/P_{H_2}): ○, preliminary and approximate results; ●, results considered most dependable; □, Emmett and Shultz; △▽, scaling and non-scaling, Jominy and Murphy; ♂, Britzke, *et al.*

The points are plotted in Fig. 3, in which the more precise experiments are designated by larger circles. Data of other investigators within the range are included for comparison. Since certain results appear to deserve greater weight than others, a brief discussion of each experiment is in order. Experiment 2 must be regarded as a preliminary run without great precision; expt. 3 was more carefully conducted and should have yielded satisfactory results. The one result of 4 appears dependable; the support failed before a second point could be obtained. A similar occurrence prevented a satisfactory check in expt. 5. In the sixth run the equilibrium point was

(4) Landolt-Börnstein, "Tabellen," Vol. II, pp. 1318–1323.

traversed in only one direction, and for this reason the results cannot be given great weight.

It was noted that some of the samples when removed from the furnace bore evidence of diffusion of iron oxide into the magnesia support. Although the specimen was in contact with its support over only a very small area, it seemed possible nevertheless that some contamination of the iron oxide might occur. The effect of such contamination was investigated by Schenck, Franz and Willeke[5] who found that the equilibrium point was very greatly affected by all of the common refractory oxides except beryllia. Accordingly a tube of this oxide was fabricated and cut into rings which were used to support the specimens in the later experiments.

The results of expt. 8 did not differ from those in which a magnesia support was used. Experiments 9 to 12 were made to determine the melting points of iron and its oxide. During 12, two equilibrium points were observed, but these must be ruled out for the reason that a crack was found in the alumina tube after the completion of the run and neither the time of occurrence nor the effect of the crack is known. Experiment 13 was conducted after a careful survey of the possible causes of minor discrepancies in the earlier runs and its results are considered the most dependable of the series.

TABLE II

SUMMARY OF EQUILIBRIUM DATA

Expt.	Temp., °C.	K	Oxygen g.	Observations	Support
2a	1165	0.792	0.08	RO	MgO
b	1188	.797	.08	OR	
c	1246	.806	.10	OR, RO	
d	1358	.834	.04	OR, RO	
3a	1253	.840	.06	OR, RO	MgO
b	1350	.867	.01	OR, RO	
c	1386	.831	.02	OR, RO	
4	1421	.804	.07	OR, RO, OR	MgO
5a	1501	.764	.06	OR	MgO
6a	1510	.706	.05	OR	MgO
b	1427	.766	.06	OR	
c	1420	.814	.10	OR	
8a	1395	.825	.09	OR, RO	BeO
b	1467	.766	.15	RO, OR	
c	1514	.717	.12	RO, OR, RO, OR	
12a	1329	.847	.15	OR, RO	BeO
b	1348	.849	.08	OR, RO	
13a	1283	.835	.41	OR, RO	BeO
b	1360	.870	.33	RO, RO, OR	
c	1380	.855	.22	OR, RO	
d	1505	.747	.24	RO, OR	
e	1510	.742	.26	OR, RO	

(5) Schenck, Franz and Willeke, *Z. anorg. allgem. Chem.*, **184**, 1 (1929).

The two lines of Fig. 3 were drawn to conform as nearly as possible to the best experimental points (expts. 3, 4, 8, 13) and to intersect at the melting point of the oxide 1369°. The slightly curved line below the melting point represents the equation which will be deduced in a later section. Attention is called to the rather extended scale upon which log K is plotted and the smallness of the heat of reaction, two factors which combine to render clearly visible the curvature occasioned by a change in heat capacity of only 2.2 calories per degree. It may be noted also that the greatest deviations from the lines do not exceed 0.02 unit in log K, while the mean deviation of all the points tabulated is only 0.0086 unit or 0.04 calorie per degree in the free energy. The uncertainty in the four best runs is somewhat less than this. The straight line above the melting point is expressed by the equation:

$$\log K = 1583/T - 1.021 \qquad (1)$$

Melting Point of Ferrous Oxide.—The lowest oxide of iron does not have the stoichiometric composition required by the formula FeO but instead has a somewhat higher oxygen content and is stable over a range of compositions. This solid solution, which is called "wüstite," has been the subject of a number of investigations among which may be mentioned those of Pfeil[6] and of Jette and Foote.[7] They have shown that the iron-rich extremity of the solid solution field is of the constant composition 76.8% iron and it is the solid solution of this composition which is taking part in the reaction under study.

The melting point of "wüstite" has been variously recorded between 1350 and 1380°. During the course of our expt. 12, an amount of oxide corresponding to about 0.4 g. of oxygen was built up on the specimen at a temperature of 1360° and under slightly oxidizing conditions. The temperature was raised about 1° per minute until a sudden loss of weight indicated the melting and dripping of the highly fluid liquid. This occurred at 1370°. A second specimen, which was coated with oxide equivalent to 0.6 g. of oxygen was heated through the same range at a rate of 0.3° per minute. The oxide dripped off at 1369°.

(6) Pfeil, *J. Iron Steel Inst. (London)*, **123**, 237 (1931).

(7) Jette and Foote, *Trans. Am. Inst. Mining Met. Engrs.*, **105**, 276 (1933).

Another method of estimating the melting point is by the intersection of the two experimental lines shown in Fig. 3. The best lines drawn through the points of expt. 13 meet at 1365°. The direct determination is considered the more dependable and accordingly the lines of Fig. 3 are drawn to intersect at 1369°. This is to be compared with 1370° found by Tritton and Hanson[8] and 1380 ± 5° reported by Bowen and Schairer.[9]

Melting Point of Iron.—Discrepancies in the published values of the melting point of iron may be due in part to impurities in the metal. Oxygen is seldom reported in analyses of iron, yet it is normally present and is generally an important impurity in vacuum-melted iron. From its solubility in liquid iron it may be calculated that its effect on the melting point may be as large as about 10°, exact calculation being impossible in the absence of dependable data on the solid solubility.

The furnace used in the equilibrium study was well adapted to a determination of the effect of oxidation upon the melting point. We did not wish to carry out a determination in dry hydrogen for fear that reduced silicon from the refractories might be transported to the specimen. Accordingly measurements were made in hydrogen containing a limited amount of water vapor, and in a mixture approaching the equilibrium ratio. In neither case was there an appreciable change in the weight of the specimen until the melting point was reached when a drop of metal weighing one to two grams melted off. There was evidence of uniform melting over the entire length of the specimens.

From the results, which are given in Table III, we may extrapolate in both directions to obtain the melting point of oxygen-free and of oxygen-saturated iron. According to Fig. 3 the equilibrium ratio at 1524° is 0.724. Extrapolation to this ratio on the one hand and to zero on the other gives, for the melting point of oxygen-saturated metal, 1524°, and for that of pure iron, 1535°. The latter agrees well with the average of previous determinations,[10] while the former is in agreement with the temperature 1523° reported by Bowen and Schairer[9] for oxidized iron.

(8) Tritton and Hanson, *J. Iron Steel Inst.* (*London*), **110**, 90 (1924).

(9) Bowen and Schairer, *Am. J. Sci.*, **24**, 177 (1932).

(10) Cleaves and Thompson, "The Metal Iron," McGraw-Hill Book Co., Inc., New York, N. Y., 1935, p. 133.

TABLE III

MELTING POINT OF IRON

Expt.	Barometer, mm.	Saturator temp., °C.	P_{H_2O}/P_{H_2} (cor.)	M. p., °C.
9	755.9	26.0	0.034	1534.0
10	755.9	27.3	.037	1534.3
11a	756.0	76.12	.674	1524.4
11b	756.0	75.93	.666	1524.4
Extrapolated			.000	1534.7
Extrapolated			.724	1523.6

Thermodynamic Treatment.—The results reported here, together with published information at lower temperatures, include data on all of the allotropic forms of iron. Thermal data on the metal are summarized in Table IV. The sources of these data have been cited in a previous paper[2] and the only change that seems necessary is a revised equation for the heat capacity of gamma iron, bringing this into agreement with the data summarized by Austin.[11] It may be remarked that the heat effect of the α–β change, which is spread over a considerable temperature range, is lumped at one temperature for the sake of simplicity and without significant loss of accuracy. On the basis of Table IV the difference in free energy of the several forms may be expressed by the equations

$$Fe(\alpha) = Fe(\gamma);\quad \Delta F^\circ = 110 - 3.65T \ln T + 0.00283T^2 + 22.347T \quad (2)$$

$$Fe(\beta) = Fe(\gamma);\quad \Delta F^\circ = 2160 + 2.30T \ln T - 0.00057T^2 + 17.430T \quad (3)$$

The specific heat at low temperatures of an impure ferrous oxide containing 77.24% iron was determined by Millar[12] and that of a similar (probably identical) material at high temperatures by White.[13] The solid oxide which was present in our equilibrium studies was the iron-saturated solid solution "wüstite" which, according to Jette and Foote,[7] has a constant composition of 76.8% iron. These materials were doubtless sufficiently alike to permit the use of the observed specific heats in the present calculation without correction for impurities. The two sets of specific heat data may be represented by the linear equation, $c_p = 0.1663 + 0.000029T$. Now in applying this to our data it must be borne in mind that we are not dealing with a simple compound FeO but with a phase in which the average oxygen atom is combined with approximately 0.95 iron atom. The free energy calculated directly

(11) Austin, *Ind. Eng. Chem.*, **24**, 1225 (1932).

(12) Millar, THIS JOURNAL, **51**, 215 (1929).

(13) White, *ibid.*, **55**, 1047 (1933).

from the equilibrium constant is that corresponding to the formation or reduction of 69 g. of this phase containing 16 g. (23.2%) of oxygen and 53 g. (0.95 g. atom) of iron. For brevity this amount of this phase will be designated "FeO (wüstite)." The corresponding heat capacity is listed in Table IV.

The heat capacities of the two gases are taken from recent calculations based upon spectroscopic data.[14,15] They may be represented with sufficient accuracy for present purposes by the two linear equations of Table IV which are designed to cover the range 298–1700°K.

TABLE IV

THERMAL DATA ON THE REACTING SUBSTANCES

Substance	Molal heat capacity cal. mole^{-1} degree^{-1}	Heat of phase changes, cal.
Fe(α)	$3.90 + 0.00680T$	$\alpha \rightarrow \beta$; $\Delta H_{1033} = 470$
Fe(β)	9.85	$\beta \rightarrow \gamma$; $\Delta H_{1183} = 218$
Fe(γ)	$7.55 + 0.00114T$	$\gamma \rightarrow \delta$; $\Delta H_{1673} = 110$
Fe(δ)	9.85	
FeO(wüstite)	$11.47 + 0.00200T$	
H_2(g)	$6.57 + 0.00074T$	
H_2O(g)	$7.09 + 0.00270T$	

In the temperature range 1183–1642°K. the change in heat capacity in the reaction is $-3.77 + 0.00104\ T$. The free energy equation is then:

$$\text{FeO(wüstite)} + H_2(g) = 0.95\ \text{Fe}(\gamma) + H_2O(g)$$
$$\Delta F^\circ = \Delta H_0 + 3.77T \ln T - 0.00052T^2 + IT \quad (4)$$

The evaluation of ΔH_0 and I will be done graphically by means of a "sigma plot." For this purpose the equation corresponding to the above is:

$$\log K = -\Delta H_0/4.575T - 1.897 \log T + 0.0001137T - I/4.575 \quad (5)$$

from which the log K and the two terms originating in ΔC_p are grouped as "Σ." In order to include available data below 910° an additional term must be included which is found from Equations 2 and 3. Including this term, sigma is defined by the equation

$$\Sigma = \log K + 1.897 \log T - 0.0001137T - 0.95(F_\gamma - F_\alpha)/4.575T \quad (6)$$

Values of Σ are plotted against reciprocal temperature in Fig. 4. The data include for comparison the older work of Eastman and Evans,[16] which is now known to have suffered the unsuspected error of thermal separation of the gases in the static system employed.

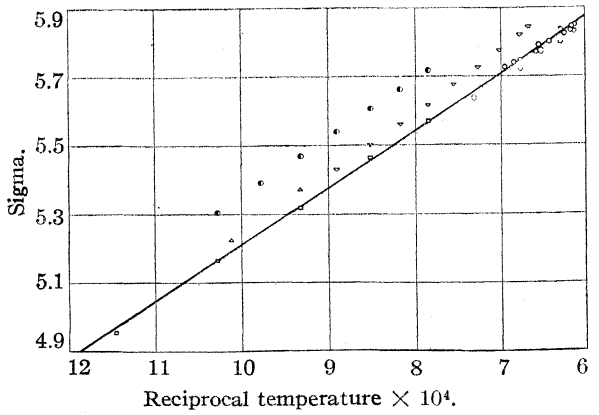


Fig. 4.—Experimental values of *sigma* of equation (6). ○, Authors; □, Emmett and Shultz; ⊙ ◡, Jominy and Murphy; △, Krings and Kempkens; ▽, Britzke, *et al.*; ◐, Eastman and Evans.

The straight line is drawn through our results and those of Emmett and Shultz.[1] The limiting oxidizing and reducing compositions of Jominy and Murphy[17] are in very good agreement with the line. Data of Krings and Kempkens[18] and of Britzke and co-workers[3] (points shown are at round temperatures) form a consistent series which, however, is in disagreement with our results.

The straight line of Fig. 4 is represented by the equation

$$\Sigma = -1653/T + 6.863 \quad (7)$$

from which the free energy change in Reaction 4 is

$$\Delta F^\circ = +7562 + 3.77T \ln T - 0.00052T^2 - 31.398T \quad (8)$$

At temperatures within the range of stability of alpha iron, Equations 2 and 8 combine to give

$$\text{FeO(wüstite)} + H_2(g) = 0.95\ \text{Fe}(\alpha) + H_2O(g) \quad (9)$$
$$\Delta F^\circ = 7457 + 7.24T \ln T - 0.00321T^2 - 52.628T$$

The free energy and heat of formation of wüstite from the elements at 25° may be obtained from the solution of Equation 9 and Rossini's[19] recently published functions for water vapor. The results are

$$0.95\ \text{Fe}(\alpha) + {}^1/_2O_2 = \text{FeO(wüstite)}$$
$$\Delta H^\circ_{298} = -63{,}380 \text{ cal.}$$
$$\Delta F^\circ_{298} = -58{,}420 \text{ cal.}$$

The corresponding value for the entropy of wüstite is 14.06 units. It is not easy to compare these results with calorimetric determinations since the latter have been based upon the erroneous assumption of a simple stoichiometric compound. Roth and his co-workers[20] report 64.2 kilocalories as the heat of formation of FeO

(14) Gordon, *J. Chem. Phys.*, **2**, 65, 549 (1934).
(15) Davis and Johnston, THIS JOURNAL, **56**, 1045 (1934).
(16) Eastman and Evans, THIS JOURNAL, **46**, 888 (1924).
(17) Jominy and Murphy, *Ind. Eng. Chem.*, **23**, 384 (1931).
(18) Krings and Kempkens, *Z. anorg. allgem. Chem.*, **183**, 225 (1929); **190**, 313 (1930).
(19) Rossini, *Bur. Standards J. Research*, **22**, 407 (1939).
(20) Roth, Umbach and Chall, *Arch. Eisenhüttenw.*, **4**, 87 (1930).

and Millar[12] reports its entropy as 12.7 ± 2.0 units.

At temperatures above the melting point of the oxide, there are no data on either its heat capacity or its composition. And since the heat effect at the gamma–delta transformation is quite small, the equilibrium involving solid iron and molten oxide may be represented by the following simple equation in which "FeO(l)" represents a quantity of the liquid oxide containing 16 g. of oxygen

$$\mathrm{FeO(l)} + \mathrm{H_2} = \mathrm{Fe}(\gamma \text{ or } \delta) + \mathrm{H_2O}$$
$$\Delta F^\circ = -7240 + 4.67T \qquad (10)$$

The heat of fusion of wüstite is found from the two free energy equations to be 10,000 calories per mole. Here the "mole" contains 16 g. of oxygen but only 53 g. of iron below the melting point and an undetermined amount in the liquid. The calculated heat thus includes the effect of any change in composition of the oxide. It may be pointed out that this is less than half the magnitude of the heat effect calculated from the data of Jominy and Murphy,[17] the discrepancy arising from disagreement in equilibrium data above the melting point of the oxide.

Summary

The equilibrium of iron and its oxide with steam and hydrogen has been investigated in the range 1200–1515°.

Below the melting point of the oxide the new results and those of Emmett and Shultz are expressed by an equation which agrees essentially with the data of Jominy and Murphy.

Above the melting point the value of $K = P_{H_2O}/P_{H_2}$ is given by: $\log K = 1583/T - 1.021$.

The melting point of the equilibrium oxide was found to be 1369°; its heat of fusion 10,000 calories per mole.

The melting points of oxygen-free and oxygen-saturated iron were found to be, respectively, 1535° and 1524°.

CAMBRIDGE, MASSACHUSETTS

RECEIVED OCTOBER 23, 1939

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, NO. 723]

An Investigation of the Complex Structure of the O–H Harmonic Bands of Substituted Alcohols, and of the Effect of Temperature on the Relative Intensities of the Multiplet Components

BY LLOYD R. ZUMWALT AND RICHARD M. BADGER

It has been observed that the fundamental and harmonic O–H vibration bands of alcohols and substituted phenols frequently consist of two or more components even in cases of substances which have only one hydroxyl group per molecule.[1,2,3] When this multiplet structure persists under conditions such as to exclude association it has often been attributed to the presence of two or more molecular species with slightly different O–H frequencies. These different species have usually been supposed to represent merely different stable molecular configurations which result from restricted rotation about one or more single bonds.

Such an explanation, however useful in some cases, must be subject to some suspicion and cannot finally be accepted without further tests since in some cases the apparent complexity of the O–H bands is probably due merely to an accidental near superposition of other harmonic or combination bands. In other instances a multiplet band may represent merely a band sequence, as has been shown to be true of the N–H bands of pyrrole.[4]

The criteria by which complex O–H bands due to the presence of several molecular species may be recognized are as follows. First, a similar pattern should be found in fundamental and harmonic regions, but the separations between the components should be roughly proportional to the number of the harmonic. Second, the relative intensities of the components should, in general, be dependent on the temperature, provided of course that equilibrium between the various molecular species is established. Third, the individual bands making up a multiplet should have different rotational structures. Pauling's explanation of the *o*-chlorophenol spectrum[5] stands up under the first two tests. The third criterion seldom can be

(1) Wulf and Liddel, THIS JOURNAL, 57, 1464 (1935).
(2) Badger and Bauer, *J. Chem. Phys.*, 4, 711 (1936).
(3) Barchewitz and Freymann, *Compt. rend.*, 204, 1728 (1937).
(4) Zumwalt and Badger, *J. Chem. Phys.*, 7, 629 (1939).
(5) L. Pauling, THIS JOURNAL, 58, 94 (1936).

applied for obvious reasons, but in the case of ethyl alcohol the two components of the O–H bands have obviously quite different structures.[2]

In some simple cases the number of components observed in the O–H bands agrees with the number of stable molecular configurations which are predicted by very reasonable considerations, but unfortunately many of the substances whose spectra have been studied are too complicated to permit of a detailed discussion at present. In view of the present interest in hindered rotation around single bonds, it has seemed worth while to study a number of substances so simple that the observations may be capable of a unique interpretation. To avoid complications due to the solvent and to possible association the investigations have been made on the vapor. Furthermore, in order to give additional support to the explanations invoked, a quantitative study of the temperature effect on the relative intensities of the components of the multiplets has been carried out in three cases. A qualitative study of the effect of temperature on *o*-chlorophenol[6] has already been made, but the small separation between the bands in the fundamental region appears to introduce some difficulty in drawing any quantitative conclusions. Consequently this substance has been included in our investigations with results which are very interesting.

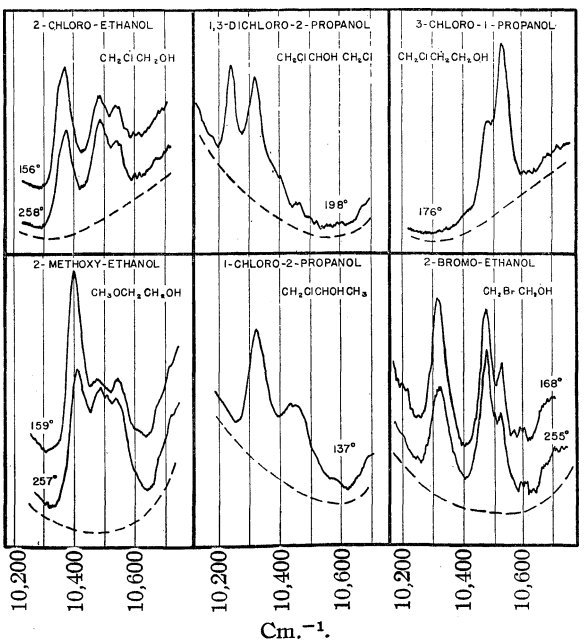


Fig. 1.—Microphotometer curves of the third harmonic O–H absorption bands of the vapors of six substituted alcohols. The temperature of the vapor is indicated in the diagrams. The dashed lines represent the trend of the background blackening.

(6) M. M. Davies, *Trans. Faraday Soc.*, **34**, 1427 (1938).

Materials.—The substances investigated were all Eastman Kodak Co. products unless otherwise specified and the boiling points given are corrected to 760 mm. pressure. The propylene chlorohydrin, ethylene bromohydrin, trimethylene bromohydrin, and *o*-chlorophenol (b. p. 174.3° at 749 mm.) were used without further purification. The refractive indices of the first three were found to be $n^{20.6}$D 1.4370, $n^{20.5}$D 1.4928 and $n^{24.5}$D 1.4885, respectively. The propyl alcohol ("practical"), ethylene chlorohydrin, 2-methoxyethanol (Mefford Chemical Company), and *sym*-glycerol dichlorohydrin ("practical") were purified by fractional distillation and boiled at 97.2, 128.9, 124.1 and 174.4°, respectively.

Measurement of the boiling points of *o*-chlorophenol under reduced pressure gave its entropy of vaporization at 175° as 21.9 cal./deg.

Apparatus and Experimental Procedure.—This investigation was carried out with the use of a Littrow glass spectrograph with a dispersion of about 70 Å. per mm. at λ 9000. Eastman 144-Q and 1-Z infrared plates were used. The absorption spectra were obtained at about one atmosphere with a path length of three meters.

Microphotometer curves for the bands of each alcohol were obtained as well as the curves for plates exposed when the absorption cell was filled with water vapor and when the absorption cell was empty. The latter were taken to get the positions and shapes of the water absorption bands (which might be superimposed on alcohol O–H bands) and to get the curve corresponding to background blackening. The sensitivity of the 144-Q plates changes very markedly with wave length in this region.

Results of Studies on the Substituted Alcohols.—The absorption maxima of the substituted alcohols studied are listed in Table I. Figure 1 gives the microphotometer curves of the O–H third harmonic bands of these alcohols. The microphotometer curves are uncorrected for change in plate sensitivity with wave length. The dashed line below the curves indicates the trend of the background blackening. The different observed trends correspond to different batches of plates used. The only appreciable water vapor absorption occurs always at frequencies a little higher than those of the alcohol O–H

TABLE I

ABSORPTION MAXIMA IN THE O–H THIRD HARMONIC BANDS OF THE VAPORS OF SEVEN SUBSTITUTED ALCOHOLS

Substance	Absorption maxima (cm.⁻¹)		
2-Chloroethanol	10,367	10,485	10,546
2-Bromoethanol	10,318	10,470	10,527
2-Methoxyethanol	10,394	10,472	10,538
3-Chloro-1-propanol	10,467	10,525	
3-Bromo-1-propanol	10,470	10,529	
1-Chloro-2-propanol	10,326	10,460	
1,3-Dichloro-2-propanol	10,243	10,325	

vibrations. The ordinates of the microphotometer curves do not have any absolute significance as they were obtained with different microphotometer settings, plate blackenings, and concentrations of the absorbing substance.

Substituted Ethanols.—From the above data it is evident that the two O–H bands which Badger and Bauer[2] found to be characteristic of primary alcohols persist in 2-methoxyethanol, ethylene chlorohydrin, and ethylene bromohydrin, though there is a slight shift to higher frequencies and considerable change in relative intensities. The weaker component has apparently become the stronger. These two bands we may attribute to molecular configurations in which the environment of the O–H group is similar to that in ethanol. In addition, however, a new strong band has appeared at a frequency around 100 cm.$^{-1}$ lower.[6a]

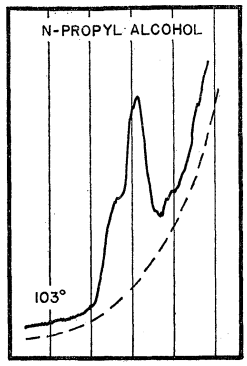


Fig. 2.—Microphotometer curve of the third harmonic O–H absorption bands of *n*-propyl alcohol.

The new band appears to be analogous to the strong long wave component which appears in the O–H bands when a halogen is substituted in the ortho position in phenol. We attribute it to chelation in a five-membered ring through the formation of a hydrogen bond between hydroxyl oxygen and other oxygen, chlorine, or bromine as the case may be. In the three compounds studied the new band is found at increasingly long wave lengths in the order just given, which is reminiscent of the observations of Wulf, Liddel and Hendricks[7] on ortho substituted phenols. As has previously been shown[8] the progressive shift to lower frequencies is an indication of increasing strength of hydrogen bond. Of the series studied the oxygen to oxygen bond appears to be the weakest and the oxygen to bromine the strongest. Possibly this is to be attributed to the differences in size of the electronegative atoms, permitting closest approach to the hydroxyl oxygen in the case of bromine.

As mentioned above, it is evident that in the substituted ethanols two types of configuration have reasonable stability in which the environment of the hydroxyl hydrogen is similar to that found in the unsubstituted primary alcohols. These configurations, however, must be less stable than the chelated structure. This is indicated by the great intensity and low frequency of the new band. Moreover, this is supported by the effect of temperature, which may be seen in Fig. 1. With increasing temperature the intensities of the short wave bands increase greatly at the expense of the low frequency component showing that they correspond to higher energy states. The temperature effect will be discussed more quantitatively below.

Substituted Normal Propyl Alcohols.—Both trimethylene chlorohydrin and trimethylene bromohydrin have O–H bands which appear to be identical with those of ordinary primary alcohols. It seems surprising that there is no indication of a hydrogen bond between halogen and oxygen with the formation of a six-membered ring, but such is the case. We may conclude that in configurations in which the oxygen halogen distance is favorable for the formation of a hydrogen bond the strain arising from the hindered rotation about the C–C single bonds is too great to permit the bond to be formed.

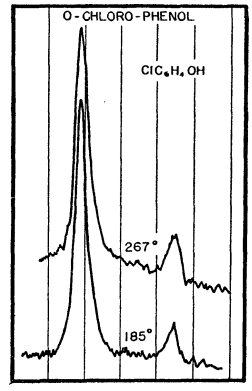


Fig. 3.—Microphotometer curve of the third harmonic O–H absorption bands of *o*-chlorophenol at two temperatures.

Substituted Secondary Alcohols.—Propylene chlorohydrin has the rather broad band characteristic of secondary alcohols and in addition a narrower, more intense component at lower frequencies. The latter may again be attributed to a chelated form with a five-membered ring involving a hydrogen bond between oxygen and chlorine.

On the substitution of the second chlorine in *sym*-glycerol dichlorohydrin the ordinary second-

(6a) Wall and Claussen [THIS JOURNAL, **61**, 2679 (1939)] failed to find any very definite evidence of chelation in ethoxyethanol and believed that they had shown its absence. They could, however, hardly expect to resolve the bands due to chelated and unchelated molecules which in this case should be separated in the fundamental region, by less than 30 cm.$^{-1}$. The chelation should undoubtedly be less in carbon tetrachloride solution than in the vapor but the curves of Wall and Claussen taken at high dilution indicate that it is not entirely absent since the band they observed is shifted to slightly longer wave lengths than normal and seems rather broad.

(7) Wulf, Liddel and Hendricks, THIS JOURNAL, **58**, 2287 (1936).

(8) Badger and Bauer, *J. Chem. Phys.*, **5**, 839 (1937).

ary alcohol band has been reduced to a mere trace while a third, new component appears at quite low frequency. We suggest that the 10,325 cm.$^{-1}$ band, as in propylene chlorohydrin, corresponds to a situation in which a hydrogen bond links the hydroxyl oxygen to one chlorine atom, while the 10,243 cm.$^{-1}$ band results from a situation in which the hydroxyl hydrogen interacts with both chlorine atoms. In the latter case we have a double ring chelation.[9]

Investigation of the Temperature Effect.—A quantitative photometric investigation was conducted of the effect of temperature on the relative intensities of the components of the O–H bands of *o*-chlorophenol, ethylene chlorohydrin and propyl alcohol. These experiments involved the keeping of the absorption cell at constant temperature and the regulation of the pressure of the vapor within the cell. The temperature of the cell was read by means of a thermometer inserted in a well in its midsection and could be kept constant by means of automatic voltage control on the heating circuit. It is believed that the actual temperature of the vapor was within three or four degrees of the corrected thermometer readings. The pressure of the vapor was controlled by regulating the temperature of a side tube which contained an excess of liquid and was at all times cooler than the absorption cell. In the experiments on *o*-chlorophenol the side tube dipped in a well agitated oil-bath, the temperature of which was constant to within two-tenths of a degree. In the other cases an auxiliary furnace was used.

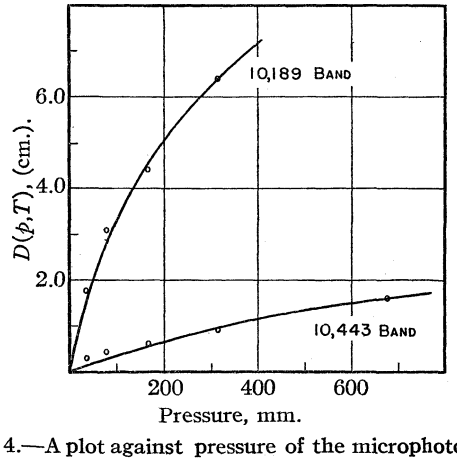


Fig. 4.—A plot against pressure of the microphotometer deflections $D_t(p,T)$ and $D_c(p,T)$ for the *o*-chlorophenol bands at 10,443 cm.$^{-1}$ and 10,189 cm.$^{-1}$, respectively. The data were obtained from a group of exposures taken on one plate with the vapor at approximately 180°, and at a series of pressures.

(9) The crystal structure of glycine indicates the occurrence of a somewhat similar situation in which one of the hydrogen atoms of the NH_3^+ group is attracted about equally strongly by two oxygen atoms; see Albrecht and Corey, THIS JOURNAL, 61, 1087 (1939).

In estimating the pressure of the vapor, data in the "International Critical Tables" were used except in the case of *o*-chlorophenol. As mentioned above, the boiling point of this substance was observed at several pressures.

The Photometric Procedure.—Precise photometry in the infrared with ammoniated plates is rather difficult, but a simplified procedure was devised which worked quite well. It involves certain assumptions which are discussed below, but these seem to be well justified and unlikely to introduce any large error. Difficulties due to the non-uniformity of the plates were largely avoided by taking all exposures of a complete series on one and the same plate, and indeed on a strip down the center of the plate where sensitization was most uniform. All exposures of a series were taken with constant illumination and equal exposure times. The warping of the absorption cell as the temperature was changed necessitated a slight compensating adjustment of one mirror in the optical train, but a fairly satisfactory constancy of background blackening through a series was attained.

Each series of exposures included two groups taken at two temperatures of the absorption cell, T_1 and T_2, respectively, and each group usually included spectra taken at several different pressures. The entire set of spectrograms was run through the microphotometer with the sensitivity of that instrument kept constant.

The interpretation of a series of records will now be described with special reference to *o*-chlorophenol. The difference between the microphotometer deflections at the band maximum and the deflection corresponding to background blackening was taken as a measure of the intensity of a band. This quantity, which is a function of pressure and temperature, we shall designate by $D_c(p,T)$ or $D_t(p,T)$ when referring, respectively, to the 10,189 cm.$^{-1}$ band (arising from molecules in the *cis* form) or the 10,433 cm.$^{-1}$ band of *o*-chlorophenol (arising from *trans* molecules). A plot of these quantities against pressure for a group of exposures taken at approximately 180° may be seen in Fig. 4.

Now the investigations of Wulf and Liddel[1] in the second harmonic region have shown that the total integral molal absorption coefficient for the

two O–H bands of *o*-chlorophenol is practically the same as for the one band of phenol and also for the one band of 2,4,6-trichlorophenol. From this it is most reasonable to conclude that the transition probabilities are practically the same for the *cis* and *trans* forms of *o*-chlorophenol, and that the concentrations of the two forms are in the ratio of the intensities of their corresponding bands.

Owing to experimental difficulties it was not possible to determine integral absorption coefficients or to compare directly the intensity of the two bands. However, if at any given temperature, T_1, the intensity of the "*cis*" band at pressure p_1 is the same as that of the "*trans*" band at p_2, it is evident that the ratio of *cis* and *trans* forms of the molecule at T_1 is given by $(n_c/n_t) = (p_2/p_1)$.

High dispersion studies have shown that the two bands have practically the same shape and breadth.[2] Furthermore, the IZ plates used have a sensitivity which is very nearly constant with wave length over a considerable range. Consequently when $D_c(p_1,T)$ and $D_t(p_2,T)$ are equal the intensity of the "*cis*" band at p_1 is equal to that of the "*trans*" band at p_2 to a good approximation.

It follows that the two curves of Fig. 4 should be practically superposable if the abscissas of the curve corresponding to the 10,443 cm.$^{-1}$ band are reduced by an appropriate factor s. Consequently we may write $(n_c/n_t) = (1/s)$, and the free energy increase for the transformation

o-chlorophenol (*cis*) ⟶ *o*-chlorophenol (*trans*) (1)

is given by the equation

$$\Delta F = RT \ln (n_c/n_t) = RT \ln (1/s) \qquad (2)$$

The energy increase for the same transformation is given by

$$\Delta E = \frac{T_2T_1}{T_2 - T_1} R \ln \frac{(n_c/n_t)_{T_1}}{(n_c/n_t)_{T_2}} = \frac{T_2T_1}{T_2 - T_1} R \ln \frac{(1/s)_{T_1}}{(1/s)_{T_2}} \qquad (3)$$

The evaluation of this expression involves obtaining data at a second temperature T_2. Fewer measurements were made at the higher temperatures owing to greater difficulty in keeping steady conditions, and consequently it was assumed that the shapes of the $D(p,T)$ curves were the same at T_2 as at T_1. This assumption is good unless the *shape* of the band envelopes differs considerably at the two temperatures. This can scarcely be the case. The bands will broaden slightly with temperature but the shape of the envelopes should not change materially.

In the evaluation of the energy difference between *cis* and *trans* forms of the molecule it is not necessary to assume equal transition probabilities for the two molecular species and equal widths and shapes of the two bands. This results from the fact that equation 3 involves the ratio of two concentration ratios.

Possibly the largest error in the determinations arises from the difficulty in precisely estimating the $D(p,T)$ quantities, due to the grain of the plate. This is particularly true in the case of the weaker band where the error of measurement may be as large as 20%.

Results of the Measurements of Temperature Effect.—Three preliminary experiments I, II and III were made on *o*-chlorophenol, and two more extensive studies, IV and V. These are summarized in Table II.

TABLE II

PHOTOMETRIC STUDY OF *o*-CHLOROPHENOL

$D_t(p,T)$ (cm.)	$D_c(p,T)$ (cm.)	T(°K.) of vapor	p(mm. Hg.) of vapor	$\Delta F°$ (kg.-cal./mole)	$\Delta E°$ (kg.-cal./mole)
		Expt. I			
0.43	3.90	453	255	2.2	
.57	5.70	453	410		
.70	3.56	542			4.3
.96	5.05	543			
		Expt. II			
0.73	4.22	459	133		
.83	5.24	459	192	2.6	
.94	6.16	459	281		
1.37	6.50	539			3.5
		Expt. III			
0.56	4.30	457	146		
.78	5.39	458	232	2.6	
.89	6.49	458	334		
.90	5.20	540			2.8
1.09	5.87	540			3.7
		Expt. IV			
0.40	1.99	460	32.6		
.43	3.41	460	79.3		
.61	4.37	461	160	3.0	
.98	6.42	461	301		
1.53	..	463	638		
0.92	4.53	534			4.3
.79	4.29	537			3.6
.87	4.50	537			3.8
		Expt. V			
0.30	1.76	450	36.7		
.50	3.10	450	78.5		
.62	4.42	451	166	2.7	
.91	6.39	450	314		
1.60	..	451	676		
0.70	3.25	537			4.5
.60	2.87	537			4.6
.58	3.14	537			3.6
			Weighted av.	2.8	3.9

An average of the several determinations shows that in the temperature range covered the energy increase for the *cis–trans* transformation is 3.9 ± 0.7 kgcal. per mole. For the same reaction the free energy increase is 2.8 ± 0.5 kgcal. per mole and the entropy increase 2.4 E. U. at 180°.

In the study of *n*-propyl alcohol it was found that the change in intensity ratio of the two O–H bands is practically within experimental error. From this we estimate that the difference in energy of the two hypothetical configurations is not greater than about 0.8 kgcal. per mole.

In ethylene chlorohydrin, also, the relative intensities of the two bands characteristic of primary alcohols did not change appreciably. Consequently the data in Table III were used to determine the difference between the average energy of the forms corresponding to these bands and the energy of the chelated structure. The former was found to exceed the latter by 2.0 ± 0.5 kgcal.

TABLE III

PHOTOMETRIC STUDY OF ETHYLENE CHLOROHYDRIN

$D_a(p,T)$[a] (cm.)	$D_b(p,T)$[a] (cm.)	$D_c(p,T)$[a] (cm.)	T(°K.) of vapor	p(mm. Hg.) of vapor	$\Delta E°$ (kg.-cal./mole)
		Expt. I			
1.00	1.61	2.87	425	490	
1.22	1.89	3.29	425	646	1.9
2.05	2.96	4.90	425	1048	
1.42	2.22	2.60	531		
		Expt. II			
1.00	1.72	2.87	420	417	
1.65	2.40	3.99	421	709	2.1
2.29	3.42	5.12	421	1120	
0.87	1.32	1.70	516		
					Av. 2.0

[a] The quantities D_a, D_b and D_c refer to the ethylene chlorohydrin absorption maxima at 10,546, 10,485 and 10,367 cm.$^{-1}$, respectively.

Discussion of the Studies on Temperature Effect.—Badger and Bauer have pointed out that there appears to be a convenient relation between the frequency shift in the O–H bands which takes place on the formation of a hydrogen bond and the energy of the bond. In a letter which will be published soon it will be shown that the data here reported confirm the existence of this relation, which will now be applied in a discussion of *o*-chlorophenol.

Our value of 2.8 kgcal. for the free energy difference between *cis* and *trans* forms of *o*-chlorophenol in the vapor state at 180° may at first seem in disagreement with the estimate of 1.4 kgcal. given by Pauling for the substance in carbon tetrachloride solution at room temperature. There is, however, no reason to suppose that this is the case. The percentage frequency difference between the two bands of the substance in solution indicates a difference in energy of two forms of only about 2.9 kgcal. as against our value of 3.9 kgcal. for the vapor. This apparent discrepancy is to be accounted for by the stabilizing effect of the solvent on the *trans* form. When the vapor of a normal alcohol is dissolved in carbon tetrachloride the shift in O–H frequency indicates an energy of interaction between solvent and the hydroxyl group of between one and two kgcal. Consequently it is not surprising that *trans o*-chlorophenol is stabilized to about this extent in carbon tetrachloride solution.

The considerable difference in entropy of the *cis* and *trans* forms is rather surprising. It appears difficult to account for it entirely in terms of the torsional oscillations of the hydroxyl hydrogen about the two potential minima. In the explanation of the double O–H bands of *o*-chlorophenol it has been assumed that there are two distinct molecular species present or, in other words, that the energy levels of the *o*-chlorophenol molecule may be divided into two classes which may be ascribed to molecules in which the hydroxyl hydrogen is performing torsional vibrations about the *cis* or *trans* minima, respectively. It does not seem possible to construct a potential function for the rotation of the hydrogen about the C–O bond which will yield a sufficient number of levels of the second class to account for the entropy difference. It is possible that the high frequency band is partly due to molecules in which the hydrogen is performing complete rotations. In the lower lying levels for which this is the case the atom will spend most of its time on the side of the molecule opposite the chlorine atom, owing to the broad shallow character of the upper minimum. For this reason the O–H frequency in this species of molecule might not differ greatly from that in a vibrating *trans* molecule.

However, a portion, and perhaps the main part, of the entropy difference may be due to another factor. In the *cis* molecular species at least two bending vibrations must have considerably higher frequencies than in the *trans* form, owing to the contribution of the hydrogen bond to the rigidity of the chelated structure.

Summary

1. An investigation has been made of the complex structure of the third harmonic O–H bands of ethylene chloro and bromohydrin, methyl cellosolve, trimethylene chloro and bromohydrin, propylene chlorohydrin, and *sym*-glycerol dichlorohydrin. These substances were all studied in the vapor state. In all cases except trimethylene chloro and bromohydrin the substitution of a halogen or a methoxy group in the alcohol has given rise to one or more new O–H bands.

2. Photometric studies have been made of the effect of temperature on the relative intensities of the components of the O–H bands in *o*-chlorophenol, propyl alcohol and ethylene chlorohydrin. It is found that in the vapor state at 180° the energy and free energy of the *trans* form of *o*-chlorophenol exceed those of the *cis* form by 3.9 ± 0.7 and 2.8 ± 0.5 kgcal., respectively.

PASADENA, CALIF. RECEIVED AUGUST 28, 1939

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

Allylic Rearrangements. X. The Reproducibility of the Standard Methods for the Preparation of Butenyl Bromide Mixtures[1]

BY WILLIAM G. YOUNG AND KENZIE NOZAKI

As a result of a recent study[2] of the composition of butenyl bromide mixtures obtained from crotyl alcohol and methylvinylcarbinol by the action of various solutions of hydrogen bromide *under controlled conditions*, a mechanism was proposed for the reaction[3] in which two simultaneous processes were considered. Process 1 assumed an opportunity for resonance of the reacting oxonium ion of the alcohol and hence for the formation of the same mixture of bromides from either the primary or secondary alcohols. Process 2, a normal substitution without resonance, gives only primary bromide from the primary alcohol and secondary bromide from the secondary alcohol. Since the values calculated for M (the fraction of alcohol reacting by Process 2), N_r (the refractive index of the bromide mixture formed by Process 1) and P_r (the percentage of primary bromide in the bromide mixture formed by Process 1 due to resonance) are dependent on the accuracy with which the composition of the butenyl bromide mixtures (prepared by the various standard methods) can be determined, it is highly desirable to test the reproducibility of the standard methods; especially since we have continually pointed out the difficulties encountered by other workers due to the extreme mobility of the bromides.

The results of the present investigation are summarized in Table I along with the results previously reported.[2,3] In general, the average deviation of the refractive index of the butenyl bromide mixture obtained from the same alcohol with a given standard method is ±0.0001 although with the standard method 3 (saturated hydrobromic acid at 0°) the mean deviation is ±0.00016. Two cases were observed where the previous results were in error. The action of hydrogen bromide gas at −20° on methylvinylcarbinol gave a bromide mixture with a refractive index 0.0010 unit lower than that previously reported, showing that a small amount of rearrangement had occurred in the previous case in spite of the special precautions which were taken to avoid it. The discrepancy observed between the results obtained by method 7 (the action of glacial acetic acid saturated with hydrogen bromide at 0°) on crotyl alcohol were traced to a different cause. A preliminary run proved that insufficient time had been allowed for the reaction (twenty-five min.). Hence the product contained traces of unreacted alcohol. This was indicated by a low Carius analysis (Br = 57.7% instead of 59.2%). As a result, the rearrangement of the sample at 100°, to get the corrected refractive index, caused the formation of dibutenyl ether which lowered the refractive index of the sample. Proof of this was found when a mixture of butenyl bromides was contaminated with a quantity of crotyl alcohol comparable with that suspected to be present in the bromide mixture prepared in

(1) This work, which was accomplished with the aid of a grant from the Board of Research of the University of California, was presented before Section C of the Pacific Division of the American Association for the Advancement of Science at Stanford University, June 29, 1939.

(2) Young and Lane, THIS JOURNAL, **59**, 2051 (1937).

(3) Young and Lane, *ibid.*, **60**, 847 (1938).

TABLE I

SUMMARY OF COMPOSITIONS OF BUTENYL BROMIDES OBTAINED FROM CROTYL ALCOHOL AND METHYLVINYLCARBINOL UNDER CONTROLLED CONDITIONS

Standard experimental method	Butenol used	$n^{25}D$ of bromide mixture (cor.) Young and Lane[2,3]	$n^{25}D$ of bromide mixture (cor.) Young and Nozaki	Compn. of bromide mixture,[a] % Primary bromide	Compn. of bromide mixture,[a] % Secondary bromide	Diff. in % primary bromide from primary and secondary alcohols
1. 48% HBr at −15°	Primary	1.4768 1.4768	1.4767 1.4769	86.0	14.0	2.8
	Secondary	1.4763 1.4762	1.4763	83.2	16.8	
2. 48% HBr + H_2SO_4 at −15°	Primary	1.4764	1.4764	84.0	16.0	4.2
	Secondary	1.4755	1.4757	79.8	20.2	
3. Saturated HBr at 0°	Primary	1.4755 1.4752	1.4756 1.4758 1.4756	79.3	20.7 ± 1.5	5.6
	Secondary	1.4746 1.4745	1.4742	73.7	26.3 ± 1.0	
4. HBr gas at −20°	Primary	1.4761	1.4763	82.9	17.1	12.2
	Secondary	1.4749	1.4739 1.4738	(70.7)	(29.3)	
7. Glacial AcOH satd. HBr gas at 0°	Primary	1.4763	1.4767	(85.5)	(14.5)	13.7
	Secondary	1.4740	1.4741	71.8	28.2	

[a] All percentages are the average of the results of both determinations except those enclosed in parentheses which are based on the present work only.

acetic acid by standard method 7. After rearrangement the contaminated bromide possessed a refractive index 0.0003 unit lower than it should, showing that ether had been formed. Consequently the time allowed for reaction by standard method 7 was increased to forty-five minutes. Using the modified procedure, both crotyl alcohol and methylvinylcarbinol gave bromide mixtures free from alcohol (Br = 59.23%). The revised values for the compositions of the bromide mixtures (columns 5 and 6) and for the differences in % primary bromide in the bromide mixtures obtained from the primary and secondary alcohols (column 7) are averages of the results of both investigations except for the two cases discussed above where the results of the present investigation are shown to be more reliable.

The Thermal Rearrangement of the Butenyl Bromides.—One objection to the previous work done in correlating the compositions of butenyl bromide mixtures produced from the butenols (by resonance process 1B) with those of the equilibrium mixtures produced by thermal rearrangement of the primary and secondary bromides under the same conditions, was that the thermal rearrangements were carried out in two-phase systems. Further work on the rearrangement of butenyl bromides (this time dissolved in a solution of hydrogen bromide in glacial acetic acid) gives a product having a refractive index qualitatively in agreement with N_r calculated[3] from the data obtained under the same conditions (standard method 7). When attempts were made to rearrange the primary and secondary butenyl bromides at room temperature in glacial acetic acid saturated with hydrogen bromide, it was discovered that addition of hydrogen bromide occurred faster than rearrangement. As a result the product was a mixture of dibromobutanes. However, at 15° in the presence of a trace of benzoyl peroxide it was possible to obtain a thermal equilibrium of the bromides before too large a quantity of dibromobutane had been formed. Although the last two runs listed in Table II show a qualitative agreement between the equilibrium refractive index of $n^{25}D$ 1.4765 and calculated value n^{25}_r 1.4764, it is recognized that the interpretation may be debatable. It should be recognized, however, that the accuracy of the work was limited in two ways. First, it was difficult to allow sufficient time to establish equilibrium without producing large quantities of dibromobutane; second, it was necessary to effect a quantitative separation of the mono and dibromides at low temperatures to avoid rearrangement of the butenyl bromide portion. Runs 1 and 2 are of little value since they were carried out with short reaction times and obviously had not come to equilibrium.

TABLE II

THE THERMAL REARRANGEMENT OF BUTENYL BROMIDES AT 15° IN GLACIAL ACETIC ACID SATURATED WITH HYDROGEN BROMIDE

Run	Butenyl bromide	$n^{25}D$ of crude bromide before fractionation	$n^{25}D$ of butenyl bromide fraction	$n^{25}D$ after rearrangement at 100°	$n^{25}D$ of butenyl bromide mixt. (corrected)[2]
1	Primary	1.4900	1.4779	1.4774	1.4772
2	Secondary	1.4820	1.4761	1.4766	1.4762
3	Primary	1.4890	1.4768	1.4771	1.4764
4	Secondary	1.4920	1.4771	1.4772	1.4766

Experimental Part

Alcohols.—Crotyl alcohol, b. p. 121–122°, was prepared by the aluminum isopropoxide method.[4,5] Methylvinylcarbinol, 96–97°, $n^{25}D$ 1.4110, was supplied by the Shell Development Company, through the courtesy of Dr. E. C. Williams.

Pure Butenyl Bromides.—Crotyl bromide, and methylvinylcarbinyl bromide were prepared as previously described.[6]

The Synthesis of Butenyl Bromide Mixtures from Crotyl Alcohol and Methylvinylcarbinol by Standard Methods.—The reproducibility of the standard methods reported by Young and Lane,[2,3] for preparing butenyl mixtures under controlled conditions, has been tested. The exact directions described by them for synthesizing and purifying the bromide mixtures have been followed except in the case of method 3 (saturated hydrobromic acid at 0°), and method 7 (glacial acetic acid saturated with hydrogen bromide at 0°) where the total reaction times were extended twenty minutes. This was done to assure completion of the reaction since in a preliminary run with method 7 the bromide mixture contained traces of crotyl alcohol which reacted with the bromide during the rearrangement at 100° and consequently interfered with the determination of the corrected refractive index. After this modification had been made the bromide preparations always contained the correct amount of bromine by Carius analysis.

The Rearrangement of Pure Butenyl Bromides in Glacial Acetic Acid Saturated with Hydrogen Bromide.—Since preliminary attempts to rearrange the butenyl bromides at 25° gave only 2,3-dibromobutane, while runs at 0° gave too slow rearrangement, it was necessary to add benzoyl peroxide[7] to speed up the rearrangement and to choose a temperature at which equilibrium of the bromide could be attained without excessive amounts of dibromides being formed. The final procedure adopted is given below: thirty-five grams of glacial acetic acid was placed in a glass-stoppered oil sample bottle and saturated with hydrogen bromide at 10°. After 8.0 g. of pure primary or secondary butenyl bromide, 0.4 g. of benzoyl peroxide and 1.5 ml. of water were added, the bottle was stoppered and the mixture shaken for fifteen to twenty minutes at 15°. The mixture was then cooled rapidly to 0° and poured over 100 g. of crushed ice and 35 g. of sodium bicarbonate in a 500-ml. separatory funnel. As soon as the initial effervescence had subsided, 35 g. of bicarbonate and more ice were added. The neutralization of the acid took nearly an hour but the ice and salt mixture present maintained a temperature several degrees below zero. The bromide layer was next washed twice with cold bicarbonate solution, then with ice water and placed over anhydrous calcium chloride at −15° for several hours. The resulting crude, dry bromide mixture was partially purified by evaporation at 2 mm. pressure. The butenyl bromide portion was then separated from dibromides by fractionation at 3 mm. pressure through a 20-cm. column which was filled with glass helices and equipped with a Hopkins condenser and an ice-filled jacket. The experimental results are shown in Table II.

Summary

The standard methods developed by Young and Lane[2] for preparing butenyl bromide mixtures from butenols under controlled conditions have been tested with both crotyl alcohol and methylvinylcarbinol. The compositions of the bromide mixtures produced are in good agreement with those previously reported except for two cases which have been explained.

The thermal rearrangement of pure primary and secondary butenyl bromides in glacial acetic acid saturated with hydrogen bromide produces equilibrium mixtures which possess refractive indices qualitatively in agreement with the calculated value of n_r or the bromide mixture produced from the butenols by process 1[3] involving resonance.

LOS ANGELES, CALIFORNIA RECEIVED AUGUST 29, 1939

(4) Young, Hartung and Crossley, THIS JOURNAL, **58**, 100 (1936).

(5) The crotonaldehyde used in preparing the crotyl alcohol was kindly furnished by the Niacet Chemicals Corporation, through the courtesy of Mr. G. M. Bramann.

(6) (a) Young and Lane, THIS JOURNAL, **59**, 2054 (1937); (b) Winstein and Young, *ibid.*, **58**, 104 (1936).

(7) Kharasch, Margolis and Mayo, *J. Org. Chem.*, **1**, 397 (1936).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BRYN MAWR COLLEGE]

The Introduction of Substituted Vinyl Groups. IV. (Primary 1-Alkenyl) Alkyl Malonic Esters

BY ARTHUR C. COPE, WALTER H. HARTUNG,[1,2] EVELYN M. HANCOCK AND FRANK S. CROSSLEY[2]

Previous articles in this series have described practical methods of preparing disubstituted malonic and cyanoacetic esters in which one substituent is a "secondary 1-alkenyl" group, RCH=C(R')—.[3] These esters were produced by alkylating alkylidene esters, obtained by condensing ketones with malonic and cyanoacetic esters.

In order to introduce "primary 1-alkenyl" groups, RCH=CH—, or RR'C=CH—, into malonic ester by a similar process, it would be necessary to start with the condensation products of aldehydes with ethyl malonate.

$$\underset{\text{I}}{RCH_2CH{=}C(COOEt)_2} \xrightarrow[\text{or } NaNH_2]{NaOR,\ Na,} \underset{\text{II}}{[RCH{=}CH{-}C(COOEt)_2]^-Na^+}$$

$$\text{II} + R'X \longrightarrow \underset{\text{III}}{RCH{=}CHC(R')(COOEt)_2} + NaX$$

Ethyl (1-butenyl)-methylmalonate has been prepared in this manner by Kon, Linstead and Maclennan.[4] The utility of the reaction as a general synthetic method remained open to question, however, both because of the ease with which substituted vinyl alkylmalonic esters undergo alcoholysis,[3a,b] and the instability of "primary alkylidene" malonic esters. These alkylidene esters (I), in the presence of alkaline reagents, readily undergo a reversal of the condensation reaction by means of which they are prepared, giving the aldehyde and malonic ester, or products derived from them.

Actually, the synthesis of *vinyl* alkylmalonic esters according to the above equation (R = H) proved to be very unsuccessful, almost all of the ethylidene malonic ester being transformed into a high boiling polymer. With alkylidene malonic esters prepared from propionaldehyde, butyraldehyde, and other higher aldehydes, however, the synthesis is successful if conditions are chosen which minimize alcoholysis and polymerization. The alkylidene esters are preferably added to sodium alkoxide–alcohol solutions at low temperatures, in the preparation of the sodium derivatives, and then alkylated rapidly by adding the alkylating agent in one portion and immediately heating to the boiling point. Under these conditions, a large part of the enolate is alkylated, and the proportion of high boiling polymer is greatly reduced.

The success of these alkylations in alcohol solution is surprising, for similar alkylations of secondary alkylidene malonic esters in alcohol gave poor yields.[3a,b] This difference in behavior on alkylation is probably due to the fact that the branched groups present in enolates derived from secondary alkylidene esters (*i. e.*, $[RCH{=}C(R')C(COOEt)_2]^-Na^+$) hinder the introduction of alkyl groups.[5] Consequently, when such enolates are treated with alkyl halides in alcohol solution, a large part of the reaction which occurs involves the sodium alkoxide with which the enolate is in equilibrium and the alkyl halide. This side reaction converts most of the enolate back into the original alkylidene ester. The primary 1-alkenyl groups present in the enolates (II) derived from primary alkylidene malonic esters, however, present no steric hindrance opposing the introduction of an alkyl group, and the alkylation of these enolates proceeds normally.

The data recorded in Table I show that in this series the yield of alkylated esters (III) depends in part upon the size of the alkylidene group in the ester employed. The yields become higher as the size of the alkylidene group increases, reaching a maximum of 86 to 93% with the isopentylidene ester. The alkylations occur more rapidly with the higher members of the series; as a result the products are in contact with the sodium enolates (and the sodium alkoxides with which they are in equilibrium) for a shorter time, and there is less opportunity for their destruction by alcoholysis.

The use of sodamide in liquid ammonia or in inert solvents is inadvisable for preparing the

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(3) (a) Cope and Hancock, THIS JOURNAL, **60**, 2644 (1938); (b) **60**, 2901 (1938); (c) **60**, 2903 (1938).

(4) Kon, Linstead and Maclennan, *J. Chem. Soc.*, 2452 (1932).

(5) Monoalkyl malonic esters containing saturated secondary alkyl groups, such as isopropyl and secondary butyl, are difficult to alkylate: *cf.* Fischer and Dilthey, *Ann.*, **335**, 337 (1904); Shonle, Keltch and Swanson, THIS JOURNAL, **52**, 2440 (1930).

TABLE I

PRIMARY 1-ALKENYL ALKYL MALONIC ESTERS

Primary 1-alkenyl group	Alkylating agent	Hours refluxed[a]	Yield, %	Boiling point, °C. (uncor.)	Mm.	$n^{25}D$	d^{25}_{25}	Molecular refraction Calcd.	Found	Formula	Carbon,[b] % Calcd.	Found	Hydrogen,[b] % Calcd.	Found
Propenyl	PrI	4	51	138–140	20	1.4371	0.9774	65.09	65.11	$C_{13}H_{22}O_4$	64.42	64.43	9.16	9.33
CH_3CH=	*i*-PrI	4.5	35[c]	135–135.5	19	1.4404	.9842	65.09	65.09	$C_{13}H_{22}O_4$	64.42	64.20	9.16	9.20
CH—	BuI	5.5	50	148–151	20	1.4390	.9687	69.71	69.77	$C_{14}H_{24}O_4$	65.58	65.38	9.42	9.51
1-Butenyl	EtI	5	75	134–135	18	1.4367	.9745	65.09	65.31	$C_{13}H_{22}O_4$	64.42	64.27	9.16	9.25
CH_3CH_2-	PrBr	5	55	142–145	19	1.4375	.9637	69.71	69.92	$C_{14}H_{24}O_4$	65.58	65.35	9.42	9.48
CH=CH—	*i*-PrBr	6	67[d]	141–143	19	1.4400	.9710	69.71	69.73	$C_{14}H_{24}O_4$	65.58	65.62	9.42	9.41
	Allyl Br	1	79	144–145	17	1.4470	.9776	69.24	69.67	$C_{14}H_{22}O_4$	66.10	66.01	8.73	8.87
	BuBr	5	59	152–156	19	1.4390	.9561	74.33	74.55	$C_{15}H_{26}O_4$	66.62	66.75	9.70	9.78
	s-BuBr	7	21	159–160	28	1.4425	.9689	74.33	74.08	$C_{15}H_{26}O_4$	66.62	66.36	9.70	9.74
Isobutenyl $(CH_3)_2C$=CH—	EtI	0.5	40[e]	140–141	24	1.4395	.9837	65.09	65.01	$C_{13}H_{22}O_4$	64.42	64.24	9.16	9.25
1-Pentenyl	EtBr	3.5	60	154–157	27	1.4374	.9656	69.71	69.77	$C_{14}H_{24}O_4$	65.58	65.41	9.42	9.56
$CH_3CH_2CH_2$-	PrBr	3	65	161–163	26	1.4381	.9551	74.33	74.49	$C_{15}H_{26}O_4$	66.62	66.42	9.70	9.94
CH=CH—	*i*-PrI	3.5	70	160–163	28	1.4410	.9627	74.33	74.34	$C_{15}H_{26}O_4$	66.62	66.48	9.70	9.69
1-Isopentenyl	MeI	0.1	93	119–122	9	1.4348	.9647	65.09	65.68	$C_{13}H_{22}O_4$	64.42	64.17	9.16	9.16
$(CH_3)_2CH$-	EtI	0.3	88	141–142	19	1.4350	.9568	69.71	70.07	$C_{14}H_{24}O_4$	65.58	65.43	9.42	9.42
CH=CH—	PrBr	1	86	154–156	26	1.4349	.9487	74.33	74.52	$C_{15}H_{26}O_4$	66.62	66.27	9.70	9.68
	i-PrBr	0.5	86	152–153.5	26	1.4372	.9545	74.33	74.41	$C_{15}H_{26}O_4$	66.62	66.75	9.70	9.63
1-Hexenyl	MeI	0.8	82	164–166	27	1.4407	.9647	69.71	70.29	$C_{14}H_{24}O_4$	65.58	65.63	9.42	9.69
$CH_3CH_2CH_2$-	EtBr	3	58	168–169.5	28	1.4410	.9612	74.33	74.45	$C_{15}H_{26}O_4$	66.62	66.37	9.70	9.61
CH_2CH=CH—														

[a] In each case, the reaction of the alkyl halide with the sodium enolate was exothermic at the boiling point, and most of the material had reacted in the first few minutes of refluxing. [b] We are indebted to Miss Corris Hofmann for semi-micro combustions. [c] Yield of the mixed ethyl and isopropyl esters obtained by alkylation in isopropyl alcohol was 82%, calculated as the ethyl ester. [d] Yield of the mixed ethyl and isopropyl esters obtained by alkylation in isopropyl alcohol was 83%. [e] The sodium enolate prepared from isobutylidene malonic ester was quite insoluble in alcohol. An impurity was removed from this ester by shaking with concd. aqueous ammonia.

sodium enolates (II) in this series. Apparently, partial decomposition occurs during the reaction with sodamide, and subsequent alkylation gives rather impure products in poor yield. The poor results obtained with sodamide in this series are in contrast with those obtained with secondary alkylidene malonic esters, which are alkylated in the highest yield by the sodamide procedure.[3a,b] Powdered sodium in inert solvents reacts readily with the primary alkylidene esters to give sodium enolates but, as in the series previously described, a part of the ester is reduced in the process, and alkylation gives a product containing the corresponding saturated ester as an impurity.

Experimental Part

The primary alkylidene malonic esters were prepared by condensing aldehydes with ethyl malonate, either in the presence of acetic anhydride,[6] or by a method using amine salts which will be described in a future communication.

Alkylation Procedures. A.—A description of the synthesis of ethyl (1-isopentenyl)-ethylmalonate will illustrate a procedure which gave good results in all of the alkylations. A solution of 8.05 g. of sodium (0.35 mole) in 300 cc. of absolute alcohol contained in a 500-cc. three-necked flask was cooled to −5°. Ethyl isopentylidene malonate, 79.8 g. (0.35 mole), was added dropwise with stirring during ten minutes. The solution was stirred for twenty minutes at −5 to −10°, after which 65.5 g. (0.42 mole) of ethyl iodide was added in one portion and the solution rapidly heated to boiling. The vigorous reaction which took place at the boiling point made it necessary to cool the flask momentarily in an ice-bath. The mixture was practically neutral to litmus after five minutes, and it was refluxed for only twenty minutes. The contents of the flask were cooled and diluted with 800 cc. of water. The ester layer was separated, and the water layer extracted four times with benzene. The combined ester and benzene extracts were washed twice with water, after which the benzene was removed in vacuum and the residue distilled through a Widmer column. The ester so prepared is one of nineteen substituted vinyl alkylmalonic esters described in Table I.

In the first preparations, the esters were shaken with concd. aqueous ammonia before the final distillation, in order to remove any alkylidene ester which might remain in the product. The portion of the alkylidene ester which is not alkylated is usually converted to a high boiling polymer during the reaction, however, and trial showed that the treatment with ammonia is superfluous, as there was no loss in weight on shaking with ammonia and no change in physical constants of the products, except in one case (*cf.* Table I). The alkylations carried out with the less active alkyl halides do not become completely neutral. In such cases, small aliquot portions were removed and titrated with standard acid from time to time. The refluxing was continued until the per cent. neutralization was constant.

In two cases in which relatively low yields of alkylated esters were obtained by the above procedure, alkylations

(6) *Cf.* Schryver, *J. Chem. Soc.*, **63**, 1344 (1893); Kötz, *J. prakt. Chem.*, [2] **75**, 477 (1907); Boxer and Linstead, *J. Chem. Soc.*, 749 (1931).

also were carried out in isopropyl alcohol solution, under conditions recently used for the alkylation of alkylidene cyanoacetic esters.[3c] In both cases the yields were higher in isopropyl than in ethyl alcohol (see footnotes to Table I). This is evidence that alcoholysis is an important factor influencing the yields in this synthesis.

B.—Ethyl butylidenemalonate reacts with powdered sodium in ether or benzene solution, just as isopropylidene malonic ester does,[3a] giving a soluble sodium derivative. Methylation with dimethyl sulfate gave a 50–60% yield of ethyl (1-butenyl)-methylmalonate, b. p. 130–132° (24 mm.). The ester was purified by shaking with ammonia and refractionation, but quantitative reductions required only 86% of the theoretical quantity of hydrogen, showing the presence of a saturated ester in the product. In preparing a disubstituted barbituric acid derivative from this partially reduced ester, by condensation with urea, in one case a small amount of 5-methyl-5-butylbarbituric acid, m. p. 179–179.5° (uncor.), was isolated,[7] proving the presence of ethyl butylmethylmalonate in the ester prepared by this method.

C.—Ethyl butylidenemalonate was treated with sodamide, in liquid ammonia solution and suspended in both ether and toluene. A sodium derivative was formed in each case, but alkylation in ether or toluene with both diethyl sulfate and allyl bromide gave poor yields (10 to 40%) of impure esters.

(7) Summaire, *Bull. soc. chim.*, **33**, 189 (1923), reports m. p. 181°.

Summary

Primary alkylidene malonic esters, $RCH_2CH{=}C(COOEt)_2$, react with sodium ethoxide and sodium isopropoxide to give sodium derivatives of primary 1-alkenylmalonic esters, $[RCH{=}CHC(COOEt)_2]^-Na^+$. These sodium derivatives may be alkylated readily, giving substituted vinyl alkyl malonic esters of the type, $RCH{=}CH{-}C(R')(COOEt)_2$.

BRYN MAWR, PENNSYLVANIA

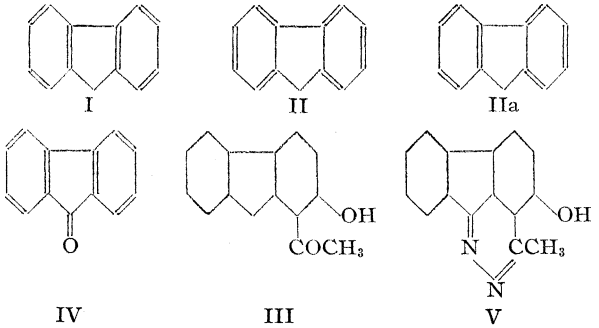
RECEIVED NOVEMBER 7, 1939

[CONTRIBUTION FROM THE DANIEL SIEFF RESEARCH INSTITUTE]

Remarks on the Structure of Fluorene

BY ERNST BERGMANN AND T. BERLIN

W. C. Lothrop has published[1] an interesting paper on the fine structure of fluorene. Some time ago, we experimented on similar lines.[2] Agreeing with the conclusions drawn by Lothrop to the effect that fluorene is not to be represented by exclusively one of the formulas I or II (and possibly IIa), we should like to supplement his evidence by reporting briefly some of our results.



IV III V

In addition to the rearrangement of 2-allyloxyfluorene, we have also studied that of 2-acetoxyfluorene. Under the influence of aluminum chloride, an isomer is formed in moderate yield, to which we ascribe the formula III of 1-acetyl-2-hydroxyfluorene on the basis of its unreactivity toward hydroxylamine, III being an *o,o'*-disubstituted acetophenone.[3] This rearranging reaction appears to take place on form I, which, by the way, is also responsible for the formation of the 9-sodium derivative of fluorene.[4] On the other hand, it has been shown before,[5] that the Kolbe reaction with 2-hydroxyfluorene leads to two isomeric 2-hydroxyfluorenecarboxylic acids, most probably the 1- and the 3-compounds. By the same reasoning as above, they would owe their formation to the fine structures I and II, respectively.

Similar observations have been made in the series of fluorenones, the quinone-like properties of which would be accounted for most fittingly by formula (IV).[6] The rearrangement product of 2-acetoxyfluorenone is 1-acetyl-2-hydroxyfluorenone, as it forms with hydrazine hydrate a pyridazine (V), analogous to that we could obtain from 1-benzoylfluorenone. The rearrangement of 2-allyloxyfluorenone, however, gave two isomers,

(1) Lothrop, THIS JOURNAL, **61**, 2115 (1939).

(2) T. Berlin, Thesis, Jerusalem University, 1939.

(3) See, *e. g.*, Claus and Foecking, *Ber.*, **20**, 3101 (1887); Baum, *ibid.*, **28**, 3207 (1895); V. Meyer and co-workers, *ibid.*, **29**, 830, *seq.* (1896).

(4) Compare Hueckel, *Z. Elektrochem.*, **43**, 779 (1937).

(5) German Patent 350,293; Friedlaender, *Fortschritte der Teerfarben-Industrie*, **18**, 599.

(6) Color! For the spectrum, see Böeseken and co-workers, *Rec. trav. chim.*, **44**, 188 (1925).

orming a well-crystallized molecular compound. After hydrogenation of the allyl double bond, two hydroxypropylfluorenones were separated, apparently the 1- and the 3-propyl-2-hydroxy compounds. This indicates that in fluorenone, too, the double bonds have no fixed position, the form represented by (IV) perhaps being somewhat favored.

Experimental

1-Acetyl-2-hydroxyfluorene (III).—2-Acetoxyfluorene (4.1 g.), prepared from 2-hydroxyfluorene[7] with acetic anhydride according to Claborn and Haller,[8] was heated at 80° for three hours with a solution of aluminum chloride (3.6 g.) in nitrobenzene (30 cc.). The reaction product was decomposed with cold dilute hydrochloric acid, the nitrobenzene removed with steam and the residue dried and extracted with carbon tetrachloride in a Soxhlet apparatus. The product soluble in carbon tetrachloride was triturated with methyl alcohol and some acetone and recrystallized from butyl alcohol or 25% acetic acid as long yellowish needles, m. p. 159°; yield, 0.6 g. *Anal.* Calcd. for $C_{15}H_{12}O_2$: C, 80.3; H, 5.4. Found: C, 79.8; H, 5.3. With hydroxylamine in alcohol, no reaction occurred.

1-Acetyl-2-hydroxyfluorenone.—2-Acetoxyfluorenone[8] (3 g.) was treated with aluminum chloride (2.8 g.) in nitrobenzene (20 cc.) as above. After removal of the solvent, the product was recrystallized from xylene as red, bent crystals, m. p. 206°. *Anal.* Calcd. for $C_{15}H_{10}O_3$: C, 75.6; H, 4.2. Found: C, 76.0; H, 4.3.

Pyridazine Derivative (V).—The diketone (300 mg.) was heated with hydrazine hydrate (64 mg.) in alcoholic solution (5 cc.), for three hours. The solvent was evaporated and the residue, after trituration with toluene containing some methyl ethyl ketone, recrystallized from toluene as yellow crystals, m. p. 197° (dec.). The combustion analysis was unsatisfactory (Calcd. for $C_{15}H_{10}ON_2$: C, 76.9; H, 4.3. Found: C, 75.0; H, 4.6); so was that of the **pyridazine derivative of 1-benzoylfluorenone;** 1-benzoyl-fluorenone[9] (500 mg.; b. p. 245°/0.4 mm.; m. p. 114–116°) was boiled with hydrazine hydrate (56 mg.) in alcohol (5 cc.) for two hours. The product obtained by evaporation of the solvent was triturated with acetone and recrystallized from benzene as yellow platelets, m. p. 181°. *Anal.* Calcd. for $C_{20}H_{12}O_2$: C, 85.7; H, 4.3. Found: C, 84.6; H, 4.5.

It may be mentioned that the rearrangement of 2-acetoxyfluorenone, when carried out at 115°, gave a substance different from the 1-acetyl-2-hydroxyfluorene described above; it crystallized from butyl alcohol, had m. p. 249° and gave analytical figures pointing to the formula $C_{15}H_{12}O_3$ (instead of $C_{15}H_{10}O_3$) (Calcd. C, 75.0; H, 5.0. Found: C, 75.3, 75.4; H, 5.4, 4.9). The structure of this compound (which might be bimolecular) has not been dealt with.

2-Allyloxyfluorenone.—2-Hydroxyfluorenone[7] (4 g.) was heated with allyl bromide (2.7 g.) and potassium hydroxide (2 g.) in alcohol (40 cc.) until neutrality (ten hours). The reaction product, separating on cooling, was dissolved in ether and extracted several times with concentrated potassium hydroxide solution. From light petroleum, containing some acetone, it gave crystals, m. p. 84–85°, yield, 2.2 g. *Anal.* Calcd. for $C_{16}H_{12}O_2$: C, 81.3; H, 5.1. Found: C, 80.7; H, 5.6.

Molecular Compound of 1-Allyl-2-hydroxy- and 3-Allyl-2-hydroxyfluorenone.—The foregoing compound (1 g.) was heated at 200° for three hours and then distilled under 0.05 mm. pressure. The red oil, distilling at 186°, was triturated with light petroleum (b. p. 130°) and recrystallized from benzene or 25% acetic acid as orange-red needles, m. p. 125–126°; yield, 0.6 g. *Anal.* Calcd. for $C_{16}H_{12}O_2$: C, 81.3; H, 5.1. Found: C, 80.9; H, 5.2.

1-Propyl- and 3-Propyl-2-hydroxyfluorenone.—The foregoing compound (2 g.) was treated with a current of hydrogen in boiling propyl alcohol (50 cc.), containing the palladous hydroxide catalyst (1 g.) of Kuhn and Stroebele,[10] for eighteen hours. The solvent was evaporated and the residue recrystallized from aqueous alcohol (1:1) as clusters of yellow needles, m. p. 202° (after repeated recrystallization from the same solvent) crystallized spontaneously (*Anal.* Calcd. for $C_{16}H_{14}O_2$: C, 80.7; H, 6.0. Found: C, 79.3; H, 6.4), while the darker-yellow isomer, m. p. 155°, appeared, when the mother liquor was concentrated. *Anal.* Calcd. for $C_{16}H_{14}O_2$: C, 80.7; H, 6.0. Found: C, 79.6; H, 5.8.

Summary

2-Acetoxyfluorene and 2-acetoxyfluorenone, on Fries rearrangement, give the 1-acetyl-2-hydroxy compounds.

From 2-allyloxyfluorenone, both 1- and 3-allyl-2-hydroxyfluorenones are obtained in the form of a molecular compound.

These facts support the conclusion drawn by Lothrop[1] that no fixed "fine structure" exists in fluorene; the dibenzocyclopentadiene formula, however, seems to prevail.

REHOVOTH, PALESTINE RECEIVED OCTOBER 17, 1939

(7) Diels, *Ber.*, **34**, 1758 (1901).

(8) Claborn and Haller, THIS JOURNAL, **59**, 1055 (1937).

(9) Koelsch, *ibid.*, **54**, 4744 (1932).

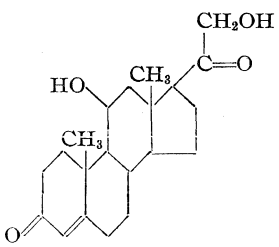
(10) Kuhn and Stroebele, *Ber.*, **70**, 785 (1937).

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY OF PRINCETON UNIVERSITY]

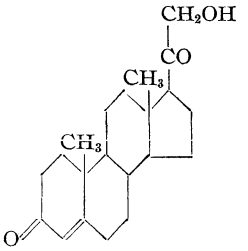
Studies on the Partial Synthesis of Corticosterone. I

BY PURNENDU NATH CHAKRAVORTY[1] AND EVERETT S. WALLIS

Through the pioneering investigations of Rogoff,[2] Swingle[3] and Hartman[4] the existence of a powerful hormone in the adrenal gland, other than adrenalin, was established. The method of Swingle and Pfiffner[5] for the preparation of concentrates of this hormone has been widely used, and has culminated in the isolation of several crystalline products, notably by three groups of investigators led by Reichstein[6] at Zürich, Kendall[7] at the Mayo Clinic and Wintersteiner[8] at Columbia University. Among these crystalline materials which have been isolated some have been found to be inactive and the structures of the few physiologically active compounds are still uncertain on certain points. Corticosterone, the most potent of the crystalline compounds, has been assigned formula I.



I



II

It has been the purpose of our investigations to find a method of synthesis of the above substance, thereby settling the structural question and also providing adequate amounts of the hormone for clinical investigations.

Stieger and Reichstein[9] have prepared a very active compound, "desoxycorticosterone" (formula II) but the starting material is rather difficult to obtain, and recent clinical tests have thrown great doubt on its value for medicinal use. In our efforts to obtain corticosterone we started from desoxycholic acid which is easily available. Of the several methods tried, that shown in the diagram seems to be most promising.

Desoxycholic acid was oxidized in the cold directly to 3-oxy-12-ketocholanic acid III by a method first described by Kaziro and Shimada.[10] The yield was very good and the material so obtained was easy to purify. The methyl ester of this acid prepared for the first time melted at 143° The acetoxy derivative (m. p. 197°) on treatment with bromine either in chloroform or acetic acid solution in the presence of hydrogen bromide gave a bromide, IV, which could be used directly for dehalogenation. The introduction of the double bond was effected with sodium ethylate, the unsaturated keto acid so obtained melting at 173°. Its acetate melts at 199°. An analysis and determination of its absorption spectra showed that it was the desired 3-oxy-12-keto-9,11-cholenic acid, V. If dehalogenation was effected with zinc and acetic acid, the saturated 3-oxy-12-ketocholanic acid was produced in good yields. It is also to be recorded that dehalogenation with sodium acetate and acetic acid failed to give the desired product.

Treatment of the above acid with semicarbazide acetate gave a semicarbazone which melted at 221°. It is interesting to note in this connection that whereas 3-oxy-12-ketocholanic acid gives a semicarbazone only after twelve hours of refluxing with the reagent, this unsaturated acid requires but two hours similar treatment. Thus, as one might expect, the conjugated double bond makes the 12-keto group more reactive. The semicarbazone thus obtained was reduced by heating it with sodium ethylate in a sealed tube for fifteen hours at 180°. On working up the reaction product the corresponding methylenic compound, VI, is obtained in readily crystallizable form. It is contaminated, as would be expected, with a small amount of its epimer, β-3-oxy-9,11-cholenic acid, but this latter compound is removed

(1) Research Assistant on Special Funds from the Rockefeller Foundation.

(2) Rogoff and Stewart, *Amer. J. Physiol.*, **84**, 660 (1928); *J. Am. Med. Assoc.*, **92**, 1569 (1929).

(3) Swingle and Pfiffner, *Science*, **71**, 321 (1930).

(4) Hartman and Brownel, *ibid.*, **72**, 76 (1930); Hartman, *Am. J. Physiol.*, **95** 670 (1930).

(5) Swingle and Pfiffner, *Am. J. Physiol.*, **96** 153, 164, 180 (1930); *ibid.*, **98**, 144 (1931). See also Pfiffner, Vars and Taylor, *J. Biol. Chem.*, **106**, 625 (1934), and Cartland and Kuizenga, *ibid.*, **116**, 57 (1936).

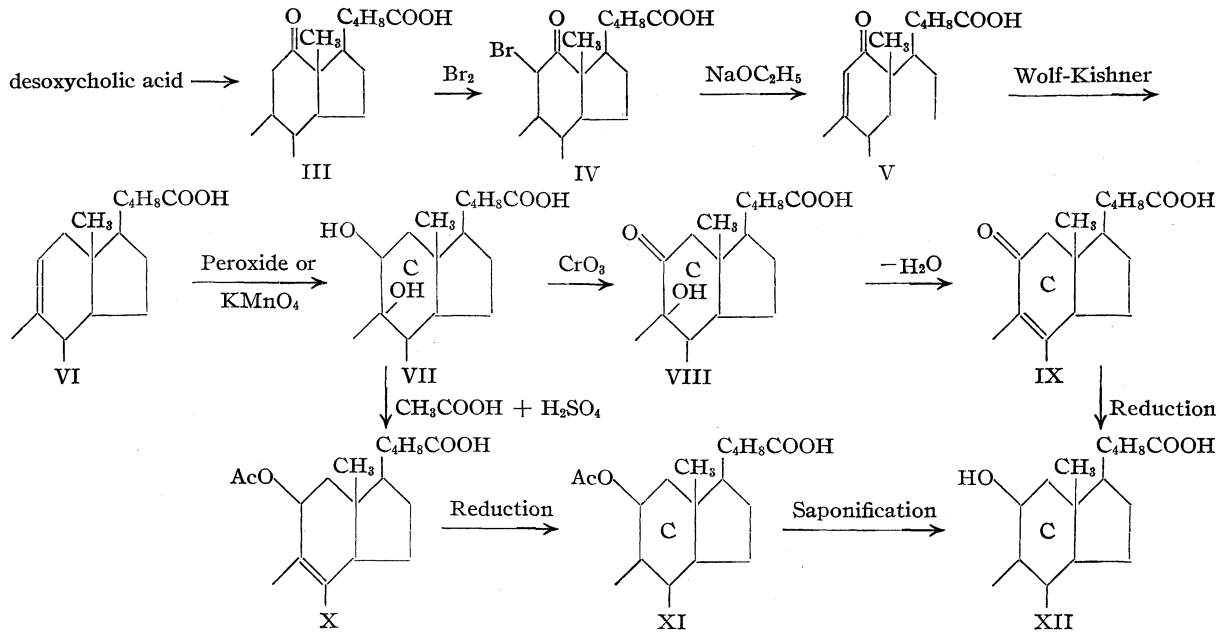
(6) Reichstein et alia, *Helv. Chim. Acta*, **19**, 29, 223, 401, 402, 979 (1936).

(7) Kendall and co-workers, *Proc. Staff Meetings Mayo Clinic*, **8**, 90 (1933).

(8) Wintersteiner, Vars and Pfiffner, *J. Biol. Chem.*, **109**, c (1934). See also Pfiffner, Vars, Bott and Swingle, *Proc. Soc. Exp. Biol. Med.*, **29**, 998, 1267 (1931–1932).

(9) Stieger and Reichstein, *Nature*, **139**, 925 (1937); *Helv. Chim. Acta*, **20**, 1164 (1937).

(10) Kaziro and Shimada, *Hoppe-Seyler, Z. physiol. Chem.*, **249**, 220 (1937). See also Bergström and Haslewood, *J. Chem. Soc.*, 541 (1939).



by recrystallization from acetone. α-3-Oxy-9,11-cholenic acid crystallizes in needles from acetone which melt at 183–184°. Further reactions of this compound will be reported in a later paper.

Experimental Part

Preparation of 3-Acetoxy-12-ketocholanic Acid.—This acid was prepared according to the method of Kaziro and Shimada[10] as described by Bergström and Haslewood.[10] It was converted into its acetoxy derivative in the usual manner.

Preparation of 3-Hydroxy-12-keto-9,11-cholenic Acid.—Five grams of 3-acetoxy-12-ketocholanic acid was dissolved in 15 cc. of glacial acetic acid, and treated with 15 cc. of a 1.05 *N* acetic acid solution of bromine. A few drops of a 34% aqueous solution of hydrogen bromide were added as a catalyst. The solution was then kept at 70° for four hours and allowed to stand overnight at room temperature. After this time it was poured into ice water and the amorphous powder which precipitated was filtered. After thorough washing with water it was dissolved in ether, and the ether solution again washed to remove all traces of hydrobromic acid. After drying with sodium sulfate the ether was evaporated to dryness and the bromide, which was obtained as a sticky reddish residue, was taken up immediately in absolute alcohol and poured into a boiling solution of sodium ethylate (prepared from 6 g. of sodium dissolved in 70 cc. of absolute alcohol). Immediately the mixture became very dark brown and some sodium bromide precipitated. Refluxing was continued for two hours, after which time a considerable amount of sodium bromide had precipitated. The condenser was then removed and after sufficient water had been added to dissolve the salt the boiling was continued to remove as much of the alcohol as possible. The reaction mixture was then cooled with ice water and to it was added an ice cold solution of 20% sulfuric acid. After standing in the icebox for one-half hour, the precipitated acid so obtained was filtered and washed free from sulfuric acid. It was then taken up in ether and the dried ether solution was decolorized with charcoal. The solution was then concentrated to a small volume and allowed to stand. (If the ether solution is perfectly dry and if the removal of hydrogen bromide has been complete, crystallization of the dissolved acid begins when the solution has reached about half its original volume.) The crystalline product so obtained was filtered and washed with cold ether. A sample of it melted at 160–165°. Recrystallization from ethyl acetate gave a product which melted at 172–173°. A melting point depression was observed when a sample of the material was mixed with a specimen of α-3-hydroxy-12-ketocholanic acid, yield 30%.

An absorption spectra study showed an absorption at wave length 242.5, a wave length which is characteristic for α,β-unsaturated ketones.

Anal. Calcd. for $C_{24}H_{36}O_4$: C, 74.2; H, 9.4. Found: C, 74.2; H, 9.8.

Preparation of 3-Hydroxy-9,11-cholenic Acid.—A portion of the above acid (0.2 g.) was refluxed for two hours with an aqueous alcoholic solution of 0.2 g. of semicarbazide acetate prepared from carbazide hydrochloride and 0.2 g. of anhydrous sodium acetate. The product was worked up in the usual manner. From benzene it came down as a gelatinous precipitate which became crystalline when filtered and washed with ether. A specimen of the crystals melted at 221°. The semicarbazone was not further purified but was directly employed for the Wolf–Kishner reduction. The heating with sodium ethylate (made from 1 g. of sodium and 15 cc. of absolute alcohol) was carried out in a sealed tube at 180° for fifteen hours. After this time the reaction product was taken up in water and boiled for one-half hour on the water-bath. After cooling with ice it was acidified with ice-cold dilute sulfuric acid. The precipitate so obtained was filtered, washed thoroughly with water and then taken up in acetone. On

crystallization needles were obtained which melted unsharply at 175°. Several recrystallizations from acetone gave a product which showed a strong positive Liebermann reaction and which melted at 183–184°, $[\alpha]^{25}D$ +27.0 (63 mg. in 5 cc. of absolute alcohol solution gave a reading of +0.68). When mixed with a specimen of 3-hydroxy-12-keto-9,11-cholenic acid a depression of the melting point was observed.

Anal. Calcd. for $C_{24}H_{38}O_3$: C, 76.96; H, 10.23. Found: C, 76.7; H, 10.5.

We wish to take this opportunity to express our thanks to the Rockefeller Foundation for a grant-in-aid which in part was used in support of this work.

Summary

1. A new route has been suggested to the preparation of sterol derivatives having a hydroxyl group C_{11}. Progress in this direction has been reported.

2. By the debromination followed by saponification of 3-acetoxy-11-bromo-12-ketocholanic acid, an unsaturated acid has been prepared which proved to be 3-hydroxy-12-keto-9,11-cholenic acid. This acid melts at 173° and possesses the characteristic absorption of the α,β-unsaturated keto derivatives.

3. The crude semicarbazone of the unsaturated keto-hydroxy acid, m. p. 221°, has been reduced according to the Wolf–Kishner method to 3-hydroxy-9,11-cholenic acid of m. p. 183–184°.

PRINCETON, NEW JERSEY RECEIVED OCTOBER 23, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NEW YORK UNIVERSITY]

Steric Hindrance in Ketone–Phenol Condensations. The Condensation of Guaiacol with Cyclic Ketones

BY JOSEPH B. NIEDERL, VICTOR NIEDERL AND JOSEPH GRUMER[1]

In a previous publication[2] the effect of steric hindrance in ketone–phenol condensations has been investigated. It was established that, while the usual condensation product is an alkylidene-diphenol,[3] this is not formed when a reaction system is selected which would lead to the formation of a cycloalkylidene-diphenol in which there is a substituent group in *ortho* position to either one of the two reacting carbon atoms involved in the condensation. In these cases only equimolar condensation is possible, leading to the formation of cycloalkylenephenols or coumarans, respectively.

For a practical application of this hypothesis, a phenolic compound having an alkoxy group in *ortho* position to the free hydroxyl group was condensed with cyclic ketones. Condensation products analogous to the ones isolated in condensations involving an ortho alkylated phenol should be obtainable. As shown in the following, similar types of condensation products could actually be isolated.

Thus, the condensation of guaiacol with cyclohexanone itself and the *m*- and *p*-methylcyclohexanone isomers, yielded the expected alkylidene-diphenols (I, II, III), while the reaction of guaiacol with *o*-methylcyclohexanone resulted in the unsaturated cyclohexenyl-guaiacol (IV).

Of the four primary condensation products (I–IV) the following derivatives were prepared and verified by analysis: crystalline acetates (Ic, IIc, IIIc), benzoates (Id, IId, IIId) and phenylurethans (Ib, IIb, IIIb) of the three alkylidene-diphenols (I, II, III) and a crystalline aryloxyacetic acid (IVa) of the unsaturated monomolecular condensation product of guaiacol with *o*-methylcyclohexanone (IV).

Experimental

Condensation Method

1,1-*bis*-(3′-Methoxy-4′-hydroxyphenyl)-cyclohexane (I).—Molar quantities of guaiacol and half molar quantities of cyclohexanone were dissolved in 100 cc. of glacial acetic acid and the mixture placed in a 1-liter, triple-necked, round-bottomed flask which was provided with a reflux condenser, a thermometer and a gas inlet tube extending to the bottom of the vessel. A vigorous stream of dry hydrogen chloride gas was passed into the system for six hours at room temperature on two consecutive days, then the flask was stoppered and left standing at room temperature for four weeks. Crystals deposited which were filtered and recrystallized from benzene; m. p. 174°; yield, 31%.

Attempts to hydrolyze the ether groups in this compound by refluxing the compound with hydrobromic acid (48%)

(1) The material presented in this paper is taken from the thesis presented by Joseph Grumer to the Graduate School of New York University in partial fulfilment of the requirements for the degree of Master of Science.

(2) J. B. Niederl and co-workers, THIS JOURNAL, **61**, 1785 (1939).

(3) M. E. McGreal and co-workers, *ibid.*, **61**, 345 (1939).

TABLE I

COMPOUNDS, FORMULAS AND ANALYSES

No.	Formula or deriv.	M. p., °C.	Empirical formula	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
	1,1-*bis*-(3′-Methoxy-4′-hydroxyphenyl)-cyclohexane								
I	$(C_6H_3(OH)OCH_3)_2C_6H_{10}$	174	$C_{20}H_{24}O_4$	73.40	73.38	7.34	6.93		
Ib	Phenylurethan	153	$C_{27}H_{29}O_5N$					3.13	3.08
Ic	Acetate	157	$C_{24}H_{28}O_6$	69.97	70.07	6.78	6.79		
Id	Benzoate	168	$C_{34}H_{32}O_6$	76.10	76.25	6.03	6.18		
	1,1-*bis*-(3′-Methoxy-4′-hydroxyphenyl)-4-methylcyclohexane								
II	$(C_6H_3(OH)OCH_3)_2C_6H_9(CH_3)$	165	$C_{21}H_{26}O_4$	73.68	73.60	7.62	7.90		
IIb	Phenylurethan	192	$C_{28}H_{31}O_5N$					3.04	3.05
IIc	Acetate	136	$C_{25}H_{30}O_6$	70.42	70.48	7.04	7.37		
IId	Benzoate	162	$C_{35}H_{34}O_6$	76.34	76.48	6.18	6.35		
	1,1-*bis*-(3′-Methoxy-4′-hydroxyphenyl)-3-methylcyclohexane								
III	$(C_6H_3(OH)OCH_3)_2C_6H_9(CH_3)$	149	$C_{21}H_{26}O_4$	73.68	73.68	7.62	7.72		
IIIb	Phenylurethan	187	$C_{28}H_{31}O_5N$					3.04	3.30
IIIc	Acetate	118	$C_{25}H_{30}O_6$	70.42	70.07	7.04	7.15		
IIId	Benzoate	171	$C_{35}H_{34}O_6$	76.34	76.56	6.18	6.38		
	1-(3′-Methoxy-4′-hydroxyphenyl)-2-methylcyclohexene-1								
IV	$C_6H_3(OH)(OCH_3)C_6H_8(CH_3)$		$C_{14}H_{18}O_2$	77.01	77.09	8.30	8.67	m. wt. 218	214
IVa	Aryloxyacetic acid	73	$C_{16}H_{20}O_4$	69.50	69.78	7.30	7.38	n. eq. 276	277

as well as with hydriodic acid (sp. gr. 1.7) proved unsuccessful. Guaiacol was obtained in the first and catechol in the second case. This would indicate that the diphenylmethane linkage is weaker than an aromatic ether linkage.

1,1-*bis*-(3′-Methoxy-4′-hydroxyphenyl)-4-methylcyclohexane (II).—Molar quantities of guaiacol and half molar quantities of *p*-methylcyclohexanone were condensed as described above and worked up in a similar manner; m. p. 165.5°; yield, 10%.

1,1-*bis*-(3′-Methoxy-4′-hydroxyphenyl)-3-methycyclohexane (III).—Molar quantities of guaiacol and half molar quantities of *m*-methylcyclohexanone were condensed as described above and worked up in a similar manner; m. p. 149°; yield 27%. In none of the above cases was the filtrate, which consisted chiefly of unreacted starting materials, investigated further.

1-(3′-Methoxy-4′-hydroxyphenyl)-2-methylcyclohexene-1 (IV).—Half molar quantities of guaiacol and *o*-methylcyclohexanone were dissolved in 50 cc. of glacial acetic acid and condensed as described above. There was no deposition of crystals. The mixture was treated on a water-bath with dry hydrogen chloride for another twelve hours. No crystallization occurred, even after standing for another two months. After this time, the reaction mixture was dissolved in 200 cc. of benzene, this solution washed several times with an equal volume of water and then extracted with 150 cc. of Claisen solution. The Claisen solution extract was acidified with dilute hydrochloric acid, the oil which separated was taken up in 100 cc. of benzene, washed with water and dried over calcium chloride. The benzene was distilled off and the residue was distilled at 14 mm. pressure. Three fractions were obtained. The lower boiling fraction (about 30%) consisted of unreacted guaiacol, the fraction boiling between 155–175° proved to be the above unsaturated phenol (IV) (approx. 20%) and the higher boiling fraction, 180°, its polymer (approx. 30%). The unsaturated phenol (IV) polymerizes slowly upon standing.

Aryloxyacetic Acid Derivative (IVa).—This derivative was prepared by dissolving the above compound (IV) in 30% sodium hydroxide solution to which sufficient methyl alcohol was added to effect solution. The calculated amount of chloroacetic acid was added, the reaction mixture gently refluxed for two hours, and worked up according to the directions given in Shriner and Fuson.[4] In testing for unsaturation, Baeyer's permanganate test was employed and found positive.[5]

Phenylurethans (Ib, IIb, IIIb).—One gram of substance was dissolved in 1 cc. of phenyl isocyanate in a test-tube which was sealed and placed in a beaker containing boiling water. The test-tube was opened when its content had solidified and the crystalline material was recrystallized from petroleum ether.

Acetates (Ic, IIc, IIIc).—One gram of the respective phenol was dissolved in 3 cc. of acetic anhydride and refluxed in an all-glass apparatus for four hours. The reaction mixture was poured into an excess of water and allowed to stand overnight, whereupon crystallization occurred. The acetates were recrystallized from 80% alcohol.

Benzoates (Id, IId, IIId).—One gram of the respective phenol was dissolved in 3 cc. of pyridine and 1.5 g. of benzoyl chloride added. The mixture was warmed over a low flame for a few minutes and then poured into 10 cc. of water and stirred thoroughly. After decanting the supernatant solution, the crystals were washed with 5 cc. of 5% sodium carbonate solution and recrystallized from alcohol.

Summary

Studies were made of the effect of substituent groups in cyclic ketones in their condensations with an ortho alkoxyphenol.

(4) Shriner and Fuson, "The Systematic Identification of Organic Compounds," J. Wiley and Sons, Inc., New York, N. Y., 1935, pp. 148–149.

(5) S. P. Mulliken, "A Method for the Identification of Pure Organic Compounds," J. Wiley and Sons, Inc., New York, N. Y., 1904, p. 79.

Cycloalkylidene-diphenols and a cycloalkylene-phenol were obtained and suitable derivatives thereof prepared. The results obtained further support the previously suggested steric hindrance hypothesis governing the condensation of cyclic ketones with ortho alkylated phenols.

WASHINGTON SQUARE COLLEGE
NEW YORK, N. Y. RECEIVED OCTOBER 28, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NEW YORK UNIVERSITY]

Steric Hindrance in Ketone–Naphthol Condensations. The Condensations of the Naphthols with Cyclohexanone

BY JOSEPH B. NIEDERL, VICTOR NIEDERL AND JESSE CHARNEY

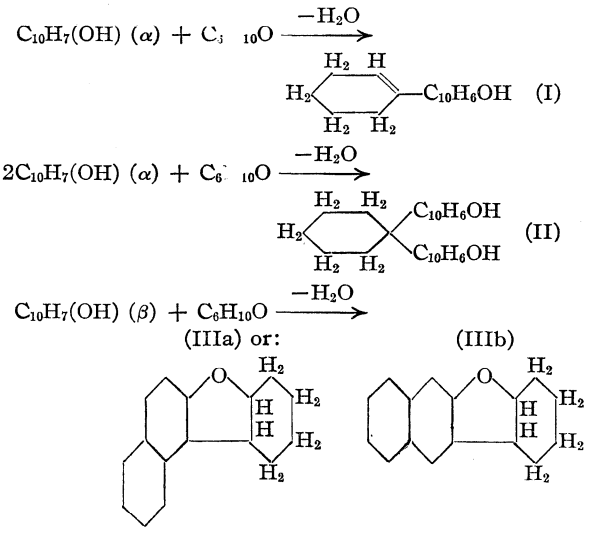
In a previous publication[1] it was asserted that in the condensation of ketones with phenols "the nature of the end product is influenced not only by the type of carbonyl compound employed, but also by the type of phenol used" and that "this influence exerts itself particularly through the position of the second substituent in the benzene ring, *i. e.*, whether it is *ortho*, *meta* or *para* to the hydroxyl group." This hypothesis was fully substantiated in a subsequent communication[2] in which condensations of various phenols with cyclohexanone derivatives were reported. In this it was shown that in cases where the alkyl radical in the final condensation product is adjacent to the carbon carrying the cyclohexenyl radical, steric hindrance effects inhibit the introduction of a second phenolic radical. Thus, instead of the normal di-phenols, unsaturated phenolic products are obtained. Further, it was indicated that when steric hindrance becomes too great, ortho alkylation takes place, leading to the formation of coumarans.

In continuation of these studies of steric hindrance in ketone–phenol condensations and in order to prove the generality of the above conclusion, these investigations were extended to the naphthols.

The results obtained were entirely in accordance with the foregoing postulation. Thus, when α-naphthol was condensed with cyclohexanone, not only was the normal di-naphthol, the 2,2-di-((4′-hydroxy)-naphthyl)-cyclohexane (II) obtained, but the cyclo-alkylene-naphthol, the 1-(4′-hydroxy)-naphthyl-cyclohexene-1 (I) was secured as well. To prove the unsaturated character of the latter, the acetate (Ia) was prepared and brominated, and the resulting crystalline dibromide (Ib) isolated. Titration of this dibromide (Ib) with 0.01 N sodium hydroxide solution gave a neutralization equivalent equal to one half the molecular weight of the compound, indicating the hydrolysis of at least one bromine atom and thus confirming the presence of bromine in the isocyclic side chain.

The condensation of β-naphthol with cyclohexanone was also studied. The condensation was slow, but positive, yielding no phenolic products, but, instead, the 2,3-tetramethylene-4,5[or 5,6]-benzocoumaran (IIIa or IIIb).

The formation of all three types of condensation product may be represented as



Experimental

1-(4′-Hydroxy)-naphthyl-cyclohexene-1 (I).—Half molar quantities of α-naphthol and cyclohexanone were placed in a 1-liter, triple-necked, round-bottomed flask which was provided with a reflux condenser, a thermometer and a gas inlet tube extending to the bottom of the vessel. The mixture was warmed until complete solution took place and then was cooled to below 30°. A vigorous stream of dry hydrogen chloride gas was passed into the system for six hours at room temperature, then the flask was stoppered and left standing for twelve hours, when com-

(1) J. B. Niederl and co-workers, THIS JOURNAL, 61, 348 (1939).
(2) J. B. Niederl and co-workers, *ibid.*, 61, 1785 (1939).

plete solidification had taken place. The mass was then crushed, washed with water and twice leached with 5% sodium hydroxide, after which it was again washed thoroughly with water. The residue was chilled until it was solid and recrystallized from a minimum quantity of 95% ethyl alcohol, separating thus any alcohol-insoluble products. The compound is no longer soluble in Claisen solution, but couples with diazotized *p*-nitroaniline; yield after recrystallization, 80%; m. p. 80°.

Anal. Calcd. for $C_{16}H_{16}O$: C, 85.71; H, 7.14. Found: C, 85.42; H, 7.22.

Acetate (Ia).—Ten grams of (I) was dissolved in 50 ml. of acetic anhydride, the solution placed in a ground-glass joint apparatus and refluxed for four hours. Then the mixture was poured into 500 ml. of water and the whole vigorously stirred. After a time the residue solidified and was separated by filtration. The crude acetate was recrystallized from 95% ethyl alcohol. The conversion to the acetate was quantitative, m. p. 94°.

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.20; H, 6.77; mol. wt., 266. Found: C, 81.09; H, 6.97; mol. wt., 265.

Di-bromide (Ib).—Ten grams of (Ib) was dissolved in 50 ml. of carbon tetrachloride and placed in a round-bottomed flask, the solution then being cooled to 5° in an ice-water-bath. The solution was stirred vigorously with the aid of a mechanical stirrer while one mole equivalent of bromine dissolved in carbon tetrachloride (1 g. of bromine per 5 ml. of solution) was added at the rate of 1 ml. per minute. When the addition of bromine was completed, the reaction mixture was poured into an evaporating dish and permitted to stand at room temperature until half the solvent had evaporated. By this time most of the dibromide had precipitated out while any substitution by-products remained dissolved. The mixture was then filtered and the crude dibromide was dissolved in the minimum quantity of acetone. A volume of water equal to one-fourth the volume of the acetone solution was added at once and stirred. In a few moments the purified dibromide crystallized from the solution and was separated by filtration; yield, 20%; m. p. 147°.

Anal. Calcd. for $C_{18}H_{18}O_2Br_2$: C, 50.70; H, 4.22; mol. wt., 426. Found: C, 50.73; H, 4.24; neut. equiv., 210.

1,1-Di-((4'-hydroxy)-naphthyl)-cyclohexane (II).—Half molar quantities of *α*-naphthol and cyclohexanone were condensed exactly as described for (I) with the single difference that the condensation was carried out at 100°. After standing for twelve hours in a tightly stoppered flask, the product was treated with 300 ml. of acetone and filtered. The residue was washed with 50 ml. of acetone and dried at room temperature. The compound was insoluble in Claisen solution but coupled with diazotized *p*-nitroaniline; yield, after treatment with acetone, 50%; m. p. 233°.

Anal. Calcd. for $C_{26}H_{24}O_2$: C, 84.78; H, 6.44; mol. wt., 368. Found: C, 84.62; H, 6.72; mol. wt., 381, 377. The molecular weight determination was performed cryoscopically according to K. Rast.[3]

Di-benzoate (IIa).—One gram of (II) was dissolved in 5 ml. of pyridine and 2 ml. of benzoyl chloride was added. The mixture was refluxed very gently for one-half hour and poured into 50 ml. of 5% sodium carbonate solution and vigorously stirred. When the product had hardened, the supernatant liquid was poured off and the residue was washed with water by decantation. A minimum amount of boiling alcohol was added to dissolve most of the residue. The alcoholic solution was then filtered and the filtrate cooled. The benzoate crystallized out and was filtered off. It was then purified by further crystallization from alcohol; m. p. 223°; mixed m. p. with (II), 207°.

Anal. Calcd. for $C_{40}H_{32}O_4$: C, 83.33; H, 5.55. Found: C, 83.48; H, 5.43.

2,3-Tetramethylene-4,5[or 5,6]-benzo-coumaran (IIIa or IIIb).—Half molar quantities of *β*-naphthol and cyclohexanone were dissolved in 80 ml. of acetic acid and condensed as described for (I). After standing for two weeks the flask was opened and the contents poured into a liter of water. The supernatant liquid was decanted and the residue twice leached with 5% sodium hydroxide solution, after which it was washed thoroughly with water. It was then chilled until semi-solid and dissolved in a very large volume of boiling alcohol. The alcoholic solution was chilled in ice. Water was added to cause the separation of the product and the resulting precipitate filtered off. After this treatment was twice repeated, the product was obtained as a nearly-white, amorphous solid; yield, 20%; m. p. 66–68°. The compound was insoluble in Claisen solution and did not undergo diazotization coupling reactions. Acetylation with acetic acid anhydride also was negative.

Anal. Calcd. for $C_{16}H_{16}O$: C, 85.71; H, 7.14; mol. wt., 224. Found: C, 85.50; H, 7.45; mol. wt., 249.

Summary

Steric hindrance phenomena encountered in certain types of ketone–phenol condensations were extended to include the condensation systems of the naphthols with cyclohexanone. From such systems and in accordance with previous postulations a cyclo-alkylidene-di-naphthol, a cyclo-alkylene-naphthol and a naphthyl-cyclohexyl-coumaran were isolated and derivatives thereof prepared.

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(3) K. Rast, as described in J. B. Niederl and V. Niederl, "Micromethods of Quantitative Organic Analysis," J. Wiley and Sons, Inc., New York, N. Y., 1938, p. 175.

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NEW YORK UNIVERSITY]

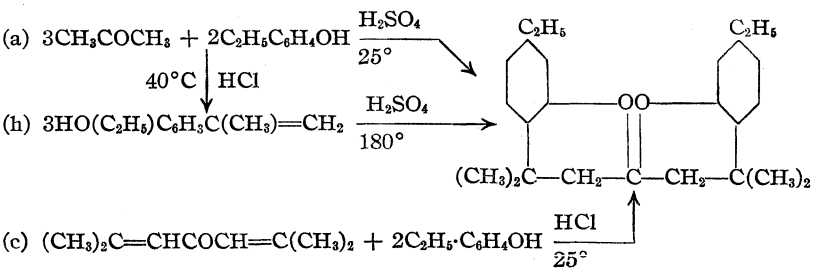
Spirochromans

BY JOSEPH B. NIEDERL AND RICHARD H. NAGEL[1]

The condensation of *m*- and *p*-cresol with acetone[2] was reinvestigated by W. Baker and D. M. Besley in 1939,[3] who not only confirmed both the empirical formulas and the "spirochroman" structures as advanced by J. B. Niederl,[4] but also assigned a similar "spirochroman" structure to their own hydroxyquinol–acetone condensation product.

To determine whether "spirochroman" formation was a phenomenon peculiar to the cresols, or whether it may be a general reaction of meta alkylated phenols with the position ortho to the phenolic hydroxyl group free, *m*-ethylphenol was condensed with acetone (a) and (b) and with phorone (c) in the presence of dry hydrogen chloride, as well as concentrated sulfuric acid. In the acetone condensation, the dimeric methovinylethylphenol, analogous to the dimer of methovinyl-methylphenol was obtained as the intermediate, when the condensation was carried out in the presence of dry hydrogen chloride at 40°. (b) This dimer was converted to the spirochroman according to the method of Böttcher[5] (b), by heating it to 180° with a small amount of sulfuric acid. The phorone condensation was direct and did not appear to have passed through any dimeric stage, which was also true in the case of the *m*- and *p*-cresol–phorone condensations.

Though the phorone product melted at 146° and the acetone compound at 114°, both gave the same tetranitro derivative, as evidenced by quantitative analyses and mixed melting point determinations. Furthermore, there was observed no depression in the melting point of an equal mixture of the two original crystalline condensation products and examination under the microscope showed that, though the crystals differed in form, it was possible to obtain crystallization by seeding a melt of the acetone compound crystals with a phorone compound crystal, and vice versa. This would seem to indicate that the dimorphism previously observed in the *m*- and *p*-cresol–acetone and the *m*- and *p*-cresol–phorone condensations and to be expected from stereochemical considerations is also exhibited by the ethyl homolog, and that the compound obtained in both cases is the 4,4,4′,4′-tetramethyl-7,7′-di-ethyl-bis-2,2′-spirochroman. Thus the course of the reaction may be presented as



Experimental

Acetone-*m*-ethylphenol

Dimeric Methovinylethylphenol (a and b).—One mole (122 g.) of *m*-ethylphenol and one-and-one-half moles (87 g.) acetone were placed in a 1-liter 3-necked round-bottomed flask provided with a reflux condenser and a gas inlet tube. Dry hydrogen chloride gas was passed into the reaction mixture at room temperature for six hours, and then the flask was tightly stoppered to keep the reactants in an atmosphere of the condensing agent, and let stand at room temperature for two weeks, in which time the mixture had turned dark brown in color and became quite viscous. The reaction mixture was poured into water and then repeatedly washed with 5% sodium carbonate solution and finally with distilled water, and then distilled. The main fraction (*ca.* 80 g.) distilled over between 200–207° at 12 mm. pressure, and on cooling an extremely viscous yellow liquid with a characteristic thymol-like odor was obtained.

Anal. Calcd. for $(C_{11}H_{14}O)_2$: C, 81.48; H, 8.64. Found: C, 81.55; H, 8.64.

Conversion to the Spirochroman (b).—Ten grams of the dimer was heated to boiling in a test-tube for half a minute with five drops of concentrated sulfuric acid. After two days, the solidified black mass was dissolved in boiling 95% ethyl alcohol and, on cooling, white rhombohedra crystallized out. These were recrystallized from the same solvent and were found to be insoluble in Claisen solution.

(1) Abstracted from a portion of the thesis to be submitted by Richard H. Nagel to the faculty of the Graduate School of New York University in partial fulfillment of the requirements for the degree of doctor of philosophy.

(2) J. B. Niederl, Ph.D. Thesis, Univ. of Graz (Austria) (1925); THIS JOURNAL, **50**, 2230 (1928); J. B. Niederl and R. Casty, *Monatsh.*, **51**, 1038 (1929); R. Casty, Ph.D. Thesis, Univ. of Graz (Austria) (1926); Th. Zincke and W. Gaebel, *Ann.*, **388**, 299 (1912); I. P. Tsukervanik and Z. N. Nazarova, *J. Gen. Chem.* (*U. S. S. R.*), **9**, 33 (1939).

(3) W. Baker and D. M. Besley, *J. Chem. Soc.*, 195 (1939).

(4) J. B. Niederl, *Z. angew. Chem.*, **43**, 467 (1931); *Monatsh.*, **60**, 150 (1932).

(5) Böttcher, Ph.D. Thesis, University of Berlin, 1930.

The conversion was practically quantitative. The pure product melted at 114° (uncor.).

Anal. Calcd. for $C_{25}H_{32}O_2$: C, 82.42; H, 8.79. Found: C, 82.48; H, 8.92.

Tetra-nitro Derivative.—About 1 g. of the crystals was dissolved in an excess of concentrated nitric acid in an Erlenmeyer flask, warmed on a steam-bath until no more fumes were given off, and then the flask was heated directly with a small Bunsen flame until a clear solution had resulted. Water was added to the cold solution, precipitating a yellow crystalline mass, which was filtered and recrystallized from 95% ethyl alcohol. The yellow crystals melted between 246–248° (uncor.). They were not analyzed, but a mixed melting point determination showed them to be identical with those obtained from the phorone–*m*-ethylphenol condensation product.

Phorone-*m*-Ethylphenol

4,4,4′,4′-Tetramethyl-7,7′-di-ethyl-bis-2,2′-spirochroman.—Three-tenths of a mole (46 g.) of phorone and 0.6 mole (82 g.) of *m*-ethylphenol were placed in a 1-liter 3-neck round-bottomed flask and dry hydrogen chloride gas was passed into the reaction mixture for six hours, the flask was stoppered tightly and allowed to stand at room temperature for one week. An excess of Claisen solution was added, precipitating a brown gelatinous mass which was filtered through a large fluted filter. The residue was washed with distilled water and dissolved in hot 50% ethyl alcohol, and on cooling white plates crystallized out. These crystals could also be obtained, though not so readily, from 95% ethyl alcohol. The crystals are insoluble in Claisen solution and melt at 146° (uncor.).

Anal. Calcd. for $C_{25}H_{32}O_2$: C, 82.42; H, 8.79. Found: C, 82.43; H, 8.68.

Tetra-nitro Derivative.—One gram of the spirochroman was heated on the water-bath in an Erlenmeyer flask with an excess of concentrated nitric acid till no more brown fumes were evolved, then heated directly with a small Bunsen flame until a clear solution resulted. On cooling, yellow needles separated, which were filtered off on a sintered glass filter funnel, and recrystallized from 95% ethyl alcohol. The melting point was 246–248° (uncor.). A mixed melting point with the nitro compound prepared from the acetone condensation product produced no depression.

Anal. Calcd. for $C_{25}H_{28}O_{10}N_4$: C, 55.15; H, 5.15. Found: C, 54.96; H, 5.13.

Summary

The condensation of acetone with meta alkylated phenols was extended to include *m*-ethylphenol. Experimental results were obtained which are in full harmony with previously advanced postulations.

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NEW YORK, N. Y. RECEIVED NOVEMBER 29, 1939

[CONTRIBUTION FROM THE WILLIAM ALBERT NOYES LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF ILLINOIS]

Change of the Ultraviolet Absorption Spectrum of Acrolein with Time

BY A. M. BUSWELL, E. C. DUNLOP, W. H. RODEBUSH AND J. B. SWARTZ

During a study of the ultraviolet absorption spectra of solutions of pure organic compounds, we observed that in the case of acrolein the data were sometimes inconsistent. In one case a solution of a given strength showed less absorption than a solution of half the concentration had shown in a previous test. A check of the records showed that the weaker solution had been examined when freshly prepared, while the stronger solution was a few days old when its absorption was determined. This suggested a systematic study of the change of the absorption spectrum of acrolein with time to determine whether this effect was due to polymerization or some other reaction.

There are several articles in the literature[1] discussing the absorption spectrum of acrolein in the vapor phase, and in solution in alcohol, water and other solvents. They report a weak absorption band at about 3200 Å. and a very strong one extending from a sharp limit at 2500 Å. toward shorter wave lengths. There are no data showing what happens to the spectra of these solutions over a period of time. This point has been investigated and is reported herewith.

Experimental

The instrument used was a Bausch and Lomb medium quartz spectrograph with a sectorphotometer. The light source was a condensed iron–tungsten alloy spark. The cells were of glass with quartz windows and were 5.14 cm. in length.

The data were read from the plates by visual comparison using a hand lens to find the matched lines. The percentage transmission was known from the sector setting and the molecular extinction coefficient was calculated from the Lam-

(1) (a) Blacet, Young and Roof, THIS JOURNAL, **59**, 608 (1937); (b) Eastwood and Snow, *Proc. Roy. Soc.* (London), **A149**, 446 (1935); (c) Thompson and Linnett, *Nature*, **134**, 937 (1934); (d) Purvis, *J. Chem. Soc.*, **127**, 9 (1925); (e) Henri, *Compt. rend.*, **199**, 849 (1934); **178**, 844 (1924); (f) Luthy, *Z. physik. Chem.*, **107**, 284 (1923); (g) Purvis and McClelland, *J. Chem. Soc.*, **103**, 433 (1913); (h) Bielecki and Henri, *Ber.*, **46**, 3627 (1913).

bert–Beer equation $I = I_0 10^{-\epsilon c d}$ where $I_0 = 100$, I = relative per cent. of light transmitted, ϵ = molecular extension coefficient, c = concentration (molar), and d = length of the path of the absorbing media in centimeters.

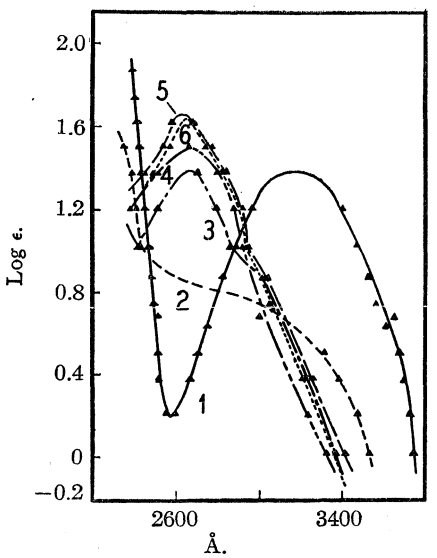


Fig. 1.—Acrolein in 50% ethyl alcohol solution: (1) immediately after making up solution; (2) after 7 days; (3) after 14 days; (4) after 21 days; (5) after 40 days; (6) after 60 days.

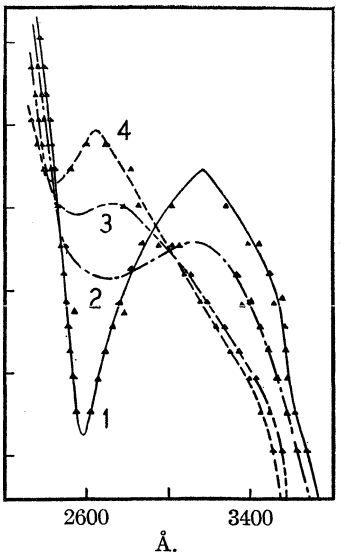


Fig. 2.—Acrolein in water: (1) immediately after making solution; (2) after 14 days; (3) after 30 days; (4) after 49 days.

The acrolein was purified and freshly distilled portions were used in making up all the solutions. The following solutions were made and tested: three solutions in 50% ethyl alcohol containing 1, 0.1 and 0.05 g. of acrolein per liter, respectively; two solutions in doubly distilled water containing 1 and 0.1 g. of acrolein per liter; and three solutions in doubly distilled water each containing 0.1 g. of acrolein per liter. To one of these last solutions a little hydroquinone was added, to another a little tannic acid and the third solution contained only acrolein and solvent. The ultraviolet absorption of each of the solutions was determined immediately after they were prepared. The solutions were then stored in glass-stoppered volumetric flasks and exposed to the diffuse light and temperature of the laboratory. Absorption tests were repeated at seven-day intervals on each of these solutions for periods up to eight weeks. In each test a small portion of the solution was removed, used for the absorption determination, and then discarded.

From the curves, Figs. 1, 2 and 3, it is seen that a definite change has taken place in the period of time indicated. In the original curves the bands correspond to those reported by Luthy[1f] and verified by others. The broad band at 3200 Å. has been assigned as due to the carbonyl and the very intense band extending from 2590 Å. toward the shorter wave length as due to the ethylenic group. There has been no mention of the band at 2670 Å. which appears after a few days. As the age of the solution increased the band at 3200 Å. disappeared and the band at 2670 Å. appeared and increased up to a time of forty days. The shoulder of the peak toward the shorter wave length also is found to diminish with increasing time.

Discussion

The new band at 2670 Å. is due to some reaction that the acrolein has undergone. This new band cannot be due to an acetal form since the same results occur in both alcoholic and water solutions (Figs. 1 and 2). It has been reported by Herold and Wolf[2] that the formation of hemiacetals can be shown by the ultraviolet absorption spectra. We also have shown that this is true for propion-

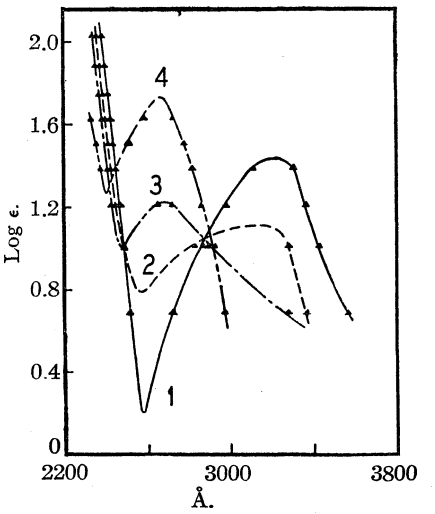


Fig. 3.—Acrolein in water: (1) immediately after making solution; (2) after 7 days; (3) after 14 days; (4) after 38 days. This solution was kept under identical conditions as those for Figs. 6 and 7.

(2) Herold and Wolf, *Z. physik. Chem.*, **12**, 165 (1931).

aldehyde, Fig. 4, where a water solution of the propionaldehyde remained unchanged for forty-two days while in an alcohol solution the absorption of the carbonyl was gradually decreased with time. The absorption of acetal in water solution was determined and is shown in Fig. 5. From these data it is shown definitely that the acrolein does not form the hemiacetal.

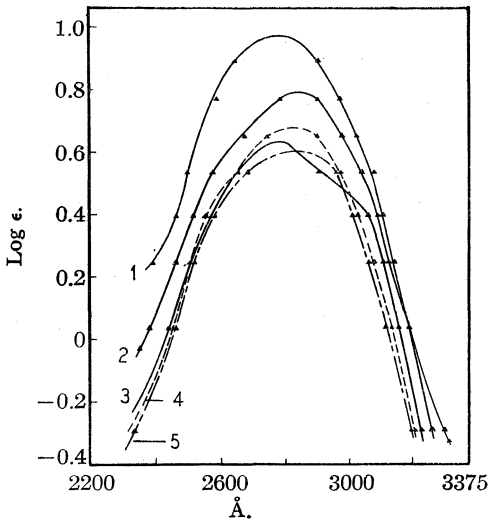


Fig. 4.—Propionaldehyde: (1) water solution remained unchanged for 42 days; (2) 50% ethyl alcohol solution immediately after making solution; (3) the alcohol solution after 9 days; (4) the alcohol solution after 16 days; (5) the alcohol solution after 42 days.

Paraldehyde has been reported as having no bands above 2500 Å. and we have verified this, Fig. 5. Comparing these data with the data for acrolein it is seen that the paraldehyde structure gives no absorption above 2500 Å. while in the aged acrolein solutions there was absorption at 2670 Å. Moreover, the aged solutions gave positive tests with fuchsin-aldehyde reagent and Tollens' reagent, thus indicating the presence of the aldehyde group. The solutions also gave a positive test with 2,4-dinitro-phenylhydrazine reagent but because of the small concentration the derivative was not isolated. This would indicate that the acrolein does not form a molecule of the paraldehyde structure.

No insoluble material formed in the solution, indicating that no long chain insoluble polymer was formed.

The absorption spectrum of allyl alcohol determined by Bielecki and Henri[3] shows that allyl alcohol is nearly transparent above 2400 Å. Since the aged acrolein solutions show absorption at 2670 Å., this eliminates the possibility of the formation of allyl alcohol.

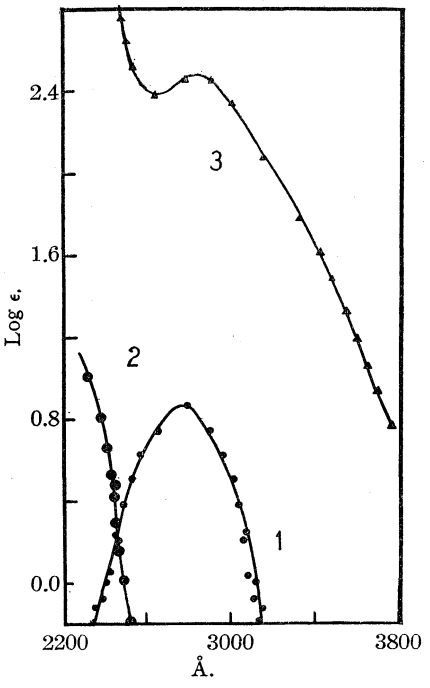


Fig. 5.—(1) Acetal in water; (2) paraldehyde in 50% ethyl alcohol; (3) aldol in 50% ethyl alcohol.

Backes[4] has shown that non-aqueous solutions of aldol show no peak above 2500 Å. while aqueous solutions have a peak at 2800 ± 10 Å. characteristic of the carbonyl group. We have verified the latter part of this statement as shown in Fig. 5 for aldol in 50% ethyl alcohol. The original carbonyl absorption of the acrolein in aqueous solution is changed completely while if the acrolein formed an aldol type of molecule the carbonyl would still be conjugated with the ethylenic linkage and should still absorb at the same wave length but should be diminished because of the disappearance of one-half the carbonyl groups. No one has ever suggested that acrolein would form the aldol and these data indicate no such formation.

From the results of the absorption spectra of the solutions to which a very minute amount of an antioxidant, either hydroquinone, Fig. 6, or tannic acid, Fig. 7, has been added, it is seen that the presence of the antioxidant has slowed down the reaction but has not stopped it. Compare Fig. 3 with Figs. 6 and 7 which show that the absorption at 3200 Å. is slower in disappearing

(3) Bielecki and Henri, *Ber.*, **46**, 2596 (1913).

(4) Backes, *Compt. rend.*, **200**, 1669 (1935).

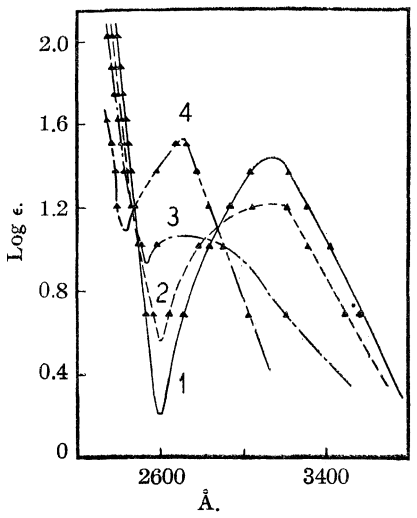


Fig. 6.—Acrolein in water plus a trace of hydroquinone: (1) immediately after making solution; (2) after 7 days; (3) after 14 days; (4) after 38 days.

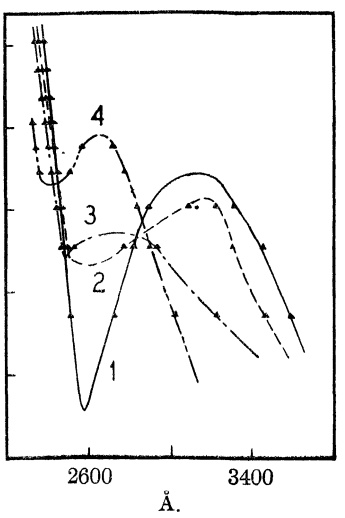


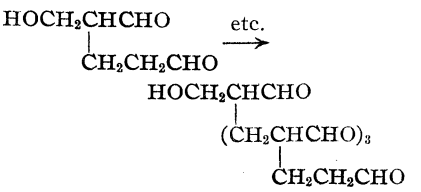
Fig. 7.—Acrolein in water plus a trace of tannic acid: (1) immediately after making solution; (2) after 7 days; (3) after 14 days; (4) after 38 days.

and that at the end of the thirty-eight-day period the new band at 2670 Å. is not as strong in the solutions which contained an antioxidant as it is in the other solution. These data suggest that the reaction may be an oxidation. In this case the product would be an acid, acrylic acid or perhaps a resin acid. The spectrum does not agree with that of acrylic acid as determined by Luthy[1f] and also the *p*H of the solution, which was 6.5 ± 0.3 when the solutions were made up and which remained constant, does not indicate any acid formation.

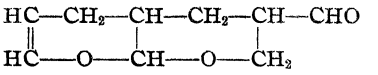
Nothing very definite can be said in regard to the ethylenic group since we have been unable to extend our working range of the spectrum below 2300 Å. In observing the results near 2350 Å., however, we notice that in every case the shoulder is diminished with time and this may be taken as an indication that the ethylenic group is disappearing.

The new band which appears at 2670 Å. is undoubtedly due to a molecule formed by the polycondensation of the acrolein. Several investigators have described the formation of a white product from the polycondensation of acrolein but have made no attempt to characterize the polymer. Gilbert and Donleavy[5] have recently shown that the polycondensation is an equilibrium reaction which they represent by the equations

$$\underset{\text{I}}{CH_2{=}CHCHO} + H_2O = HOCH_2CH_2CHO + \text{I} =$$



Sherlin, *et al.*,[6] have reported on the polymerization of acrolein in anhydrous condition at 170° and have proposed the formula



This molecule, with water added to the double bond, may be in equilibrium with the chain molecule as prepared by Gilbert and Donleavy.[5] The absorption data agree with the equilibrium reaction proposed by Gilbert and Donleavy[5] in which the ethylenic group disappears and the carbonyl group is changed, giving absorption at a shorter wave length. This would be expected since the conjugation disappears, causing the shift to the shorter wave length. The absorption data show that an antioxidant slows down the reaction, which is known to be the case for the above reaction. A sample of the polymer described by Gilbert and Donleavy[5] was prepared and its alcohol solution was found to give an absorption peak at the same wave length as that for the aged acrolein solutions.

Summary

The change in the absorption spectrum of acrolein in water and alcoholic solutions has been determined over a period of time. The effect of hydroquinone and tannic acid on the spectrum also has been determined.

The absorption due to the carbonyl of the acrolein changes with time, and the change is slowed down by the presence of an antioxidant. A band which appears at 2670 Å. is probably due to the carbonyl of the polymer since the product described by Gilbert and Donleavy[5] gives the same absorption band.

Curves for propionaldehyde in water and 50% alcohol solutions, for acetal in water, paraldehyde in 50% alcohol and aldol in 50% alcohol are also given for comparison.

URBANA, ILLINOIS RECEIVED JULY 13, 1939

(5) Gilbert and Donleavy, THIS JOURNAL, 60, 1911 (1938).

(6) Sherlin, *et al.*, *J. Gen. Chem.* (*U. S. S. R.*), 8, 22 (1938); *C. A.*, 32, 5398 (1938).

[CONTRIBUTION FROM THE DEPARTMENTS OF CHEMISTRY AT SMITH COLLEGE AND CORNELL UNIVERSITY]

The Action of Ethyl Azide and Phenyl Azide on Fuming Sulfuric Acid[1]

BY K. W. SHERK, A. G. HOUPT[2] AND A. W. BROWNE

The action of hydrogen azide on fuming sulfuric acid has been shown[3] to yield aminomonopersulfuric acid which is capable of acting both as an aminating agent and as a strong oxidizing agent. In the attempt to throw more light upon the structure and nature of this compound and its possible derivatives, a study has been made of the action of fuming sulfuric acid on two derivatives of hydrogen azide: phenyl azide and ethyl azide. This work also was undertaken in the attempt to determine the conditions under which the monazene (NH=) radical or its substitution products might polymerize or condense to form compounds of the diazene series of hydronitrogens, as exemplified by the condensation of RN= residues to form azo compounds.[4]

Phenyl Azide.—The formation of *p*-aminophenol and its *o*-sulfonic acid, respectively, by the action of phenyl azide on dilute and concentrated sulfuric acid, as noted by Bamberger[5] is in a sense analogous to the formation of hydroxylamine as a product of the action of hydrogen azide on concentrated sulfuric acid. Since no hydroxylamine is formed when the fuming acid is used in place of the ordinary concentrated acid, it seemed likely that the phenyl derivative of aminomonopersulfuric acid, rather than *p*-aminophenol, might be obtainable from the action of phenyl azide on fuming sulfuric acid.

The phenyl azide used in the present work was prepared from nitrosyl chloride and phenylhydrazine.[6] It was separated by steam distillation and dried with anhydrous sodium sulfate. The introduction of this reagent into fuming sulfuric acid, even when the acid was cooled in an ice-salt mixture and thoroughly stirred, resulted in considerable charring. At room temperature, each drop of the phenyl azide, as it struck the acid, detonated with a violet flash and formed a purple-black smoke. To overcome these difficulties the phenyl azide was introduced in the form of vapor by drawing a slow stream of dried air through the azide and then through the fuming acid at room temperature. In this way 12 g. of phenyl azide was drawn into 20 ml. of 20% fuming acid in eighteen hours. Almost from the outset evolution of nitrogen took place, and the acid assumed a maroon color. After the azide had been introduced the acid solution was allowed to stand until gas evolution had ceased.

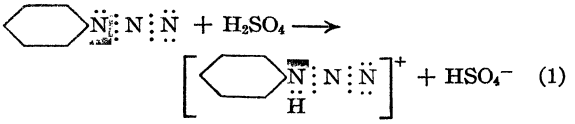
The solution was poured into vigorously agitated, ice-cold, dry ether with the result that a bulky, rose colored precipitate was formed. This was washed with dry ether until the washings were free from sulfate ion. A yield of 11 g. of a very hygroscopic solid was obtained. On exposure to air a sample of this product quickly became blue and sticky.

The solid dissolves in water to yield a solution from which needle-like crystals are at once deposited. These are soluble in dilute sodium hydroxide and reprecipitated by acid. A sample of this product of hydrolysis weighing several grams was prepared, redissolved, reprecipitated, washed with water and alcohol, and dried. Qualitative tests and further analysis proved the compound to be *p*-aminophenol *o*-sulfonic acid monohydrate. *Anal.* Calcd. for *p*-aminophenol *o*-sulfonic acid monohydrate: neut. equiv., 207.1; S, 15.48; N, 6.76; H_2O, 8.70. Found: neut. equiv., 207; S, 15.28; N, 6.76, 6.74, 6.77; H_2O, 8.53.

The original hygroscopic material, when heated, chars without melting. Its aqueous solution gives a positive phenol test, and fails to liberate iodine from acidified potassium iodide solution. It yields at once, even at room temperature, a heavy precipitate of barium sulfate when treated with barium chloride and hydrochloric acid. Although analysis was hindered by the hygroscopic nature of the substance, the following data were obtained. Found: S, 21.75, 21.90, 21.95; N, 4.90, 4.92; atomic ratio S:N, 1.986/1.

In conjunction with the observed formation of *p*-aminophenol *o*-sulfonic acid and sulfuric acid by hydrolysis, this strongly indicates that the original substance was mainly phenylaminomonopersulfuric acid *m*-sulfonic acid. Unlike aminomonopersulfuric acid, this compound does not liberate iodine from potassium iodide in acid solution but hydrolyzes immediately and rearranges to *p*-aminophenol *o*-sulfonic acid. It shows no tendency to form monopersulfuric acid.

Mechanism of the Reaction between Phenyl Azide and Fuming Sulfuric Acid.—The first step may be considered to consist of the coördination of a hydrogen ion to the alpha nitrogen of the azide group.



(1)

(1) This article is based in part upon the thesis submitted to the Faculty of the Graduate School of Cornell University by A. G. Houpt in partial fulfilment of the requirements for the degree of Master of Arts. The work of K. W. Sherk has been supported by the personal generosity of Mr. Haymo V. Pfister of the Pfister Chemical Company.

(2) Present address: American Cyanamide Company, Stamford, Conn.

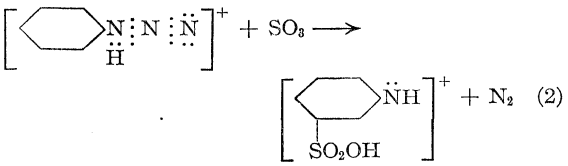
(3) Specht, Browne and Sherk, THIS JOURNAL, **61**, 1083 (1939).

(4) Bertho, *Ber.*, **57B**, 1138 (1924).

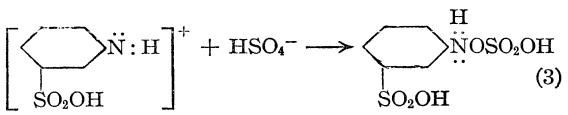
(5) Bamberger, *Ann.*, **424**, 233–296 (1921); **443**, 192–210 (1925).

(6) Tilden and Miller, *J. Chem. Soc.*, **63**, 256 (1893).

The coördination link reduces the stability of the azide group with the result that two atoms of nitrogen split off as nitrogen gas. Sulfonation occurs subsequently to the coördination as indicated by the meta position of the sulfonate group.



The unstable residue unites with a bisulfate ion to form phenylaminomonopersulfuric acid *m*-sulfonic acid.



This product probably exists in the isomeric form obtained by a shift of the hydrogen from the nitrogen to the adjacent oxygen as seems likely in the case of aminomonopersulfuric acid.[3]

Ethyl Azide.—This reagent was prepared by the action of diethyl sulfate on sodium azide.[7] It was washed with water to remove ethanol, and was dried with anhydrous sodium sulfate. About 8 g. of the azide in the form of vapor was introduced by means of a current of dry air into 15 ml. of 20% fuming sulfuric acid at 80° in eighteen hours. After the evolution of nitrogen had ceased, the clear, slightly yellow solution was slowly poured into vigorously agitated, ice-cold, dry ether. The heavy yellowish precipitate was washed with dry ether until it was free from sulfuric acid. During this operation the solid gradually assumed an orange color and became sticky. *In vacuo*, over phosphorus pentoxide, it soon changed to a deep-orange paste, and finally, after several days, to a brittle orange-colored glass.

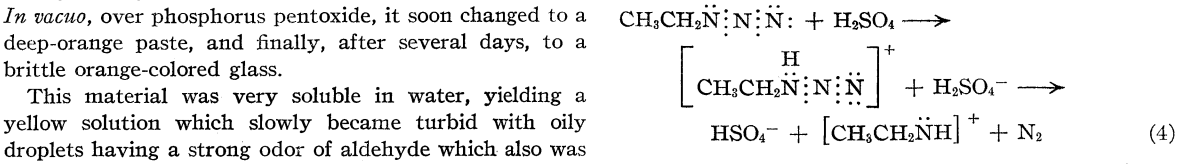
This material was very soluble in water, yielding a yellow solution which slowly became turbid with oily droplets having a strong odor of aldehyde which also was manifested by the glassy solid itself. The solution was strongly acidic and contained sulfate ions. Distillation yielded a clear, colorless, aqueous solution which contained formaldehyde and another aldehyde, assumed under the circumstances to be acetaldehyde. To separate the formaldehyde from the other, a sample of the distillate was treated with an excess of concentrated ammonium hydroxide solution. This converted the formaldehyde to hexamethylenetetramine and the acetaldehyde to aldehyde-ammonia. The solution was made barely acid to methyl red and distilled until no more aldehyde came over. There was no formaldehyde in the distillate. Acetaldehyde was present, however, and was confirmed by the preparation of the *p*-nitrophenylhydrazine derivative.

The residue in the flask was made strongly acid with 1:1 sulfuric acid and distillation resumed. The new distillate gave strong tests for formaldehyde, which was confirmed by the *p*-nitrophenylhydrazine derivative.

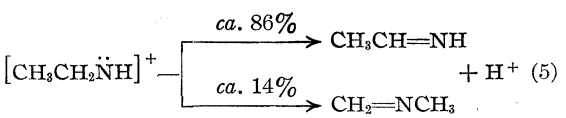
The residue from the distillation of the aldehydes was made alkaline with sodium hydroxide, and distilled into cold water. This distillate contained ammonia and methylamine, which were identified by conversion to benzamide and dinitromethylaniline, respectively. The distillate would not reduce ammoniacal silver nitrate nor Fehling's solution, and therefore contained no hydroxylamine derivatives.

From these results it seems that the unstable yellow solid formed by the action of fuming sulfuric acid on ethyl azide yields, upon hydrolysis, sulfuric acid and a mixture of acetaldehyde, formaldehyde, ammonia and methylamine. No other products such as N-ethylhydroxylamine, ethylidene imine, or ethylene imide could have been present as final products since the volatile bases did not reduce potassium permanganate or ammoniacal silver nitrate solution. The estimation of ammonia and methylamine was accomplished by the method of François[8] in which a solution of the weighed hydrochlorides was used. The mixture was found to contain 0.86 mole of ammonia to 0.14 mole of methylamine. The relative strength of the tests given for acetaldehyde and formaldehyde indicated that these substances were present in a similar ratio.

Mechanism of the Reaction between Ethyl Azide and Fuming Sulfuric Acid.—From the behavior of hydrogen azide and phenyl azide toward fuming sulfuric acid, it was expected that ethyl azide would react with the fuming acid to form ethylaminomonopersulfuric acid, which would hydrolyze to yield N-ethylhydroxylamine. The first step of the reaction is probably the union of a hydrogen ion with the ethyl azide and the subsequent loss of two nitrogen atoms.



The unsaturation of the nitrogen is relieved by a shift of a hydrogen or of a methyl group from the alpha carbon to the adjacent nitrogen, rather than by combination with a bisulfate ion to form a derivative of aminomonopersulfuric acid.



The fact that the solution of the glassy yellow product contained sulfate ions indicates that it was probably a mixture of the sulfates of the bases

(7) Staudinger and Hauser, *Helv. Chim. Acta*, **4**, 872 (1921).

(8) François, *Compt. rend.*, **144** 857 (1907); from "Allen, Commercial Organic Analysis," 5th ed., Vol. V, P. Blakiston's Son and Co., Phila., 1927, p. 287.

shown in equation 5. The hydrolysis of these compounds would account for all of the observed products.

Since no products containing nitrogen linked to nitrogen have been obtained by the interaction of either phenyl or ethyl azide and fuming sulfuric acid, the possibility that diazene or its homologs might be formed by the interaction of hydrogen azide and the fuming acid seems rather remote under the prevailing conditions. The mechanism already suggested for this reaction[3] is confirmed by the behavior of phenyl azide toward the fuming acid.

Summary

1. The action of fuming sulfuric acid upon phenyl azide apparently results in the formation of phenylaminomonopersulfuric acid *m*-sulfonic acid, which on hydrolysis yields *p*-aminophenol *o*-sulfonic acid.

2. The action of fuming sulfuric acid upon ethyl azide results in the formation of products which on hydrolysis yield sulfuric acid and a mixture of acetaldehyde, formaldehyde, ammonia and methylamine.

3. A useful method for the separation of formaldehyde and acetaldehyde has been described.

4. No compounds containing nitrogen linked to nitrogen were obtained as products of either reaction. The analogy between these reactions, particularly that of the phenyl azide, and that of hydrogen azide and fuming sulfuric acid has been noted.

NORTHAMPTON, MASS. RECEIVED OCTOBER 30, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

The Heat Capacities, Heats of Transition and Fusion, and Entropies of Ethylene Dichloride and Ethylene Dibromide

BY KENNETH S. PITZER

Internal rotation in ethylene dichloride and ethylene dibromide has been studied by dielectric constant[1] measurements, electron diffraction,[2] and Raman spectra.[3] Although it has been proved that the rotation is considerably restricted, many aspects are yet to be worked out. With this in mind, the low temperature heat capacities, heats of fusion, and heats of transition for both substances have been measured, leading of course to entropy values. Work is in progress on the heat capacities of these substances in the gas phase.

These substances are also interesting because of the transitions they undergo as solids. Ethylene dibromide shows a sharp transition at 249.54° K., while ethylene dichloride has a large peak in its heat capacity curve near 177°K.

Apparatus and Materials.—The vacuum calorimeter used in this investigation already has been described.[4] The value 273.10°K. was taken for the ice point, and the defined calorie, 4.1833 International joules, was used throughout.

The calorimetric samples were purified by washing with water, drying, and repeatedly fractionating. The impurity in each case was estimated from the rise in heat capacity below the melting point, and found to be 0.058% in the case of ethylene dichloride and 0.26% in ethylene dibromide. Although impurities of this magnitude make the true heat capacity below the melting point uncertain, they do not appreciably affect the final entropy values.

Melting and Transition Temperatures.—The melting points were observed for different fractions melted and were corrected for impurities. The transition temperature in ethylene dibromide was similarly measured. The results are presented in Table I together with the values obtained by other observers.

Heat Capacities.—The heat capacities were measured by the usual method and are listed in Tables II and III shown graphically in Fig. 1. The temperature increments employed can be judged by the spacing of the reported results. In the anomaly in ethylene dichloride small increments were necessary to show that the true curve is rounded at the peak. This special series of measurements is included at the end of Table II. The results of other special measure-

(1) Beach and Stevenson, *J. Chem. Phys.*, **6**, 635 (1939); Zahn, *Phys. Rev.*, **40**, 291 (1932); **38**, 521 (1931).

(2) Beach and Turkevich, THIS JOURNAL, **61**, 303 (1939); Beach and Palmer, *J. Chem. Phys.*, **6**, 639 (1938).

(3) Ta-You Wu, *ibid.*, **7**, 965 (1939), who gives additional references.

(4) Latimer and Greensfelder, THIS JOURNAL, **50**, 2202 (1928); Pitzer and Coulter, *ibid.*, **60**, 1310 (1938).

TABLE I

MELTING AND TRANSITION TEMPERATURES FOR ETHYLENE DIBROMIDE AND DICHLORIDE (0°C. = 273.10°K.)

M. p. of $C_2H_4Cl_2$	M. p. of $C_2H_4Br_2$	Trans. temp. of $C_2H_4Br_2$	Observer
237.6	283.10		Timmermans and Martin[a]
240.6			Hammick and Howard[b]
	283.07		LeBlanc and Möbius[c]
	282.3	249	White and Morgan[d]
		248.4	Morino[e]
237.2 ± 0.1	283.0 ± 0.2	249.54 ± 0.1	This research

[a] Timmermans and Martin, *J. chim. phys.*, **23**, 733 (1926); *ibid.*, **25**, 411 (1928). [b] Hammick and Howard, *J. Chem. Soc.*, 2915 (1932). [c] LeBlanc and Möbius, *Ber. Verhandl. sächs. Akad. Wiss., Leipzig, Math.-phys. Klasse*, **85**, 75 (1933). [d] White and Morgan, *J. Chem. Phys.*, **5**, 655 (1937). [e] Morino, *J. Chem. Soc. Japan*, **60**, 222 (1939).

ments indicated slow thermal equilibrium near the peak, but no detectable hysteresis.

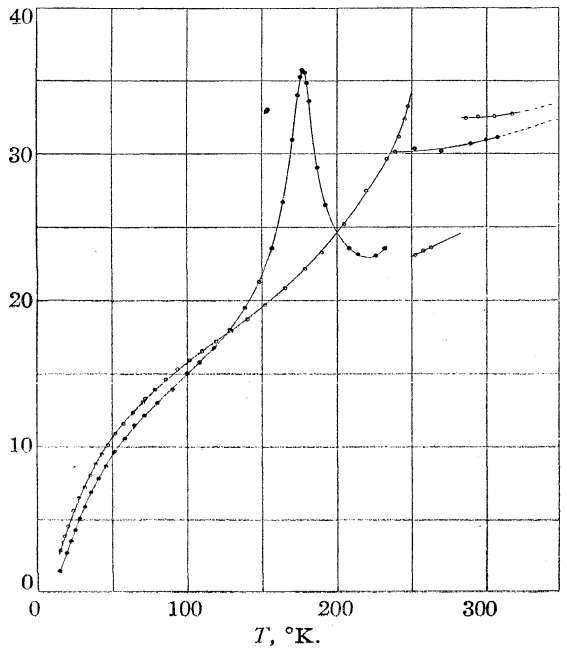


Fig. 1.—The molal heat capacity of ethylene dichloride (solid circles) and ethylene dibromide (open circles) in cal. per degree.

The error in the heat capacities is probably less than 0.2% under optimum conditions. At the highest temperatures rapid heat exchange by radiation is troublesome, while at the lowest temperatures the resistance thermometer is less sensitive. Just below the melting point, the premelting effect obscures the true heat capacity curve. The listed results have been corrected for this effect on the basis of Raoult's law, which may not be followed accurately. This uncertainty is greater in the ethylene dibromide, due to both the larger impurity and the proximity of the transition to the melting point. The observed heat capacities above the transition fit the following expression within experimental error: $C_p = A + BT + C/(T_{M.P.} - T)^2$. In this expression the first two terms represent the true heat capacity, assumed to vary linearly with temperature over this short range, and the third term the "Raoult's law" premelting. Since a series of six evenly spaced observations was available, as compared to three constants, the agreement is real evidence for the correctness of this treatment. It cannot be regarded as conclusive, however, and only the three measurements farthest from the melting point are included in Table III.

While the presence of small impurities renders the heat capacity uncertain just below the melting point, any appreciable error in this region is compensated in the heat of fusion, so that the

TABLE II

THE MOLAL HEAT CAPACITY OF ETHYLENE DICHLORIDE, $C_2H_4Cl_2$, MOL. WT. 98.966

T, °K.	C_p	T, °K.	C_p
15.12	1.432	170.48	30.91
19.85	2.676	176.15	35.16
22.41	3.488	181.50	33.54
25.10	4.201	186.99	28.96
28.35	4.990	192.46	26.46
31.94	5.823	199.99	24.89
35.92	6.791	208.30	23.50
40.69	7.768	214.23	23.06
45.71	8.621	226.32	23.00
51.83	9.595	232.01	23.48
58.39	10.51	liquid	
64.83	11.41	238.68	30.01
71.49	12.06	252.27	30.24
80.07	12.93	269.98	30.08
90.10	13.87	289.23	30.61
99.92	14.98	299.88	30.86
108.20	15.75	307.53	31.04
118.16	16.71	peak of anomaly	
128.43	17.93	174.13	33.93
138.94	19.43	175.92	35.19
148.25	21.21	177.18	35.63
156.78	23.49	178.44	35.52
164.21	26.66	179.69	34.82

TABLE III

THE MOLAL HEAT CAPACITY OF ETHYLENE DIBROMIDE, $C_2H_4Br_2$, MOL. WT. 187.88

T, °K.	C_p	T, °K.	C_p
15.25	2.851	129.71	17.90
17.94	3.792	140.49	18.69
20.28	4.502	152.12	19.66
23.78	5.605	165.53	20.82
27.59	6.460	178.99	22.13
31.49	7.209	189.94	23.24
35.20	8.019	204.98	25.20
39.08	8.820	219.72	27.42
43.10	9.471	232.93	29.62
47.36	10.10	241.58	31.15
52.11	10.86	245.23	32.37
57.59	11.55	247.83	33.22
63.87	12.31	transition	
70.54	13.04	252.69	23.09
71.78	13.25	257.79	23.35
78.08	13.87	262.86	23.58
85.48	14.58	melting point	
93.84	15.29	286.48	32.41
101.37	15.89	294.38	32.48
110.05	16.53	305.47	32.56
119.54	17.18	318.04	32.71

total entropy or heat content is not seriously altered.

Heats of Fusion and Transition.—Table IV contains the observed heats of fusion and transition. The temperature intervals and times of heating are also listed. In each heat of fusion a correction was made for the amount "premelted" at the initial temperature. It is believed that the uncertainties given in Table IV are sufficient to cover any calorimetric errors. However, a failure of the premelting effect to even approximate Raoult's law might possibly lead to errors about five times those listed. As stated above, the total entropy is not rendered uncertain by this latter possibility.

TABLE IV

HEATS OF FUSION AND TRANSITION

Temp. interval, °K.	Time of heat input, min.	$\Delta H°$ cal./mole
Fusion of $C_2H_4Cl_2$ at 237.2°K.		
229.22–244.45	24	2112.1
229.88–248.33	33	2112.0
		Av. value 2112.0 ± 2
Fusion of $C_2H_4Br_2$ at 283.0°K.		
275.62–294.51	24	2617.1
272.47–294.05	25	2614.5
		Av. value 2615.8 ± 5
Transition of $C_2H_4Br_2$ at 249.54°K.		
247.17–258.64	14	465.5
248.97–258.96	10	462.3
247.17–250.29	14	463.7
		Av. value 463.8 ± 2

Entropies.—The entropies were calculated by the usual graphical integrations, together with extrapolations to the absolute zero based on the Debye theory. The heat capacity does not fit a single Debye function (three degrees of freedom) satisfactorily for either substance, but does fit twice a Debye function (corresponding to six degrees of freedom). This latter assumption is consistent with the idea that the tendency of the molecules to oscillate torsionally leads to torsional waves similar to the more common compressional waves. Lord, Ahlberg and Andrews[5] found this assumption very successful in the case of benzene and discussed its justification in greater detail.

Measurements are now in progress on the heats of vaporization of both substances, and on heat capacities as gases. Consequently, it seems best to postpone calculations and discussions of the entropies of gaseous ethylene dichloride and dibromide until these data are available.

Discussion of Transitions.—Some comment seems worth while on the nature of the transition in ethylene dibromide and the gradual transition or anomaly in the chloride. Measurements of the dielectric constant by White and Morgan[6] show only small changes in passing through these regions. The dielectric constant becomes large only above the melting point for either substance. This probably means that the molecules retain configurations of small dipole moment until they melt. Rotation of whole molecules about their long axis might set in, however, without allowing internal rotation. The internal rotation is considerably restricted even in the gas phase.[1,2]

If this explanation is accepted, the results for either substance by itself would seem reasonable, since similar thermal effects have been observed for the beginning of rotation within other crystals. However, the difference seems very great for two such similar compounds. The following explanation is offered as plausible but by no means proved.

If the coöperative or coupling effect between the rotation of one molecule and its neighbors is relatively small, then the whole curve for the chloride becomes understandable and the rather

(5) Lord, Ahlberg and Andrews, *J. Chem. Phys.*, **5**, 649 (1937).
(6) See note d, Table I.

TABLE V

MOLAL ENTROPY OF ETHYLENE DICHLORIDE

0–15.0°K.	Debye extrapolation	0.505
15.0–237.2	Graphical–solid	33.500
237.2	Fusion (2112.0/237.2)	8.904
237.2–298.1	Graphical–liquid	6.935
	Entropy of liquid at 298.1°K.	49.84 ± 0.15 cal./deg.

TABLE VI

MOLAL ENTROPY OF ETHYLENE DIBROMIDE

0–15.00°K.	Debye extrapolation	1.106
15.00–249.54	Graphical–solid II	36.490
249.54	Transition (463.8/249.54)	1.859
249.54–283.0	Graphical–solid I	2.989
283.0	Fusion (2615.8/283.0)	9.243
283.0–298.1	Graphical–liquid	1.688
	Entropy of liquid at 298.1°K.	53.37 ± 0.2 cal./deg.

gradual rise in the bromide curve from 150 to 250°K. is also to be expected. Above 250°K. some fundamentally different crystal structure, based on rotating molecules, becomes more stable for the ethylene dibromide, and a sharp interphase transition of the usual sort occurs. If one considers lattices comprising points which represent only the centers of gravity of the molecules, then the writer proposes that the lattice for ethylene dichloride will be essentially the same above and below the peak or "transition." Probably the lattice for ethylene dibromide below the transition is also similar; however, it is suggested that above the transition the ethylene dibromide lattice is quite different. The marked similarity of the heat capacity curves below 100°K. gives some confirmation to the suggestion that the low temperature lattices are similar. Also a comparison of the extra entropy associated with the peak in ethylene dichloride (about 2.8 cal. per deg.) with that in the abnormal rise and the transition in ethylene dibromide (about 3.7 cal. per deg.) is in reasonable agreement with this picture. The latter might be expected to be somewhat larger because it includes a change in lattice in addition to molecular rotation. Thus the observations are accounted for in a general way, although x-ray studies would be needed to prove that these ideas are correct.

Since submitting this paper for publication, Railing[7] has published results of a somewhat similar investigation. His measurements do not extend below 90°K. and he did not attempt to make an entropy calculation. A comparison of certain results is presented.

		Railing	This Research
Melting point, °K.	$C_2H_4Cl_2$	237.6	237.2±0.1
	$C_2H_4Br_2$	283.03	283.0±0.2
Transition temp., °K.	$C_2H_4Br_2$	250.6	249.54±0.1
Heat of fusion, cal.	$C_2H_4Cl_2$	2090±21	2112.0±2
	$C_2H_4Br_2$	2590±26	2615.8±5
Heat of transition, cal.	$C_2H_4Br_2$	450±9	463.8±2

For the greater part, the heat capacity results agree well within the 1–2% error suggested by Railing. However, near the transitions, melting points, or other irregularities, appreciable discrepancies arise, particularly with the dichloroethane. This is not too surprising when one considers the method of measurement employed by Railing, as described by Stull.[8] Briefly, this involves continuous introduction of energy with temperature measurements at the same time. Under these conditions, temperature gradients certainly exist, and a thermometer reading may not correspond to the temperature which would be attained at thermal equilibrium with the same heat content. In most regions, the error in temperature should remain almost constant, leading to correct heat capacities. However, near transitions, melting points, etc., these temperature gradients may change rapidly, leading to considerable error in the heat capacity results. Since, with the method used in this research, temperatures are measured only when thermal equilibrium has been essentially attained, the results of the present investigation are not subject to this error.

In this connection the writer is not convinced as to the reality of the variation of heat capacity depending on thermal history, which was found by Railing for liquid ethylene dichloride. He reports that one curve is obtained "immediately after melting" and another with liquid which has been cooled to just above the melting point. Presumably, in the first case the introduction of energy is not stopped after the fusion is completed and the liquid heat capacity measurements begin with the thermal gradients that existed under the conditions of melting. These gradients may differ considerably from those of the

(7) Railing, THIS JOURNAL, **61**, 3349 (1939).

(8) Stull, THIS JOURNAL, **59**, 2726 (1937).

recently cooled liquid. The observed differences, depending on rate of freezing, can similarly be explained as arising from differences in heat conductivity within the sample, which depends on the size of crystals among other factors.

The results of the present investigation neither support nor definitely disprove these effects reported by Railing. They do, however, offer strong evidence against the slow *cis–trans* isomerization suggested by him in explanation. The presence of *cis* and *trans* isomers would be expected to produce variations in the melting point and other peculiar effects which were definitely not observed. Also, according to Railing's suggestions, absorption of heat and apparent cooling would be expected after melting the material. No such cooling effect was observed in the heat of fusion experiments.

Summary

The thermal behavior of ethylene dichloride and ethylene dibromide was investigated from 15°K. to room temperature, for which range values of the heat capacities are given. The following melting points (0°C. = 273.10°K.) and heats of fusion were determined: $C_2H_4Cl_2$, 237.2 ± 0.1°K., 2112.0 ± 2 cal./mole; $C_2H_4Br_2$, 283.0 ± 0.2°K., 2615.8 ± 5.0. The following temperature and heat of transition values were determined: $C_2H_4Br_2$, 249.54 ± 0.10°K., 463.8 ± 2.0 cal./mole. From these data, the following values of entropy at 298.1°K. were calculated: $C_2H_4Cl_2$(l), 49.84 ± 0.15 cal./deg. mole; $C_2H_4Br_2$-(l), 53.37 ± 0.20 cal./deg. mole.

Ethylene dichloride shows no sharp transition but has a peak in the heat capacity curve near 177°K. which may correspond partially to the transition in ethylene dibromide. A possible explanation of the transitions is offered.

BERKELEY, CALIF. RECEIVED NOVEMBER 21, 1939

[CONTRIBUTION FROM THE MALLINCKRODT CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

The Viscosity of Solutions of Electrolytes as a Function of the Concentration. VI. Potassium Bromide and Lanthanum Chloride

BY GRINNELL JONES AND ROBERT ELIOT STAUFFER

The general objective of this paper and of the others of this series is a study of the viscosity of solutions of electrolytes as a function of the concentration, temperature and nature of the salt. The earlier papers[1] should be consulted for a more detailed theoretical discussion and for a description of the experimental technique.

The potassium bromide used in this work was prepared by S. Baeckström.[2]

The lanthanum chloride was originally purified from other rare earths by the late Professor Charles James and had been used in previous investigations in this Laboratory[3] and recovered by precipitation as the oxalate. The oxalate was ignited to the oxide, dissolved in a solution of hydrochloric acid in ethyl alcohol, filtered through a sintered glass filter, chilled with ice and hydrogen chloride gas passed into the solution until the lanthanum chloride was precipitated. The salt was dried by centrifugal drainage and reprecipitated from alcohol in the same manner. The use of ethyl alcohol instead of water gives better yields. A suitable quantity for each solution was placed in a platinum boat inside of a quartz tube and heated to 600° for four hours in a stream of hydrogen chloride gas without fusion. The salt was cooled in an atmosphere of hydrogen chloride gas and then the acid gas replaced by dried air and the boat put into a weighing bottle by the use of a Richards bottling apparatus. The solutions were then made up by weight.

The solutions prepared from the salt dried in this manner had a *p*H of about 6.0 when tested with brom thymol blue, which agrees with the earlier work of Kolthoff and Elmquist,[4] and of Jacques[5] and of Jones and Bickford.[6] No corrections were applied for this slight hydrolysis. Erratic results were obtained at first and the cause was traced to a slight deposit of lanthanum hydroxide in the capillary tube of the viscometer. However, it was found that the deposit was formed during the rinsing of the viscometer with hot water after a series of measurements, which in-

(1) Grinnell Jones and M. Dole, THIS JOURNAL, **51**, 2950 (1929); Grinnell Jones and S. K. Talley, *ibid.*, **55**, 624, 4124 (1933); *Physics*, **4**, 215 (1933); Grinnell Jones and H. J. Fornwalt, THIS JOURNAL, **57**, 2041 (1935); **58**, 619 (1936); **60**, 1683 (1938); Grinnell Jones and R. E. Stauffer, *ibid.*, **58**, 2558 (1936); **59**, 1630 (1937); Grinnell Jones and S. M. Christian, *ibid.*, **59**, 484 (1937); Grinnell Jones and E. Ferrell, *J. Chem. Soc.*, 325 (1939).

(2) Grinnell Jones and S. Baeckström, THIS JOURNAL, **56**, 1519 (1934).

(3) Grinnell Jones and C. F. Bickford, *ibid.*, **56**, 602 (1934); Grinnell Jones and L. T. Prendergast, *ibid.*, **58**, 1376 (1936).

(4) I. M. Kolthoff and R. Elmquist, THIS JOURNAL, **50**, 959 (1928).

(5) A. G. Jacques, Dissertation, Harvard University, 1931, p. 344.

(6) Grinnell Jones and C. F. Bickford, THIS JOURNAL, **56**, 605 (1934).

fluenced subsequent measurements with water or other solutions. By rinsing at first with hydrochloric acid instead of with water the tubes were kept clean and more consistent and reliable measurements obtained.

In some cases a correction not exceeding a few hundredths of one per cent. was applied by interpolation to bring the results to the round concentration given, but if the correction required was substantial the actual data are given and the interpolated values at the round concentration are shown in parentheses. The lanthanum chloride solutions were measured at both 25 and 0° but measurements were made at 0° only on the potassium bromide solutions because measurements on this salt at 25° already had been made in this Laboratory.

The kinetic energy correction has been applied to the data, but no correction[7] has been applied for surface tension effects because the surface tension data are not available.

TABLE I

DENSITY AND RELATIVE VISCOSITY OF POTASSIUM BROMIDE SOLUTIONS AT 0°

c	d^0_4	η	$(\eta - 1)/c$	Jones and Dole equation Simple $\Delta\eta \times 10^5$	Jones and Dole equation Extended $\Delta\eta \times 10^5$
0.00025	(0.99989)	1.00007	+0.28	+ 4	+4
.0005	.99994	1.00005	+ .10	+ 3	+3
.001	.99995	0.99992	− .08	− 7	−7
.002	1.00004	.99985	− .07	− 4	−4
.005	1.00032	.99950	− .10	− 5	−5
.01	1.00077	.99896	− .10	+ 5	+5
.02	1.00165	.99760	− .12	+ 4	+4
.05	1.00435	.99330	− .134	− 2	−8
.1	1.00869	.98635	− .136		−4
.2	1.01747	.97284	− .136		+5
.5	1.04353	.93649	− .127		−1
1	1.08629	.88866	− .111		
2	1.17007	.82882	− .0856		
2.98978	1.25120	.80363	− .0657		
(3)	(1.25203)	(.80341)			
3.750	1.31269	.80234	− .05271		

	Range of validity, M	Av. deviation, %
Root equation		
$d^0_4 = 0.999871 + 0.089603c - 0.003196c^{3/2}$	3.75	0.002
Jones and Dole equation		
$\eta = 1 + 0.00450\sqrt{c} - 0.15377c$	0.05	.004
$\eta = 1 + 0.00450\sqrt{c} - 0.15459c + 0.04244c^2$	.5	.005

Interpretation of the Data.—The densities of these solutions can be expressed over the entire range of concentration studied by equations of the form suggested by Root[8] with an average deviation of only 0.002%. These equations are

for KBr at 0°; $d^0_4 = 0.999871 + 0.089603c - 0.003196c^{3/2}$

for $LaCl_3$ at 25°; $d^{25}_4 = 0.997074 + 0.229324c - 0.01184c^{3/2}$

at 0°; $d^0_4 = 0.999871 + 0.23665c - 0.01521c^{3/2}$

These salts give the Grüneisen effect as usual.

(7) The correction factor for this instrument should be computed by the equation

$$f = 1 + 0.0076\,\frac{\sigma_0/\rho_0 - \sigma_c/\rho_c}{\sigma_0/\rho_0}$$

see Jones and Fornwalt, THIS JOURNAL, **60**, 1691 (1938).

TABLE II

DENSITY AND RELATIVE VISCOSITY OF LANTHANUM CHLORIDE SOLUTIONS AT 25°

c	d^{25}_4	η	$(\eta - 1)/c$	Jones and Dole equation Simple $\Delta\eta \times 10^5$	Jones and Dole equation Extended $\Delta\eta \times 10^5$
0.00025	(0.99713)	1.00067	+2.68	+5	+ 5
.0005	(.99718)	1.00091	+1.82	−5	− 5
.001	.99729	1.00152	+1.52	−1	0
.0025	.99763	1.00291	+1.16	−3	0
.005	.99820	1.00499	+1.00	+1	+ 6
.01	.99933	1.00879	+0.879	+8	+19
.025	1.00275	1.01891	+ .756	−8	+20
.05	1.00839	1.03517	+ .703	+1	+25
.1	1.01965	1.06632	+ .6632	−1	−26
.25	1.05299	1.16314	+ .6525		+ 3
(.5)	(1.10755)	(1.34913)			
.502687	1.10812	1.35132	+ .6988		
.990638	1.21256	1.83815	+ .84607		
(1)	(1.21454)	(1.84945)			

	Range of validity, M	Av. deviation, %
Root equation		
$d^{25}_4 = 0.997074 + 0.229324c - 0.01184c^{3/2}$	1.0	0.002
Jones and Dole equation		
$\eta = 1 + 0.0304\sqrt{c} + 0.5672c$	0.1	.004
$\eta = 1 + 0.0304\sqrt{c} + 0.5551c + 0.14629c^2$	.25	.011

TABLE III

DENSITY AND RELATIVE VISCOSITY OF LANTHANUM CHLORIDE SOLUTIONS AT 0°

c	d^0_4	η	$(\eta - 1)/c$	Jones and Dole equation Simple $\Delta\eta \times 10^5$	Jones and Dole equation Extended $\Delta\eta \times 10^5$
0.00025		1.00051	+2.0	− 5	− 5
.0005		1.00072	+1.44	−14	−13
.001	1.00011	1.00129	+1.29	− 6	− 5
.0025	1.00047	1.00266	+1.06	+ 8	+11
.005	1.00107	1.00444	+0.888	+10	+16
.01	1.00221	1.00751	+ .751	− 1	+ 9
.025	1.00570	1.01614	+ .646	−12	+ 9
.05	1.01150	1.03003	+ .6006	+ 9	+32
.1	1.02302	1.05621	+ .5621	− 2	−28
(.25)	(1.05708)	(1.13849)			+ 3
.250395	1.05717	1.13872	+ .5540		
.250462		1.13876			
(.5)	(1.11267)	(1.30258)			
.505272	1.11443	1.30640	+ .6064		
.997033	1.22039	1.76661	+ .7689		
(1)	(1.22102)	(1.77023)			

	Range of validity, M	Av. deviation, %
Root equation		
$d^0_4 = 0.999871 + 0.23665c - 0.01521c^{3/2}$	1.0	0.001
Jones and Dole equation		
$\eta = 1 + 0.02780\sqrt{c} + 0.47440c$	0.1	.007
Jones and Dole		
$\eta = 1 + 0.02780\sqrt{c} + 0.46276c + 0.14190c^2$	.25	.013

(8) W. C. Root, THIS JOURNAL, **55**, 850 (1933).

The solutions of potassium bromide at 0° give another example of a salt which causes a diminution in viscosity at moderate concentration but nevertheless gives an increase in viscosity at extreme dilution.

The viscosity of these solutions relative to that of pure water can be expressed by the Jones and Dole equation; $\eta = 1 + A\sqrt{c} + Bc$ as follows

for KBr at 0°; $\eta = 1 + 0.0045\sqrt{c} - 0.15377c$; valid up to 0.05 N

for $LaCl_3$ at 25°; $\eta = 1 + 0.0304\sqrt{c} + 0.5672c$; valid up to 0.1 M

for $LaCl_3$ at 0°; $\eta = 1 + 0.0278\sqrt{c} + 0.4744c$; valid up to 0.1 M

Table IV gives a comparison of the values of the coefficient of the square root term (A) determined experimentally and that computed by the Falkenhagen and Vernon equation.

TABLE IV

COMPARISON OF THE THEORETICAL AND EXPERIMENTAL VALUES OF THE COEFFICIENT OF THE SQUARE ROOT TERM

	Equiv. cond. used in calcg. cation	anion	A computed	A exper.
KBr at 0°	40.6	43.1	0.0044	0.0045
$LaCl_3$ at 25°	71	76.34	.0280	.0304
	68	76.34	.0288	
$LaCl_3$ at 0°	35.5	41.3	.0270	.0278
	35	41.3	.0272	

These results furnish additional evidence in support of that given in the earlier papers of this series that the Falkenhagen and Vernon equation is essentially correct both as to the influence of valence type and temperature.

Cox and Wolfenden[9] have made a series of measurements on dilute solutions of lanthanum chloride at 18° from which they find an experimental value of A of 0.037 ± 0.002. They compute a theoretical value of 0.0318 but do not state the value of the equivalent conductivities and other parameters which they used in these calculations. They say "Aqueous solutions of magnesium sulfate and lanthanum chloride do not give results in accordance with the Falkenhagen equation and these electrolytes are the first cases to be investigated which have shown an unmistakable divergence. Such a divergence is not unexpected as it is characteristic of the behavior of electrolytes of higher valence-type in respect to other properties such as those of heats of dilution, etc. The discrepancy is presumably associated with the higher terms of the ionic atmosphere theory."

Our data do not confirm this conclusion as to lanthanum chloride. Our experimental data are consistently lower than theirs and agree much better with computed values of A.

The only other measurements on potassium bromide at 0° which we have found in the literature are by Taylor and Ranken[10] on 1, 2 and 3 N KBr. These results are appreciably higher than ours and since data on dilute solutions are lacking they are not significant in determining the experimental value of A.

Summary

1. The absolute densities and relative viscosities of many solutions of potassium bromide have been determined at 0° and of solutions of lanthanum chloride at 25 and 0°.

2. These results confirm the Root equation for densities, the Jones and Dole equation for viscosities and the Falkenhagen and Vernon equation for the influence of the interionic attraction on the viscosity.

CAMBRIDGE, MASS. RECEIVED NOVEMBER 25, 1939

(9) W. M. Cox and J. H. Wolfenden, *Proc. Roy. Soc.* (London), **145A**, 475 (1934). L. W. Öholm, *Soc. Sci., Fennica., Commentationes Phys.-Math.*, **9**, No. 2, 1937, gives measurements on lanthanum chloride solutions at 20°.

(10) W. W. Taylor and C. Ranken, *Proc. Roy. Soc. Edinburgh*, **25**, 231 (1904).

[CONTRIBUTION FROM THE MALLINCKRODT CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

The Viscosity of Solutions of Electrolytes as a Function of the Concentration. VII. Silver Nitrate, Potassium Sulfate and Potassium Chromate

BY GRINNELL JONES AND JOHN HENRY COLVIN

The earlier papers of this series[1] should be consulted for a discussion of the objectives and theoretical significance of the work and for a description of the experimental procedure.

Silver nitrate was purified[2] by solution in water, precipitation by the addition of freshly distilled nitric acid, and separation from the mother liquor by centrifugal drainage. This process was carried out three times in succession. It was then fused in a porcelain casserole, taking care to avoid overheating above the melting point, and then poured in small portions into a platinum dish to cool and solidify. Potassium chromate was recrystallized three times with centrifugal drainage, then dried and finally heated just below its melting point. The purified material gave a negative test for sodium, chloride and sulfate. Potassium sulfate was purified in the same manner as the chromate. It gave a negative test for sodium and chloride.

The results are summarized in Tables I to VI in which the concentrations, c, are expressed in gram molecular weights per liter, and viscosities, η, are given relative to that of water at the same temperature. A small kinetic energy correction has been applied to the data but no correction for the effect of surface tension has been made.[3] Figures in parentheses were not actually measured but were estimated by interpolation over a small range of concentration.

The densities of these solutions can be expressed by the equations given in the tables having the form suggested by Root,[4] throughout the entire range of concentration studied and with average deviation of less than 0.002%. It is remarkable that this equation should be valid for

TABLE I

DENSITY AND RELATIVE VISCOSITY OF SILVER NITRATE SOLUTIONS AT 25°

c	d^{25}_4	η	$(\eta - 1)/c$	Jones and Dole equation Simple $\Delta\eta \times 10^5$	Jones and Dole equation Extended $\Delta\eta \times 10^5$
0.002	0.99736	1.00036	0.18	−1	− 1
.005	.99778	1.00068	.136	+1	+ 1
.01	.99853	1.00110	.110	+2	+ 3
.015	.99919	1.00148	.099	+3	+ 5
.02	.99992	1.00177	.0885	−2	0
.05	1.00414	1.00364	.0728	−3	0
.10	1.01118	1.00652	.0652	+1	− 3
.20	1.02518	1.01224	.0612		− 5
.50	1.06709	1.03088	.06178		+ 6
.99719	1.13601	1.06783	.06802		+11
(1.0)	(1.13643)	(1.06806)			
2.0	1.27363	1.16788	.08394		− 2
(3.0)	(1.40942)	(1.29888)			
3.00425	1.41002	1.29951	.09970		
(4.0)	(1.54407)	(1.46261)			
4.0115	1.54565	1.46471	.11584		
4.99808	1.67745	1.66223	.13250		
5.000	(1.67775)	(1.66264)			

	Range of validity, M	Av. deviation, %
Root equation		
$d^{25}_4 = 0.997074 + 0.141956c - 0.002603c^{3/2}$	5	0.002
Jones and Dole equation		
$\eta = 1 + 0.0063\sqrt{c} + 0.04517c$	0.1	.002
$\eta = 1 + 0.0063\sqrt{c} + 0.043805c + 0.017845c^2$	2	.003

(1) The preceding paper, VI, THIS JOURNAL, **62**, 335 (1940), gives references to the earlier papers.

(2) T. W. Richards and G. S. Forbes, *ibid.*, **29**, 816 (1907); E. B. Rosa, G. W. Vinal and A. S. McDaniel, *Bull. Bur. Standards* **9**, 539 (1913).

TABLE II

DENSITY AND RELATIVE VISCOSITY OF SILVER NITRATE SOLUTIONS AT 0°

c	d^{0}_4	η	$(\eta - 1)/c$	Jones and Dole equation Simple $\Delta\eta \times 10^5$	Jones and Dole equation Extended $\Delta\eta \times 10^5$
0.001	0.99991	1.00013	+0.130	0	0
.002	1.00016	1.00017	+ .085	+1	+1
.005	1.00059	1.00021	+ .042	+2	+3
.01	1.00132	1.00018	+ .018	+2	+3
.015	1.00204	1.00007	+ .005	−3	−2
.02	1.00278	1.00000	.000	−2	−2
.05	1.00714	0.99939	− .0122	+1	−6
.1	1.01438	0.99847	− .0153		0
.2	1.02880	0.99701	− .01495		+2
.5	1.07174	0.99782	− .0109		0
(1)	(1.14233)	(1.01373)			
1.00326	1.14293	1.01393	+ .01349		
(2)	(1.28164)	(1.08445)			
2.0157	1.28381	1.08576	+ .04255		
(3)	(1.41870)	(1.19439)			
3.03205	1.42306	1.19842	+ .06543		
(4)	(1.55418)	(1.33998)			
4.05174	1.56115	1.34860	+ .08604		
(5)	(1.6882)	(1.52342)			
5.05	1.69487	1.53375	+ .1057		

	Range of validity, M	Av. deviation, %
Root equation		
$d^{0}_4 = 0.999871 + 0.146431c - 0.003923c^{3/2}$	5	0.002
Jones and Dole equation		
$\eta = 1 + 0.00515\sqrt{c} - 0.03542c$	0.05	.002
$\eta = 1 + 0.00515\sqrt{c} - 0.03656c + 0.049844c^2$	.5	.002

(3) See footnote (7) of the previous paper for the method of applying this correction.

(4) W. C. Root, THIS JOURNAL, **55**, 850 (1933).

silver nitrate solutions even up to 5 molar, which contain more than 50% of salt by weight.

TABLE III

DENSITY AND RELATIVE VISCOSITY OF POTASSIUM SULFATE SOLUTIONS AT 25°

c	d^{25}_4	η	$(\eta - 1)/c$	Jones and Dole equation: Simple $\Delta\eta \times 10^5$	Jones and Dole equation: Extended $\Delta\eta \times 10^5$
0.0005	0.99715	1.00039	0.78	−2	− 1
.001	.99723	1.00062	.62	−2	− 1
.002	.99736	1.00103	.51	+1	+ 2
.005	.99779	1.00198	.396	+2	+ 4
.01	.99850	1.00334	.334	0	+ 4
.02	.99990	1.00586	.293	0	+ 7
.05	1.00407	1.01281	.256	−1	+11
.1	1.01094	1.02380	.238	0	+ 9
.2	1.02443	1.04535	.227		−16
.3	1.03774	1.06760	.225		+ 6
.5	1.06386	1.11470	.229		

	Range of validity, M	Av. deviation, %
Root equation		
$d^{25}_4 = 0.997074 + 0.142388c - 0.012497c^{3/2}$	0.3	0.001
Jones and Dole equation		
$\eta = 1 + 0.01406\sqrt{c} + 0.19350c$	.1	.001
$\eta = 1 + 0.01406\sqrt{c} + 0.18951c + 0.033146c^2$	.3	.006

TABLE IV

DENSITY AND RELATIVE VISCOSITY OF POTASSIUM SULFATE SOLUTIONS AT 0°

c	d^0_4	η	$(\eta - 1)/c$	Jones and Dole equation: Simple $\Delta\eta \times 10^5$	Jones and Dole equation: Extended $\Delta\eta \times 10^5$
0.0005	0.99993	1.00028	0.56	−1	−1
.001	1.00001	1.00040	.40	−2	−1
.002	1.00015	1.00061	.30	0	+1
.005	1.00061	1.00101	.20	−2	+1
.01	1.00137	1.00157	.157	+1	+6
.02	1.00284	1.00241	.120	+1	+8
.05	1.00724	1.00441	.0882	0	−2
(.1)	(1.01447)	(1.00787)			
.101044	1.01463	1.00795	.0787		−3
(.2)	(1.02851)	(1.01606)			
.20083	1.02876	1.01614	.0804		0
(.3)	(1.04237)	(1.03020)			
.30138	1.04270	1.03040	.1009		

	Range of validity, M	Av. deviation, %
Root equation		
$d^0_4 = 0.999871 + 0.15149c - 0.01709c^{3/2}$	0.3	0.001
Jones and Dole equation		
$\eta = 1 + 0.01216\sqrt{c} + 0.03390c$	.05	.001
$\eta = 1 + 0.01216\sqrt{c} + 0.02798c + 0.12556c^2$	.2	.003

Although silver nitrate solutions at 25° have a viscosity greater than that of water throughout the range of concentration studied, yet at 0° the viscosity is less than that of water in the range from 0.02 M to about 0.6 M, but greater than that of water in both the more dilute and more concentrated ranges.

TABLE V

DENSITY AND RELATIVE VISCOSITY OF POTASSIUM CHROMATE SOLUTIONS AT 25°

c	d^{25}_4	η	$(\eta - 1)/c$	Jones and Dole equation: Simple $\Delta\eta \times 10^5$	Jones and Dole equation: Extended $\Delta\eta \times 10^5$
0.0005	0.99716	1.00036	0.72	−1	− 1
.001	.99723	1.00053	.53	−4	− 4
.002	.99739	1.00090	.45	0	+ 1
.005	.99786	1.00170	.34	0	+ 2
.01	.99863	1.00284	.284	−1	+ 2
.02	1.00018	1.00492	.246	0	+ 5
.05	1.00481	1.01062	.212	+4	+16
.1	1.01236	1.01940	.194	−2	− 8
.2	1.02753	1.03732	.1866		− 2
(.5)	(1.07174)	(1.09446)			0
.50178	1.07199	1.09457	.1885		
(1)	(1.14309)				
1.0005	1.14316	1.20946	.20936		
1.9992	1.27891	1.53171	.26596		
(2)	(1.27902)	(1.53204)			
(2.5)	(1.34424)	(1.7584)			
2.52209	1.34708	1.76931	.30503		

	Range of validity, M	Av. deviation, %
Root equation		
$d^{25}_0 = 0.997074 + 0.157186c - 0.01167c^{3/2}$	1	0.0014
Jones and Dole equation		
$\eta = 1 + 0.013305\sqrt{c} + 0.15210c$	0.1	.002
$\eta = 1 + 0.013305\sqrt{c} + 0.148502c + 0.042218c^2$	.5	.004

TABLE VI

DENSITY AND RELATIVE VISCOSITY OF POTASSIUM CHROMATE SOLUTIONS AT 0°

c	d^0_4	η	$(\eta - 1)/c$	Jones and Dole equation: Simple $\Delta\eta \times 10^5$	Jones and Dole equation: Extended $\Delta\eta \times 10^5$
0.0005	0.99995	1.00025	0.50	+1	+ 1
.001	1.00003	1.00032	.32	−1	− 1
.002	1.00019	1.00046	.23	0	+ 1
.005	1.00070	1.00070	+ .14	+1	+ 3
.01	1.00155	1.00090	.09	−2	+ 2
.02	1.00315	1.00122	.061	+2	+ 7
.05	1.00799	1.00157	.0314	0	− 3
.1	1.01593	1.00223	.0223		−10
.2	1.03181	1.00496	.0248		+ 6
(.5)	(1.07745)	(1.0249)			0
.504656	1.07814	1.02536	.05025		
(1)	(1.1503)	(1.0913)			
1.0078	1.15149	1.09270	.09198		
1.948675		1.32130	.16488		
(2)	(1.2878)	(1.3343)			
2.01707	1.28991	1.33989	.16851		
(2.5)	(1.3532)	(1.5224)			
2.54422	1.35890	1.54108	.21267		

	Range of validity, M	Av. deviation, %
Root equation		
$d^0_4 = 0.999871 + 0.166225c - 0.0157573c^{3/2}$	2.5	0.002
Jones and Dole equation		
$\eta = 1 + 0.01104\sqrt{c} - 0.01790c$	0.05	.001
$\eta = 1 + 0.01104\sqrt{c} - 0.023107c + 0.114591c^2$	.5	.003

Both potassium sulfate and potassium chromate solutions have viscosities greater than that of

water at the same temperature throughout the concentration range, and as usual the relative viscosity at 25° for any given concentration is greater than for the same concentration at 0°.

The viscosities of these solutions relative to that of pure water at the same temperature can be expressed by the Jones and Dole equation: $\eta = 1 + A\sqrt{c} \pm Bc$ as follows:

Silver nitrate at 25°: $\eta = 1 + 0.0063\sqrt{c} + 0.04517c$ valid up to 0.1 M

at 0°: $\eta = 1 + 0.00515\sqrt{c} - 0.03542c$ valid up to 0.05 M

Potassium sulfate at 25°: $\eta = 1 + 0.01406\sqrt{c} + 0.19350c$ valid up to 0.1 M

at 0°: $\eta = 1 + 0.01216\sqrt{c} + 0.03390c$ valid up to 0.05 M

Potassium chromate at 25°: $\eta = 1 + 0.013305\sqrt{c} + 0.1521c$ valid up to 0.1 M

at 0°: $\eta = 1 + 0.01104\sqrt{c} - 0.01790c$ valid up to 0.05 M

The following table gives a comparison of the values of the coefficients of the square root term (A) determined experimentally with that computed by the Falkenhagen and Vernon equation.

TABLE VII

COMPARISON OF THE THEORETICAL AND EXPERIMENTAL VALUES OF THE COEFFICIENT OF THE SQUARE ROOT TERM

	Equivalent conductance used in calcg. cation	anion	A computed	A exptl.
$AgNO_3$ at 25°	61.92	71.44	0.0056	0.0063
$AgNO_3$ at 0°	32.9	40.4	.00505	.00515
K_2SO_4 at 25°	73.52	79.8	.0131	.0140[6]
K_2SO_4 at 0°	40.4	41	.0122	.0121[6]
K_2CrO_4 at 25°	73.52	79.3	.0131	.0133
K_2CrO_4 at 0°	40.4	42.6	.0119	.0110

These results confirm the conclusions drawn in the earlier papers in this series that the Falkenhagen and Vernon equation correctly gives the influence of both valence type and temperature on the values of the coefficient of the square root term.

Although earlier measurements[5] on solutions of these salts have been numerous, none of them extend to sufficiently dilute solutions to give a reliable determination of the A coefficient, or are as precise as our measurements.

Simon[6] has proposed a law, "the molecules of isomorphous substances modify equally the viscosity of water in which they are dissolved, at the same temperature and in certain ranges of concentration." He supports this thesis by his own data on potassium sulfate and potassium chromate. Our data show that Simon's rule is a rough approximation only at 25°, but fails grossly at 0°. Thus, for example, at 0° and at a concentration of 0.2 M the solution of potassium chromate has a viscosity of 0.5% greater than that of water, whereas the solution of potassium sulfate has a viscosity 1.6% greater than that of water. Indeed the coefficient of the linear term actually has a different sign for the two salts.

Summary

1. The absolute densities and the relative viscosities of many solutions of silver nitrate, potassium sulfate and of potassium chromate have been determined at 0° and at 25°.

2. These results confirm the Root equation for densities, the Jones and Dole equation for the viscosities, and the Falkenhagen and Vernon equation for the influence of interionic attraction on the viscosity.

3. These results do not confirm Simon's proposed law that isomorphous substances have the same influence on the viscosity.

CAMBRIDGE, MASSACHUSETTS

RECEIVED NOVEMBER 25, 1939

(5) For earlier measurements on $AgNO_3$ see: A. A. Blanchard, THIS JOURNAL, **26**, 1324 (1904); J. Wagner, *Z. physik. Chem.*, **5**, 40 (1889); A. Sachanov, *Z. Elektrochem.*, **19**, 588 (1913); J. W. Ingram, *J. Chem. Soc.*, 543 (1930).

For earlier measurements on K_2SO_4 see: A. Sprung, *Pogg. Ann. der Physik*, **159**, 1 (1876); S. Arrhenius, *Z. physik. Chem.*, **1**, 285 (1887); B. E. Moore, *Phys. Rev.*, **3**, 321 (1896); J. Wagner, *Z. physik. Chem.*, **5**, 40 (1889); E. Grüneisen, *Wiss. Abhandl. physik.-tech. Reichsanstalt*, **4**, 237 (1905); G. Tigerstedt, *Soc. Sci. Fennica, Commentationes Phys.-Math.*, **1**, No. 5 (1922); M. Bobtelsky and Malkowa-Janowskaja, *Z. anorg. allgem. Chem.*, **165**, 249 (1927); W. J. Sulston, *Proc. Phys. Soc. London*, **47**, 657 (1935).

For earlier measurements on K_2CrO_4 see: A. Sprung, *Pogg. Ann. der Physik*, **159**, 1 (1876); K. F. Slotte, *Wied. Ann. der Physik*, **14**, 13 (1881); K. Schneider, Diss., Rostock, 1910; L. J. Simon, *Compt. rend.*, **178**, 1607 (1924).

(6) L. J. Simon, *Compt. rend.*, **178**, 1607 (1924).

[CONTRIBUTION FROM THE BAKER CHEMISTRY LABORATORY OF CORNELL UNIVERSITY]

The Action of Fluorine upon some Simple Aliphatic Chlorinated Hydrocarbons

BY WILLIAM T. MILLER

In beginning an investigation of the reactions of elementary fluorine with organic compounds it was observed that fluorine prepared without especial precautions may contain considerable amounts of oxygen due to the presence of water in the electrolyte.[1] Such a gaseous mixture is unsuitable for reacting with organic compounds because of its very great oxidizing action. To avoid this difficulty a carefully standardized method of preparation was developed and shown by analysis to yield nearly pure fluorine.[2]

The present paper describes a simple technique for bringing fluorine into reaction with organic compounds,[3] and reports the reactions of some chlorinated hydrocarbons with undiluted fluorine obtained using this procedure. This work is part of a research program designed to establish and investigate the general type reactions of fluorine with organic compounds.

Earlier work with the chlorinated hydrocarbons is rather limited. Humiston[4] found that the reaction between chloroform vapor and fluorine over fluorspar sand yielded free chlorine, phosgene (O_2 present?) and unidentified carbon fluorides as well as considerable carbon and tarry material. Similarly, pure fluorine containing compounds could not be isolated from the reaction between fluorine and tetrachloroethylene in carbon tetrachloride solution. Bockemüller,[5] however, has successfully carried out the fluorination of tetrachloroethylene at −80° in difluorodichloromethane solution and at 0° in carbon tetrachloride using fluorine diluted with carbon dioxide. At −80° difluorotetrachloroethane, fluoropentachloroethane and difluoroöctachlorobutane (characterized only as a liquid b. p. 139–142° at 13 mm.) were obtained as reaction products. At 0° no difluorotetrachloroethane was isolatable and only small amounts of fluoropentachloroethane and difluoroöctachlorobutane were found.

(1) For other observations see: Cuthbertson and Prideaux, *Trans. Roy. Soc. (London)*, **A205**, 395 (1906); Fredenhagen and Krefft, *Z. Elektrochem.*, **35**, 671 (1929); Ruff and Miltschitzky, *Z. anorg. Chem.*, **221**, 155 (1934).

(2) Miller and Bigelow, THIS JOURNAL, **58**, 1585 (1936).

(3) Compare: U. S. 2,013,030 and 2,013,035; *C. A.*, **29**, 6900 (1935).

(4) Humiston, *J. Phys. Chem.*, **23**, 572 (1919).

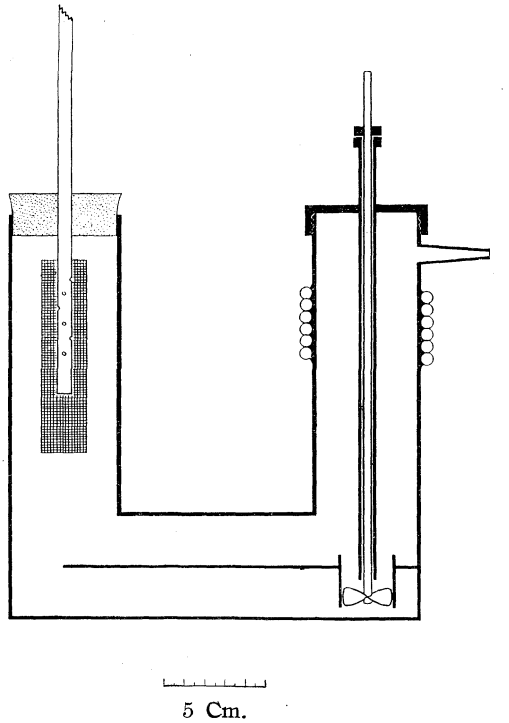
(5) Bockemüller, *Ann.*, **506**, 20 (1933).

Experimental Results

Materials.—Fluorine was obtained by essentially the procedure previously described.[2]

The chlorinated hydrocarbons were obtained by refractionating C. P. grade materials through a 50 × 1 cm. column packed with glass helices after suitable washing. Fractions with a boiling point range of 0.2° or less were utilized. Boiling points are uncorrected unless otherwise noted.

Samples for halogen analysis were decomposed by fusion with sodium peroxide. Chlorine was then determined gravimetrically and fluorine by titrating aliquots of the carefully neutralized fusion mixture with cerium nitrate solution using a procedure modeled after that of Kurtenacker and Jereuka[6] as modified by Scott and Henne.[7]



5 Cm.

Fig. 1.—Reaction vessel.

General Method.—Reactions were carried out in apparatus of the design shown in Fig. 1, which was constructed from brass tubing with silver soldered joints. One arm of the U-shaped vessel was closed by a rubber stopper which supported the fluorine inlet tube, and the other by a threaded cap which was fitted with a stirrer as indicated in the drawing. The rubber stopper was protected on the inside by a covering of thin copper foil, and in case of a too sudden reaction functioned as a safety

(6) Kurtenacker and Jereuka, *Z. anal. Chem.*, **82**, 210 (1930).

(7) Scott and Henne, *Ind. Eng. Chem., Anal. Ed.*, **7**, 299 (1935).

valve. In use the vessels were filled up to the horizontal division. The stirrer then acted as a pump to force a rapid counter-current flow of liquid along the horizontal section which divided the lower part of the vessel. Fluorine was passed in at a 5 amp. rate through a roll of copper gauze[8] and temperature control was obtained by surrounding the reaction vessel with a suitable bath.

Chloroform.—The inertness and high vapor pressure of chloroform make reaction in a suitably packed tube[9] preferable to the procedure used in this work. Small puffs due to sudden reaction occurred at regular intervals. From 150 g. of chloroform which was caused to react for three hours at 0°, 149.5 g. of washed and dried water-white product was obtained. Distillation yielded 21.0 g., b. p. 23–59°, and 0.8 g. of crystalline residue after removal of the main chloroform fraction. Redistillation yielded 8.5 g. of fluorotrichloromethane, b. p. 23.0–25.0° (reported 24.1°).[10] The purified crystalline residue (m. p. 184° subl.) was shown to be hexachloroethane.

Pentachloroethane.—This compound may be heated sufficiently to bring about smooth reaction without at the same time obtaining a too great vapor concentration. From 350 g. of pentachloroethane which was caused to react for ten hours at 90 ± 3°, 297 g. of partially crystalline (at 0°) product was obtained.

Preliminary distillation yielded the following fractions: (1) 7.6 g., b. p. 88–100°; (2) 28.5 g., b. p. 100–130°; (3) 57.4 g., b. p. 130–140° (solid); (4) 11.8 g., b. p. 140–148°; (5) 12.9 g., b. p. 148–156°; (6) 91.6 g., b. p. 156–159°; (7) 45.2 g., oily semi-solid residue. Small amounts of hydrogen chloride gas were evolved during this first distillation. By repeated fractionation the following products were isolated.

sym.-Difluorotetrachloroethane.—5.0 g.: b. p. 91.0–92.0°; $n^{25}D$ 1.4133; m. p. 22–24°. Previously reported: m. p. 24.65°; b. p. 92.8°; $n^{25}D$ 1.4130.[11]

Tetrachloroethylene.—15.6 g.: b. p. 117.5–118.0°. Chlorination in sunlight yielded only hexachloroethane.

Fluoropentachloroethane.—83.1 g.: b. p. 137.0–139.0°. A redistilled sample melted at 99.8–100.0° in a sealed tube. Previously reported: m. p. 101.3°; b. p. 137.9°.[11]

Pentachloroethane.—93.4 g.: b. p. 159.0–160.0°.

Hexachloroethane.—28.5 g.: m. p. 174–181° subl. A recrystallized sample melted 183.0–184.0° subl.; shown to be hexachloroethane.

Decachlorobutane.—Distillation of the residue (8.4 g.), remaining from the above separations, at 2.0 mm. pressure, yielded 4.2 g. of mobile oil, b. p. 100–116°, from which no pure products were isolated. However, by extracting the still residue with hot alcohol and evaporating the filtered extract, 1.9 g. of oily crystalline material was obtained of m. p. 61–69°. This substance was extremely soluble in usual organic solvents but only slightly soluble in glacial formic acid. Three recrystallizations by slow evaporation of its solution in 1:1 glacial formic and acetic acids yielded 0.1 g., m. p. 80.0–81.0°. Calcd. for C_4Cl_{10}: C, 11.92; Cl, 88.07; H, 0.0; mol. wt., 403. Found: C, 12.1; Cl, 88.0; H, 0.11; mol. wt., 397.[12]

Considerably improved recovery was found possible in subsequent runs for which, however, complete separations were not carried out. For example, 343 g. of crude material was obtained from a similar ten-hour reaction starting with 365 g. of pentachloroethane.

Tetrachloroethane.—From 327 g. of tetrachloroethane which was caused to react at 50 ± 2° for fourteen hours, 310 g. of washed and dried product was recovered. Preliminary distillation yielded the following fractions: (1) 7.9 g. to b. p. 90°; (2) 18.4 g., b. p. 90–95°; (3) 5.8 g., b. p. 93–113°; (4) 75.3 g., b. p. 113–118°; (5) 11.4 g., b. p. 118–142°; (6) 168.3 g., b. p. 142–150°; (7) 21.2 g. residue. Continued fractionation yielded:

Trichloroethylene and sym-Difluorotetrachloroethane.—Separation of these substances cannot be accomplished by distillation; however, trichloroethylene was shown to be present and separated by preparing its mercury salt $Hg(CCl{=}CCl_2)_2$, m. p. 82–83°.[13] Difluorotetrachloroethane was obtained slightly impure; m. p. 19–23°, b. p. 92–93°.

Fluorotetrachloroethane.—($CHCl_2CFCl_2$), 67.8 g., b. p. 115.5–116.5°, was obtained from fraction (4). For a redistilled sample of constant b. p. 115.7°: d^{20}_4 1.6218; $n^{20}D$ 1.4487. Previously reported: b. p. 116.6°; d^{20}_4 1.6223; $n^{20}D$ 1.4487.[14]

Tetrachloroethane.—Fraction (6) was principally unreacted tetrachloroethane.

Pentachloroethane.—11.2 g. was obtained from fraction (7); b. p. 159.0–160.0°. No hexachloroethane could be isolated.

Tetrachloroethylene.—From 335 g. of tetrachloroethylene which was caused to react at 0° for twelve hours, 354 g. of washed and dried product was recovered. Complete absorption of the fluorine occurred.

Preliminary distillation yielded the following fractions: (1) 15.4 g., b. p. 40–80°; (2) 58.5 g., b. p. 80–115°; (3) 30.6 g., b. p. 115–120° (the distillation was interrupted at this point because of decomposition to yield some free chlorine, and then continued under reduced pressure without a fractionating column); (4) 138.4 g. to b. p. 125° at 35 mm.; (5) 6.1 g., b. p. 125–155° at 35 mm.; (6) 88.7 g., b. p. 155–173° at 35 mm.; (7) 11.5 g. residue. Careful fractionation yielded the following pure products:

sym-Difluorotetrachloroethane.—55.0 g., b. p. 89–94°. Redistillation yielded 42.7 g., b. p. 92.0–93.0°. A redistilled sample of constant b. p. 92.3° melted at 24.43–24.73° corr.

Fluoropentachloroethane.—49.7 g., b. p. 136.0–138.0°. A redistilled sample melted at 99.0–99.5° in a sealed tube. The yield of fluoropentachloroethane varied considerably between runs and in one case a minimum of 18.0 g. was obtained together with 40.0 g. $C_2F_2Cl_4$ and 50.5 g. $C_4F_2Cl_8$.

Difluoroöctachlorobutane.—(Presumably 1,4-), 66.0 g., m. p. 4.0–5.0°; b. p. 152.5° at 20.0 mm.; $n^{20}D$ 1.5256; d^{20}_4 1.9272: Calcd. for $C_4Cl_8F_2$: Cl, 76.7%; MR_D 59.39.[15] Found: Cl, 76.6%; MR_D 58.86.

A residue of 11.1 g. remained from the above separations, b. p. principally 102–130° at 1 mm.

(8) Fredenhagen and Cadenbach, *Ber.*, **67**, 928 (1934).
(9) Miller, Calfee and Bigelow, THIS JOURNAL, **59**, 198 (1937).
(10) Ruff and Keim, *Z. anorg. Chem.*, **201**, 245 (1931).
(11) Locke, Brode and Henne, THIS JOURNAL, **56**, 1726 (1934).
(12) In fluoropentachloroethane solution; unpublished work.
(13) Schmalguss and Werner, *Z. anal. Chem.*, **97**, 314 (1934).
(14) Henne and Ladd, THIS JOURNAL, **58**, 403 (1936).
(15) Smyth, "Dielectric Constant and Molecular Structure," Chemical Catalog Company, New York, N. Y., 1931, pp. 152–153.

Tetrachloroethylene in Trifluorotrichloroethane Solution.—Sixty-five grams of tetrachloroethlyene dissolved in 150 cc. of trifluorotrichloroethane[16] was caused to react with a slight excess of fluorine at 0°. Careful fractionation of two such reaction products yielded: 46.9 g. of *difluorotetrachloroethane*, b. p. 91–93°; 10.1 g. of *fluoropentachloroethane*, b. p. 137–138°; 49.5 g. of *difluorooctachlorobutane*, b. p. 152–153° at 20 mm. *Hexachloroethane* also was identified, but was present only as a trace.

Trichloroethylene.—From 340 g. of trichloroethylene which was caused to react at 0° for ten hours, 347 g. of washed and dried product was obtained. Preliminary distillation yielded: (1) Approximately 5 cc. of liquid uncondensed by 11° cooling water but retained by a dry-ice cooled trap; (2) 10.0 g., b. p. 32–40°; (3) 4.6 g., b. p. 40–65°; (4) 40.5 g., b. p. 65–85.5°; (5) 153.9 g., b. p. 85.5–86.5°; (6) 15.6 g., b. p. 86.5–114.0° (mostly 113–114°); (7) 17.7 g., b. p. 48–80° at 93 mm.; (8) 11.6 g., to b. p. 123° at 25 mm.; (9) 48.0 g., b. p. 123–125.5° at 25 mm.; (10) 13.4 g. brown viscous residue.

Fractions (1) and (2) were brominated in sunlight. Distillation of the product yielded 3 g., b. p. 31.0–32.0°, $n^{20}D$ 1.338; an intermediate fraction of 3.5 g. to b. p. 160°; and 0.9 g., b. p. 160–162°, $n^{23}D$ 1.5194, which contained bromine. Reported for fluoro-1,2-dichloro-1,2-dibromoethane: b. p. 163.5°; $n^{23}D$ 1.5160.[14]

Refractionation of samples (4) to (7) inclusive yielded: *1,2-Difluoro-1,2,2-trichloroethane and fluorotrichloroethylene*, 14.9 g., b. p. 71.5–73.0°. Redistilled sample: b. p. 72.3–72.6°; $n^{20}D$ 1.3967; d^{20}_4 1.5555. Previously reported for CHClF—CCl_2F: b. p. 72.5; d^{20}_4 1.5587; $n^{20}D$ 1.3942;[14] for CFCl=CCl_2: b. p. 72.1°; d^{20}_4 1.5541; $n^{20}D$ 1.4360.[11] Chlorination of this product yielded *sym*-difluorotetrachloroethane principally (b. p. 92.0–92.3°, m. p. 22–24°, $n^{25}D$ 1.4135) and a small residue of fluoropentachloroethane (m. p. 75–82°, b. p. 135°).

Fluorotetrachloroethanes.—CHFCl—CCl_3 and $CHCl_2$—$CFCl_2$, 18.7 g.: b. p. 114.0–116.0°. Redistilled sample, b. p. 115.9–116.0°; $n^{20}D$ 1.4488; d^{20}_4 1.6192. Previously reported for CHFCl—CCl_3: b. p. 117.0°; $n^{20}D$ 1.4525;[14] d^{20}_4 1.6253. For $CFCl_2$—$CHCl_2$, see above. Chlorination yielded only fluoropentachloroethane (m. p. 96.0–98.0°).

Hexachlorobutene.—Distillation of sample (9) combined with the residue from the lower boiling fractions yielded: (11) 8.9 g., b. p. 70–122° at 25 mm.; (12) 42.4 g., b. p. 122.0–125.5° at 25 mm.; (13) 5 g. residue. Crystallization of (12) from 30–60° b. p. petroleum ether yielded 20.6 g. of white crystalline material (m. p. 6–9°). Several recrystallizations yielded: 6 g., m. p. 9.5–11.0°; b. p. 125.5° at 25 mm.; $n^{20}D$ 1.5442; d^{20}_4 1.6880. It contained no fluorine. Calcd. for $C_4H_2Cl_6$: C, 18.28; H, 0.76; Cl, 80.94; mol. wt., 262.8; MR_D 50.61. Found: C, 18.3; H, 0.73; Cl, 81.0; mol. wt. (Rast), 261; MR_D 49.17. This substance did not add bromine or chlorine in sunlight, and differs in properties from 1,1,2,3,4,4-hexachlorobutene-2.[17]

The lower melting fraction from sample (12) contained fluorine as well as chlorine.

Octachlorobutane.—Sample (13) partially solidified on cooling to 0° and 2.5 g. of material melting above room temperature was obtained. Several recrystallizations from petroleum ether and from methyl alcohol yielded 1.2 g. of white crystals, m. p. 75.0–76.0°. This compound did not contain fluorine and had no noticeable odor. Calcd. for $C_4H_2Cl_8$: C, 14.40; H, 0.60; Cl, 84.98. Found: C, 14.5; H, 0.65; Cl, 84.7. This substance appeared to have a structure other than 1,1,2,2,3,3,4,4-octachlorobutane.[18]

Trichloroethylene in Trifluorotrichloroethane Solution.—Fifty-five grams of trichloroethylene was dissolved in 160 cc. of trichlorotrifluoroethane[16] and caused to react at 0° for six and one-half hours. The products from three duplicate reactions were combined for distillation which yielded after removal of the solvent to b. p. 50°: (1) 2.9 g., b. p. 50–72°; (2) 29.0 g., b. p. 72–75°; (3) 15.4 g., b. p. 75–114°; (4) 20.9 g., b. p. 114–116°; (5) still residue.

Difluorohexachlorobutane.—Crystallization of sample (5) from 30–60° b. p. petroleum ether with dry-ice cooling yielded 14.6 g. of white crystals, m. p. 47–52°. Several recrystallizations from this solvent and from methyl alcohol yielded 2.5 g., m. p. 55–56°. Calcd. for $C_4H_2F_2Cl_6$: C, 16.01; H, 0.67; F, 12.63; Cl, 70.74. Found: C, 16.0; H, 0.67; F, 12.8; Cl, 70.8.

Lower melting isomers of difluorohexachlorobutane were indicated as being present in the soluble residue from the above separation by distillation, determination of molecular refraction and analysis.

Discussion

The physical as well as chemical properties of fluorine must be taken into account in considering actual reaction conditions. It has been found to be insoluble in carbon tetrachloride within the limit of measurement[19] and in general a slight solubility for fluorine in compounds of this type may be expected from its low boiling point (−188°). Consequently, the reactions observed in this work occur principally in the gas phase and at the liquid surface under essentially "non-ionic" conditions,[20] and radical type mechanisms in which the fluorine molecule is split symmetrically are considered to be of greatest importance. It is suggested that some of the observed differences of kind between the reactions of fluorine with organic compounds and the reactions of the other halogens may be found in this direction.

In addition to the expected substitution products which were obtained from chloroform and pentachloroethane, hexachloroethane and dodecachlorobutane were isolated in small amounts. This converse of the Wurtz–Fittig type of reaction has also been observed to occur when fluoroform reacts by sparking with fluorine.[21]

(16) "Freon 113" Kinetic Chemicals Inc., Carney's Point, N. J.

(17) Müller and Hüther, *Ber.*, **64**, 589 (1931).

(18) Müller and Luber, *ibid.*, **65**, 285 (1932).

(19) William T. Miller, unpublished work.

(20) Waters, "Physical Aspects of Organic Chemistry," D. Van Nostrand Co., New York, N. Y., 1937, p. 84.

(21) Ruff and Bretschneider, *Ber.*, **69**, 299 (1936).

With olefins the dimerization observed by Bockemüller[5] in the case of tetrachloroethylene was confirmed and also established for trichloroethylene. The products obtained may be termed *dimer addition products*, and it is assumed that in compounds of this type the fluorine atoms are in the 1,4-positions. Chlorine fluoride was formed in the reaction mixtures and substitution and addition products resulting from its action were isolated. Chlorine fluoride seems to add normally to ethylenic compounds without the formation of dimers since no monofluorobutane derivatives were found. In fact, the formation of dimer addition products from simple olefins appears to be a type of reaction peculiar to fluorine among the halogens.

Summary

The reactions of some simple chlorinated aliphatic organic compounds with fluorine have been studied. Using pure fluorine, charring was not observed in any case and reactions were easily controlled. The types of reaction observed were: substitution of hydrogen attached to saturated carbon; substitution of hydrogen attached to double bonded carbon; addition to ethylenic bonds; dimerization of saturated molecules by removal of two hydrogens; dimerization of ethylene derivatives accompanied by the addition of two fluorine atoms; secondary reactions due to the presence of chlorine fluoride.

The reaction conditions used and results obtained are discussed briefly. Essentially "nonionic" conditions prevailed and the hypothesis was advanced that radical type mechanisms of reaction in which the fluorine molecule is split symmetrically are of greatest significance.

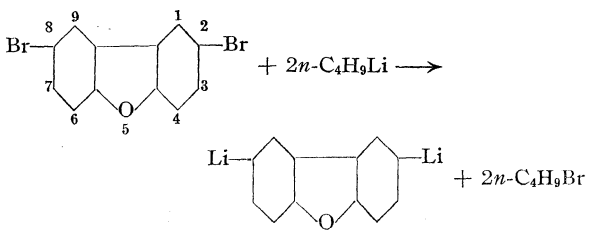
ITHACA, NEW YORK RECEIVED AUGUST 25, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

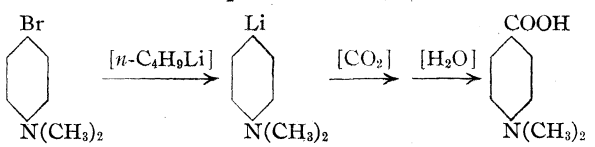
Halogen–Metal Interconversion with *m*- and *p*-Bromodimethylanilines[1]

BY HENRY GILMAN AND IRVING BANNER

The two chief transformations which resulted when an organolithium compound reacted with a nuclear-brominated aryl-alkyl or diaryl ether were: (1) metalation or replacement of a nuclear hydrogen by lithium[2] and (2) halogen–metal interconversion or the replacement of nuclear halogen by lithium.[2,3] The metalation occurred when the halogen was *para* to the ether linkage; and halogen–metal interconversion took place when the halogen was *ortho* to the ether linkage. Subsequently[4] it was shown that it was not necessary to have bromine *ortho* to an ether linkage to have a halogen–metal interconversion, for 2,8-dibromodibenzofuran and *n*-butyllithium gave an excellent yield of 2,8-dibenzodifurylenedilithium. When bromine is *meta* to the ether linkage as in 3-bromodibenzofuran, both metalation and interconversion probably occur, for the acids isolated subsequent to carbonation were 3-dibenzofurancarboxylic acid and 4-dibenzofurancarboxylic acid.[4] The reaction with 1-bromodibenzofuran, in which the bromine is also *meta* to the ether linkage, is exclusively interconversion.[5] Actually, as the accompanying paper[6] on methoxy-halogenodibenzofurans illustrates, interconversion is the predominant reaction of bromo ethers.



We are reporting at this time the reaction of *n*-butyllithium with *m*- and *p*-bromodimethylanilines. Reaction was to be expected because of the related activating effects of dialkylamino and alkoxy groups. In each case a halogen–metal interconversion took place.



Unlike the case with *p*-bromoanisole, there was

(1) This is paper XXVIII in the series of relative reactivities of organometallic compounds. The preceding paper is THIS JOURNAL, **61**, 1513 (1939).

(2) Gilman and Jacoby, *J. Org. Chem.*, **3**, 108 (1938); Wittig and co-workers, *Ber.*, **71**, 1903 (1938), and **72**, 89 (1939); Gilman, Langham and Jacoby, THIS JOURNAL, **61**, 106 939).

(3) Gilman, Cheney and Willis, *ibid.*, **61**, 951 (1939).

(4) Gilman, Willis and Swislowsky, *ibid.*, **61**, 1371 (1939).

(5) Unpublished studies.

(6) Gilman, Swislowsky and Brown, THIS JOURNAL, **62**, 348 (1940).

no evidence of significant nuclear metalation. The reaction may prove of synthetic value with amines having nuclear halogen, as already has been demonstrated with halogenated carbazoles.[5]

Not only does *p*-bromodimethylaniline react differently from *p*-bromoanisole toward *n*-butyllithium, but it also undergoes a different reaction with another metalating agent, mercuric acetate. Whitmore[7] obtained a 74% yield of N,N-dimethyl-4-bromo-2-acetoxymercurianiline by treating *p*-bromodimethylaniline with mercuric acetate in alcohol at low temperatures for several days.

Experimental Part

Preparation of *o*- and *m*-Bromodimethylanilines.—These bromodimethylanilines were prepared by customary reactions but in yields somewhat higher than those reported.[8]

To a mixture of 100 g. (0.58 mole) of *o*-bromoaniline and 100 cc. of water, contained in a 1-liter, three-necked flask provided with a mechanical stirrer, was added three equivalents (219 g.) of methyl sulfate in the following manner. One equivalent of the methyl sulfate was added with stirring and the mixture allowed to stand until homogeneity was reached. The contents were then carefully neutralized with a 25% solution of potassium hydroxide, during which cooling was effected in an ice-bath. The second equivalent of methyl sulfate was then added and the process repeated, except that a slight excess of base was added. Finally, the third equivalent was added, and the mixture was allowed to stand for one hour after stirring. The alkaline mixture was extracted with ether, and the ethereal extracts were washed with water, dried over potassium carbonate and then distilled at 100–101° (12 mm.). The yield was 81.5 g. or 70%.

The *m*-bromodimethylaniline was prepared in a related manner from 100 g. (0.58 mole) of *m*-bromoaniline and 219 g. of methyl sulfate. The yield of product distilling at 118–119° (8 mm.) was 63 g. or 54%. The melting point of the picrate (134–135°) agreed with that described in the literature.[8]

Pure *p*-bromodimethylaniline was obtained by recrystallization of a commercial product from alcohol. All samples of the bromodimethylanilines were shown to be free of primary and secondary amines. Houben and co-workers[9] have shown that some N-ethylanilines when treated first with ethylmagnesium iodide to form –N(C_2H_5)(MgI) types, and then with carbon dioxide at 225° for twenty-four hours, undergo nuclear carboxylation.

***m*-Bromodimethylaniline and *n*-Butyllithium.**—A solution of 8 g. (0.04 mole) of *m*-bromodimethylaniline in 50 cc. of ether was added to a filtered solution of 0.055 mole of *n*-butyllithium.[10a] The reaction was carried out in a nitrogen atmosphere and in a flask provided with a mechanical stirrer. After refluxing for twenty hours, the mixture was cooled, and then carbonated by adding it jet-wise to solid carbon dioxide.[10b]

The resulting mixture was extracted thoroughly with a 5% potassium hydroxide solution. The ether layer was washed with a little water and the washings combined with the aqueous layer.

The aqueous layer was concentrated, made slightly acidic with acetic acid, and then exhaustively extracted with an ether–chloroform mixture. After drying the ether–chloroform solution over sodium sulfate, the solvents were removed by distillation. The brownish oily residue was crystallized from water to yield 1.7 g. or 26% of *m*-dimethylaminobenzoic acid melting at 150–150.5°. The melting point reported[11] is 151°. The acid was derivatized by preparing the methyl ester hydrochloride, which melted at 175–176°.[12]

The yellowish ether layer yielded 1.1 g. of an as yet unidentified oil distilling between 90–115° (13 mm.).

In a check experiment, the yield of *m*-dimethylaminobenzoic acid was 32%, and the yield of oil from the ether solution was 1.3 g.

***p*-Bromodimethylaniline and *n*-Butyllithium.**—A reaction mixture of 8 g. (0.04 mole) of *p*-bromodimethylaniline in 50 cc. of ether and 0.055 mole of *n*-butyllithium in ether was refluxed for twenty hours, then carbonated, and worked up by the general procedure described for *m*-bromodimethylaniline. The yield of *p*-dimethylaminobenzoic acid (m. p. 240–241°) was 41%, and the compound was derivatized as the methyl ester[13] (m. p. 102°). From the ether layer was obtained an unidentified oil distilling between 100–130° (20 mm.). This oil did not yield a picrate of *p*-bromodimethylaniline, a compound which forms readily from pure reactants in ethanol and melts at 140–141°.

In a check experiment, the yield of *p*-dimethylaminobenzoic acid was 56%, and the yield of oil from the ether extracts was 1.5 g.

Experiments were not carried out with either *m*- or *p*-bromodimethylaniline to establish optimal conditions for the halogen–metal interconversion. However, it is highly probable that the yields can be improved by reducing the time of refluxing with the *n*-butyllithium. In this connection, it is interesting to note that forty seconds are sufficient to give a 23% interconversion in the reaction between 4-bromodibenzofuran and *n*-butyllithium in ether.

Summary

A halogen–metal interconversion takes place in the reaction of *m*- and *p*-bromodimethylanilines with *n*-butyllithium to give *m*- and *p*-dimethylaminophenyllithiums, respectively.

AMES, IOWA RECEIVED DECEMBER 7, 1939

(7) Whitmore, THIS JOURNAL, **41**, 1846 (1919); see, also, Whitmore, Cade and Leucks, *ibid.*, **51**, 1952 (1929).

(8) For *o*-bromodimethylaniline, see Auwers, *Ber.*, **40**, 2530 (1907); and von Braun, *ibid.*, **49**, 1105 (1916). For *m*-bromodimethylaniline, see Wurste and Scheibe, *ibid.*, **12**, 1818 (1879); Vorländer and Siebert, *ibid.*, **52**, 287 (1919); Hodgson and Wignall, *J. Chem. Soc.*, 1144 (1927).

(9) Houben and co-workers, *Ber.*, **42**, 3729, 4488 (1909).

(10) (a) Gilman, Zoellner and Selby, THIS JOURNAL **54**, 1957 (1932); (b) Gilman and Van Ess, *ibid.*, **55**, 1258 (1933).

(11) Griess, *Ber.*, **6**, 587 (1873).

(12) The melting point of methyl *m*-dimethylaminobenzoate hydrochloride reported by Cumming, *Proc. Roy. Soc.* (*London*), **A78**, 103 (1906), is 175–177°.

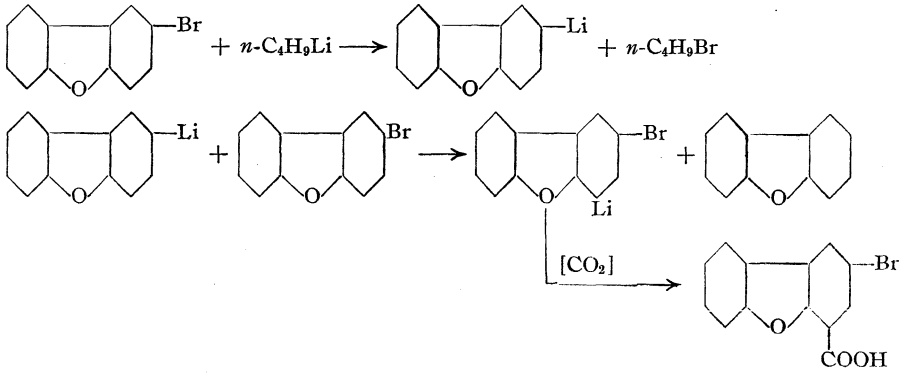
(13) Bischoff, *Ber.*, **22** 343 (1889).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE, AND PANHANDLE AGRICULTURAL AND MECHANICAL COLLEGE]

Dibenzofuran. XVI. The Two-Stage Metalation of 2-Bromodibenzofuran[1]

BY HENRY GILMAN, WRIGHT LANGHAM AND H. B. WILLIS

In an earlier study,[2] incidental to an attempt to prepare 2-bromo-6-dibenzofurancarboxylic acid, it was shown that metalation of 2-bromodibenzofuran by *n*-butyllithium gave, subsequent to carbonation, 2-bromo-4-dibenzofurancarboxylic acid. The isolation from that reaction of appreciable quantities of dibenzofuran suggested that a halogen-metal interconversion first took place and that this reaction was followed by metalation as follows.

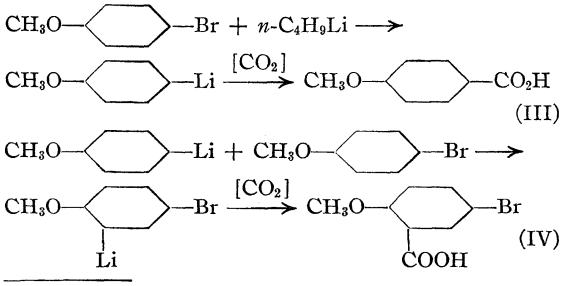


We are now presenting evidence in support of this two-stage metalation. When 2-bromodibenzofuran is treated with *n*-butyllithium for a short time, reaction (I) occurs predominantly, and carbonation results in the formation of excellent yields of 2-dibenzofurancarboxylic acid to the exclusion of any 2-bromo-4-dibenzofurancarboxylic acid. The bromo-acid probably results in accordance with reaction (II) when the reaction mixture (with equivalent quantities of reactants) is heated for a relatively long period.[2]

The preliminary reaction involving a halogen-metal interconversion is now known to take place quite readily when the halogen is bromine or iodine. This interconversion reaction is not limited to halogenated ethers, but has been observed with simple and multiple halogenated derivatives of aromatic hydrocarbons[3] and with *m*- and *p*-bromodimethylanilines.[4] The first report on such a reaction with *n*-butyllithium was probably the study by Marvel and co-workers[5] with *o*- and *m*-bromotoluenes.[6] The other reported studies on the interconversion reaction have been with *ortho*-bromo ethers.[7]

It is uncertain whether a halogen–metal interconversion precedes all metalations of halogen containing compounds. An examination of the results of metalation, particularly by *n*-butyllithium, of bromo- and iodo-ethers, reveals that in almost every case a halogen–metal interconversion first takes place.[8] However, there is no unequivocal case for interconversion preceding metalation when the nuclear halogen is chlorine or fluorine. In such cases, the rate of direct metalation is apparently decidedly greater than the rate of halogen–metal interconversion.

Two other illustrations of interconversion preceding metalation are the reactions of *p*-bromoanisole and *p*-iodoanisole with *n*-butyllithium. Under conditions reported earlier,[9] carbonation



(1) Paper XV, THIS JOURNAL, **61**, 3149 (1939).

(2) Gilman, Cheney and Willis, *ibid.*, **61**, 951 (1939).

(3) See p. 1372 of Gilman, Willis and Swislowsky, *ibid.*, **61**, 1371 (1939), for studies by W. Langham.

(4) Gilman and Banner, *ibid.*, **62**, 344 (1940).

(5) Marvel, Hager and Coffman, *ibid.*, **49**, 2323 (1927).

(6) Under their conditions (Ref. 5) of long-timed reactions in sealed tubes and with petroleum ether as a medium, they observed that *p*-bromotoluene and *n*-butyllithium gave *p*-*n*-butyltoluene on hydrolysis. With our experimental conditions (short-time, non-sealed containers, and ether as a medium) interconversion took place as usual to give *p*-toluic acid subsequent to carbonation.

(7) Citations to the earlier literature are given in Ref. 3.

(8) Illustrations with some bromo-ethers of dibenzofuran are given in the accompanying paper by Gilman, Swislowsky and Brown, THIS JOURNAL, **62**, 348 (1940).

(9) Gilman and Jacoby, *J. Org. Chem.*, **3**, 108 (1938); Wittig, Pockels and Dröge, *Ber.*, **71**, 1903 (1938); Gilman, Langham and Jacoby, THIS JOURNAL, **61**, 106 (1939).

of the reaction mixture of *p*-bromoanisole and *n*-butyllithium gave 5-bromo-2-methoxybenzoic acid [reaction (IV)]. We are now reporting that by employing a large excess of *n*-butyllithium, and milder conditions, the *p*-methoxybenzoic acid is formed exclusively and in good yields [reaction (III)].

When equivalent quantities of halide and organolithium compound are used, the reaction time is the most important factor in determining the products which result. This is strikingly illustrated in the reaction of *p*-iodoanisole with *n*-butyllithium. In this case, the *p*-methoxybenzoic is formed predominantly if not exclusively in thirty minutes, whereas after six hours only 5-iodo-2-methoxybenzoic acid is isolated. Also, when equivalent quantities of *p*-bromoanisole and *n*-butyllithium are added dropwise and separately to a reaction chamber and then allowed to react but one minute prior to carbonation, a 10% yield of *p*-methoxybenzoic acid (free from any bromo acid) results. It is rather certain that even with a long period of reaction, interconversion is the main reaction when a large excess of *n*-butyllithium is used.

Experimental Part

2-Bromodibenzofuran and *n*-Butyllithium.—To a solution of 2 g. (0.0081 mole) of 2-bromodibenzofuran in 25 cc. of benzene was added approximately 0.009 mole of *n*-butyllithium in 25 cc. of ether. The solution was refluxed for thirty minutes, and then poured upon dry-ice and ether. The yield of the crude 2-dibenzofurancarboxylic acid was 1.7 g. (87.3%). One recrystallization from glacial acetic acid gave a product which melted at 241–242°.

The methyl ester, prepared from the acid and diazomethane in ether, melted at 81–82° after crystallization from dilute alcohol. A mixed melting point with an authentic specimen of methyl 2-dibenzofurancarboxylate was not depressed. Incidentally, the melting point of methyl 2-dibenzofurancarboxylate is 82–83° and not 73–74° as reported previously.[10]

Anal. Calcd. for $C_{14}H_{10}O_3$: OCH_3, 13.72. Found: OCH_3, 13.45.

In a check experiment, the yield of 2-dibenzofurancarboxylic acid was 84.5%.

In another experiment 2-dibenzofuryllithium was prepared as described above, from 0.0081 mole of 2-bromodibenzofuran and 0.009 mole of *n*-butyllithium, and after fifteen minutes an additional 0.032 mole of 2-bromodibenzofuran was added. Upon carbonation after six hours of refluxing, the only acid isolated was 2-bromo-4-dibenzofurancarboxylic acid.

With three equivalents of *n*-butyllithium to one of 2-bromodibenzofuran, in a 1:1 ether–benzene mixture heated for six hours at 50°, the yield of 2-dibenzofurancarboxylic acid was 64%, and no 2-bromo-4-dibenzofurancarboxylic acid was isolated.

p-Bromoanisole and *n*-Butyllithium.—When an ether solution of equivalent quantities of *p*-bromoanisole (0.1 mole) and *n*-butyllithium was heated at 34° for twenty hours and then carbonated, the acids obtained were *p*-methoxybenzoic (10%) and 5-bromo-2-methoxybenzoic (10%). Under corresponding conditions, but with a more concentrated mixture which permitted refluxing at 50°, the yield of 5-bromo-2-methoxybenzoic acid was 28%. In a third experiment, a mixture of 0.05 mole of *p*-bromoanisole and 0.05 mole of *n*-butyllithium in a 1:1 ether–benzene solvent was refluxed for twenty hours at 50°, and then carbonated to yield 22% of 5-bromo-2-methoxybenzoic acid.

In a fourth experiment, two equivalents of *p*-bromoanisole were used. A mixture of 0.18 mole of *p*-bromoanisole and 0.09 mole of *n*-butyllithium in 150 cc. of ether was refluxed for a few minutes; then 150 cc. of dry benzene was added and the temperature of refluxing was 50°. Carbonation of 50-cc. aliquots of the reaction mixture after refluxing for one hour, five hours and ten hours gave 47, 47, and 52%, respectively, of 5-bromo-2-methoxybenzoic acid. Carbonation of the remainder of the reaction mixture after a total of twenty hours of refluxing reduced the average yield to 45%. Possibly some of the organolithium compound is used up in ether cleavage in the extended period of refluxing.

In a fifth experiment two equivalents of *n*-butyllithium were used and the reaction was run in ether at room temperature for ten minutes. From 0.02 mole of *p*-bromoanisole and 0.04 mole of *n*-butyllithium there was obtained 1.6 g. (52%) of crude *p*-methoxybenzoic acid (m. p. 168–171°). Pure *p*-methoxybenzoic acid melts at 183–184°. The crude acid gave a qualitative test for bromine, but no bromo acid was isolated.

In a sixth experiment 0.02 mole of *p*-bromoanisole and 0.02 mole of *n*-butyllithium were added separately and dropwise to a reaction chamber and carbonation was effected at intervals after the reactants had been in contact for one minute. This method gave a total yield of 0.3 g. (10%) of *p*-methoxybenzoic acid which melted at 178–180° and showed no qualitative test for bromine.

***p*-Iodoanisole and *n*-Butyllithium.**—A solution of 0.03 mole of *p*-iodoanisole and 0.03 mole of *n*-butyllithium in 100 cc. of ether was allowed to stand for thirty minutes with no external heating. Carbonation of a 25-cc. aliquot gave a 52% yield of crude *p*-methoxybenzoic acid melting at 176–180°. After one hour of refluxing, carbonation of a 25-cc. aliquot gave a 52% yield of crude *p*-methoxybenzoic acid melting at 172–175°. After six hours of heating, a 25-cc. aliquot yielded 0.45 g. of acidic material with a melting point range of 154–165°. At the end of ten hours of heating there was obtained a 35% yield of 5-iodo-2-methoxybenzoic acid.

The 5-iodo-2-methoxybenzoic acid was identified by a mixed melting point determination with an authentic specimen.[11]

Anal. Calcd. for $C_8H_7O_3I$: neut. equiv., 278. Found: neut. equiv., 278.

(10) Gilman and Van Ess, THIS JOURNAL, **61**, 1365 (1939).

(11) For the preparation of 5-iodo-2-hydroxybenzoic acid see Hübner, *Ber.*, **12** 1347 (1879); Goldberg, *J. prakt. Chem.*, [2] **19**, 368 (1879).

In a second experiment, carbonation at the end of fifteen minutes gave a 50% yield of crude *p*-methoxybenzoic acid, melting at 170–174°. From a third experiment in which the reaction mixture was heated at 50° in a 1:1 ether–benzene solvent for five hours, the yield of pure 5-iodo-2-methoxybenzoic acid was 24%.

Orienting experiments have shown that it is possible to metalate alcohols (like benzyl alcohol), phenols, and primary and secondary amines. Also, halogen–metal interconversions take place with a variety of bromo and iodo compounds containing, in addition, other functional groups like amino, hydroxy, and acids and their derivatives. For example, *o*-bromophenol and *n*-butyllithium give, subsequent to carbonation and hydrolysis, a 60% yield of salicylic acid; and under corresponding conditions *o*-bromoaniline gives a 36% yield of anthranilic acid.

Summary

It has been shown that the metalations reported previously of some halogenated ethers involve a two-stage procedure. First, there is a halogen–metal interconversion, and, second, the organometallic compound formed in this manner then metalates the original halogenated ether. The interconversion reaction is more rapid. For example, in fifteen minutes, 2-bromodibenzofuran reacts with *n*-butyllithium to give excellent yields of 2-dibenzofuryllithium. Upon protracted refluxing, this RLi compound then metalates 2-bromodibenzofuran to give 2-bromo-4-dibenzofuryllithium.

Related observations are reported with *p*-bromoanisole and *p*-iodoanisole.

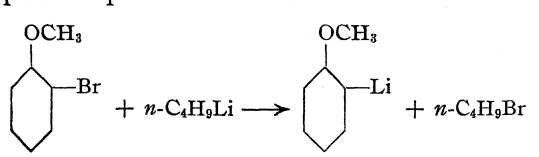
AMES, IOWA
GOODWELL, OKLAHOMA RECEIVED DECEMBER 7, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

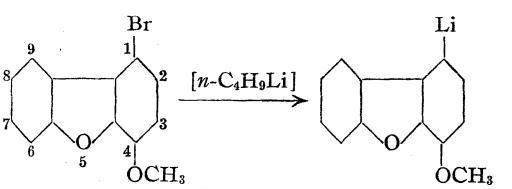
Dibenzofuran. XVII. The Reaction of Bromo-Ethers with *n*-Butyllithium[1]

BY HENRY GILMAN, JACK SWISLOWSKY AND GEORGE E. BROWN

The recent availability of a series of bromomethoxy derivatives of dibenzofuran has provided essential material for an examination of the scope of halogen–metal interconversion reactions. In the first published illustrations of this reaction with bromo-ethers,[2] the bromine replaced by lithium was always *ortho* to an ether linkage. A typical simple illustration is



We are now reporting reactions of *n*-butyllithium with a series of bromomethoxydibenzofurans in which the bromine atoms are disposed in most of the important positions with respect to the ether linkages. In these eight compounds, a bromine atom is not only *ortho*, *meta* and *para* to a methoxy group, but also *ortho* and *meta* to the oxygen bridge in dibenzofuran. We have found that in every case the predominant reaction is a halogen–metal interconversion.



Some of the reactions reported are synthetically valuable. For example, 1-bromo-3,4-dimethoxydibenzofuran has not as yet yielded either an organomagnesium[3] or an organolithium[4] compound when treated with the respective metals under general conditions for the formation of these organometallic compounds. However, *n*-butyllithium reacts promptly with 1-bromo-3,4-dimethoxydibenzofuran to give a satisfactory yield of 3,4-dimethoxy-1-dibenzofuryllithium.

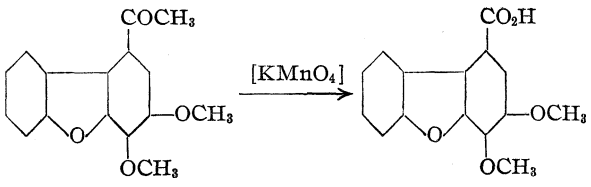
The structures of the several reaction products were established by conventional procedures involving carbonation to the corresponding acids which were in turn compared with authentic specimens. The acid resulting from 1-bromo-3,4-dimethoxydibenzofuran was shown to be identical with 3,4-dimethoxy-1-dibenzofurancarboxylic acid prepared as follows

(1) Paper XVI, THIS JOURNAL, **62**, 346 (1940).

(2) General references on this reaction are contained in the accompanying papers: (a) Gilman and Banner, *ibid.*, **62** 344 (1940), and (b) Gilman, Langham and Willis, *ibid.*, **62**, 346 (1940).

(3) The activated magnesium–copper alloy was not used.

(4) Gilman, Zoellner and Selby, THIS JOURNAL, **55**, 1252 (1933).



Experimental Part

1-Bromo-2-methoxydibenzofuran.—A solution of *n*-butyllithium, prepared from 4.15 g. (0.03 mole) of *n*-butyl bromide and 0.5 g. (0.07 g. atom) of lithium in 20 cc. of ether, was added at once to 2.77 g. (0.01 mole) of 1-bromo-2-methoxydibenzofuran[5] in 40 cc. of warm benzene. A white precipitate formed immediately and the solvent began to reflux gently. Heat was applied, and after ten minutes of refluxing with stirring the mixture was carbonated by addition to solid carbon dioxide. After removal of the solvent by distillation the residue was extracted with hot potassium hydroxide solution, from which was obtained 1.8 g. (73.5%) of acid melting at 135–140°. Two recrystallizations from dilute ethanol gave 1.15 g. (47%) of acid melting at 155–157°. A mixed melting point with an authentic sample of 2-methoxy-1-dibenzofurancarboxylic acid (m. p., 156–157°)[5] showed no depression. The methyl ester, prepared from the acid and diazomethane in ether, melted at 100° and did not depress the melting point of an authentic sample of methyl 2-methoxy-1-dibenzofurancarboxylate (m. p. 99.5–100°).[6]

1-Bromo-4-methoxydibenzofuran.—A solution of *n*-butyllithium prepared from 0.11 g. (0.16 g. atom) of lithium and 10 g. (0.073 mole) of *n*-butyl bromide in 50 cc. of dry ether was filtered rapidly into a solution of 13.85 g. (0.05 mole) of 1-bromo-4-methoxydibenzofuran in 100 cc. of dry benzene. A gray precipitate formed immediately. The suspension was refluxed with stirring for one-half hour, and then carbonated by pouring upon crushed solid carbon dioxide. On working up the mixture in a customary manner there was obtained 8.3 g. (68.5%) of 4-methoxy-1-dibenzofurancarboxylic acid (m. p. 278°). Identification was completed in two ways: first, by a mixed melting point determination with an authentic specimen of the acid; and, second, by conversion to methyl 4-methoxy-1-dibenzofurancarboxylate and comparison of this ester with one prepared from an authentic specimen of the corresponding acid.[7]

Methyl 4-Methoxy-1-dibenzofurancarboxylate.—Addition of an excess of diazomethane solution to a suspension of 0.1 g. of 4-bromo-1-dibenzofurancarboxylic acid in ether gave a quantitative yield of methyl 4-methoxy-1-dibenzofurancarboxylate. This ester melted at 125° after crystallization from methanol.

Anal. Calcd. for $C_{15}H_{12}O_4$: methoxyl, 24.22. Found: methoxyl, 24.18.

3-Bromo-2-methoxydibenzofuran.—An ether solution of *n*-butyllithium (0.015 mole) was added in one portion to 1.39 g. (0.005 mole) of 3-bromo-2-methoxydibenzofuran[5] in 60 cc. of warm benzene. The mixture was stirred and refluxed for fifteen minutes and then carbonated. The 2-methoxy-3-dibenzofurancarboxylic acid isolated melted at 197–199° and weighed 0.710 g. (58.6%). Recrystallization from glacial acetic acid yielded 0.490 g. (40.5%) of acid melting at 206–207°. A mixed melting point with an authentic specimen of the acid (m. p. 206–207°)[5] showed no depression. The methyl 2-methoxy-3-dibenzofurancarboxylate obtained from the acid resulting from the interconversion reaction was shown to be identical with an authentic specimen.[6]

In another experiment in which only one-half the amount of *n*-butyllithium was used and where the time of refluxing was ten minutes, the yield of crude acid was 24.5%.

6-Bromo-4-methoxydibenzofuran.—To 60 mg. (0.000216 mole) of 6-bromo-4-methoxydibenzofuran[8] dissolved in 2.4 cc. of warm benzene was added 1.2 cc. of an ether solution of *n*-butyllithium (0.0005 mole), and the solution was stirred and heated. Just before the boiling point was reached, a white precipitate appeared which gradually became heavier. Carbonation was carried out at the end of fifteen minutes. There was obtained 30 mg. (57.4%) of crude acid which sintered at 210° and melted at 223–225° with decomposition. The pure 4-methoxy-6-dibenzofurancarboxylic acid melts at 243–245°.[9]

The methyl ester prepared from the acid and diazomethane did not depress the melting point of authentic methyl 4-methoxy-6-dibenzofurancarboxylate (m. p. 123–124°).

1-Bromo-3,4-dimethoxydibenzofuran.—A mixture prepared from *n*-butyllithium (0.03 mole) in ether and 4.6 g. (0.015 mole) of 1-bromo-3,4-dimethoxydibenzofuran[8] in 100 cc. of benzene was refluxed with stirring for one-half hour. Carbonation gave 2.22 g. (54%) of acid melting at 234–235°. Crystallization from ethanol yielded needles melting at 236°. The acid was shown to be 3,4-dimethoxy-1-dibenzofurancarboxylic acid by the method of mixed melting points. In addition, the methyl ester was shown by the same process to be identical with an authentic specimen prepared by the oxidation of 1-acetyl-3,4-dimethoxydibenzofuran followed by methylation.[8,10]

3,4-Dimethoxy-1-dibenzofurancarboxylic Acid.—A suspension of 0.27 g. (0.001 mole) of 1-acetyl-3,4-dimethoxydibenzofuran in 75 cc. of water was oxidized by alkaline permanganate to give a 50% yield of 3,4-dimethoxy-1-dibenzofurancarboxylic acid. The acid melted at 236° after crystallization from ethanol.

Anal. Calcd. for $C_{15}H_{12}O_5$: methoxyl, 22.79. Found: methoxyl, 22.40.

Methyl 3,4-Dimethoxy-1-dibenzofurancarboxylate.—This ester was prepared in a quantitative yield from the corresponding acid and diazomethane. On crystallization from dilute ethanol the ester melted at 78°.

Anal. Calcd. for $C_{16}H_{14}O_5$: methoxyl, 32.55. Found: methoxyl, 32.40.

1-Bromo-4,6-dimethoxydibenzofuran.—An ether solution of 0.008 mole of *n*-butyllithium was added to a solution of 2.15 g. (0.007 mole) of 1-bromo-4,6-dimethoxydibenzofuran[11] in 60 cc. of benzene. After refluxing and

(5) Kindly provided by P. R. Van Ess.
(6) Kindly provided by R. L. Bebb.
(7) Gilman, Parker, Bailie and Brown, THIS JOURNAL, **61**, 2838 (1939).
(8) Kindly provided by L. C. Cheney.
(9) Unpublished studies by T. H. Cook.
(10) Gilman and Cheney, THIS JOURNAL, **61**, 3149 (1939).
(11) Kindly provided by T. H. Cook.

stirring for one-half hour, the mixture was carbonated to give a 60% yield of acid melting at 296°. The identity of the acid as 4,6-dimethoxy-1-dibenzofurancarboxylic acid was established by converting it to the methyl ester and comparing this ester with an authentic specimen.[10]

1,9 - Dibromo - 2,8 - dimethoxydibenzofuran.—This dibromo compound was prepared by bromination of 2,8-dihydroxydibenzofuran and subsequent methylation.[12] The 1,9-positions of the bromine atoms are assigned provisionally on the basis of the behavior of the related 2-hydroxydibenzofuran upon bromination.[13]

To 1.5 g. (0.00389 mole) of the dibromo compound dissolved in 120 cc. of benzene was added an ether solution of *n*-butyllithium (0.035 mole). The mixture was refluxed and stirred for two hours and then carbonated to yield 820 mg. (66.6%) of acid melting at 210–220°. Two recrystallizations from glacial acetic acid raised the melting point to 270–271°, and a mixed melting point with the acid obtained from direct dimetalation of 2,8-dimethoxydibenzofuran[12] followed by carbonation was not depressed. The methyl ester, prepared from the acid, methanol and dry hydrogen chloride melted at 128–129° after crystallization from methanol.

This dimethyl 2,8-dimethoxy-1,9-dibenzofurandicarboxylate did not depress the melting point of the dimethyl ester[12] obtained from the 2,8-dimethoxydibenzofurandicarboxylic acid resulting from direct dimetalation of 2,8-dimethoxydibenzofuran.

3,7-Dibromo-2,8-dimethoxydibenzofuran.—To 0.7 g. (0.00183 mole) of the dibromo-2,8-dimethoxydibenzofuran melting at 260–261° and tentatively designated as the 3,7-isomer,[12] dissolved in 60 cc. of benzene was added an ether solution of 0.018 mole of *n*-butyllithium. After stirring and refluxing for seven hours, the mixture was carbonated. The resulting acidic material weighed 650 mg. and from this was isolated by sublimation several tenths of a gram of benzoic acid.[14] The residual acid, 2,8-dimethoxy-3,7-dibenzofurandicarboxylic acid, was recrystallized three times from glacial acetic acid to yield 0.1 g. (17.5%) of needles which melted at 290° with decomposition.

Anal. Calcd. for $C_{16}H_{12}O_7$: methoxyl, 19.62. Found: methoxyl, 19.62.

Thirty milligrams of the dimethoxy-dibasic acid was esterified by methanol and dry hydrogen chloride to yield 18 mg. (50%) of dimethyl 2,8-dimethoxy-3,7-dibenzofurandicarboxylate. This ester crystallized from methanol as needles melting at 183–184°.

Anal. Calcd. for $C_{18}H_{16}O_7$: methoxyl, 36.05. Found: methoxyl, 36.50.

(12) Unpublished studies.

(13) Gilman and Van Ess, THIS JOURNAL, **61**, 1365 (1939).

Summary

The halogen–metal interconversion reaction has been shown to be the predominant reaction with a series of bromo-ethers of dibenzofuran in which a bromine is not only *ortho*, *meta* and *para* to a methoxy group, but also *ortho* and *meta* to the oxygen bridge.

Although no organomagnesium or organolithium compound can be prepared from 1-bromo-3,4-dimethoxydibenzofuran with magnesium or lithium, respectively, under ordinary conditions, a reaction takes place readily and satisfactorily with *n*-butyllithium to give 3,4-dimethoxy-1-dibenzofuryllithium.

(14) It is known that benzene and *n*-butyllithium give on protracted refluxing small quantities of phenyllithium, the carbonation of which yields benzoic acid.

AMES, IOWA RECEIVED DECEMBER 7, 1939

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, NO. 754]

The Synthesis of 3,5-Difluoro- and 3-Fluoro-5-iodo-*dl*-tyrosine

BY JAMES ENGLISH, JR., JAMES F. MEAD AND CARL NIEMANN

Tyrosine and thyronine are different from all other amino acids in that they alone are found in nature as nuclear substituted halogen derivatives and in all cases it has been observed that the halogen atoms are contiguous to either a phenolic or aryloxy group.[1] Until recently the only halogenated amino acid of unambiguous physiological importance was the hormone thyroxine. However, the synthesis of 3-fluorotyrosine by Schiemann and Winkelmuller[2] and the subsequent pharmacological investigations of G. Litzka, K. Kraft, and W. May[3] have shown that other halogenated amino acids must be added to this category. As part of a study on the halogenated tyrosines and thyronines this communication describes the synthesis of 3,5-difluoro- and 3-fluoro-5-iodo-*dl*-tyrosine.[4]

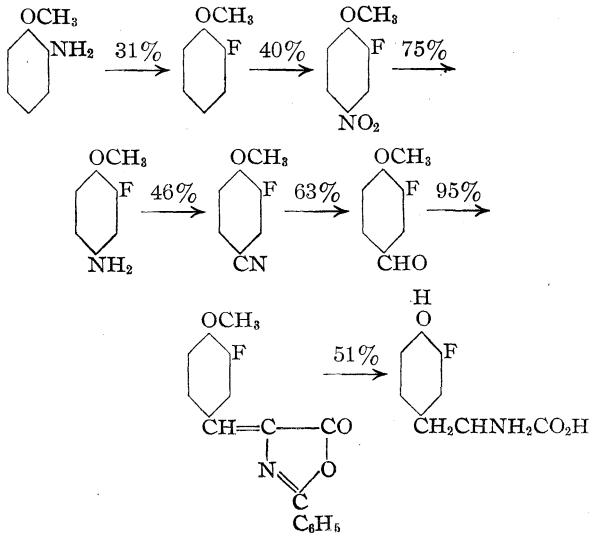
(1) (a) C. R. Harington, *Fortschritte Chem. organ. Naturstoffe*, **2**, 103 (1939); (b) C. L. A. Schmidt, "The Chemistry of the Amino Acids and Proteins," C. Thomas, Springfield, Ill., 1938.

(2) G. Schiemann and W. Winkelmuller, *J. prakt. Chem.*, **135**, 101 (1932).

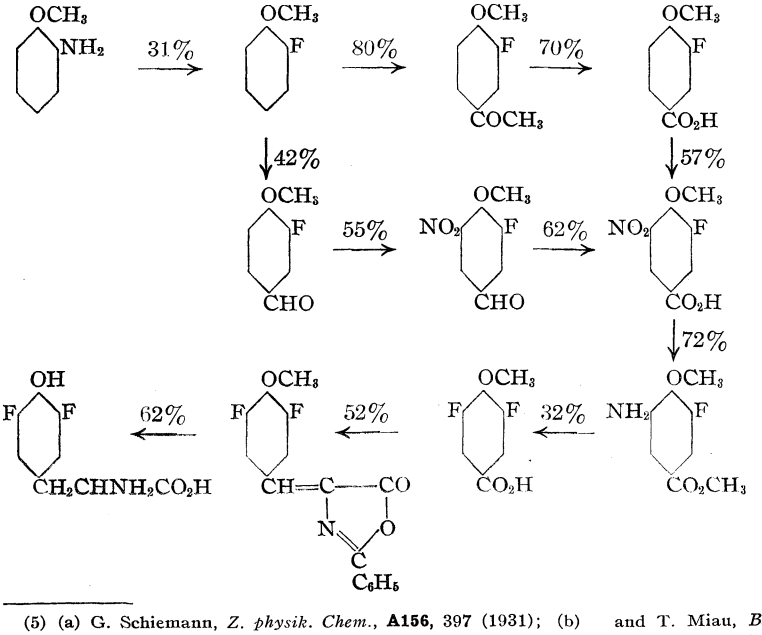
(3) (a) G. Litzka, *Arch. exptl. Path. Pharmakol.*, **183**, 427, 436 (1936); (b) *Klin. Wochschr.*, **15**, 1568 (1936); (c) *Z. ges. exptl. Med.*, **99**, 518 (1936); (d) *Deut. med. Wochschr.*, **63**, 1037 (1937); (e) H. May and G. Litzka, *Z. Krebsforsch.*, **48**, 376 (1939); (f) K. Kraft, *Z. physiol. Chem.*, **245**, 58 (1936); (g) K. Kraft and R. May, *ibid.*, **246**, 233 (1937); (h) W. May, *Klin. Wochschr.*, **14**, 790 (1935); **16**, 562 (1937).

(4) This research is being conducted as a coöperative project with Professor Paul Phillips of the University of Wisconsin.

3-Fluoro-5-iodo-*dl*-tyrosine was prepared by the direct iodination of 3-fluoro-*dl*-tyrosine. The latter amino acid was prepared by two methods. The first was a modification of a synthesis described by Schiemann[2,5] and differed only in starting with *o*-anisidine rather than *o*-phenetidine. A second synthesis was based upon the reactions



The synthesis of 3,5-difluoro-*dl*-tyrosine was attended with some difficulty; however, after several unsuccessful attempts this amino acid was obtained in a 0.73% yield from *o*-anisidine by the following series of reactions



(5) (a) G. Schiemann, *Z. physik. Chem.*, **A156**, 397 (1931); (b) *J. prakt. Chem.*, **140**, 97 (1934).

Experimental

I. Synthesis of 3-Fluoro-*dl*-tyrosine

***o*-Fluoroanisole.**[5,6]—To 2.60 kg. of freshly distilled *o*-anisidine in 5.2 l. of concd. hydrochloric acid was added 1.53 kg. of sodium nitrite in 2 l. of water. Throughout the above and succeeding operation the reaction mixture was stirred vigorously and the temperature was not allowed to rise above 0°. Five liters of fluoboric acid, prepared from 4.05 l. of technical 52% hydrofluoric acid and 1.86 kg. of boric acid,[7] was added to the clear solution of the diazotized amine and the mixture maintained at −10° for one hour. The precipitate was then recovered, washed successively with water, ethanol, and ether, and dried *in vacuo* over sulfuric acid. The yield of diazonium fluoborate was 2.70 kg. or 57.5% of the theoretical amount. The diazonium salt was then decomposed, in 540-g. portions, in a manner identical with that described in *Organic Syntheses*.[7] The crude fluoroanisole was taken up in ether, the ethereal solution washed successively with dilute sodium hydroxide and water and finally dried over sodium sulfate. Fractional distillation gave 820 g. of *o*-fluoroanisole, b. p. 69–70° (26 mm.), a yield of 53.5% from the diazonium fluoborate or an over-all yield of 30.8% from *o*-anisidine.

Anal. Calcd. for C_7H_7OF (126): C, 66.7; H, 5.6. Found: C, 66.8; H, 5.9.

2-Fluoro-4-nitroanisole.[5b,6]—The nitration of *o*-fluoroanisole according to the directions given by Schiemann and Miau[6b] consistently gave 39–40% of the theoretical amount of 2-fluoro-4-nitroanisole, m. p. 104.5°, instead of the 70% reported by these authors. All attempts to improve the yield by modification of the procedure with respect to temperature, duration of the reaction, and concentration of the nitric acid were without effect. In no case was the compound of m. p. 53° described by Holmes and Ingold[6a] as a 2-fluoro-4-nitro-anisole obtained.

2-Fluoro-4-aminoanisole.[5b,6b]—The reduction of 2-fluoro-4-nitroanisole with hydrochloric acid and stannous chloride as described by Schiemann and Miau[6b] gave 65–75% of the theoretical amount of 2-fluoro-4-aminoanisole, m. p. 82.0°, which confirms the observations of these authors.

2-Fluoro-4-cyanoanisole.—To 51 g. of 2-fluoro-4-aminoanisole in 110 ml. of concd. hydrochloric acid and 100 ml. of water was added 26 g. of sodium nitrite in 50 ml. of water. The diazonium salt was then added, with vigorous stirring, to a solution, maintained at 60–70°, of 105 g. of potassium cyanide and 92 g. of copper sulfate in 500 ml. of water layered with 100 ml. of benzene. The reaction product was taken up in an additional quantity of benzene and the solution dried over sodium sulfate. Fractional distillation gave 25 g. (46%) of the nitrile,

(6) (a) E. L. Holmes and C. K. Ingold, *J. Chem. Soc.*, **129** 1328 (1926); (b) G. Schiemann and T. Miau, *Ber.*, **66**, 1179 (1933).

(7) *Organic Syntheses*, **13**, 46 (1933).

b. p. 96–98° (1.5 mm.), m. p. 95–96°. After repeated recrystallization the substance melted at 96.5°.

Anal. Calcd. for C_8H_6ONF (151): N, 9.3; Found: N, 9.4.

3-Fluoroanisaldehyde.[2]—(A) To a solution of 15 g. of stannous chloride in 80 ml. of ether, previously saturated with hydrogen chloride, was added 8 g. of 2-fluoro-4-cyanoanisole in 100 ml. of ether.[8] The reaction mixture was allowed to stand overnight after hydrogen chloride had been passed through it, with stirring, for four hours. The precipitate was recovered, decomposed with warm water, the aldehyde taken up in ether and the ethereal solution dried over sodium sulfate. Fractional distillation gave 63% of the theoretical amount of 3-fluoroanisaldehyde, b. p. 93° (4.5 mm.), m. p. 29–30°.

Anal. Calcd. for $C_8H_7O_2F$ (154): C, 62.4; H, 4.5. Found: C, 62.4; H, 4.6.

(B) Twenty grams of *o*-fluoroanisole was added to 27 g. of zinc cyanide[9] suspended in 100 ml. of benzene. After the solution was saturated with hydrogen chloride, 24 g. of aluminum chloride was added and the reaction mixture was heated at 40–50° for four hours. The complex, after standing overnight, was decomposed by refluxing with 10% hydrochloric acid and the crude aldehyde was isolated as described above. Fractional distillation gave 6.5 g. of *o*-fluoroanisole and 7.0 g. of 3-fluoroanisaldehyde, m. p. 29–30°. The yield of aldehyde was therefore 29% of the theoretical amount, based on the original starting material, or 42% on the basis of *o*-fluoroanisole consumed.

4-(3′-Fluoro-4′-methoxybenzal)-2-phenyl-oxazolone-5.[2]—Six grams of 3-fluoroanisaldehyde was condensed with hippuric acid in the presence of acetic anhydride and sodium acetate,[2,10] and 11 g. (95%) of 4-(3-fluoro-4-methoxybenzal)-2-phenyl-oxazolone-5, m. p. 207° (cor.), was obtained.

3-Fluoro-*dl*-tyrosine.[2]—Thirty grams of the above azlactone gave, on reduction and hydrolysis,[2] 10.3 g. of 3-fluoro-*dl*-tyrosine, dec. p. 275–278° with rapid heating. The yield of amino acid from 3-fluoroanisaldehyde was 49% of the theoretical amount.

Anal. Calcd. for $C_9H_{10}O_3NF$ (199): C, 54.3; H, 5.0; N, 7.0. Found: C, 54.4; H, 5.2; N, 6.9.

3-Fluoro-5-iodo-*dl*-tyrosine.—To 7 g. of 3-fluorotyrosine in 8 *N* ammonium hydroxide was added 9 g. of iodine dissolved in the minimum amount of potassium iodide solution and the mixture was allowed to stand overnight. The crystalline precipitate was then recovered, dissolved in alkali and reprecipitated by the careful addition of acid. The mother liquors were concentrated *in vacuo* to remove the excess ammonia and carefully acidified, whereupon a further quantity of 3-fluoro-5-iodo-*dl*-tyrosine was obtained. After recrystallization from 50% ethanol the compound melted with decompn. at 192°. The yield was 5.4 g. or 47% of the theoretical amount.

Anal. Calcd. for $C_9H_9O_3NFI$ (324.9): C, 32.9; H, 2.8; N, 4.3. Found: C, 32.9; H, 3.1; N, 4.1.

(8) H. Stephen, *J. Chem. Soc.*, **127**, 1874 (1925).

(9) (a) R. Adams and J. Levine, THIS JOURNAL, **45**, 2373 (1923); (b) R. Adams and E. Montgomery, *ibid.*, **46**, 1518 (1924).

(10) E. Erlenmeyer, Jr., *Ann.*, **275**, 1 (1893).

II. Synthesis of 3,5-Difluoro-*dl*-tyrosine

3-Fluoro-4-methoxyacetophenone.—To 750 g. of *o*-fluoroanisole in 2.4 l. of carbon disulfide was added, with cooling, 1.80 kg. of aluminum chloride and 6.5 g. of acetic anhydride.[11] The reaction mixture was refluxed for one hour and then poured into ice water. The solid was recovered and recrystallized (charcoal) from ethanol. The yield of 3-fluoro-4-methoxyacetophenone, m. p. 92° was 700–800 g. or 70–80% of the theoretical amount.

Anal. Calcd. for $C_9H_9O_2F$ (168): C, 64.3; H, 5.4. Found: C, 64.1; H, 5.3.

3-Fluoro-4-methoxy-5-nitroacetophenone.—Twenty-two and one-half ml. of nitric acid, sp. gr. 1.5 in 45 ml. of concd. sulfuric acid was added, with stirring, at −10°, to 90 g. of 3-fluoro-4-methoxyacetophenone in 270 ml. of sulfuric acid. After thirty minutes the mixture was poured onto ice and the product isolated by extraction with ether and distillation *in vacuo;* 50 g. (44%) of 3-fluoro-4-methoxy-5-nitroacetophenone, b. p. 144–147° (4 mm.), was obtained. The crystalline phenylhydrazone, m. p. 160–161° dec., was prepared for analysis.

Anal. Calcd. for $C_{15}H_{14}O_3N_3F$ (303): N, 13.9. Found: N, 13.9.

3-Fluoro-5-nitroanisaldehyde.—Fourteen grams of 3-fluoroanisaldehyde was dissolved in 200 ml. of concd. sulfuric acid at −10° and while maintaining this temperature there was added 8.8 g. of nitric acid, sp. gr. 1.5. The resulting solution was allowed to stand at −10° for three hours and then poured into ice water. A white crystalline solid was recovered. This product was recrystallized from isopropyl ether, yielding 10 g. (55%) of 3-fluoro-5-nitroanisaldehyde m. p. 57–58°. Reaction of the aldehyde with hydroxylamine gave an oxime m. p. 138–139°.

Anal. Calcd. for $C_8H_7O_4N_2F$ (214): N, 13.1. Found: N, 13.1.

3-Fluoroanisic Acid.[2]—Two hundred and seventy-five grams of potassium permanganate dissolved in the minimum quantity of hot water was added to 100 g. of 3-fluoro-4-methoxyacetophenone suspended in 1 l. of water (at 80°) containing 2 g. of potassium hydroxide. After the reaction was completed the manganese dioxide was removed and the filtrate acidified with sulfuric acid. The solution was then heated to 95–98° and sufficient ethanol was added to dissolve the precipitate, 70.3 g. (70%) of 3-fluoroanisic acid, m. p. 208–210°, crystallized from this solution on standing at 0° for twenty-four hours.

Anal. Calcd. for $C_8H_7O_3F$ (170): C, 56.5; H, 4.1. Found: C, 56.6; H, 4.2.

3-Fluoro-5-nitroanisic Acid.—(A) Forty-eight grams of 3-fluoroanisic acid was added in small portions to 250 ml. of nitric acid, sp. gr. 1.5, with efficient stirring at −5°. The clear solution was allowed to stand at 0° for two hours and then poured into ice water. The 3-fluoro-5-nitroanisic acid separated as a white solid which was recovered, washed with cold water, and recrystallized from benzene, m. p. 166°. The yield was 35 g. or 57% of the theoretical amount.

Anal. Calcd. for $C_8H_6O_5NF$ (215): C, 44.7; H, 2.8; N, 6.5. Found: C, 44.7; H, 2.9; N, 6.6.

(11) C. R. Noller and R. Adams, THIS JOURNAL, **46**, 1892 (1924).

(B) Three grams of 3-fluoro-5-nitroanisaldehyde was refluxed for one hour with 25 ml. of water and 1.5 g. of potassium permanganate. The reaction product was filtered and upon acidification 2.0 g. (62%) of 3-fluoro-5-nitroanisic acid of m. p. 165° was obtained. After recrystallization the substance melted at 166°.

(C) Oxidation of 3-fluoro-4-methoxy-5-nitroacetophenone with potassium permanganate at 100° (see B above) gave 3-fluoro-5-nitroanisic acid of m p. 164–165°, recrystallized 166°. The yield was poor.

Methyl 3-Fluoro-4-methoxy-5-nitrobenzoate.—The esterification of 3-fluoro-5-nitroanisic acid was conducted in the usual manner with methanol and hydrogen chloride. From 200 g. of the acid 160 g. (80%) of the ester b. p. 128–131° (3 mm.), m. p. 50°. was obtained.

Anal. Calcd. for $C_9H_8O_5NF$ (229): N, 6.1 Found: N, 6.4.

Methyl 3-Fluoro-4-methoxy-5-aminobenozate.—One hundred and forty grams of the above nitro compound was dissolved in methanol and reduced catalytically with the aid of platinic oxide. Upon evaporation of the solvent, 110 g. (90%) of the amine, m. p. 53°, was obtained. After recrystallization from isopropyl ether the compound melted at 55°.

Anal. Calcd. for $C_9H_{10}O_3NF$ (199): N, 7.0. Found: N, 7.2.

3,5-Difluoroanisic Acid.—To 30 g. of methyl 3-fluoro-4-methoxy-5-aminobenzoate in 25 ml. of concd. hydrochloric acid was added, at −5°, 11 g. of sodium nitrite dissolved in the minimum quantity of water; 60 ml. of fluoboric acid (see above) was then added to the clear solution of the diazotized amine, still maintaining the temperature at −5°. After the reaction mixture had stood for some time at 0°, the insoluble diazonium fluoborate was recovered, washed in the usual manner and dried *in vacuo* over sulfuric acid. The yield was 38 g. or 89% of the theoretical amount. The diazonium fluoborate (38 g.) was then decomposed by dry distillation and 13 g. of methyl 3,5-difluoro-4-methoxybenzoate, was obtained. Without further purification the ester was saponified with alcoholic potassium hydroxide and upon acidification of the reaction mixture 9.0 g. (32%) of crude 3,5-difluoroanisic acid was obtained. Several recrystallizations from benzene gave 8.0 g. (28%) of pure difluoroanisic acid, m. p. 162°.

Anal. Calcd. for $C_8H_6O_3F_2$ (188): C, 51.1; H, 3.2. Found: C, 51.3; H, 3.3.

4-(3′,5′-Difluoro-4′-methoxybenzal)-2-phenyloxazolone-5.—Eight grams of 3,5-difluoroanisic acid was heated on a steam-bath for three hours with thionyl chloride. The excess reagent was removed by distillation *in vacuo* at 100° and the crude acid chloride, m. p. 15–20°, was converted into 3,5-difluoroanisaldehyde without further purification. The reduction was accomplished by refluxing a solution of the acid chloride in 25 ml. of xylene, containing 1 g. of 5% palladium barium sulfate and 45 mg. of quinoline sulfur poison,[12] while passing in hydrogen for three hours. At the end of this time no more hydrogen chloride was being evolved and the reaction mixture was filtered, extracted with a small quantity of dilute hydrochloric acid, washed with water, dried over sodium sulfate, and the xylene removed *in vacuo*. The residual liquid aldehyde was converted into the azlactone in the usual manner and from this reaction 7.0 g. (52%) of 4-(3′,5′-difluoro-4′-methoxybenzal)-2-phenyloxazolone-5, m. p. 165–169° dec., was obtained.

Anal. Calcd. for $C_{17}H_{11}O_3NF_2$ (315): N, 4.4. Found: N, 4.6.

α-N-Benzoylamino-3,5-difluoro-4-methoxycinnamic Acid.—The above azlactone was saponified with alcoholic sodium hydroxide and after acidification of the reaction mixture α-N-benzoylamino-3,5-difluoro-4-methoxycinnamic acid, m. p. 200–201°, was obtained.

Anal. Calcd. for $C_{17}H_{13}O_4NF_2$ (333): C, 61.2; H, 3.9; N 4.2. Found: C, 61.0; H, 4.2; N, 4.1.

3,5-Difluoro-*dl*-tyrosine.—Seven grams of 4-(3′,5′-difluoro-4′-methoxybenzal)-2-phenyloxazolone-5 and 7 g. of red phosphorus in 65 ml of hydriodic acid, sp. gr. 1.7, and 50 ml. of acetic anhydride, was refluxed for five hours. The reaction mixture was then worked up in the usual manner and 3.7 g. of the crude amino acid was obtained. Recrystallization from water gave 3.0 g. (62%) of 3,5-difluoro-*dl*-tyrosine, m. p. 263–265° dec.

Anal. Calcd. for $C_9H_9O_3NF_2$ (217): C, 49.8; H, 4.2; N, 6.5. Found: C, 49.7; H, 4.3; N, 6.3.

3-Fluoro-4-methoxy-5-aminobenzyl Alcohol.—(A) Four grams of 3-fluoro-5-nitroanisaldehyde in 30 ml. of ethanol was shaken with 50 mg. of platinic oxide and 0.1 ml. of 0.1 *M* ferrous chloride, in the presence of 3–4 atm. of hydrogen, for thirty minutes. After removing the catalyst and solvent the residual dark oil was distilled *in vacuo;* 0.95 g. (27%) of 3-fluoro-4-methoxy-5-aminobenzyl alcohol, b. p. 141° (2 mm.), m. p. 55°, was obtained.

Anal. Calcd. for $C_8H_{10}O_2NF$ (171): N, 8.2. Found: N, 8.2.

(B) 3-Fluoro-5-nitroanisaldehyde (6.3 g.) dissolved in 25 ml. of dry isopropyl alcohol was treated with 2 g. of aluminum isopropoxide and the mixture slowly distilled until no more acetone could be detected in the distillate. The residue was poured into water, extracted with ether and the ethereal solution dried over sodium sulfate. Fractional distillation gave 65% of the theoretical amount of 3-fluoro-4-methoxy-5-nitrobenzyl alcohol, b. p. 155–159° (3 mm.). The alcohol thus obtained was reduced quantitatively with platinic oxide and hydrogen to give 3-fluoro-4-methoxy-5-aminobenzyl alcohol, m. p. 55°.

All attempts to convert 3-fluoro-4-methoxy-5-aminobenzyl alcohol to the corresponding diazonium fluoborate, either by diazotization in the usual manner or by diazotization in fluoboric acid,[13] were unsuccessful. In a control experiment 3-amino-4-methoxybenzyl alcohol gave a 60% yield of the diazonium fluoborate.

3-Fluoro-4-methoxy-5-aminoacetophenone.—This substance was prepared by the reduction of the corresponding nitro compound in ethanol solution with platinic oxide and hydrogen. The amine, b. p. 138° (2.5 mm.), was converted into the hydrochloride which did not exhibit a true m. p. but decomposed slowly from 160–175°.

(12) K. W. Rosenmund and F. Zetsche, *Ber.*, **54**, 425 (1921).

(13) C. M. Suter, E. J. Lawson and P. G. Smith, THIS JOURNAL, **61**, 161 (1939).

Anal. Calcd. for $C_9H_{11}O_2NFCl$ (219.5): N, 6.4. Found: N, 6.5.

All attempts to prepare the diazonium fluoborate from this amine by the usual procedures were unsuccessful.

Methyl 3,5-Diamino-4-methoxybenzoate.—The methyl ester of 3,5-dinitroanisic acid[14] was reduced catalytically in an ethanol solution and a quantitative yield of the diamine, m. p. 157°, was obtained.

On tetrazotizing the diamine according to the method given by Schiemann and Pillarsky,[15] 55% of the theoretical amount of crystalline tetrazonium fluoborate separated very slowly from the reaction mixture. It was found impossible to control the decomposition of this salt so as to give a practical yield of difluoroanisic acid.

2,6-Diamino-4-nitrophenol.[16]—Hydrogen sulfide was passed into a solution of 75 g. of picric acid in 500 ml. of 28% ammonia and 500 ml. of water. Heat was evolved and cooling was necessary to prevent the temperature from rising above 75°. When the solution cleared and when heat was no longer evolved, the passage of hydrogen sulfide was stopped and the mixture evaporated *in vacuo* until the residue was practically free of ammonia. After filtration the solution was acidified, the precipitate extracted with dilute hydrochloric acid and the extract filtered. Careful addition of acid to the filtrate gave, on cooling, 45% of the theoretical amount of 2,6-diamino-4-nitrophenol, m. p. 169° dec.

Anal. Calcd. for $C_6H_7O_3N_3$ (169): N, 24.8. Found: N, 24.6.

Eight grams of the diamine heated on a steam-bath for one hour with 100 ml. of acetic acid and 9.5 g. of acetic anhydride gave a 65% yield of 2,6-diacetoamino-4-nitrophenol, m. p. 235° with decompn.

2,6-Diamino-4-nitroanisole.—Finely powdered 2,6-diacetamino-4-nitrophenol was treated, at 0° for twenty-four hours with an ethereal solution of diazomethane. A 75% yield of 2,6-diacetamino-4-nitroanisole, m. p. 211°, was obtained by recrystallizing the precipitate with ethyl acetate. 2,6-Diamino-4-nitroanisole, m. p. 180–181°, was obtained in an 85% yield from the diacetyl derivative by saponification with 5 *N* sodium hydroxide.

Anal. Calcd. for $C_7H_9O_3N_3$ (183): N, 22.9. Found: N, 23.0.

A 52% yield of the tetrazonium fluoborate was obtained from the above diamine but it was found that the salt decomposed explosively giving a very small amount of oily product.

2,6-Difluoro-4-nitroanisole.—To 2.4 g. of 2-fluoro-4-nitro-6-aminoanisole,[6b] m. p. 108°, in 3.6 ml. of concd. hydrochloric acid was added 0.9 g. of sodium nitrite in 2 ml. of water and the resulting filtered solution treated with 4 ml. of fluoboric acid. The diazonium fluoborate was obtained in a 60% yield. The decomposition of this salt was difficult to control and it was found impossible to obtain more than a 10% yield of 2,6-difluoro-4-nitroanisole, m. p. 35°.

Anal. Calcd. for $C_7H_5O_3NF_2$ (189): N, 7.4. Found: N, 7.5.

Summary

The synthesis of 3,5-difluoro- and 3-fluoro-5-iodo-*dl*-tyrosine from *o*-anisidine has been described.

PASADENA, CALIFORNIA RECEIVED DECEMBER 1, 1939

(14) F. Ullmann, *Ann.*, **366**, 94 (1909).
(15) G. Schiemann and R. Pillarsky, *Ber.*, **62**, 3039 (1929).
(16) P. Griess, *Ann.*, **154**, 202 (1870).

[CONTRIBUTION FROM THE KENT AND GEORGE HERBERT JONES CHEMICAL LABORATORIES, UNIVERSITY OF CHICAGO]

dl-Threonic Acid from 3-Hydroxy-crotonic Acid

BY J. W. E. GLATTFELD AND E. C. LEE[1]

While *dl*-erythronic lactone can be prepared without difficulty and in quantity directly from 3-hydroxy-isocrotonic lactone[2] which itself is easily obtained in good yield as a by-product in the synthesis of *dl*-2,3-dihydroxybutyric acid,[3] the epimeric tetronic acid, *dl*-threonic acid, is still a rare chemical. The only synthesis of the last-named acid that is reported in the literature was accomplished by Braun.[4] Glycerol-1,3-dichlorohydrin is the starting material and this is converted into *dl*-threonic acid by a procedure consisting of six steps. While the yield in each step is good (varying from 25 to 81%) the over-all yield is only about 2% of the theoretical.[5] As none of the intermediates is available commercially, it becomes necessary to start with glyceroldichlorohydrin in each attempt to synthesize *dl*-threonic

(1) The material in this article is taken from a dissertation submitted by E. C. Lee in August, 1936, to the faculty of the Division of the Physical Sciences in the University of Chicago in partial fulfilment of the requirements for the Ph.D. degree. Dr. Lee died in June, 1939. This article has been prepared by the senior author.
(2) Braun, THIS JOURNAL, **51**, 235 (1929).
(3) Glattfeld, Leavell, Spieth and Hutton, *ibid.*, **53**, 3164 (1931).
(4) Braun, *ibid.*, **52**, 3167 (1930); **54**, 1133 (1932).

(5) Braun also prepared one of the intermediates, 2-hydroxy-3-chloro-butyronitrile from epichlorohydrin and hydrogen cyanide (Lespieau) in 65% yield as against 25% from glycerol-1,3-dichlorohydrin. This would make the over-all yield of *dl*-threonic acid from the former 6.5% as against 2% from the latter. In spite of the lower yield, Braun seems to consider the dichlorohydrin as the starting material in this procedure for he says [*ibid.*, **52**, 3168 (1930)] "Lespieau's method has the great disadvantage that the handling of anhydrous hydrogen cyanide above its boiling point is very inconvenient. The *new procedure* (italics the author's) avoids this; it involves the treatment of dichlorohydrin with sodium cyanide in aqueous suspension."

acid. This acid is a possible source of *dl*-threose, which is necessary for the study of the saccharinic acid rearrangement of the tetroses which has been undertaken in these laboratories. It is for this reason that efforts to simplify Braun's synthesis or to find a new synthesis for this substance are being continued as opportunity offers. Some improvements have been made in Braun's procedure. These will be reported in another paper. In the present article, the transformation of 3-hydroxy-crotonic acid into *dl*-threonic acid is reported.

The starting material in this synthesis is acrolein. This has been transformed into *dl*-threonic acid with an over-all yield of 4.1% of the theoretical in five steps: acrolein $\xrightarrow{(1)}$ vinylglycolic nitrile $\xrightarrow{(2)}$ ethyl vinylglycolate $\xrightarrow{(3)}$ ethyl 3-bromo-crotonate $\xrightarrow{(4)}$ 3-hydroxy-crotonic acid $\xrightarrow{(5)}$ *dl*-threonic acid.

3-Hydroxy-crotonic acid was not recorded in the literature until 1932, when its preparation was reported by Kirrman and Rambaud.[6] The first three steps in their synthesis were the same as the first three listed under the new procedure indicated above. They then transformed the ethyl 3-bromo-crotonate into ethyl 3-acetoxy-crotonate, which in turn was hydrolyzed to 3-hydroxy-crotonic acid. The entire sketchily-described procedure of Kirrman and Rambaud was repeated. From one mole of acrolein, a few grams of the hydroxy-acid was obtained, but when five moles of acrolein was used, none was obtained. The severe treatment of the 3-bromo-ester with sodium acetate in boiling acetic acid was suspected of causing rearrangement, the longer period of heating required with larger quantities affording more opportunity for this to take place. Conversion of the bromo-ester to the acetoxy-ester was therefore eliminated, the former being hydrolyzed directly to 3-hydroxy-crotonic acid in improved yield by means of aqueous potassium carbonate. Incidentally, the preparation of ethyl vinylglycolate was studied and the yield reported in the literature[7] (49% from acrolein) improved by about 10%.

Experimental Part

Preparation of Ethyl Vinylglycolate (Steps 1 and 2).—The procedure was that used by Lobry de Bruyn[8] and by Van der Sleen.[7] Although these authors give detailed descriptions of the procedure a few comments on it should be made.

The addition of hydrogen cyanide to the acrolein proceeds slowly in a perfectly dry medium. Too much water on the other hand, causes polymerization of both the acrolein and the cyanohydrin. Ether of the proper water content was obtained by washing ordinary ether with saturated salt solution, strong permanganate solution, and water consecutively, shaking up the ether with sodium sulfate, and storing it over the sulfate for fifteen hours. Instead of adding glacial acetic acid in portions to the mixture of acrolein, ether and potassium cyanide, it was found advantageous to add the cyanide (pulverized but not dried) in portions to an ether solution of acrolein and glacial acetic acid at 10° (not lower). After all of the cyanide (1.5 moles) had been added, the reaction mixture was allowed to stand for two hours (no longer) with occasional shaking. Water was then added to dissolve the salt and the extraction with ether and subsequent distillation carried out as soon and as rapidly as possible. The last of the ether was removed at reduced pressure, yielding the crude cyanohydrin as a residue. This was transformed into the ethyl ester essentially by the procedure of Van der Sleen, 2 moles of acrolein (112 g.) giving 160 g. of the ester: a 61% yield.

Preparation of Ethyl 3-Bromo-crotonate (Step 3).—To a vigorously stirred mixture of 54 g. of phosphorus tribromide and 5 cc. of pyridine[9] kept at 20°, was added dropwise a solution of 10 g. of pyridine in 65 g. (0.5 mole) of ethyl vinylglycolate over a period of one and one-half hours. The mixture was stirred an additional half-hour, and then subjected to distillation at 13 mm. until considerable fuming occurred and the distillate became orange. The entire product was redistilled twice to free it of colored material and to complete the rearrangement and then fractionated. The second portion, which distilled at 77.5–84.5° at 6 mm., weighed 49 g.; a yield of 51% on the basis of the ethyl vinylglycolate.

Preparation of 3-Hydroxy-crotonic Acid (Step 4).—A mixture of 49 g. (0.25 mole) of the ester and 83 g. (0.5 mole) of hydrated potassium carbonate in 200 cc. of water kept at 80° was vigorously stirred for four hours at the end of which time it was cooled to 10°. Under vigorous stirring, 75 cc. of concentrated hydrochloric acid was added. Troublesome foaming due to escaping carbon dioxide was controlled by the occasional addition of a small amount of ether. The solution after filtration to remove a small amount of dark oil was concentrated under reduced pressure at 60°. The slightly-colored crystalline residue was heated with 57 cc. of acetone, the solution filtered while hot, and the material on the filter paper washed with three 25-cc. portions of acetone. The combined filtrates were filtered once more and then reduced in volume as completely as possible in vacuum at 45°. The warm residue, partly crystalline, was dissolved in 23 cc. of hot ethyl acetate. The solution was allowed to stand in an ice–salt mixture for an hour. The crystals were separated, washed with a minimum of ethyl acetate, and then recrystallized from 11 cc. of ethyl acetate. The product was dried, first in the air on a porous plate, and then in a desic-

(6) Kirrman and Rambaud, *Compt. rend.*, **194**, 1168 (1932); **196**, 487 (1933).

(7) Van der Sleen, *Rec. trav. chim.*, **21**, 211 (1902).

(8) Lobry de Bruyn, *ibid.*, **4**, 221 (1885).

(9) Bouis, *Ann. chim.*, **9**, 411 (1928).

cator over concentrated sulfuric acid. It weighed 7.1 g.; a yield of 27.8% on the basis of the bromo-ester. The product melted at 108°, the recorded melting point of 3-hydroxy-crotonic acid.

Preparation of *dl*-Threonic Acid (Step 5).—To 10.2 g. (0.1 mole) of 3-hydroxy-crotonic acid in 500 cc. of water and 2.5 cc. of a 1% aqueous solution of osmic acid was added 6.4 g. (0.033 mole) of silver chlorate in two portions separated by an interval of twenty-four hours. After forty-eight hours the silver chloride was removed by filtration, and the filtrate reduced in volume as completely as possible in vacuum at 60° and 15 mm. The sirupy residue was dissolved in 30 cc. of acetone, the solution filtered from a small amount of dark material, and most of the acetone evaporated from a crystallizing dish on the steam-bath. The material was then stored in a vacuum desiccator over concentrated sulfuric acid until bubbling ceased. The partly crystalline mass was then dissolved in 10 cc. of ethyl acetate and the solution chilled in an ice–salt bath. The crystals were separated and washed with a mimimum of ethyl acetate. The product, which melted at 97°, weighed 6.5 g.; a yield of 48% based on the hydroxy acid. A small portion of the product was recrystallized from the same solvent. This material melted at 99°. It showed no depression of the melting point when mixed with a sample of *dl*-threonic acid which had been prepared by Braun.

Summary

The work of Kirrman and Rambaud on the preparation of 3-hydroxy-crotonic acid was successfully repeated. The yield, however, was very low.

Their procedure has been modified so that 3-hydroxy-crotonic acid can now be obtained in four steps from acrolein in 8.6% yield.

3-Hydroxy-crotonic acid has been oxidized to *dl*-threonic acid with silver chlorate and osmic acid in 48% yield. The over-all yield of threonic acid, from acrolein in five steps, (4.1%) compares favorably with that obtained by Braun (2.5%) in six steps from glycerol-1,3-dichlorohydrin.

CHICAGO, ILLINOIS RECEIVED OCTOBER 16, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, NATIONAL CENTRAL UNIVERSITY, CHINA]

Keto-cyclol Tautomerism of 1,6-Diketones. 1,4-Dibromo-1,4-dibenzoylbutane*

BY TSI-YU KAO

In seeking for a direct method for the preparation of 1,2-dibenzoylcyclobutane (IV) the action of molecular silver on 1,4-dibromo-1,4-dibenzoylbutane was tried. Since silver is a monovalent element it appeared altogether unlikely that it would lead to a Reformatsky condensation such as that reported by Fuson and Farlow.[1] These authors treated 1,4-dibromo-1,4-dibenzoylbutane with zinc and obtained besides 1,4-dibenzoylbutane (III) three other compounds: 2-phenyl-3-benzoylcyclopentanone, 1-phenyl-5-benzoyl-1-cyclopentene (IX), and its oxide (VIII).

Molecular silver actually gave a small yield of the desired cyclobutane derivative, but the chief product was 1-phenyl-5-benzoyl-1-cyclopentene oxide (VIII). The formation of this substance is explained adequately by the keto-cyclol tautomerism of 1,6-diketones. This mechanism explains equally well the formation of the cyclopentene derivatives from the dibromo compound (I) by the action of zinc dust.

While the cyclol forms of simple 1,6-diketones have not been isolated, there is considerable evidence that their existence is possible. For example, Baeyer and Liebig[2] obtained 1-cyclopentenealdehyde as well as adipaldehyde by oxidation of α,α'-dihydroxysuberic acid. Marshall and Perkin[3] showed that 1,4-diacetylbutane when distilled or boiled with alcoholic potash gave 1-acetyl-2-methyl-1-cyclopentene. By the action of sodamide on 1,4-dibenzoylbutane Bauer[4] obtained two isomeric cyclopentene derivatives: 2-phenyl-3-benzoyl-1-cyclopentene and 1-phenyl-2-benzoyl-1-cyclopentene. The latter was prepared by Skraup and Guggenheimer[5] by heating 1,4-dibenzoylbutane at 300–310°. Similarly, 2,4,5-triphenyl-1-benzoyl-1-cyclopentene results when 1,4-dibenzoyl-2,3-diphenylbutane is treated with sodium ethylate.[6] All of these transformations can be explained as due to the elimination of water from the cyclol form of the diketone or diacid.

Still more striking evidence for the existence of the cyclol forms has been furnished by Vogel,[7] who showed that 2,2,3,3-tetramethyl-1,4-diacetylbutane exists only in the cyclol form.

(*) Original manuscript received January 16, 1939.

(1) Fuson and Farlow, THIS JOURNAL, **56**, 1593 (1934).

(2) Baeyer and Liebig, *Ber.*, **31**, 2107 (1898).

(3) Marshall and Perkin, *J. Chem. Soc.*, **57**, 241 (1890).

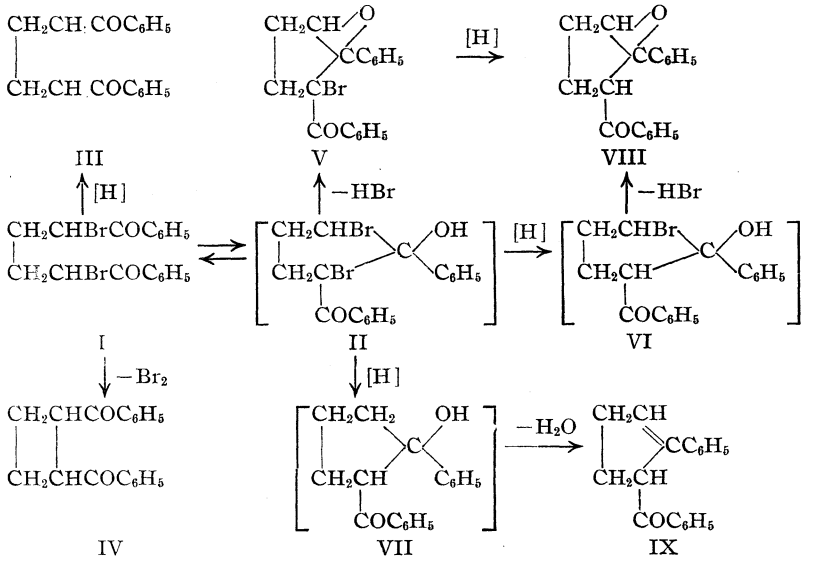
(4) Bauer, *Compt. rend.*, **155**, 288 (1912).

(5) Skraup and Guggenheimer, *Ber.*, **58B**, 2495 (1925).

(6) Conant and Cutter, THIS JOURNAL, **48**, 1026 (1926).

(7) Vogel, *J. Chem. Soc.*, **128**, 594 (1927).

The results presently reported can be explained similarly by assuming 1,4-dibromo-1,4-dibenzoylbutane to exist in both the keto (I) and the cyclol (II) forms. Removal of bromine from the keto form by the action of molecular silver yields 1,2-dibenzoylcyclobutane, and elimination of hydrogen bromide and one bromine atom from the cyclo form gives rise to the cyclopentene oxide (VIII). The probable course of these reactions is represented by the diagram



Debromination of I and II yields, respectively, 1,4-dibenzoylbutane and the cyclopentene (IX), presumably formed from the cyclol, VII. The oxide (VIII) could be formed either by elimination of hydrogen bromide from the cyclol, VI, or by debromination of the bromo oxide (V).

The latter method of formation has been shown to be possible. The bromo oxide (V) is formed when the dibromide (I) is treated with sodium cyanide,[8] diethylamine or sodium acetate. The sodium derivative of ethyl malonate produces the same change. When the bromo compound (V) is treated with zinc dust and sodium iodide in acetone it gives the oxide (VIII). This reaction serves also to establish the structure of the bromo oxide (V).

Experimental

Action of Molecular Silver on 1,4-Dibromo-1,4-dibenzoylbutane.—A mixture of 15 g. of the dibromide, 32 g. of sodium iodide and 15 g. of molecular silver (prepared by the method of Gomberg and Cone[9]) was covered with acetone and heated for eight hours under reflux. The mixture was filtered while hot and the filtrate allowed to run into a large volume of water. The residue was washed two or three times with hot acetone and finally extracted with acetone in a Soxhlet apparatus. The acetone solution obtained in this way was also poured into water. It usually contained very little organic material.

The water–acetone mixture was heated to remove the acetone and the product separated by filtration and dried. The filtrate, which was always turbid, was extracted twice with benzene to make sure that no material was lost; very little was recovered, however. The yellow product was first extracted with petroleum ether (b. p. 40–60°) in a Soxhlet apparatus for four hours and then with ethyl alcohol (in portions) until all of the organic compounds were removed. This usually required about twenty-four hours.

From the petroleum ether was obtained a solid melting at 115–140°. Fractional crystallization from alcohol gave *cis*-1,2-dibenzoylcyclobutane (m. p. 121–122°) and 1-phenyl-5-benzoyl-1-cyclopentene oxide (m. p. 169.5–170.5°) in yields of 13 and 37%, respectively. Both compounds were identified by the method of mixed melting points. The former was the more soluble and was contained in the mother liquors from which the latter had crystallized. A small amount of 1,4-dibenzoylbutane also was isolated.

1-Phenyl-5-bromo-5-benzoyl-1-cyclopentene Oxide.—A mixture of 4.2 g. of 1,4-dibromo-1,4-dibenzoylbutane, 17 g. of diethylamine and 30 cc. of dry benzene was refluxed for about thirty minutes. The bromo compound dissolved to give a wine-red solution. The mixture was filtered to remove the crystals of diethylamine hydrobromide which were then washed with benzene. The washings were added to the filtrate and the solvent was distilled under diminished pressure. The clear, viscous oily residue was dissolved in ether and the solution washed successively with hydrochloric acid and water. After the solution was dried the solvent was removed and the residue crystallized from alcohol: yield, 2 g. (59%); m. p. 138–139°.

The same compound was obtained by using sodium cyanide or sodium acetate instead of diethylamine but yields were low.

Action of the Sodium Derivative of Ethyl Malonate on 1,4-Dibromo-1,4-dibenzoylbutane.—This experiment was originally carried out with the intention of making ethyl 2,5-dibenzoyl-1,1-cyclopentanedicarboxylate. The product, however, was identical with the bromo compound of Kao and Fuson and proved to be 1-phenyl-5-benzoyl-5-bromo-1-cyclopentene oxide (V).

To a solution of 1.2 g. of metallic sodium in 50 cc. of absolute ethyl alcohol was added first 4.2 g. of ethyl malonate and then a solution of 10 g. of the dibromide in 100 cc. of dry benzene. The stopper of the reaction flask was secured with a wire and the vessel was placed in a water-

(8) Kao and Fuson, THIS JOURNAL, **54**, 313 (1932).
(9) Gomberg and Cone, *Ber.*, **39**, 3286 (1906).

bath which was heated to boiling and kept at that temperature for five hours. The contents were evaporated nearly to dryness and the residue crystallized from ethyl acetate. The bromo compound melted at 138–139°; yield, 64% of the theoretical amount.

Debromination of 1-Phenyl-5-bromo-5-benzoyl-1-cyclopentene Oxide.—A mixture of 7 g. of the bromo oxide, 7 g. of zinc dust, 10 g. of sodium iodide and 100 cc. of dry acetone was refluxed for eight hours. The mixture was filtered and the residue washed several times with hot acetone. The acetone solution was poured into a large volume of water and the precipitated oxide purified by recrystallization. It melted at 169–170° and was identified by the mixed melting point method as 1-phenyl-5-benzoyl-1-cyclopentene oxide. The yield was 0.7 g.

Summary

Treatment with molecular silver converts 1,4-dibromo-1,4-dibenzoylbutane into a mixture of 1,4-dibenzoylbutane, 1,2-dibenzoylcyclobutane and 1-phenyl-5-benzoyl-1-cyclopentene oxide. With the sodium derivative of ethyl malonate the dibromide yields 1-phenyl-5-benzoyl-5-bromo-1-cyclopentene oxide. The latter is also formed from the dibromide by the action of diethylamine Treatment of the oxide with zinc dust and sodium iodide in acetone converts it to the bromine-free cyclopentene oxide.

These transformations are interpreted on the assumption that the dibromide exists in tautomeric keto and cyclol forms.

CHUNKING, SZECHUAN, CHINA

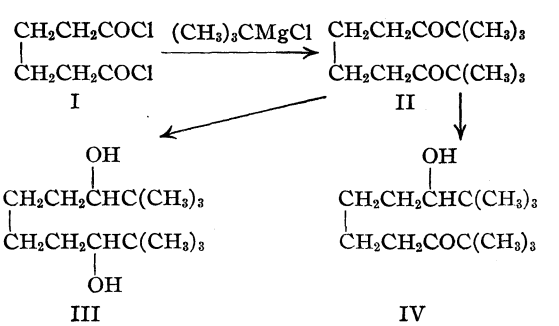
RECEIVED DECEMBER 4, 1939

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

1,4-Dibromo-1,4-dipivalylbutane

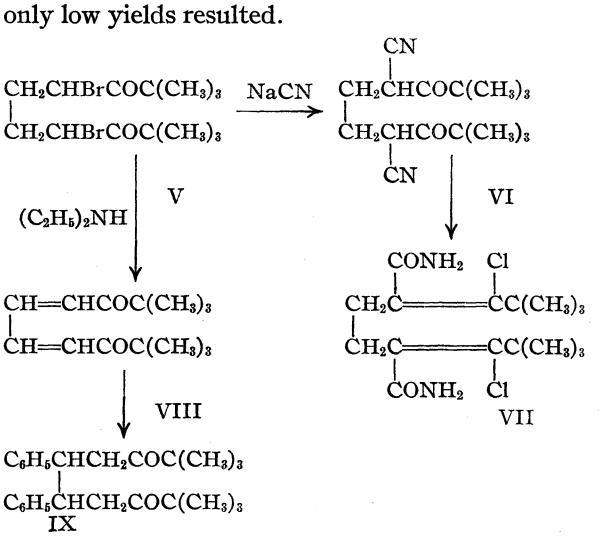
BY REYNOLD C. FUSON AND JOHN W. ROBINSON, JR.

1,4-Dibromo-1,4-dipivalylbutane (V) has been synthesized for use in connection with a general study of ring closures of 1,4-dihalogen compounds. The primary problem from the synthetic point of view was that of making the parent diketone, 1,4-dipivalylbutane (II). This compound was obtained in yields of 25% by treatment of adipyl chloride with *t*-butylmagnesium chloride. An excess of the Grignard reagent must be avoided at all times to minimize reduction of the diketone. Incomplete reaction gave δ-pivalylvaleric acid [$(CH_3)_3CCO(CH_2)_4CO_2H$]. It was impossible to



eliminate completely the formation of this by-product; the average yield of this substance was about 20%.

The use of an excess of *t*-butylmagnesium chloride gave an oil which evidently contained the diol (III) or the hydroxy ketone (IV) or both. An attempt was made to obtain the desired diketone by oxidation of the oil with chromic acid but only low yields resulted.



The dibromide (V) was formed without difficulty but only one of the two possible stereoisomeric forms was isolated. Its structure was proved by cleavage to pivalic acid by the action of alkali on the pyridinium salt.

Treatment of the dibromide with sodium cyanide was found to give the corresponding dinitrile (VI) together with a liquid which had the composition of the cyanocyclobutane derivative which might be expected by analogy with the behavior of

dibromoadipic esters.[1] On the other hand, the conversion of 1,4-dibromo-1,4-diaroylbutanes to dihydro-1,4-pyrans under these conditions[2] suggests that the liquid might be the dihydro-1,4-pyran, isomeric with the cyclobutane derivative. The data at hand do not permit a decision between these two possibilities.

Treatment with diethylamine dehydrohalogenated the dibromide (V) giving 1,4-dipivalyl-1,3-butadiene (VIII). This compound failed to condense with maleic anhydride, but reacted with phenylmagnesium bromide to yield 1,4-dipivalyl-2,3-diphenylbutane (IX). Catalytic hydrogenation converted the diene to the saturated diketone (II).

The dicyano diketone (VI) gave two moles of gas in the Grignard machine,[3] but attempts to alkylate it and to effect ring closure through the disodium derivative were fruitless. The cyano groups showed extraordinary resistance to the action of hydrolytic agents. Long heating with aqueous sodium hydroxide, for example, did not alter the compound. However, heating with concentrated hydrochloric acid in a closed tube produced a remarkable transformation. The product proved to be a chloro amide which probably has the structure VII. This is a novel type of reaction for β-keto nitriles; presumably its realization in this instance is to be ascribed to the steric hindrance afforded by the *t*-butyl radical.

Experimental

Synthesis of 1,4-Dipivalylbutane

A. By Condensation of Adipyl Chloride with *t*-Butylmagnesium Chloride.—To an ice cold solution of 0.136 mole of adipyl chloride in 400 cc. of absolute ether was added gradually over a two-hour period 0.30 mole of *t*-butylmagnesium chloride in 500 cc. of absolute ether. Vigorous stirring was used during the addition and the temperature of the reaction mixture maintained at 0°. Stirring was continued for three hours after the addition was complete.

The mixture was decomposed at 0° with ammonium chloride and worked up in the usual way. The ether solution was washed with aqueous sodium carbonate solution and dried. Evaporation of the ether left an oil which could be crystallized from low-boiling petroleum ether. In this way 6.5 to 8.5 g. of 1,4-dipivalylbutane was obtained melting at 52–52.5°.

Anal. Calcd. for $C_{14}H_{26}O_2$: C, 74.28; H, 11.58. Found: C, 74.19; H, 11.40.

The di-2,4-dinitrophenylhydrazone when purified by repeated crystallization from chloroform melted at 251–252° (uncor.).

Anal. Calcd. for $C_{26}H_{34}N_8O_8$: C, 53.23; H, 5.84; N 19.09. Found: C, 52.87; H, 5.97; N, 18.81.

Distillation of the filtrate from the crystallization of 1,4-dipivalylbutane gave 5 g. of a neutral oil boiling at 119–124° (3.5 mm.). It appeared to be impure 2,2,9,9-tetramethyl-3,8-decanediol (III).

Anal. Calcd. for $C_{14}H_{30}O_2$: C, 72.98; H, 13.12. Found: C, 71.56; H, 11.12.

The sodium carbonate solution was acidified with hydrochloric acid and extracted with ether. In this way there was obtained 5 g. of δ-pivalylvaleric acid boiling at 151–153° (2 mm.) and melting at 45–47°.

Anal. Calcd. for $C_{10}H_{18}O_3$: C, 64.48; H, 9.74. Found: C, 64.53; H, 9.61.

B. By Oxidation of the Neutral Oil.—One gram of the neutral oil boiling at 119–124° (3.5 mm.) was treated with 1 g. of chromic acid in glacial acetic acid solution. Only a small amount of the diketone could be isolated.

1,4-Dibromo-1,4-dipivalylbutane.—The bromination of 1,4-dipivalylbutane in warm carbon tetrachloride proceeded rapidly to give a 90% yield of the dibromide. The product crystallized from an ether–petroleum ether mixture, m. p. 119.5–120°.

Anal. Calcd. for $C_{14}H_{24}O_2Br_2$: C, 43.77; H, 6.30. Found: C, 43.67; H, 6.29.

Cleavage to pivalic acid was effected by the following procedure. One gram of the dibromide was dissolved in 10 cc. of ethyl acetate, 5 g. of pyridine was added and the mixture allowed to stand for twenty-four hours. The solid which formed was removed by filtration and the filtrate heated nearly to boiling; an additional quantity of the solid resulted. The solid was dissolved in 10 cc. of water and treated with cold 5% sodium hydroxide solution. An intense red color developed. The solution was acidified with dilute sulfuric acid and extracted five times with ether. In this way pivalic acid was isolated, m. p. 34–35°.

1,4-Dipivalyl-1,3-butadiene.—A solution of 4 g. of 1,4-dibromo-1,4-dipivalylbutane and 20 g. of diethylamine in 100 cc. of dry benzene was boiled under reflux for fourteen hours. The diethylamine hydrobromide was removed by filtration and the filtrate concentrated to about 15 cc. under reduced pressure. Cooling the benzene solution to 0° caused the butadiene to separate in white cotton-like crystals. These were recrystallized from methanol, m. p. 145–146°. The yield was 21% of the theoretical.

Anal. Calcd. for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.90; H, 10.22.

The di-2,4-dinitrophenylhydrazone melted at 280–282°.

Anal. Calcd. for $C_{26}H_{30}N_8O_8$: C, 53.60; H, 5.19. Found: C, 53.32; H, 5.19.

Reduction was carried out in two ways.

A. With Sodium Hydrosulfite.—This method gave a solid melting at 70–72° which decolorized solutions of permanganate in acetone and discharged the color of carbon tetrachloride solutions of bromine without evolution of hydrogen bromide. The compound was not studied further.

(1) Fuson and Kao, THIS JOURNAL, **51**, 1536 (1929); Fuson, Kreimeier and Nimmo, *ibid.*, **52**, 4074 (1930).

(2) Fuson, Kuykendall and Wilhelm, *ibid.*, **53**, 4187 (1931).

(3) Kohler, Fuson and Stone, *ibid.*, **49**, 3181 (1927).

B. With Hydrogen.—Raney nickel was used as the catalyst. The product had a melting point of 52–53° which was not depressed by the addition of 1,4-dipivalylbutane.

Reaction of the Butadiene with Phenylmagnesium Bromide.—This reaction was carried out in the usual manner. A solid was isolated melting at 206–207° which is the melting point given for 2,3-diphenyl-1,4-dipivalylbutane.[4]

1,4-Dicyano-1,4-dipivalylbutane.—A mixture of 8 g. of 1,4-dibromo-1,4-dipivalylbutane, 4 g. of powdered sodium cyanide, 120 cc. of absolute alcohol and 120 cc. of dry ethyl acetate was refluxed for forty hours. Removal of the solvents left a dark brown residue to which was added 150 cc. of water. The aqueous solution was extracted with four 50-cc. portions of ether. The resulting solution was evaporated to dryness and the residue crystallized from alcohol. The dinitrile was obtained in yields of 1.4 to 1.7 g., m. p. 92–93°.

Anal. Calcd. for $C_{16}H_{24}N_2O_2$: C, 69.53; H, 8.75; N, 10.13. Found: C, 69.75; H, 8.72; N, 10.17.

Reaction of the Dinitrile with Hydrochloric Acid.—A mixture of 0.5 g. of the dinitrile and 10 cc. of concentrated hydrochloric acid was heated in a closed tube (capacity about 30 cc.) for two hours at 140–150°. A solid was obtained which after recrystallization from benzene melted at 198–200°. The yield was 0.33 g.

Anal. Calcd. for $C_{16}H_{26}Cl_2N_2O_2$: C, 55.02; H, 7.50; N, 8.02; Cl, 20.30; mol. wt., 349. Found: C, 55.18; H, 7.43; N, 7.46; Cl, 20.70; mol. wt., 330.

(4) Hill and Susselman, THIS JOURNAL, **53**, 4424 (1931).

The alcoholic filtrate left after the separation of the dicyano compound was found to contain a neutral oil boiling at 163–168° (6 mm.); $n^{20}D$ 1.4722.

The 2,4-dinitrophenylhydrazone was crystallized from alcohol, m. p. 225–227°.

Anal. Calcd. for $C_{21}H_{27}N_5O_5$: C, 58.76; H, 6.34; N, 16.30. Found: C, 58.30; H, 6.49; N, 16.45.

An **oxime** was formed by heating a mixture of 1 g. of the oil, 1.5 g. of hydroxylamine hydrochloride, 3 g. of potassium acetate and 10 cc. of water. It was crystallized from alcohol, m. p. 183–185°.

Anal. Calcd. for $C_{15}H_{24}N_2O_2$: C, 68.15; H, 9.15. Found: C, 68.28; H, 8.96.

Repetition of the foregoing test using sodium hydroxide in place of potassium acetate gave an **isomeric oxime** melting at 146–148°.

Anal. Calcd. for $C_{16}H_{24}N_2O_2$: C, 68.15; H, 9.15; N, 10.59. Found: C, 68.23; H, 9.14; N, 10.47.

Summary

1,4-Dipivalylbutane (II) has been prepared by the action of *t*-butylmagnesium chloride on adipyl chloride.

1,4-Dibromo-1,4-dipivalylbutane (V) has been converted to the corresponding dicyano compound (VI) and to 1,4-dipivalyl-1,3-butadiene (VIII).

URBANA, ILLINOIS RECEIVED DECEMBER 4, 1939

[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

The 1,2,4-Trimesityl 1,4-Diketones and Related Compounds, Including the Stereoisomeric Mono and Dienols[1]

BY ROBERT E. LUTZ AND CHARLES J. KIBLER

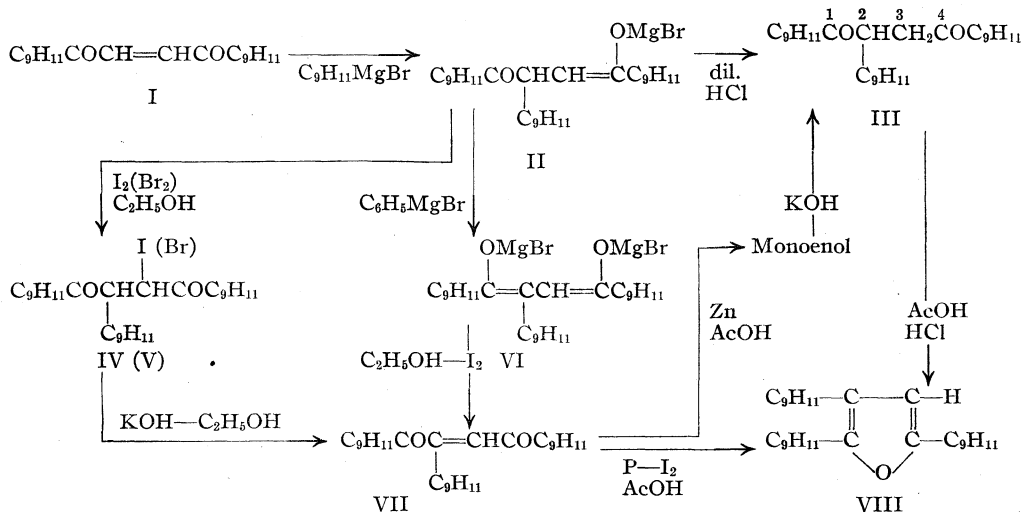
The preparation of this series of compounds was undertaken in order to extend the study of the hindering effect of mesityl groups. It was expected that here the damping of the keto–enol shift and the consequent increase in the persistence of enolic forms would make it possible to prepare some of the stereoisomeric mono and dienols or, at least, to obtain evidence of their existence. Furthermore, it was hoped that new information might be obtained concerning the properties of highly hindered enolic groups and the mechanism of certain reactions which supposedly proceed through enolic intermediates, particularly furan ring closure.[2] This report deals with a preliminary investigation in which these objectives were in a degree accomplished.

(1) This paper was presented at the Boston meeting of the American Chemical Society, September 14, 1939.

(2) Lutz and Reveley, THIS JOURNAL, **61**, 1854 (1939).

The Saturated 1,4-Diketone (III).—The starting point in the synthesis of these compounds was di-(trimethylbenzoyl)-ethylene (I). Addition of mesitylmagnesium bromide at 20° gave the monoenolate II by 1,4-addition, the reaction proceeding quickly but stopping at this point. When the reaction mixture was hydrolyzed by means of dilute hydrochloric or acetic acid, the saturated diketone III was produced in good yield; the free monoenol could not be isolated and was quite mobile, ketonizing quickly to the saturated diketone even when dilute acetic acid under mild conditions was used.

That the reaction between mesitylmagnesium bromide and di-(trimethylbenzoyl)-ethylene actually stopped at the stage of the monoenolate, II, was demonstrated (a) by conversion of the product with alcoholic iodine or bromine into the



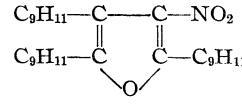
monohalogeno saturated diketones IV and V, (b) by the failure of the product to undergo oxidation to the unsaturated diketone VII when hydrolyzed in the presence of iodine or quinone, a reaction characteristic[2] of dienolates of the type of VI, and (c) by actual enolization upon more drastic treatment with the Grignard reagent to the true dienolate VI which was readily oxidizable to the unsaturated diketone when treated in the usual way with alcoholic iodine.

From these results it appears that the newly introduced mesityl group in the 1,4-addition product II definitely hinders enolization at the adjacent carbonyl. This effect is to be contrasted with the absence of any such marked hindrance in the case of the reactions between phenyl[2,3] and mesityl[4] magnesium bromides and dibenzoylethylene, and between phenylmagnesium bromide and di-(trimethylbenzoyl)-ethylene,[3] where even under mild conditions dienolates corresponding to VI are obtained.

The Unsaturated 1,4-Diketone (VII).—The trimesityl unsaturated 1,4-diketone of this series can be made in either of two ways: (a) through elimination of halogen acid from the halogeno saturated diketones IV and V by means of alcoholic potassium hydroxide, or (b) by hydrolysis under oxidizing conditions with alcoholic iodine, of the dienolates obtained by the action of a Grignard reagent on suitable compounds in this series such as the monoenolate II, the halogeno saturated diketones IV and V, or the saturated diketone III.

The unsaturated diketone VII is distinctly less reactive than the other compounds of this type which have been studied, as would be expected in view of the extreme hindrance offered by the three mesityl groups. It is reduced by zinc and boiling acetic acid through a 1,6-mechanism to a monoenol (to be described later) which is easily ketonized to the saturated diketone III; and the phosphorus–iodine–acetic acid reagent converts it directly into trimesitylfuran, VIII. Attempts to convert it into trimesitylacetoxyfuran by means of acetic anhydride and sulfuric acid failed.

2,3,5-Trimesitylfuran (VIII).—Trimesitylfuran (VIII) was obtained from the saturated diketone III in excellent yield by the prolonged action of boiling acetic acid saturated with dry hydrogen chloride. Furanization was effected also, although less efficiently, by the action of hydriodic acid at 170° and by the phosphorus–iodine–acetic acid reagent.



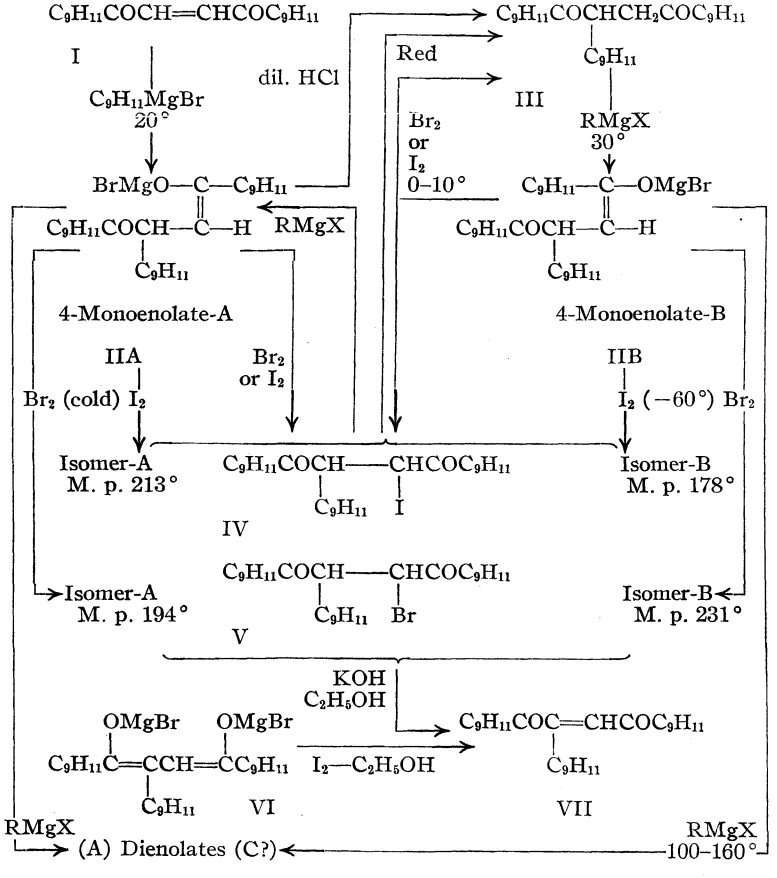
IX

The action of nitric–acetic acid mixtures on the furan produces a mononitro derivative without disrupting the furan nucleus. The nitro group presumably is located in the β-position as formulated in IX.[5] The resistance of the furan nucleus here toward oxidative ring fission constitutes another illustration of the striking stabilizing influence of two mesityl groups in the 2,5-positions, an effect which is presumably due to the hindrance of the mesityl groups toward addition of the reagents at the ends of the diene system.

(3) Lutz and Tyson, THIS JOURNAL, **56**, 1341 (1934).
(4) Lutz and Kibler, *ibid.*, **61**, 3007 (1939).
(5) The β-position is the reactive one in all of the analogous compounds studied. (Lutz and Kibler, a study of 2,5-dimesitylfurans to be published shortly.)

The Halogeno Saturated 1,4-Diketones, IV and V.—The halogeno trimesityl 1,4-diketones IV and V are of special interest because of their ready conversion into one of the two possible stereoisomeric 4-monoenolates (II) by the action of Grignard reagents, and also because of the various stereochemical relationships involved. The bromo and the iodo compounds exist each in two stable diastereoisomeric forms. These are prepared by the action of the appropriate halogen on one or the other of the isomeric (*cis-trans*) 4-monoenolates IIA and B which will be described separately below. The reactions are illustrated in the second diagram where the configurations and stereochemical relationships have been indicated as far as they have been determined. In order to simplify the naming of these various compounds, particularly the different types of enolates, the chain has consistently been numbered as in formula III.

The structures of the halides, given as IV and V, follow from the formation of both pairs of isomers



in the same reaction, namely, the halogenation of the 4-monoenolate-A (IIA) in which the position of the enolic group is known from the mode of preparation through 1,4-addition of mesitylmagnesium bromide to di-(trimethylbenzoyl)-ethylene (I). The stereoisomeric halides of the type A are best obtained in quantity by the action of the appropriate halogen on this 4-monoenolate-A and are obtained almost exclusively under controlled conditions. The B-isomers are obtained almost exclusively by halogenation at −60° of the stereoisomeric 4-monoenolate-B which is obtained by direct partial enolization of the saturated diketone III (to be described below).

The existence of these stereoisomeric halides is somewhat surprising in view of the instability of di-(trimethylbenzoyl)-bromo[5] and chloro[6]-ethanes, $C_9H_{11}COCH_2CH(Br \text{ or } Cl)COC_9H_{11}$, which lose hydrogen halide even during crystallization under relatively mild conditions. The halides in this series withstand the prolonged action of sodium acetate in boiling alcohol. Hydrogen halide is eliminated only by the action of the more powerful reagent, potassium hydroxide, with the formation of the unsaturated diketone VII.

On the other hand, the halogens are very easily eliminated from these compounds by reduction with zinc and acetic acid and also with sodium bisulfite or potassium iodide in acetic acid. The latter two reductions are of a type characteristic for α-halogeno ketones, and particularly halogen derivatives of β-diketones. The iodides, of course, are much more easily reduced than the bromides, and liberate iodine from potassium iodide in acetic acid at room temperature, whereas the bromides react thus only at elevated temperature. The product of reduction in all cases is the saturated diketone III.

The 4-Monoenolate-A (IIA).—The monoenolate obtained by the 1,4-addition of mesitylmagnesium bromide to di-(trimethylbenzoyl)-ethylene is designated as the 4-monoenolate-A. It is obtained also by the action of a Grignard reagent on any one of the halogeno satu-

(6) Lutz and Wood, THIS JOURNAL, **60**, 229 (1938).

rated diketones IV or V. It is characterized by the reactions with bromine and iodine. When it is brominated a mixture of two stereoisomeric halides A and B results with the isomer-A in the larger proportion; at lower temperatures the bromide of type A is obtained as the chief product. In iodination chiefly the iodo diketone-A is obtained even at room temperature, and only very small amounts of the isomer-B can be detected; at low temperature the iodide-A appears to be formed exclusively.

The direction of enolization in the 4-monoenolate-A indicated in formula IIA is certain from the mode of formation by the addition of mesitylmagnesium bromide to di-(trimethylbenzoyl)-ethylene (I).

The 4-Monoenolate-B (IIB).—The existence of the stereoisomeric 4-monoenolate, designated as isomer-B, was discovered in studying the direct enolization of the saturated diketone III by means of different Grignard reagents. Methylmagnesium iodide reacts rapidly with evolution of *one* molecule of methane, but the secondary reaction involving enolization of the other carbonyl group, with evolution of the second molecule of methane and the formation of a dienol, takes place very slowly and only at elevated temperatures. In respect to this secondary enolization the 4-monoenolate-B is distinctly different from the 4-monoenolate-A which undergoes this reaction easily at a moderate temperature and gives the dienolate-A quickly and in good yield. The rigorous proof of the existence of the 4-monoenolate-B and its stereoisomerism with the isomer-A is the halogenation with iodine or bromine at a lowered temperature with the formation of the iodo and bromo diketones-B consistently and almost exclusively in good yield.

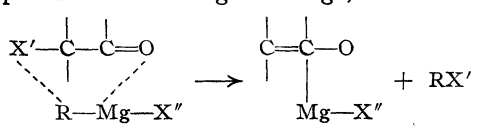
In some of the first experiments in which the reaction between iodine and the 4-monoenolate-B was carried out at room temperature or at 10°, largely the saturated diketone III was obtained and the full extent of the presence of the 4-monoenolate-B was overlooked; this result was found to be due to the high rate of ketonization of the 4-monoenolate-B at ordinary temperatures, which apparently is greater than in the case of the 4-monoenolate-A, and which under the conditions of this experiment enables ketonization to compete on favorable terms with iodination. When the halogenation was carried out at −60° the ketonization was relatively slow and became negligible, and at the same time the stereochemical mode of reaction was much more sharply defined.

The Configurations at the 4-Enolic Group.—There exists a basis for assignment of configurations at the 4-enol group in the striking fact that the configuration greatly influences the ease of the secondary enolization at the hindered 1-carbonyl. It seems reasonable to assume that the configuration offering the greater resistance to this secondary enolization will be that with the 4-mesityl group in the *cis* position with respect to the rest of the chain since this arrangement should involve the greater degree of steric hindrance. Thus the 4-monoenolate-B which undergoes the secondary enolization with great difficulty should have the configuration indicated in formula IIB, and the 4-monoenolate-A which is very easily converted into a dienolate should have the structure IIA. This argument is strengthened by the fact that the relative rates of ketonization at the 4-enolic group are consistent with the conclusion. Assuming that the ketonization of a free 4-enolic group would be hindered to the greater degree when the enolic hydroxyl group is *cis* with respect to the residue of the chain, and to the lesser degree when *cis* with respect to the hydrogen atom, then again, the 4-monoenolate-A must have the configuration indicated in IIA and the 4-monoenolate-B the structure IIB.

Stereochemical Relationships and Mechanism of Reaction.—It is clear from the foregoing discussion that the *cis* and *trans* isomeric 4-monoenolates IIA and B actually exist and are stable, and that halogenation of these isomers occurs in a consistent stereochemical manner. Whether the reaction is *cis* or *trans*, however, is not known because no information is available concerning the actual configurations of the halides produced.

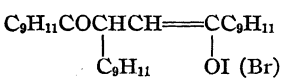
The halides IV and V, both the A and B-isomers, react readily with the Grignard reagent, the first stage of the reaction proceeding very rapidly in the cold with the formation of one and the same 4-monoenolate, isomer-A. Since the two 4-monoenolates, A and B, appear to be stable once formed, it may safely be assumed that the reaction is not guided or influenced by the configuration of the starting material as is the addition of halogen to the two monoenolates. This result would be expected because it is not easy to conceive of a marked stereochemical guiding influence emanating from the kind of configurational difference (diastereoisomerism) involved in the two types of halides.

In the formation of the 4-monoenolate by the two different methods, namely, the direct enolization of the saturated diketone III and the interaction of a Grignard reagent and the halogeno diketones A or B (IV or V), opposite stereochemical results are obtained. This is not surprising because the two reactions differ sharply in that α-hydrogen is involved in the one case and α-halogens in the other, with the elimination, respectively, of hydrocarbon and alkyl halide. This does not necessarily indicate different mechanisms in the two reactions, however. Probably, the mechanism of the reaction in the case of the halides is a simple 1,4-reaction between alkyl-magnesium halide and the conjugated system of carbonyl group and carbon–halogen linkage, as follows:



The enolizing action of the Grignard reagent on the saturated diketone may possibly follow a similar path but with opposite stereochemical results.

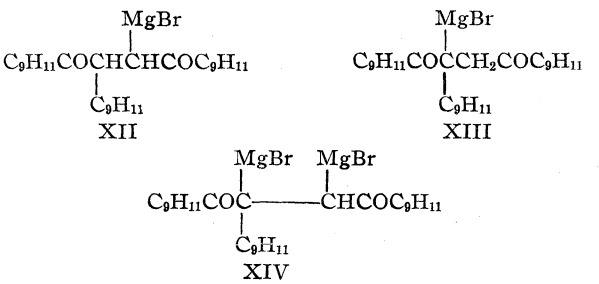
Alternative Formulations.—The hypohalite structures for the halogeno diketones IV and V (namely, X and XI), although perhaps not excluded, are highly improbable. On the basis of these formulations, which involve *cis–trans* rather than diastereoisomerism, each type of isomer should react with the Grignard reagent to give a different stereoisomeric 4-monoenolate since the 4-monoenolates-A and B are known to be stable under these conditions; actually, however, this is not the case.



X (XI)

cis and *trans*

The various mono and dienolates described in this paper may of course be formulated as true Grignard reagents, namely, XII, XIII and XIV[7]; no stereoisomerism is possible with XIII, but XII and XIV would involve diastereoisomerism instead of *cis–trans* isomerism. In view of the possibility that the whole conjugated system of the enolate group, namely, C=C—O or C=C—O—Mg, may function in reaction as a unit, and that conversely the system O=C—C—Mg might also react as a unit with one addend going to oxygen, it may not be possible from the reactions of the various compounds to decide conclusively as to which type of structure is correct. However, the true enolate formulations have been assumed here because they seem best to account for all of the reactions studied so far, particularly hydrolysis which leads to definite mono and dienols, and the existence of two isomeric 1-monoenols (described below) which would be impossible on the basis of formula XIII alone.



The Stereoisomeric 1-Monoenolates and the Dienolates.—In the foregoing discussion the question of enolization exclusively at the end of the molecule carrying the 2-mesityl group has not entered. Just as with the 4-monoenolates, the 1-monoenolates should exist in *cis* and *trans* forms, but due to the hindrance of the extra mesityl group these monoenolates should be harder to form, and the free 1-monoenols, once formed, should be extraordinarily persistent. Since the saturated diketone III enolizes first at the 4-carbonyl, it was necessary to go to the dienolates and then, avoiding oxidation to the unsaturated diketone, to allow the dienol to ketonize partially, the mobile 4-enol group ketonizing first and leaving the more persistent 1-enol. One of the two possible 1-monoenols has thus been obtained and in this case it was isolated as a metastable crystalline solid; also, there is definite evidence for the existence of the stereoisomer. These two 1-monoenols are best considered along with the stereoisomeric dienolates of which four are possible; of the latter, the existence of at least two has been demonstrated; furthermore, one free dienol has been isolated crystalline. The study of these dienolates, of course, is handicapped by the sensitivity of the free dienols toward oxygen, and the mobility of the free 4-enol group.

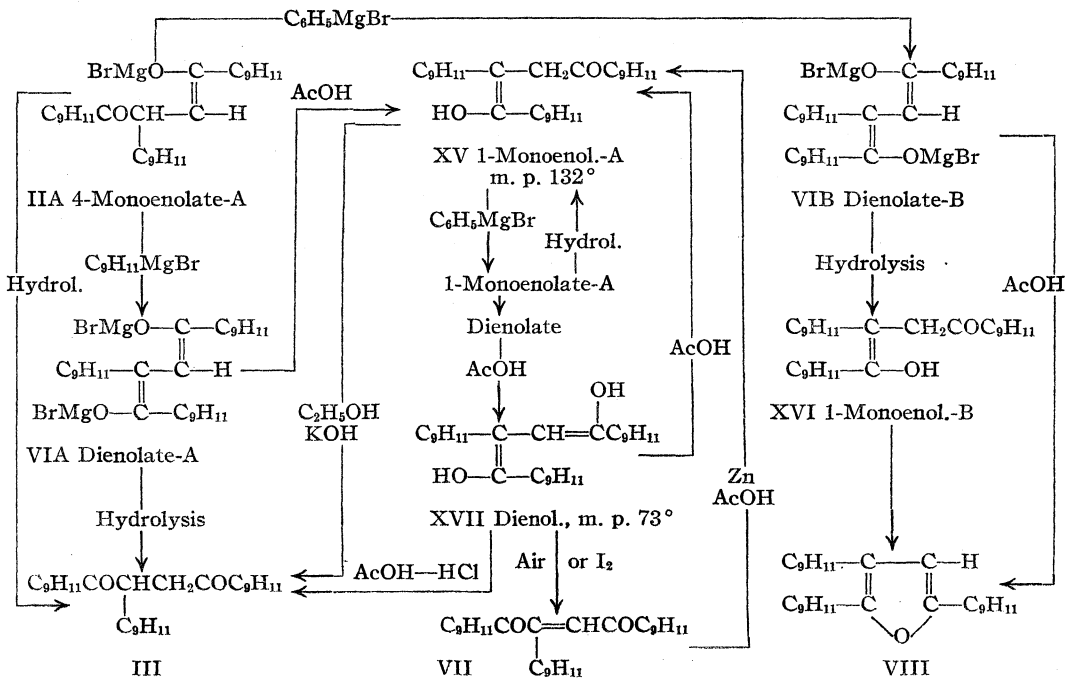
The Dienolate-A (VIA).—The dienolate VIA, arbitrarily named isomer-A, has been obtained from the 4-monoenolate-A by the enolizing action of mesitylmagnesium bromide. The preparation of this dienolate is most conveniently carried out by allowing an excess of mesitylmagnesium bromide to react either with di-(trimethylbenzoyl)-ethylene (I) or the halides IV or V, followed by

(7) *Cf.* Fuson, Fugate and Fisher, THIS JOURNAL, **61**, 2362 (1939).

heating for a short time to enolize the remaining and hindered 1-carbonyl group. That a dienolate was actually present was shown by hydrolysis in alcoholic iodine solution with resulting oxidation to the unsaturated diketone VII.

The configuration at the 4-enol group is undoubtedly the same as that in the 4-monoenolate-A because this group was already formed and possessed the configuration indicated before enolization at the 1-carbonyl took place (inversion appears to be unlikely under the conditions).

and acetic acid reduction of the unsaturated diketone VII. The structure XV follows for this monoenol since it is distinctly different from the two 4-monoenols-A and B and since the partial ketonization of the dienol would be expected to occur far more rapidly at the more mobile 4-enol group. The configuration is obviously similar to that of the corresponding 1-enol group in the dienolate-A, with the 1 and 2-mesityl groups *trans* to each other as indicated in formula XV. This configuration is assigned on the basis of the ready



The dienolate-A was characterized by its behavior upon hydrolysis; treatment with acetic acid gave the 1-monoenol-A and the use of the stronger acid, dilute hydrochloric acid, produced the saturated diketone III. The end result is in sharp contrast with that obtained on hydrolysis of the 1-monoenolate-B and the dienolate-B (described below) where trimesitylfuran (VIII) is formed exclusively under comparable conditions. The inability of the dienolate-A to go to the furan has been used as the basis for assignment of the configuration at the 1-enol group. The complete configuration is given in formula VIA.

The 1-Monoenolate-A (XV).—When the hydrolysis of the dienolate-A was carried out cautiously using acetic acid, the 1-monoenol-A was produced. It was isolated in crystalline form and characterized. It was obtained also by the zinc ketonization exclusively to the saturated diketone III and the absence of furanization which is the sole result when the isomeric 1-monoenolate-B XVI and the dienolate-B (VIB) are hydrolyzed under comparable conditions.

The 1-monoenol-A is rearranged readily to the saturated diketone III; however, it does not react with ferric chloride, bromine or diazomethane although it reacts instantly with methylmagnesium iodide with evolution of one molecule of methane. The failure of these typical enol tests must be attributed to the combined hindering effects of the two mesityl groups. The failure of the ferric chloride test might be expected, however, since it is known that another mesityl ketone,[8] $(C_6H_5)_2$-$CHCH{=}C(OH)C_9H_{11}$, does not give the color test although it reacts normally with bromine. It is

(8) Kohler and Thompson, THIS JOURNAL, 59, 888 (1937).

evident then that the dimesityl enol group, $C_9H_{11}\overset{|}{C}=C(OH)C_9H_{11}$, has none of the usual enol properties except some of those due to the active hydrogen.

Because of the inability of the enolic group of the 1-monoenol-A to react normally, the proof that it is really an enol should be examined. The evidence is as follows: the compound is isomeric with the saturated diketone and must be the enol by difference; it has an active hydrogen atom, is metastable and is convertible into the saturated diketone by the catalytic action of acids or bases.

In this connection, because of the difficulty of distinguishing between the keto and the 1-monoenol forms in this series, it was necessary to consider the saturated diketone III and the evidence that it is not itself an enol form. The saturated diketone does not react with bromine or iodine and is stable toward alkali or acid as catalysts for ketonization. It is enolized rapidly by methylmagnesium iodide with evolution of only *one* molecule of methane, and the resulting 4-monoenolate-B is shown to be the monoenolate by its reaction with one molecule of halogen to give the B-halides IV and V. From these facts then there can be no question that the saturated diketone is correctly formulated.

Reduction of the unsaturated diketone VII with zinc and boiling acetic acid, as mentioned above, proceeds slowly with the formation of the 1-monoenol-A. Reduction undoubtedly is 1,6, with the 4-enol group of the resulting dienol quickly ketonizing under these conditions.

A Crystalline Dienol.—The crystalline dienol XVII was isolated in one of the reactions studied. The 1-monoenol-A XV was treated with an excess of phenylmagnesium bromide and the resulting dienolate (probably A) was decomposed cautiously in dilute alcohol acidified with acetic acid, the free dienol separating in crystalline form. A purified sample absorbed oxygen from the air and was completely oxidized in the solid state within one week in contact with air, and reacted immediately with one equivalent of iodine; it gave in both cases the unsaturated diketone VII in approximately quantitative yields. It reacted instantly with methylmagnesium iodide with evolution quantitatively of two molecules of methane. Treatment with acetic acid caused partial ketonization to the 1-monoenol-A. Thus the configuration at the 1-enol group must correspond to that of the 1-monoenol-A as indicated in formula XVII. The configuration at the 4-enol group has not yet been ascertained.

The Dienolate-B (VIB).—As described above, the 4-monoenolate-A (IIA) reacts further with mesitylmagnesium bromide to give the dienolate-A (VIA). However, if *phenyl*magnesium bromide is used instead to bring about enolization of the hindered carbonyl group, a dienolate of distinctly different properties is obtained. The new dienolate is designated as the isomer-B (formula VIB). That this new product is actually a dienolate is shown by hydrolysis and oxidation by means of alcoholic iodine to the unsaturated diketone VII.

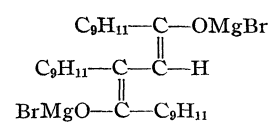
The new dienolate-B is characterized by hydrolysis. Under the usual conditions trimesitylfuran is produced exclusively, a result entirely different from that in the case of the dienolate-A where only the saturated 1,4-diketone is obtained under similar conditions. On the basis of this fact and the mode of preparation, the formula VIB has been assigned.

The 1-Monoenol-B (XVI).—Decomposition of the dienolate-B in acetic acid gave an oil which evidently was not the dienol since it did not undergo oxidation to the unsaturated diketone VII. The oil was distillable in the vacuum oven but resisted attempts at crystallization. On standing it slowly and spontaneously changed to the furan VIII which was not immediately isolable at the beginning. Under no conditions could it be converted into the saturated diketone III. It is evident that this oil contains the fourth monoenol which is therefore designated as the 1-monoenol-B XVI. In view of the ease of furan ring closure here, coupled with the fact that the 1-monoenol-A does not undergo furanization except under drastic conditions capable of dehydrating any of the compounds in the series, it is possible with reasonable assurance to assign a definite configuration at the 1-enol group both in the dienolate-B and in the 1-monoenol-B, with the 1- and the 2-mesityl groups *cis* to each other, as indicated in formulas XVI and VIB.

In the formation of the dienolate-B from the 4-monoenol-A, it is probable that the 4-enolate group remains unchanged in configuration, and in consequence it seems likely that both the dienolates-A and -B and the 4-monoenolate-A are identical in respect to the 4-enolic group, as formulated in the diagram. The new dienolate-B, then, presumably differs from the dienolate-A only in the

configuration at the 1-enol group. Whether or not this be true, it is noteworthy that the enolization at the 1-carbonyl of the 4-monoenolate-A goes in different ways with mesityl and phenylmagnesium bromides to produce configurationally opposite arrangements at the 1-enolic grouping.

The Possible Existence of a Third Dienolate (C).—The saturated diketone III when enolized by the action of the Grignard reagent gives first the 4-monoenolate-B, as described above. When the secondary enolization is forced under drastic conditions a second molecule of methane is evolved, but some decomposition occurs and the result is not of quantitative significance. The formation of some dienolate was demonstrated by oxidation with iodine to the unsaturated diketone, but the yield was poor. If no rearrangement at the 4-enol group took place, then this must be a third dienolate, C (formula XVIII), with the 4-enol group corresponding in configuration to that of the 4-monoenolate-B, and differing in this respect from the dienolates-A and -B; and since no furan was obtained from the reactions the configuration at the 1-enol must correspond to that of the 1-monoenol-A (as indicated). However, in view of the poor yields, the production of a mixture of products, and the possibility of rearrangement at the 4-enol group under the drastic conditions involved, and in the absence of any definite characterizing reaction, this question must be regarded as unsettled. It is conceivable that the configuration of the 4-monoenolate-B may actually inhibit enolization at the 1-carbonyl with rearrangement necessarily preceding the secondary enolization, and in such a case the dienolate formed here would be either A or B (VIA or B). Unfortunately, attempts to test these points were not successful.



XVIII

Dienolate—C (?)

The Bearing of the Results on the Mechanism of Furan Ring Closure.—The foregoing results are entirely consistent with the probable mechanism of furan formation[2] involving addition of an enolic hydroxyl to a γ-carbonyl followed by loss of a molecule of water. According to this theory the dienols should not be capable of giving the furan directly. The two stereoisomeric dienols which are known with certainty (IVA and B) do not do so (one of them gives the furan but only after partial ketonization and consequent destruction of the dienol system). It is hoped that the two remaining theoretically possible dienols can be isolated and tested in this connection since it is conceivable that one of them might undergo direct furanization, even though the dienol form has now been shown to be unnecessary to this reaction in at least one instance.[9]

If the suggested mechanism of furanization is correct, then in cases of unsymmetrical compounds where the enol groups, as here, can exist in four forms (two *cis–trans* pairs), two of the isomers with the enolic hydroxyl and chain in the *cis* relationship could theoretically give the furan.[10] However, if one of the two γ-carbonyl groups is unreactive due to great steric hindrance (as in the case of the 1-carbonyl group in this series), then only one of these two isomers of favorable configuration would be at all likely to undergo furanization. In the trimesityl series under discussion, neither of the two stereoisomeric 4-monoenols IIA and B gives the furan. One of these, of course, would have a favorable configuration but in this case furanization would not be expected because of the enormous and undoubtedly prohibitive steric hindrance at the γ-carbonyl coupled with the mobility and speed of ketonization of the 4-enolic group. Of the two 1-monoenols the A-isomer XV cannot be furanized under ordinary conditions and undergoes ketonization exclusively, but the B-isomer XVI gives the furan directly and spontaneously and is the only compound in the series to do so. Here then is a definite case of spontaneous furanization through a monoenol where the dienol certainly cannot be involved, and where there evidently exists the only possible combination of factors which would be favorable to this reaction, namely, the *cis* configuration with respect to the enolic hydroxyl and the chain bearing the γ-carbonyl, a marked persistence of the

(9) *Cf.* also the supposed monoenol of 1,4-diphenyl-2-mesitylbutanedione-1,4 (Ref. 4).

(10) Kleinfeller and Trommsdorff [*Ber.*, **72**, 257 (1939)] have made the suggestion that the failure of their substituted saturated 1,4-diketone to undergo dehydration to the furan was not because of any difficulty of enolization but rather because of enolization in one-half of the molecule to an enolic group of unfavorable configuration. Presumably, these authors in referring to the "enolform" involved in dehydration mean the dienol since they state that only one of the four possible stereoisomers would have a configuration favorable for ring closure. If the monoenols were meant, then of the four possible isomers (two *cis–trans* pairs), two would have configurations favorable to ring closure, assuming, of course, a mechanism of reaction such as has been suggested in Ref. 2 According to this theory of the mechanism, however, there is no obvious explanation of the failure of this saturated 1,4-diketone to undergo dehydration (perhaps it will do so if suitable conditions are found).

enol group due to hindrance by the substituted mesityl groups, and a γ-carbonyl with a minimum of hindrance and capable of reaction, given time to do so.

The inconsistency in the ease of furanization of various saturated 1,4-dimesityl 1,4-diketones is understandable in terms of some resultant of the various factors which have been discussed.[11]

Continuation of the work on this series of compounds with extension to tetraaryl types is in progress.

Experimental Part

1,2,4-Trimesitylbutanedione-1,4, III.—In a typical experiment 5.7 g. of finely powdered di-(trimethylbenzoyl)-ethylene was added in half-gram portions to a thoroughly stirred solution of four equivalents of mesitylmagnesium bromide in 45 cc. of absolute ether. The temperature was held at 20° as the immediate and vigorous reaction proceeded. The resulting clear brown solution was stirred for fifteen minutes, cooled to 0° and poured into ice water acidified with dilute hydrochloric acid. The product was extracted by means of ether, the solution on concentration depositing 5.3 g. of triphenylbutanedione. After repeated crystallization from acetone it was obtained as slender needles melting at 147–147.5°.[12] It is very soluble in acetone, butanone, ethyl acetate and ligroin but difficultly soluble in methanol and ethanol.

Anal. Calcd. for $C_{31}H_{36}O_2$: C, 84.5; H, 8.2. Found: C, 84.5; H, 8.2.

Bromination in chloroform solution did not give a crystalline product.

Reaction with methylmagnesium iodide at room temperature according to the Zerewitinoff method in isoamyl ether gave a precipitate and showed evolution quantitatively of one molecule of methane; further evolution of methane did not occur even on long standing. At 100°, fifteen hours were required for a half of a molecule more of methane to form. On hydrolysis of the products in alcoholic iodine and working up in the usual way, some unsaturated as well as saturated diketone was isolated. A yield of 20% of unsaturated diketone was isolated upon hydrolysis in alcoholic iodine.

2,3,5-Trimesitylfuran, VIII.—Dehydration of the saturated 1,4-diketone (III) with acetic anhydride and sulfuric acid in the usual way failed. The effective procedures developed are described below, the best one being (a).

(a) A solution of 0.5 g. of III in 15 cc. of concd. acetic acid containing 0.6 cc. of water was refluxed gently for thirty hours with a continuous stream of dry hydrogen chloride passing through at the rate of about 20 bubbles per minute. The solution on cooling deposited 0.41 g. of nearly pure furan and 0.13 g. more was recovered from the filtrate. On repeated crystallization from concd. acetic acid or ethanol, it melted at 106.5°. It crystallizes slowly.

Anal. Calcd. for $C_{31}H_{34}O$: C, 88.1; H, 8.1. Found: C, 87.84; H, 7.9.

(b) A mixture of 0.2 g. of III and 1 cc. of hydriodic acid (sp. gr. 1.7, protected with hypophosphorous acid) was heated in a sealed tube at 160–170° for one hour. The product upon standing for several days in ethanol deposited the furan in 50% yield.

(c) A mixture of 0.2 g. of III, 8 cc. of concd. acetic acid, 6 drops of hydriodic acid (sp. gr. 1.7) and 0.1 g. each of red phosphorus and of iodine, was refluxed for one hour (the peculiar conditions here used were chosen for a control experiment). When the mixture was poured into water and worked up in the usual way, 0.13 g. of the furan was isolated.

Bromination of the furan with phosphorus pentabromide at 90° for half an hour gave an amorphous solid melting at 120–150°. Analysis indicated it to be a tetrabromide.

Anal. Calcd. for $C_{31}H_{30}OBr_4$: Br, 43.4. Found: Br, 41.7.

4(?)-Nitro-2,3,5-trimesitylfuran, IX.—A suspension of 0.2 g. of VIII in 2 cc. of concd. acetic acid at 15° was treated with 0.4 cc. of a 1–3 mixture of concd. nitric and acetic acids. On standing for thirty minutes the suspended solid dissolved, and scratching and seeding caused deposition of 0.12 g. of the mononitro derivative which on repeated crystallization from isopropanol was obtained as rhombic prisms melting at 206.5–207°.

Anal. Calcd. for $C_{31}H_{33}O_3N$: C, 79.6; H, 7.1; N, 3.0. Found: C, 79.9; H, 7.1; N, 3.2.

3-Iodo-1,2,4-trimesitylbutanedione-1,4-A, IV.—The solution of magnesium 4-monoenolate-A, prepared from 20 g. of di-(trimethylbenzoyl)-ethylene and 90 cc. of an ether solution of two equivalents of mesitylmagnesium bromide, was decomposed by adding it slowly to a vigorously stirred solution of 20 g. of iodine in 400 cc. of ethanol cooled in an ice-bath, the temperature varying between 0 and 10°. The product crystallized directly from the ethanol solution. After standing for half an hour at 0° with stirring to ensure complete precipitation, enough concd. hydrochloric acid was added to dissolve the magnesium hydroxide, and the product was filtered off; yield 26.5 g. of practically pure material. The yields in different runs varied from 74–79%. After repeated crystallization from concd. acetic acid and from ethyl acetate it was obtained as colorless rectangular plates melting at 213° with decomposition and liberation of iodine.

Anal. Calcd. for $C_{31}H_{35}O_2I$: C, 65.7; H, 6.2. Found: C, 65.8; H, 6.2.

Small amounts of the isomeric iodo compound B were obtainable by fractional crystallization of the residues from this experiment.

Reduction was brought about in four ways as follows:

(a) A sample of the iodo compound reacted with potassium iodide in concd. acetic acid at room temperature with liberation of approximately one equivalent of iodine (titrated) and formation of trimesitylbutanedione III in quantitative yield.

(11) 1,4-Dimesitylbutanedione-1,4, $C_9H_{11}COCH_2CH_2COC_9H_{11}$ [Lutz, Johnson and Wood, THIS JOURNAL, **60**, 716 (1938)] and the saturated diketone of this series, III, for example, are dehydrated only with considerable difficulty, whereas 2,3-dimethyl-1,4-dimesitylbutanedione-1,4, $C_9H_{11}COCH(CH_3)CH(CH_3)COC_9H_{11}$ [Lutz and Taylor, *ibid.*, **55**, 1593 (1933)] is converted into the corresponding furan with extraordinary ease.

(12) Melting points of all analytical samples are corrected.

(b) The action of zinc dust in boiling concd. acetic acid (three min.) gave III.

(c) Refluxing for one hour in 60% ethanol with an excess of sodium bisulfite gave III.

(d) Hydrogenation in ethyl acetate using platinum oxide catalyst liberated iodine and gave III in good yield.

Alcoholic potassium hydroxide, refluxed for one hour, converted the iodo compound into the unsaturated diketone VII. Refluxing with an excess of anhydrous sodium acetate in ethanol for eight hours was without effect.

3-Iodo-1,2,4-trimesitylbutanedione-1,4-B, IV.—Solutions of the magnesium 4-monoenolate-B from the action of an excess of phenyl, ethyl or methylmagnesium halide at room temperature on trimesitylbutanedione, III, were poured into excess of cooled alcoholic iodine. From 0.4 g. of III, upon decomposition in alcoholic iodine at −10 to −15°, 0.25 g. of IVB was obtained, and from the mother liquors 0.15 g. of unchanged material (III). The iodide was not pure, however, and contained a little of the higher melting isomer-A. When the decomposition in alcoholic iodine was carried out at −60° the yield of the iodo compound-B was about the same but it was practically pure. Exhaustive crystallization from ethyl acetate and from concd. acetic acid gave a product of constant melting point of 178° (elongated hexagonal plates). It did not give a mixture melting point depression with the higher melting isomer-A but did with the bromo compound, isomer-A.

Anal. Calcd. for $C_{31}H_{35}O_2I$: C, 65.7; H, 6.2. Found: C, 65.5; H, 6.1.

Examination of the mother liquors of the above experiment failed to reveal the presence of even small amounts of the unsaturated diketone VII which would be expected as a result of oxidation of small amounts of dienolate by the iodine.

Reaction with the Grignard Reagent.—A sample (0.1 g.) of IVB was added to 1 cc. of ether containing two equivalents of ethylmagnesium bromide at 20° and the resulting mixture immediately was poured into 15 cc. of boiling concd. acetic acid. On diluting with water and crystallizing from ethanol 0.05 g. of the saturated diketone III was obtained.

In a similar experiment in which the ether solution was heated for five minutes and then poured into boiling acetic acid, a mixture of about equal parts of the saturated and unsaturated diketones III and VII was obtained, indicating that part of the material had been enolized at both of the carbonyls. Phenylmagnesium bromide, used instead of ethylmagnesium bromide, caused complete enolization to the dienolate under these conditions.

Reduction with sodium bisulfite in boiling 60% ethanol (thirty minutes) gave a quantitative yield of III.

The action of potassium hydroxide in excess in boiling ethanol (one hour) converted the iodide in good yield into the unsaturated diketone VII.

3-Bromo-1,2,4-trimesitylbutanedione-1,4-A, V.—A solution of the 4-monoenolate-A (II) and 12 cc. of an ether solution of two equivalents of ethylmagnesium bromide at 20° was cooled immediately to 0° and added to 25 cc. of ethanol solution containing 1.5 g. of bromine also at 20°. The product crystallized and was filtered off (2.4 g.). Fractional crystallization from acetone and from isopropanol gave 1.35 g. of nearly pure bromo diketone VA and 0.1 g. of the stereoisomer (B). The isomer-A was purified by repeated crystallization from isopropanol and melted at 192.5–193.5°.

Anal. Calcd. for $C_{31}H_{35}O_2Br$: C, 71.7; H, 6.8. Found: C, 71.7, 71.9; H, 6.9, 6.8.

When the 4-monoenolate-A solution was decomposed in alcoholic bromine at higher temperatures (10°) a difficultly separable mixture of the bromodiketones A and B was obtained.

Ethylmagnesium bromide at 20° enolized the bromodiketone-A quickly and when the mixture was decomposed in alcoholic iodine at 10° the iododiketone-A (IV) was obtained exclusively and in good yield.

The bromodiketone-A was not affected by the prolonged action of boiling ethanolic sodium acetate (twelve hours), but when refluxed for thirty minutes with a 95% methanolic solution of an excess of potassium hydroxide, the unsaturated diketone VII was obtained.

Reduction with sodium bisulfite in 60% ethanol (refluxing for four hours) gave the saturated diketone III.

3-Bromo-1,2,4-trimesitylbutanedione-1,4-B, V.—A solution of the 4-monoenolate-B, prepared by the action of phenyl, methyl or ethylmagnesium halide on III, was decomposed in alcoholic bromine. In a typical experiment starting with 0.2 g. of III, decomposing in alcoholic bromine at −60°, 0.2 g. of nearly pure bromodiketone-B was obtained (80%). Repeated crystallization from acetone gave a pure product melting at 230–231°.

Anal. Calcd. for $C_{31}H_{35}O_2Br$: C, 71.7; H, 6.8; Br, 15.4. Found: C, 71.5; H, 7.1; Br, 15.5.

When in several different experiments the solution of the 4-monoenolate-A was decomposed in alcoholic bromine at temperatures ranging from 0 to −15°, a mixture of the isomers A and B was obtained.

Ethylmagnesium bromide at 20° reacted rapidly with the bromodiketone-B. On decomposition in alcoholic iodine at 10°, the iododiketone-A was obtained exclusively in good yield.

Reduction in the usual way with zinc dust and concd. acetic acid gave III.

Sodium acetate in boiling ethanol (two hours) was without effect, but refluxing for two hours in 95% ethanol containing an excess of potassium hydroxide gave the unsaturated diketone in nearly quantitative yield.

1,2,4-Trimesityl-2-butenedione-1,4, VII.—A suspension of 4 g. of the iododiketone IVA in 125 cc. of ethanol and 3 g. of potassium hydroxide was refluxed for one hour, giving a dark red solution which was diluted with water cautiously as it cooled, the product separating in 90% yield. On repeated crystallization from methanol, ethanol or ligroin it was obtained as colorless needles which melted at 142–144°, turning yellow as it melted. It became colorless on solidification. Its solutions in common solvents are yellow.

Anal. Calcd. for $C_{31}H_{34}O_2$: C, 84.9; H, 7.8. Found: C, 85.1; H, 7.6.

The unsaturated diketone VII is obtainable similarly as described from the other halides IVB and V (A and B). Methanol may be substituted for ethanol as the solvent but it is not as satisfactory due to the difficult solubility of the halides.

Various attempts to make the acetoxyfuran by means of acetic anhydride and concd. sulfuric acid failed, no reaction occurring even at boiling temperature.

The unsaturated diketone was not changed on exposure to sunlight in ethanol or in chloroform containing iodine.

Reduction.—Zinc dust and concd. acetic acid produced the 1-monoenol-A (see this compound). Sodium hydrosulfite in dilute ethanol as medium did not bring about reduction. The combination 8 cc. of concd. acetic acid, 4 drops of water, 0.1 g. of iodine and 0.1 g. of red phosphorus, refluxed for one hour, gave the furan VIII in good yield.

1,2,4-Trimesitylbutane-1,4-dione-4-enolate-A, IIA.—A solution of this enolate is obtained by the action of mesitylmagnesium bromide on the saturated 1,4-diketone III as already described. Since neither it nor the free enol could be isolated, this compound was characterized by its reactions as follows:

(a) The reaction with iodine and bromine leads to the iodo and bromodiketones IVA and VA.

(b) Decomposition in an alcoholic solution of quinone or ferricyanide produced only the saturated diketone III and no unsaturated diketone VII, showing that significant amounts of the dienolate were absent.

(c) When decomposed in dilute hydrochloric acid the saturated diketone III was formed exclusively.

(d) Decomposition by dropping the ether solution slowly into boiling concd. acetic acid in an apparatus arranged to collect the ether boiled off, gave the saturated diketone III exclusively and in good yield.

(e) Mesitylmagnesium bromide in isopropyl ether with refluxing for two hours under an atmosphere of nitrogen converts it into the dienolate-A (see this compound). When ethyl ether was used and the mixture refluxed for two hours and decomposed in alcoholic iodine in the usual way, only the iododiketone-A was obtained, showing that the higher temperature obtainable in boiling isopropyl ether is required to produce the dienolate.

(f) Phenylmagnesium bromide converted it readily into the dienolate-B (see this compound), the reaction proceeding upon five minutes of refluxing with ethyl ether as solvent.

Preparation of the 4-Monoenolate-A from the Iododiketone IVA.—This method is the most convenient and the product is obtainable thus free from tarry secondary products which are formed in the reaction between mesitylmagnesium bromide and di-(trimethylbenzoyl)-ethylene. The general procedure was to add the sample of iododiketone to 3–4 equivalents of phenylmagnesium bromide in ether, controlling the temperature by means of an ice-bath to 20°, and allowing the solution to stand not more than two to three minutes before use. The other three halogeno diketones can be used in the same experiment and ethyl or mesitylmagnesium bromides can be used with equal success.

The 4-monoenolate-A from the iododiketone-A was characterized by application of the tests (a), (d) and (f) listed under the first preparation described above. The products from the iododiketone-B and from the bromodiketones A and B were characterized by application of (a) with conversion into the iododiketone-A.

An attempt was made to isolate the 4-monoenolate-A under mild conditions by hydrolysis in ice water acidified with dilute acetic acid, extraction by ether, and evaporation at room temperature. An oil was obtained which crystallized promptly from ethanol as the saturated diketone III. Similarly a solution of the 4-monoenolate-A was decomposed in ice water and extracted with ether without acidification, separated, the ether layer dried over anhydrous sodium sulfate for a few minutes, and added to an ether solution of an excess of diazomethane. Only the saturated diketone was recovered.

1,2,4-Trimesitylbutane-1,4-dione-4-monoenolate-B, IIB.—The action of phenyl, ethyl or methylmagnesium halide in ether on trimesitylbutanedione III at room temperature gives the 4-monoenolate-B. The reaction was carried out under a variety of conditions, in some cases with refluxing, but heating proved to be unnecessary and introduced some dienolate. The enolization of the second and hindered carbonyl here is much more difficult to bring about than in the case of the 4-monoenolate-A. The solutions of the 4-monoenolate-B on decomposition in alcoholic bromine or iodine gave the B-halides IV and V when the temperature was lowered. At temperatures from 0–25° mixtures of the bromides (largely B) were obtained, but with iodine ketonization took place so rapidly that the saturated diketone III was obtained in large amounts (over 75% in one case) along with smaller amounts of the iododiketone IVB.

Characterization of the 4-monoenolate-B was best made by halogenation at lowered temperature (−60°). Hydrolysis of a sample in boiling concd. acetic acid gave only the saturated diketone III, and careful examination of the products failed to reveal the presence of trimesitylfuran. The 4-monoenolate-B was decomposed in a cooled (10°) solution of quinone in ethanol, but only the saturated diketone could be isolated, showing that there was little dienolate present in the sample. Unsuccessful attempts were made to isolate the free 4-monoenol-B by hydrolysis of the enolate in ice water acidified with acetic acid and extraction with ether. The oil obtained crystallized quickly at room temperature when triturated with isopropanol, giving the saturated diketone.

1,2,4-Trimesitylbutane-1,4-dione-1-monoenol-A, XV.—A mixture of 8 g. of the unsaturated diketone VII, 20 g. of zinc dust, and 125 cc. of concd. acetic acid was refluxed with mechanical stirring for one hour. On filtration and dilution with ice water the product coagulated and was filtered, dried and recrystallized from ligroin. The yields averaged 60%. On repeated crystallization from ligroin it was obtained as cubic prisms melting at 131–131.5°.

Anal. Calcd. for $C_{31}H_{36}O_2$: C, 84.5; H, 8.2. Found: C, 84.3; H, 8.2.

The 1-monoenol-A was obtained also from the hydrolysis of the dienolate-A (see that compound). It crystallized from ethanol with water of crystallization and melted with effervescence at 95–100°, solidified and remelted at 130°. On standing the hydrate loses its solvent of crystallization and reverts to the anhydrous form. It does not give a color reaction with alcoholic ferric chloride nor does it react at all readily with alcoholic bromine or with diazomethane (in ether for eighteen hours). In a quantitative test it reacted with methylmagnesium iodide at room temperature under nitrogen with evolution of 0.93

molecule of methane. Phenylmagnesium bromide at 20° gives the monoenolate also as was shown by decomposition in alcoholic iodine and recovery of the 1-monoenol-A unchanged, with little or no oxidation to the unsaturated 1,4-diketone. Under more drastic conditions the monoenol reacts with phenylmagnesium bromide to give the dienolate-A (see that compound).

The 1-monoenol-A, when heated with iodine, red phosphorus and concd. acetic acid for one hour, gave trimesitylfuran. The saturated diketone III is furanized under these conditions also.

The action of potassium hydroxide in 95% ethanol (refluxed for one hour) produced the saturated diketone.

1,2,4-Trimesitylbutanedione-1,4 Dienolate-A, VIA.—The dienolate-A was obtained as an ether insoluble powder by adding di-(trimethylbenzoyl)-ethylene to mesitylmagnesium bromide in isopropyl ether (giving first the 4-monoenolate-A) followed by refluxing for two hours under an atmosphere of nitrogen. A dienolate which was presumably the same was obtained by adding the 1-monoenol-A, XV, to an ether solution of an excess of phenylmagnesium bromide and refluxing for thirty minutes. These dienolates from the two sources appeared to be identical since they gave similar results when tested in the following experiments carried out independently on samples prepared in the two ways.

(a) The suspension of product was poured into an ethanol solution of an excess of iodine (10°), and the mixture was then diluted with water containing sodium bisulfite (acidified) to destroy the excess of iodine. The resulting oil was crystallized from ethanol and a good yield of the unsaturated diketone VII was obtained.

(b) Decomposition in boiling acetic acid andre fluxing for one hour after expulsion of all of the ether, gave an oil from which only the saturated diketone III could be isolated. No furan was detected. The presence of the magnesium salts evidently was responsible for ketonization of the 1-monoenol-A in this reaction.

(c) When the ether solution of the dienolate was poured into concd. acetic acid magnesium salts crystallized and were filtered off. The ether was then boiled off; the remaining solution in concd. acetic acid was then refluxed for one hour and diluted with water. Extraction with ether and concentration gave the 1-monoenol-A, XV, which was crystallized from ligroin or isopropanol and identified.

While the identity of the two samples with respect to configuration at the 1-enol group is certain, the identity of configurations at the 4-enol group is not rigorously proved because in one case (dienolate-A) the group was formed before and in the other case after enolization at the 1-enol group, and because the tests listed do not distinguish between the 4-monoenolate configurations. Attempts to prove the point by converting both samples of dienolate to the same crystalline dienol were unsuccessful. The dienol (described below) was isolated only in the second case when the dienolate was prepared from the 1-monoenol-A. The failure to isolate the dienol from the first preparation (dienolate-A) is of no significance in view of the experimental difficulties involved, particularly the difficulty of crystallizing, the presence of mesitylene from excess Grignard reagent, and the sensitivity of the dienol itself. It is hoped that in the further investigations under way derivatives may be obtained which will throw light on this question.

1,2,4-Trimesitylbutanedione-1,4 Dienol, XVII.—Two-tenths gram of the 1-monoenol-A (XV) was added to 4 cc. of phenylmagnesium bromide solution in ether (concn. 0.001 mole per g.) and the mixture was refluxed for thirty minutes, the dienolate precipitating. On cooling to 0° and adding 20 cc. of 80% ethanol containing 2 cc. of concd. acetic acid, followed quickly by 50 cc. of water, a white solid separated and was filtered quickly and crystallized from ethanol. The first crop of crystals melted low and successive crops of material were then obtained (rectangular plates) which melted sharply at 70–71°. In another run a sample melting at 72–73° was obtained. The yield was 0.1 g. The compound in the solid state was oxidized by air and after standing for a week was converted quantitatively into the unsaturated diketone VII. The change proceeded rapidly when the material was treated with iodine in ethanol, and in a quantitative experiment where the excess of iodine was estimated by titration with sodium thiosulfate, one molecule of iodine was used up with the formation of the unsaturated diketone in quantitative yield. In the Zerewitinoff apparatus with methylmagnesium iodide at room temperature 1.89 molecules of methane was liberated with the formation of a white precipitate.[13]

Rearrangement to the saturated diketone III was brought about by heating a solution of the dienol in concd. acetic acid containing a small amount of concd. hydrochloric acid for fifteen minutes. Rearrangement to the 1-monoenol-A (without isolating the dienol from the magnesium dienolate) was described under the preparation of this compound.

While the configuration at the 1-enol group is certain the configuration at the 4-enol group has not been established relative to the 4-monoenolates-A and B.

1,2,4-Trimesitylbutanedione-1,4 Dienolate-B, VIB.—The dienolate-B is obtained in two ways: (1) by the enolization of the 4-monoenolate-A in diethyl ether after its preparation from di-(trimethylbenzoyl)-ethylene and mesitylmagnesium bromide; this was done by adding *phenyl*-magnesium bromide to the mixture and refluxing for thirty minutes; and (2) by the action of phenylmagnesium bromide on the iododiketone IVA in ethyl ether, with refluxing for five minutes.

The dienolate-B differs from the A-isomer by its solubility in ether. The probable identity of the materials from the two sources was established by the following experiments carried out on each sample separately.

(a) Samples were decomposed in alcoholic iodine solution at 10° and worked up in the usual way, giving the unsaturated diketone VII and showing that they actually contained the dienolate.

(b) Solutions were decomposed by adding them slowly to boiling concd. acetic acid in an apparatus arranged to collect the ether which volatilized, the solution then being

(13) Unfortunately before carbon and hydrogen analyses could be carried out on the above described sample, oxidation to VII had occurred. New samples prepared subsequently were not as good and analyses were unsatisfactory (carbon was low). It did not seem worth while to delay publication further, however, and the formulation of the dienol is therefore based on the quantitative data described.

refluxed for one hour, diluted with water and extracted with ether. Crystallization of the resulting oil from isopropanol gave trimesitylfuran VIII exclusively, no saturated diketone being detected.

In one experiment the dienolate-B was decomposed in cold dilute acetic acid and only traces of the furan were isolable from the oily product which could be distilled in the vacuum oven. This oil is very evidently the **1-monoenolate-B.**

From the fact that the two samples of the dienolate-B give the furan rather than the saturated diketone, it is certain that they both have the same configuration at the 1-enol group as indicated in formula VIB. Both samples, of course, must have the same configuration at the 4-enol group (corresponding to that of the 4-monoenolate-A) since this group was formed in both experiments before enolization occurred at the 1-carbonyl group.

Summary

1,2,4-Trimesitylbutanedione-1,4 was obtained as the result of 1,4-addition of mesitylmagnesium bromide to di-(trimethylbenzoyl)-ethylene. The 4-monoenolate-A was first formed (proved by halogenation) and was further enolized to the dienolate (proved by oxidation).

1,2,4-Trimesityl-2-butenedione-1,4 was obtained by oxidation of the dienols and by elimination of halogen acid from the 3-halogeno-1,2,4-trimesitylbutane-1,4-diones.

2,3,5-Trimesitylfuran and its mononitro derivative are described.

The 3-halogeno-1,2,4-trimesityl-1,4-butanediones have been obtained each in diastereoisomeric forms.

The existence of two 4-monoenolates, A and B, was demonstrated: A was formed by the addition of mesitylmagnesium bromide to di-(trimethylbenzoyl)-ethylene or by the action of any Grignard reagent on the 3-halogeno-1,2,4-trimesitylbutane-1,4-diones, and B by the enolization of the saturated 1,4-diketone. They were characterized by halogenation to the stereoisomeric halogeno diketones. A basis for assignment of configurations is discussed.

The 1-monoenol-A (m. p. 145°) was obtained by partial ketonization of the dienolate. It lacked most of the usual enolic properties. Ketonization gave the saturated diketone. Enolization gave a crystalline dienol which was metastable and easily oxidized to the unsaturated 1,4-diketone.

The existence of two dienolates, A and B, was demonstrated. A was obtained from the 4-monoenolate-A by enolization with mesitylmagnesium bromide, and was converted by hydrolysis and ketonization to the saturated diketone. B was obtained by the action of phenylmagnesium bromide on the 4-monoenolate-A and was characterized by hydrolysis with spontaneous formation of trimesitylfuran.

Configurations at the 1-enol group are assigned on the basis of the relative ease of furan formation and ketonization.

The mechanism of furan ring closure is discussed in the light of this work.

CHARLOTTESVILLE, VIRGINIA
RECEIVED OCTOBER 17, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE CALCO CHEMICAL DIVISION OF THE AMERICAN CYANAMID COMPANY]

Sulfanilamide Derivatives. V. Constitution and Properties of 2-Sulfanilamidopyridine[1]

BY M. L. CROSSLEY, E. H. NORTHEY AND MARTIN E. HULTQUIST

Although 2-sulfanilamidopyridine[2] (now named "sulfapyridine" by the American Medical Association) has received wide publicity as a result of its use in the treatment of pneumonia,[3] attention has been drawn to the fact that practically nothing has been published on its physical and chemical properties, and no evidence has been given in support of the assigned structure.[4]

We had independently synthesized this compound as part of our program on N^1-substituted sulfanilamides and had made a pharmacological study, but the announcements from England were made before we were prepared to publish our information. We offer the following evidence on constitution as well as data on the properties of the carefully purified compound.

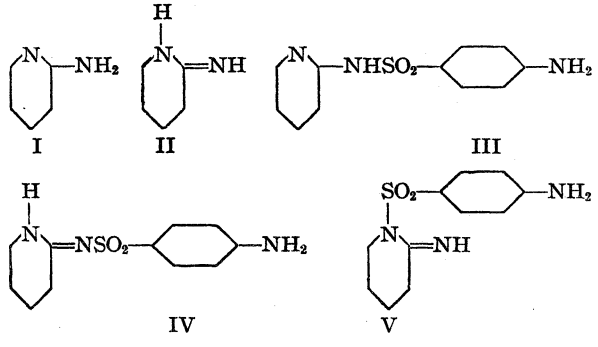
(1) Presented in part before the Division of Medicinal Chemistry, A. C. S. Meeting, Baltimore, Md., April, 1939.

(2) See Sulfanilamide Derivatives I, THIS JOURNAL, **60**, 2217 (1938), for nomenclature.

(3) Whitby, *Lancet*, **1**, 1210 (1938); synthesized by J. A. Ewins and M. A. Phillips.

(4) Marshall, *J. Am. Med. Assoc.*, **112**, 352 (1939).

2-Sulfanilamidopyridine was synthesized by reaction of N-acetylsulfanilyl chloride with 2-aminopyridine, followed by hydrolysis of the acetyl group. 2-Aminopyridine is a well-known compound, but can exist in tautomeric forms having the structures I and II, so that it is necessary to decide which form represents the structure of its sulfanilyl derivative. Structures III, IV and V represent the possibilities through replacement of a hydrogen attached to nitrogen in formulas I and II. 2-Aminopyridine derivatives



having structure II undergo hydrolysis on boiling in sodium hydroxide solution with evolution of ammonia and production of pyridone.[5]

Actually, no hydrolysis of 2-sulfanilamidopyridine occurred on boiling with 50% sodium hydroxide, or weaker strengths. When hydrolyzed by boiling with 36% hydrochloric acid, practically quantitative yields of sulfanilic acid and 2-aminopyridine were obtained. This evidence supports structure III and is against IV and V.

Further evidence in support of III is that the compound forms a monosodium salt which hydrolyzes in water to give a *p*H of 10 to 11. This is characteristic of all sulfonamides of the structure —SO_2NH—.[6] While structures IV and V might conceivably give rise to monosodium salts, it would be predicted from the behavior of the sodium salt of 2-aminopyridine that these would be more highly hydrolyzed in water and would give rise to higher *p*H values than those found.

These facts and deductions lead one to the conclusion that structure III is correct and justify the name 2-sulfanilamidopyridine.

Physical Properties of 2-Sulfanilamidopyridine.—2-Sulfanilamidopyridine is soluble to the extent of approximately 1.05 g./100 cc. in water at 100°; 0.11 g./100 cc. at 40°; 0.05 g./100 cc. at 20°.

It melts with slight decomposition in a capillary tube, over the range: 190.4 (first shrinking)—190.9 (first meniscus)—191.5° (complete melting). On the Dennis block a value of 192.8° was obtained on warming from room temperature, and the same value was obtained by placing the material in contact with the hot bar.

The compound crystallizes from alcohol in small, glistening rhombs. It is white, odorless and tasteless.

Chemical Properties.—2-Sulfanilamidopyridine dissolves readily in strong hydrochloric acid, presumably forming a hydrochloride or dihydrochloride. Potentiometric titration on addition of hydrochloric acid, however, gives a smooth curve without indication of salt formation, so that it is evident that the hydrochloride is highly dissociated. 2-Sulfanilamidopyridine forms a sodium salt which may be isolated and purified.[7]

The solution in hydrochloric acid may be titrated quantitatively by diazotization with sodium nitrite. The reaction is in equimolecular proportions and involves only the amino group of the sulfanilamide part of the molecule.

On heating a sample of the material in a test-tube to about 220° decomposition occurs with development of a brown color and evolution of sulfur dioxide and aniline (a similar but slower decomposition occurs at the melting point and explains the wide range). This is in contrast to sulfanilamide, which develops a blue or violet color and evolves ammonia and aniline.

Purified 2-sulfanilamidopyridine had the following microanalysis[8]: Calcd. for $C_{11}H_{11}O_2N_3S$: C, 52.99; H, 4.45; N, 16.86; S, 12.86. Found: C, 53.02, 53.06; H, 4.66, 4.55; N, 16.72, 16.72; S, 12.76, 12.93.

When assayed by titration with 0.1 *N* sodium nitrite to an end-point on starch iodide paste, the results were 100.2, 100.0. Molecular weight determinations using *m*-dinitrobenzene (K_f 12.49, setting point 89.70°) gave: 251.5, 251.5, 251.0, 248.0. Calcd. 249.29.

Experimental Part

2-(N^4-Acetylsulfanilamido)-pyridine.—18.8 g. (0.2 mole) of 2-aminopyridine (purified by double vacuum fractionation and three recrystallizations from 1 part benzene and 2 parts hexane; melting range 57.0–58.0°; setting point 57.90°) was dissolved in 75 cc. of anhydrous dioxane; 23.5 g. (0.1 mole) of N-acetylsulfanilyl chloride (recrystallized twice from toluene and once from chloroform; m. p. 148.5–149.5°) was added. The mixture was warmed to 95° and held fifteen min. On cooling and stirring, the oily layer crystallized. The crystals were filtered and washed with 25 cc. of dioxane, then 25 cc. of alcohol, and finally with 150 cc. of water. The dry weight was 27 g. or 92.8% based on N-acetylsulfanilyl chloride.

The crude 2-(N^4-acetylsulfanilamido)-pyridine was recrystallized from 200 cc. of dioxane and 125 cc. of water with use of activated charcoal and the crystals were washed with dilute dioxane. On drying, the material partially melted and changed crystalline form indicating loss of

(5) H. Maier-Brode and J. Altpeter, "Das Pyridin und seine Derivate in Wissenschaft und Technik," Verlag Wilhelm Knapp, Halle, 1934, p. 99.

(6) For structure of such salts see N. V. Sidgwick, "The Organic Chemistry of Nitrogen," Clarendon Press, Oxford, 1937, p. 158.

(7) Marshall, Bratton and Litchfield, *Science*, **88**, 597 (1938).

(8) Purification and determination of physical constants were carried out by W. J. Mader. Microanalyses were made under the direction of G. L. Royer.

dioxane of crystallization. After two recrystallizations from 70% alcohol, the melting range was 225.2° (first softening), 226.6° (first meniscus), 228.1° (final melting). This value was unchanged by recrystallization from 30% acetic acid, diacetone alcohol, and 70% alcohol. On the Dennis block, the material melted at 230.5° when placed on the hot bar or at 229.0° when warmed from room temperature. When a sample was heated at 230° for five minutes, then remelted, the range was 190.0–227.5°, indicating thermal decomposition.

Anal. Calcd. for $C_{13}H_{13}O_3N_3S$: C, 53.59; H, 4.50; N, 14.43; S, 11.00. Found: C, 53.47; H, 4.56; N, 14.53; S, 10.95.

The condensation was also run in pyridine in which case equimolecular amounts of 2-aminopyridine and N-acetylsulfanilyl chloride were used. The crude product so obtained contained a yellow impurity which was difficult to remove.

2-Sulfanilamidopyridine.—The acetyl derivative was hydrolyzed by boiling 29.1 g. (0.1 mole) with 10 g. (0.25 mole) of sodium hydroxide and 150 cc. of water for two hours. The excess sodium hydroxide was neutralized to *p*H 11, activated charcoal was added, and the hot mixture clarified, giving a colorless solution. On acidifying to *p*H 6, 23.1 g. of colorless crystals was obtained equal to 92.5%.

After two recrystallizations from 70% alcohol, the compound had the properties noted above, which remained unchanged on further recrystallizations from alcohol and chlorobenzene.

Hydrolysis of 2-Sulfanilamidopyridine.—Seventy-five grams (0.3 mole) of 2-sulfanilamidopyridine was boiled with 300 cc. of concentrated hydrochloric acid for one hour. After twenty min. crystals started to separate. The mixture was cooled to 15°, the crystals filtered, and washed with a little cold water; weight of crystals: 46.7 g. Titration by nitrite gave 100.2% purity, calculated as sulfanilic acid. The material decomposed gradually above 300°.

The mother liquor was evaporated to 50 cc. and a little more sulfanilic acid removed. Sodium hydroxide was then added in great excess and the oil layer separated. The aqueous layer was extracted with toluene. The toluene extract combined with the oil was dried over solid sodium hydroxide and distilled. The cut from 205 to 212° amounted to 21.0 g., with 2.0 g. of forerun and 1.3 g. of still residue; the total was 24.3 g. or 86% calculated as 2-aminopyridine. The setting point of the main cut was 57.9°, unchanged by admixture with 2-aminopyridine. The material did not resemble ordinary 2-aminopyridine in odor when freshly distilled, but on standing in the air for twenty-four hours the normal odor returned.

The aqueous mother liquors were titrated with sodium nitrite and accounted for 2.7 g. calculated as sulfanilic acid. Total recovery was 49.4 g. or 95.4%.

Melting Range Behavior.—Capillary melting ranges were determined by immersing the tube in a bath preheated to 180°. The values given are corrected. No difference was noted in melting range through use of sealed tubes filled with nitrogen. Some decomposition occurred on melting, as shown by heating a sample at 193° for five minutes in air and in nitrogen. The resulting melting ranges then were: sample melted in air, 154.0–184.5–189.9°; sample melted in nitrogen, 165.0–186.0–190.5°. This would indicate that decomposition on melting was both thermal and oxidative.

Summary

1. The preparation of 2-sulfanilamidopyridine and its physical and chemical properties are described.

2. Evidence in favor of the accepted formula for this compound is given.

BOUND BROOK, N. J. RECEIVED NOVEMBER 16, 1939

[CONTRIBUTION FROM RYERSON PHYSICAL LABORATORY, UNIVERSITY OF CHICAGO]

X-Ray and Optical Properties of Built-up Films

BY SEYMOUR BERNSTEIN

The discrepancy of about 3.6% between X-ray and optical measurements of the thickness per layer of barium–copper stearate films has been reported by C. Holley and S. Bernstein[1] and by C. Holley.[2] Investigations of refraction corrections in the X-ray measurements and possible phase change corrections in the optical measurements show that these cannot account for the discrepancy. Further investigation indicates that the discrepancy must be explained in terms of the structure of the films.

(1) C. Holley and S. Bernstein, *Phys. Rev.*, **52**, 525 (1937).
(2) C. Holley, *ibid.*, **53**, 534 (1938).

Phase Changes on Reflection

The film thicknesses were measured optically by measuring the fringe displacement between a step of 100 layers to 1000 or more layers of film deposited on an optical flat, as described by Mr. Holley.[2] In order to determine whether the phase change on reflection from the surface of the 100 layer portion was different from the phase change on reflection from the surface of the thicker portion of the films, a 1900-100 layer film was coated with aluminum by evaporation. Before having been covered with aluminum the

TABLE I

OPTICAL AND X-RAY MEASUREMENTS OF FILM THICKNESS

Film no.	Type	No. of layers	Average $\delta \times 10^6$	d_0, Å.	d_r, Å.	$d_0 - d_r$, Å.
1	Ba-Cu stearate	1100-100	5.1	48.57	50.45	−1.88
2	Ba-Cu stearate	1100-100	4.3	48.44	50.25	−1.81
3	Cu stearate	328	...	47.82	47.20	0.62
4	Cu stearate	1100-100	5.9	46.91	46.38	.53
5	Cu stearate	1100-100	4.7	47.67	46.91	.76
6	Cu stearate	404	...	48.08	47.15	.93
7	Ba stearate	319	6.1	48.52	49.92	−1.40
8	Ba stearate	316	...	48.19	50.30	−2.11
9	Pb arachidate	300	6.1	...	56.26	...

displacement between the 100 layer and the 1900 layer portion was an integral number of fringes, that is, the fringes were continuous across the boundary between the two portions. The fringes were continuous also after the film had been covered with aluminum. Since the total displacement was sixteen whole fringes, to account for the discrepancy of 3.6% the fringes from the thick and thin portions of the film should have shifted relative to each other by more than half a fringe. If the assumption is made that the thickness of aluminum on the thick and thin portions of the film was the same, then the fact that no shift of fringes was observed indicates that the discrepancy could not be due to phase changes on reflection.

Optical and X-Ray Measurements

The results of the film measurements are given in Table I. All of the films of Table I were kindly built for the writer by Dr. Katharine B. Blodgett of the General Electric Company. In Table I, d_0 denotes the thickness of a double layer as determined optically. All of the films of less than 1000 layers in thickness were measured[3] by Dr. Blodgett with an optical spectrometer. Films 1 and 2 were measured optically by C. Holley with the interferometer method described by him.[2] Films 4 and 5 were measured optically with the interferometer by the author. All of the X-ray measurements given in Table I were also made by the author. The symbol d_r used in Table I denotes the grating-space of the films, corrected for refraction and based upon the ruled grating wave length scale.

The X-ray apparatus used has been described by Mr. C. Holley.[2] The X-ray measurements were made by two methods. (1) The X-ray lines were reflected on both sides of the direct beam and the glancing angles determined from the distance between two corresponding orders and the distance from the axis of rotation to the photographic plate. (2) X-Ray reflections from the film were matched against those from a gypsum crystal. With the film used as the crystal, a photograph was taken of the fifth-order tungsten $L\alpha_1$ line, for example. The film was then replaced by a gypsum crystal and a photograph taken of the first order tungsten $L\gamma_1$ line. The photographic plate remained in the same position during the two exposures. The glancing angle of the $L\alpha_1$ line from the film was then determined from the known glancing angle of the reference line reflected from gypsum, by use of the distance between the lines, measured on the photographic plate and the distance from the plate to the axis of rotation of the crystal. The time of exposure for both methods was about three hours per order.

The index of refraction of the films for X-rays was determined from the absolute measurements of the first method by use of the apparent grating-spaces in the different orders according to the method of Stenstrom.[4]

The experimentally determined value of the unit decrement, δ, for all of the films was found to be more than 1.5 times as great as the value 3.4×10^{-6} calculated by Lorentz dispersion theory from the density measurements of barium–copper stearate films determined by R. W. Mattoon. This discrepancy between the observed and calculated index of refraction cannot account for the discrepancy between X-ray and optical measurements of the grating-space because the entire correction for refraction in the fifth order of the tungsten $L\alpha_1$ line amounts to only 0.3%.

The optical measurement given in Table I for Film 4 is the result of 200 measurements of the fractional part of a fringe, made before the film was exposed to X-rays. The measurement shown for Film 5 is the result of two sets of 200 measure-

(3) K. B. Blodgett, THIS JOURNAL, 57, 1007 (1935).

(4) Compton and Allison, "X-Rays in Theory and Experiment," p. 280.

ments of the fractional part of a fringe, one set of 200 measurements having been taken before, and one set after, exposing the film to X-rays. The average of one set of measurements was the same as the average of the other set to 0.01 fringe. The total number of fringes for Films 3 and 4 was eight.

From Table I, the following conclusions can be made. (1) The X-ray grating-space is greater than the optically measured thickness of a double-layer for barium–stearate and barium–copper stearate films; for copper stearate films the optical measurement is the greater. (2) For barium stearate and barium–copper stearate films the difference between the X-ray and optical measurements is about 3.5%; for copper stearate films this difference is about 0.7%.

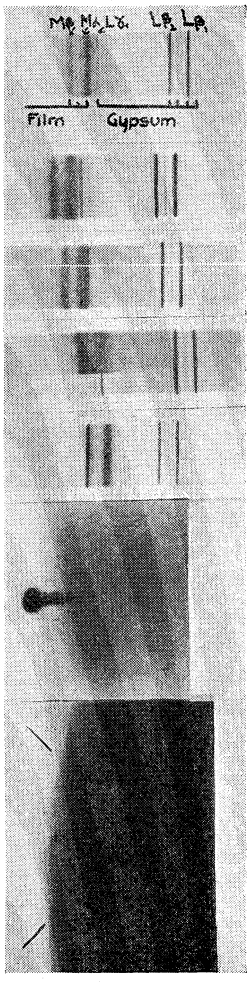


Fig. 1.—Barium stearate.

Fig. 2.—Barium stearate.

Fig. 3.—Barium–copper stearate.

Fig. 4.—Barium–copper stearate.

Fig. 5.—Copper stearate.

Fig. 6.—Rotation photograph of metal stearate film.

Fig. 7.—Rotation photograph of ethyl stearate film.

Variation of Measurements with Film Composition.—Measurements of a set of films of varying proportions of barium stearate and copper stearate show that although a change in film thickness measured optically is accompanied by a change in X-ray measured thickness of the same sign, there is no close correspondence between the magnitudes of changes in the optical and X-ray measurements of film thickness.

TABLE II

Fig.	Film no.	Barium acetate, *M*	$KHCO_3$, *M*	Copper acetate, *M*	KCN, *M*
1	7	10^{-4}	....	.....	....
2	10	10^{-4}	2×10^{-4}	.....	5×10^{-4}
3	11	10^{-4}	2×10^{-4}	3.5×10^{-6}	....
4	12	0.3×10^{-4}	2×10^{-4}	3.5×10^{-6}	....
5	3	.....	....	10^{-4}	....

The variation of X-ray grating-space with film composition can be observed in Figs. 1, 2, 3, 4, and 5. The solutions used by Dr. Blodgett in building the films with which these photographs were taken are given in Table II. Corresponding optical and X-ray measurements were made for Film 7 of Fig. 1 and Film 3 of Fig. 5. In going from the pure barium stearate film of Fig. 1 to the pure copper stearate film of Fig. 5, the X-ray grating-space decreases from 49.92 to 47.20 Å., a difference of 5.5%; while the optical measurement of the thickness of a double layer decreases from 48.52 to 47.82 Å., a decrease of approximately 1.5%. The X-ray and optically measured thicknesses both decrease with increasing copper content and with simultaneously decreasing barium content, but the X-ray grating-space decreases at a much greater rate.

Skeletonized Films.—Dr. Blodgett and Dr. Irving Langmuir have described the process of skeletonizing a film.[5] After a film is built it is dipped into benzene. That portion of the film which consists of pure stearic acid is dissolved by the benzene; the portion which consists of metal stearate remains on the slide. If the proportion of stearic acid in the film is too high the film collapses. If the proportion of stearic acid is not too high the optically measured film thickness changes by only 1 or 2%.

X-Ray measurements were made of a skeletonized and an unskeletonized film of lead arachidate. The two films were built by Dr. Blodgett at the same time from the same solution, after which one of them was dipped into benzene for one minute. According to Dr. Blodgett a test film made from the same solution showed that 40% of the material had been removed by soaking

(5) K. B. Blodgett and I. Langmuir, *Phys. Rev.*, **51**, 980 (1937).

the film in benzene for one minute and that a change in thickness of 1 or 2% had taken place. The X-ray measurements for the two films are given in Table III. These measurements show that the grating-spaces of the skeletonized and unskeletonized films are the same within experimental error. The relative intensities of the first three orders for the two films were also the same.

TABLE III

COMPARISON OF GRATING-SPACES OF A SKELETONIZED AND AN UNSKELETONIZED FILM

	Distances in cm.		
	1R to 1L	2R to 2L	3R to 3L
Unskeletonized film	3.207	6.285	9.382
Skeletonized film	3.204	6.287	9.387
Difference, %	−0.1	+0.04	+0.05

In Table III, the values given are the distances measured on the plate from a given order of WLα_1 line on one side of the direct beam to the same order on the opposite side of the direct beam. Thus 1R to 1L denotes the distance from the first order Lα_1 line on one side of the beam to the first order Lα_1 line on the opposite side of the direct beam.

This identity of the grating-spaces of the skeletonized and unskeletonized films seems to indicate that the X-ray photographs give a measure of the grating-space of crystals of metal stearate contained within the films, and that such a measurement should not be compared with an optical measurement of the film thickness.

Rotation Photographs of Metal Stearate Films.—The zero layer-line reflections from which the grating-space measurements of Table I were made have shown that the films have a regular arrangement of molecules in a direction perpendicular to the surface upon which they are built. The question arises as to whether or not the films have regular arrangements of molecules in planes parallel to the surface on which they are built.

Figure 6 is a rotation photograph taken with one of the barium–copper stearate films. Only the zero layer-line reflections appear. The background is badly fogged because of scattering from the glass plate upon which the films were built. However, it may be concluded that either reflections on layer-lines other than the zero layer-line are very much weaker than the zero layer-line reflections or that they do not appear at all. The fact that they do not appear would indicate that the films do not have a regular arrangement over an appreciable area in planes inclined at an angle to the surface of the slides upon which the films are built or in planes parallel to these surfaces. Every one of several other films of barium–copper stearate, copper stearate, and barium stearate also showed only zero layer-line reflections.

Suggested Structure of Metal Stearate Films.—The following film structure is suggested as one which is consistent with the results described above.

The film consists of many small crystals of metal stearate embedded in a matrix of amorphous stearic acid or stearic acid crystals. These crystals of metal stearate all have the same, or nearly the same, orientation in a direction perpendicular to the slide upon which the film is built but have a random arrangement in planes parallel to the foundation surface. The X-ray measurements are a measure of the grating-space of the metal stearate crystals. The optical measurements are a statistical average of the thickness per layer.

The similarity in the X-ray photographs taken with X and Y films[6,7] indicates that the film structure is independent of the type of deposition.

The suggested film structure is also consistent with Dr. Langmuir's interpretation[8] of the contact potential measurements of Porter and Wyman.[9]

Films of Ethyl Stearate.—Stenhagen reported[10] the use of ethyl stearate, along with a number of other substances, in building films. These films differ from stearate films in that there is no question of degree of saturation. In the case of stearate films, the stearic acid on the water surface is partly changed to metal stearate by the metal ions in solution. In the case of ethyl stearate, if the *p*H of the water is not too low or too high, the ethyl stearate placed on the water surface is transferred unchanged to the slide.

Stenhagen found the following X-ray and optical values for ethyl stearate films: X-ray grating-space, 25.7 Å.; optical measurement of the thickness per layer, 28.0 ± 0.5 Å. The writer built several films of Eastman Kodak Company ethyl stearate and found the apparent X-ray grating-space in the second order to be 25.2 Å. Stenhagen, in his optical measurement, assumed that the index of refraction for ethyl stearate films is

(6) C. Holley and S. Bernstein, *Phys. Rev.*, **49**, 403 (1936).
(7) S. Bernstein, THIS JOURNAL, **60**, 1511 (1938).
(8) I. Langmuir, *ibid.*, **60**, 1190 (1938).
(9) E. F. Porter and J. Wyman, *ibid.*, **60**, 1083 (1938).
(10) E. Stenhagen, *Trans. Faraday Soc.*, **34**, 1328 (1938).

the same as the index for barium–copper stearate films. The average of the two X-ray measurements is about 9% less than the optical measurement. This difference cannot be due to Stenhagen's assumption of the equality of index of refraction of barium–copper stearate and ethyl stearate films.

The available evidence, then, seems to indicate that the discrepancy found for metal stearate films persists in the case of ethyl stearate films.

A rotation photograph taken with an ethyl stearate film differed from those of the metal stearate films in that reflections other than those of the zero layer-line appeared for the ethyl stearate film. The rotation photograph is shown in Fig. 7. The presence of these reflections indicates that in the case of ethyl stearate films all of the small crystals have the same orientation.

The suggestion that many small crystals form of themselves within the films is indicated also by the fact that the average of the two X-ray grating-space values for ethyl stearate is the same as the value for one of the natural crystalline forms of ethyl stearate found by T. Malkin.[11] Also, as Stenhagen already has pointed out,[10] these tiny crystals can be seen in the ethyl stearate films under a microscope.

The writer is greatly indebted to the following people for their help: To Dr. Katharine B. Blodgett of the General Electric Company for her coöperation. In addition to building many of the films and making optical measurements of some of them, Dr. Blodgett gave freely of her time to the discussion of the many problems which arose in the course of the investigation. To Professor Arthur H. Compton and Dr. Elmer Dershem for their careful guidance. To the Charles A. Coffin Foundation of the General Electric Company for the grant of a fellowship which enabled him to continue with the work.

(11) T. Malkin, *J. Chem. Soc.*, 2796 (1931).

Summary

X-Ray refraction corrections and possible optical phase change corrections fail to account for the discrepancy between X-ray and optical measurements of the thickness of built-up stearate films. The results indicate that the discrepancy must be explained in terms of the film structure. X-Ray measured thicknesses of barium–copper stearate and barium stearate films are greater than the corresponding optical measurements; X-ray measured thicknesses of copper stearate films are less than the corresponding optically measured thicknesses. Measurements of a set of barium–copper stearate films of varying proportions of barium stearate and copper stearate show that the film thickness varies greatly with film composition and that a change in X-ray measured thickness is not accompanied by a change in optically measured thickness of the same magnitude. Skeletonized and unskeletonized films of the same original composition were found to have the same X-ray grating-space. Metal stearate films give only zero layer-line reflections. An ethyl stearate film showed other than zero layer line reflections in addition to those of the zero layer line. A film structure is suggested which is consistent with the X-ray and optical measurements and with reported contact potential measurements.

CHICAGO, ILL. RECEIVED NOVEMBER 20, 1939

[CONTRIBUTION FROM THE CHEMISTRY LABORATORIES OF NEW YORK UNIVERSITY]

The Catalytic Decomposition of Azodicarbonate Ion

BY CECIL V. KING

In his attempts to make diimide HN=NH, Thiele[1] prepared the potassium salt of azodicarbonic acid, by alkaline hydrolysis of azodicarbonamide. He found this salt fairly stable in alkaline solution in the cold, though it decomposes in a few minutes on heating. It is very soluble in water, but decomposes rapidly and is all gone in one to two minutes. In acid solutions the decomposition is even more rapid. Thiele found quantitative formation of nitrogen and hydrazine; the reaction takes place as follows

Alkaline solution

$$2\ \begin{matrix}\mathrm{N{-}COO^-}\\ \|\\ \mathrm{N{-}COO}\end{matrix} + 4OH^- \longrightarrow N_2 + N_2H_4 + 4CO_3^= \quad (1)$$

Faintly alkaline solution

$$2\ \begin{matrix}\mathrm{N{-}COO^-}\\ \|\\ \mathrm{N{-}COO}\end{matrix} + 4H_2O \longrightarrow N_2 + N_2H_4 + 4HCO_3^- \quad (2)$$

Acid solution

$$2\ \begin{matrix}\mathrm{N{-}COO^-}\\ \|\\ \mathrm{N{-}COO}\end{matrix} + 4H^+ \longrightarrow N_2 + N_2H_4 + 4CO_2 \quad (3)$$

Obviously these equations do not represent the mechanism of the decomposition; Thiele suggested the intermediate formation of diimide, which instantly gives nitrogen and hydrazine

$$2N_2H_2 \longrightarrow N_2 + N_2H_4$$

The rapid decomposition in acid solution and greater stability in basic solution suggest an acid catalyzed reaction. Preliminary study in alkaline buffers showed great sensitivity to general acid catalysis. The rate was found to be measurable in solutions of sodium hydroxide from 0.01 *M* to 0.10 *M*.

Experimental

Materials, Apparatus and Procedure

Sodium azodicarbonate was made by the method described by Thiele[1] for the potassium salt. Three preparations evolved 94, 95 and 90%, respectively, of the theoretical amount of nitrogen from acid solution. Microanalyses indicated little if any carbonate impurity, but rather some other nitrogen-containing compound.

Sodium hydroxide stock solutions free from carbonate were prepared; distilled water was not freed from carbonate since carbonate is formed in the decomposition. **Sodium acetate** buffers were made by neutralizing samples of acetic acid and adding excess sodium hydroxide. **Acetoxime** was made and purified by redistillation. Other chemicals were the best commercial grade available.

Nitrogen evolution was followed in an apparatus similar to that described by Brönsted and Duus.[2] The reaction flasks were of 100 cc. capacity and 60 cc. of solution was used for each measurement. The thermostat temperature was kept at 24.9 ± 0.02°. Since the manometers were not thermostated, the room temperature was kept constant to ±0.5° during any one experiment. In most of the experiments 73-mg. samples of azodicarbonate were used, making this concentration 0.0075 *M*. In all except salt effect experiments the ionic strength of the solution was kept at $\mu = 0.1225$ by addition of sodium chloride as an inert salt if necessary.

Hydrogen Ion and Water Catalysis.—In sodium hydroxide solutions, the previous considerations suggest the rate equation:

$$dx/dt = k_1 C_{N_2(COO)_2^=} C_{H_3O^+} + k_2 C_{N_2(COO)_2^=} C_{H_2O} \quad (4)$$

In all solutions used equation (1) is valid for the decomposition, *i. e.*, only carbonate ion is produced during at least the first quarter of the reaction. Also

$$C_{H_2O^+} = K_w/C_{OH^-}$$

where K_w is the ion product of water at the ionic strength in question. Neglecting the water catalysis and the change in ionic strength during reaction

$$dx/dt = kC_{N_2(COO)_2^=} \times K_w/C_{OH^-}$$

where dx/dt = moles decomposing per minute. Since two hydroxyl ions are used for each azodicarbonate ion

$$\frac{dx}{dt} = kK_w \frac{a - x}{b - 2x}$$

where a and b are initial moles of azodicarbonate and hydroxyl ion, respectively. This may be integrated to give

$$\frac{kK_w t}{2.3(b - 2a)} = \log \frac{a}{a - x} + \frac{2x}{2.3(b - 2a)} \quad (5)$$

Omission of the water catalysis term of equation (4) was found to be justified in practice. In the faster experiments it is too small to change the form of the rate equation appreciably, and in the slower experiments at higher hydroxyl ion concentrations the last term of equation (5) becomes small and the entire rate almost of the unimolecular form.

(1) Thiele, *Ann.*, **271**, 127 (1892).

(2) Brönsted and Duus, *Z. physik. Chem.*, **117**, 299 (1925).

Rate constants were evaluated by plotting log $(a-x) - 2x/2.3\ (b - 2a)$ *vs.* t (in minutes). The negative slope of the straight line obtained, multiplied by $2.3(b - 2a)$, gives kK_w. Typical plots are shown in Fig. 1. Deviations from linearity occur for solutions of low hydroxyl ion concentration, where bicarbonate ion is formed and equation (1) is valid only near the beginning of the reaction. In this case the rate constant is obtained from the first few readings. In the special case where $b = 2a$, the rate equation becomes $kK_w = 2x/t$ and a plot of x *vs.* t should be linear. This was found true for the first few readings.

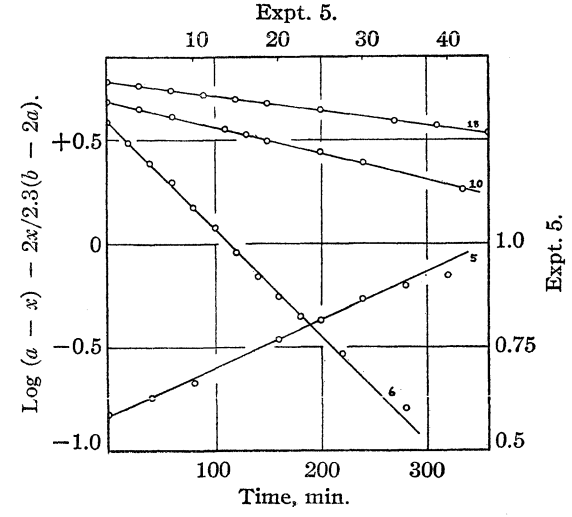


Fig. 1.—Determination of rate constants: expt. 6—divide time scale by 2, expt. 5—$(b - 2a)$ is negative.

It is evident that correct initial pressure readings must be obtained to evaluate equation (5). The azodicarbonate dissolves rapidly when dropped into the solution, and in the slower experiments no correction was necessary for slow attainment of pressure equilibrium. In the faster experiments pressure readings were taken at frequent intervals for several minutes, and an extrapolation made to an initial pressure in agreement with the rate curve.

The rate constants obtained in sodium hydroxide, with sodium chloride added to maintain a constant total ionic strength of 0.1225, are given in Table I. The increasing values of kK_w with increasing hydroxyl ion concentration are obviously due to the increasing proportion of catalysis by water. Division by the initial hydroxyl ion concentration of each experiment gives "constants," kK_w/b, which are comparable dimensionally with the unimolecular rate constants ob-

TABLE I

CATALYSIS BY HYDROGEN ION AT 24.9°

$C_{N_2(COO)_2^-} = 0.0075\ M$ in first thirteen experiments, 0.015 M in last four. Sodium chloride added to make ionic strength 0.1225.

Expt.	C_{OH^-}, M	$C_{H_3O^+}$, $M \times 10^{13}$	kK_w	k'
5	0.01	16.65	0.0001064	0.01064
35	.01	16.65	.0001133	.01133
6	.02	8.33	.0001150	.00575
13	.025	6.66	.0001143	.00457
7	.03	5.55	.0001180	.00393
14	.035	4.76	.0001224	.00350
8	.04	4.16	.0001169	.00292
9	.05	3.33	.0001222	.00244
10	.06	2.78	.0001276	.00213
11	.07	2.38	.0001352	.00193
12	.08	2.08	.0001340	.001675
17	.09	1.85	.0001279	.001421
18	.10	1.67	.0001385	.001385
15	.025	6.66	.0001242	.00497
16	.03	5.55	.0001282	.00421
19	.035	4.76	.0001323	.00378
20	.04	4.16	.0001369	.00342

tained in similar reactions in which the pH remains unchanged during the reaction. These values, which we shall call k', are given in Table I and plotted *vs.* hydrogen ion concentration in Fig. 2. The value of K_w used to calculate the hydrogen ion concentration was 1.665×10^{-14}, taken for $\mu = 0.1225$ from the data of Harned and Mannweiler for sodium chloride solutions.[3] This assumes K_w to be the same in sodium hydroxide and sodium chloride solutions, and also to be unaffected by the small amount of bivalent ion present.

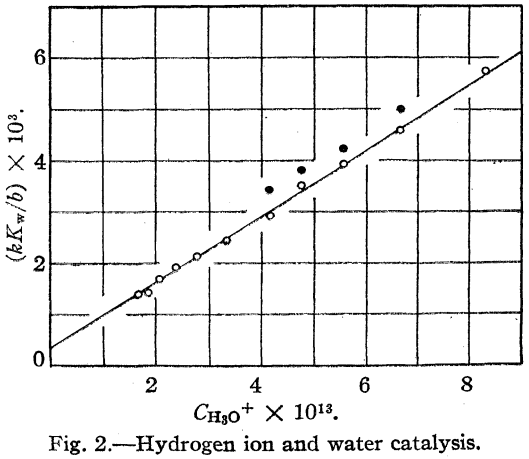


Fig. 2.—Hydrogen ion and water catalysis.

The position of the straight line of Fig. 2 was determined by the method of least squares. Its equation is

$$k' = (3.287 \times 10^{-4}) + (6.388 \times 10^9\ C_{H_3O^+}) \quad (6)$$

(3) Harned and Mannweiler, THIS JOURNAL, **57**, 1873 (1935).

The slope is the molar hydrogen ion catalytic constant, $k_m(H_3O^+) = 6.39 \times 10^9$, and the intercept g ves the water catalysis constant, $k_{H_2O} = 3.29 \times 10^{-4}$. The latter value divided by the water concentration gives the molar water constant, $k_m(H_2O) = 5.92 \times 10^{-6}$.

Salt Effect.—Experiments 15, 16, 19 and 20 (Fig. 2) were run with 0.015 *M* sodium azodicarbonate instead of 0.0075 *M* as in all other experiments, while the ionic strength remained 0.1225 as before. That the higher values of k' are due to specific salt effects rather than lack of validity of equation (5) is indicated by the experiments of Table II, in which 0.02 *M* sodium hydroxide was used throughout and sodium chloride and sodium sulfate added to increase the ionic strength. Values of k' are plotted in Fig. 3 *vs.* ionic strength; bivalent ions apparently exert a smaller negative salt effect than univalent ions. The type and magnitude of the salt effect are in agreement with the Brönsted theory, but the smaller effect of bivalent ions must be ascribed to the peculiarities of this particular case.

TABLE II

THE EFFECT OF IONIC STRENGTH. $C_{NaOH} = 0.02$ *M*, $C_{N_2(COO)_2^-} = 0.0075$ *M*; 24.9°

C_{NaCl}, *M*	μ	k'
0	0.0425	0.00667
0	.0425	.00661
0.04	.0825	.00613
.08	.1225	.00575
.12	.1625	.00547
.12	.1625	.00577
.16	.2025	.00551
$C_{Na_2SO_4}$, *M*	μ	k'
0.0133	0.0825	0.00637
.0267	.1225	.00598
.04	.1625	.00587
.0533	.2025	.00558

Catalysis by Acetic Acid.—Rate constants in solutions of sodium hydroxide and sodium acetate were found to be appreciably higher than in sodium hydroxide and sodium chloride of the same ionic strength. If we assume no change in K_w and the same primary salt effect, the increase may be ascribed to catalysis by molecular acetic acid. Several experiments are detailed in Table III. The acetic acid concentration (C_{HAc}) was calculated from the equation

$$C_{HAc} = \frac{K_w}{K_{HAc}} \frac{C_{Ac^-}}{C_{OH^-}}$$

where $K_w = 1.665 \times 10^{-14}$ ($\mu = 0.1225$) and

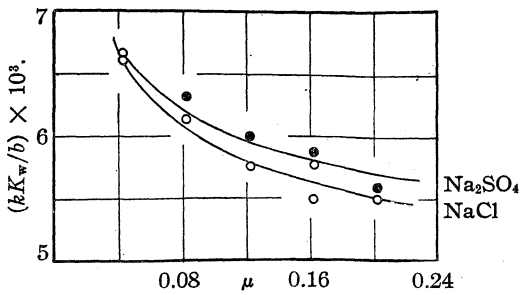


Fig. 3.—Salt effect.

$K_{HAc} = 2.87 \times 10^{-5}$ at this ionic strength.[4] Values of the hydrogen ion and water catalysis calculated from equation (6) are subtracted from k' to give $\Delta k'$.

TABLE III

CATALYSIS BY ACETIC ACID: $C_{N_2(COO)_2^-} = 0.0075$ *M*, $\mu = 0.1225$, 24.9°

C_{NaOH}, *M*	C_{NaAc}, *M*	C_{HAc}, *M* $\times 10^9$	k'	$\Delta k'$	k_m (HAc) $\times 10^{-5}$
0.01	0.09	5.49	0.01185	0.00088	1.60
.01	.09	5.49	.01259	.00162	2.98
.01	.09	5.49	.01190	.00093	1.70
.02	.08	2.44	.00627	.00064	2.62
.02	.08	2.44	.00593	.00030	1.23
.02	.08	2.44	.00594	.00031	1.27
					Av. 1.90

Since the acetate ion concentration remains sensibly constant during the decomposition when hydroxyl ion is present in excess, the rate equation for these solutions has the same form as equation (5). The molar catalytic constants obtained are not very accurate or even consistent, largely because the entire error of each determination is included in the relatively small increase in rate. The average value of Table III, k_m (HAc) $= 1.9 \times 10^5$, may be regarded as an approximation for the acetic acid catalysis.

Ammonium Ion Catalysis.—Catalysis by ammonium ion was measured similarly by adding ammonia to sodium hydroxide solutions and noting the increase in rate. Assuming that the ammonia present does not affect the ionization of water or the primary salt effect, this increase may be ascribed to the ammonium ion. Since the ammonia concentration is little changed during the decomposition if excess hydroxyl ion is present, the rate equation again has the same form as equation (5). The ammonium ion concentration can be calculated from $C_{NH_4^+} = K_{NH_3}C_{NH_3}/C_{OH^-}$, using $K_{NH_3} = 3.95 \times 10^{-5}$ at this ionic strength.[5]

(4) Harned and Hickey, THIS JOURNAL, **59**, 1284 (1937).
(5) Harned and Robinson, *ibid.*, **50**, 3157 (1928).

The rates obtained are given in Table IV. Again the rate increases are erratic since the entire error falls on the increase. The average value k_m (NH_4^+) = 7.3 is taken as the molar catalytic constant.

TABLE IV

CATALYSIS BY AMMONIUM ION: $C_{N_2(COO)_2^-}$ = 0.0075 *M*, μ = 0.1225, 24.9°

C_{NaOH}, *M*	C_{NH_3}, *M*	$C_{NH_4^+}$, *M* × 10^4	*k'*	$\Delta k'$	k_m (NH_4^+)
0.02	0.12	2.37	0.00713	0.00148	6.24
.02	.12	2.37	.00674	.00107	4.60
.02	.09	1.78	.00736	.00171	9.60
.02	.09	1.78	.00655	.00088	5.06
.02	.06	1.19	.00630	.00065	5.46
.02	.06	1.19	.00677	.00110	9.41
.02	.03	0.59	.00575	.00010	1.70
.02	.03	.59	.00624	.00057	10.0
.01	.12	4.74	.01507	.00410	8.65
.01	.06	2.37	.01415	.00318	13.4
					Av. 7.4

Catalysis by Acetoxime.—The molar catalysis by an acid as weak as acetoxime should be much smaller than that by acetic acid or ammonium ion, but on the other hand higher concentrations of molecular acid (HA) can be maintained in the alkaline solutions necessary. Equation (5) is unusable in this case, since both hydroxyl ion and the weak acid anion decrease in concentration as the reaction proceeds. The correct rate equation

$$dx/dt = C_{N_2(COO)_2^-}(k_1C_{H_3O^+} + k_2C_{H_2O} + k_3C_{HA})$$

cannot easily be transformed into usable form even if the water catalysis be neglected. Fortunately this equation approaches the unimolecular form; it can be seen from the expression

$$C_{HA} = \frac{K_w}{K_{HA}} \frac{C_{A^-}}{C_{OH^-}}$$

that since both C_{A^-} and C_{OH^-} are diminishing, C_{HA} remains relatively constant and $C_{H_3O^+}$ increases less than in the preceding cases. Satisfactory "unimolecular" rate constants can be obtained by plotting log $(a - x)$ *vs. t;* in some cases the plot is perfectly linear over two-thirds of the reaction and in other cases the slope near the beginning of the reaction can be used.

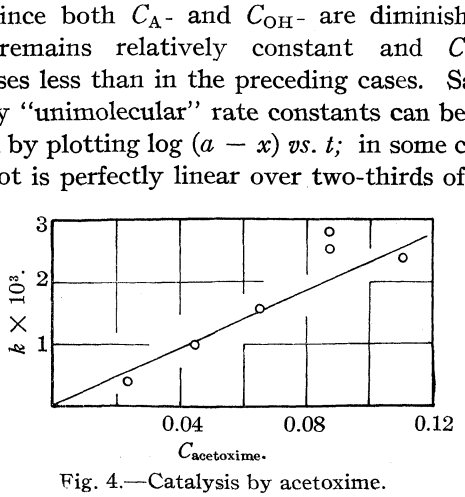


Fig. 4.—Catalysis by acetoxime.

TABLE V

CATALYSIS BY ACETOXIME: $C_{N_2(COO)^-}$ = 0.0075 *M*, μ = 0.1225, 24.9°, K_{HA} = 6.0 × 10^{-13}

Initial C_{NaOH}, *M*	Initial $C_{Acet.}$, *M*	C_{OH^-} *M*	C_{HA}, *M*	$k_{uni.}$	$k_{H_3O^+, H_2O}$	k_{HA}
0.05	0.05	0.0226	0.0226	0.00546	0.00508	0.00038
.05	.075	.0193	.0443	.00690	.00590	.00100
.05	.10	.0150	.0650	.00905	.00749	.00156
.05	.125	.0121	.0871	.01173	.00921	.00252
.05	.125	.0121	.0871	.01202	.00921	.00281
.05	.15	.0100	.1100	.01346	.01108	.00238

Rate constants obtained in this manner are given in Table V. Hydroxyl ion and unneutralized acetoxime concentrations were calculated using K_{HA} = 6.0 × 10^{-13}, a value calculated by Scudder[6] for 25° from measurements of Lundén on the rate of ethyl acetate hydrolysis in barium hydroxide partly neutralized by acetoxime.[7] Values of *k'*, called $k_{H_3O^+, H_2O}$ in Table V, were calculated for these hydroxyl ion concentrations from equation (6). The acetoxime constants, k_{HA}, are plotted *vs.* C_{HA} in Fig. 4, and the slope of the straight line is taken as the molar catalytic constant, k_m (HA) = 0.023.

It is doubtful whether the value K_{HA} = 6.0 × 10^{-13} is correct under the experimental conditions here, or whether a more satisfactory value could be calculated from Lundén's experimental results. Use of a smaller value for K_{HA} and a larger value for K_w leads to a somewhat better linear relation in Fig. 4, but due to lack of more precise rate measurements and probable complications of a type to be described later, it seems better to accept the above value as approximately correct.

Catalysis by Maltose.—In solutions containing maltose the rate is also approximately of the unimolecular form. Some difficulty arose from slow decomposition of the maltose; while it was usually unnecessary to take pressure readings for more than sixty minutes, over a period of several hours the solutions turned brown, and final pressure readings were one to five millimeters higher than usual. Since this led to rate constants that were evidently too low, new values of the rate constants were calculated using for the total pressure rise the average for preceding experiments in which the same azodicarbonate sample was used. This gives fairly consistent results, but of course introduces some error.

(6) Scudder, "Conductivity and Ionization Constants of Organic Compounds," D. Van Nostrand Co., New York, N. Y., 1914.

(7) Lundén, *Z. physik. Chem.*, **54**, 532 (1906).

Rate constants so determined are given in Table VI, together with the calculated hydroxyl ion and unneutralized maltose concentrations, hydrogen ion and water catalysis calculated from equation (6), and finally the maltose catalysis constants. The latter are plotted *vs.* unneutralized maltose concentrations in Fig. 5, and the slope of the straight line is taken as the molar catalysis constant, k_m (HM) = 0.038.

TABLE VI

CATALYSIS BY MALTOSE: $C_{N_2(COO)_2^=}$ = 0.0075 *M*, μ = 0.1225, 24.9°, K_{HM} = 1.4 × 10^{-12}

Initial C_{NaOH}, *M*	Initial $C_{Malt.}$, *M*	C_{OH^-}, *M*	C_{HM}, *M*	$k_{uni.}$	$k_{H_3O^+, H_2O}$	k_{HM}
0.05	0.05	0.0174	0.0174	0.00753	0.00590	0.00163
.10	.10	.0261	.0261	.00512	.00400	.00112
.10	.10	.0261	.0261	.00529	.00400	.00129
.10	.15	.0128	.0628	.00989	.00724	.00265
.10	.18	.0094	.0894	.01329	.00958	.00371
.10	.18	.0094	.0894	.01231	.00958	.00273
.10	.20	.0079	.1079	.01564	.01119	.00445
.10	.20	.0079	.1079	.01548	.01119	.00429
.10	.20	.0079	.1079	.01546	.01119	.00427
.10	.25	.0056	.1556	.02151	.01553	.00598

In calculating the values of Table VI, the dissociation constant of maltose was taken as 1.4 × 10^{-12}. This is somewhat lower than the value determined by Michaelis and Rona[8] at 18°, namely, 1.8 × 10^{-12}. Use of the latter value changes the position of the catalytic constants so that, in Fig. 5, no satisfactory straight line can be drawn through them and through the origin. In general too high values of the dissociation constant lead to a curve which is concave downward, too low values to a curve concave upward. The change is not sensitive enough for accurate estimation of the dissociation constant.

Catalysis by Sucrose.—In mixtures of sodium hydroxide and sucrose, the rate is again "unimolecular" over the first portion of the decomposition. Three series of experiments were run: (a) various concentrations of sucrose were added to 0.03 *M* sodium hydroxide, thus maintaining the total base concentration (C_{OH^-} + C_{S^-}) constant; (b) solutions were made up at nearly constant hydroxyl ion concentration (or *p*H) with varying sucrose concentrations; and (c) the total base concentration was kept at 0.06 *M*. In each case the ionic strength was kept at 0.1225 by addition of sodium chloride where necessary. Details are given in Table VII, where hydroxyl ion and unneutralized sucrose concentrations are given, then rate constants, hydrogen ion and water catalysis calculated from equation (6), and finally the portion of the total catalysis due to sucrose. Hydroxyl ion concentrations were calculated using K_{HS} = 2.4 × 10^{-13} for the sucrose dissociation constant, a value determined by Michaelis and Rona[8] by hydrogen electrode measurements in sodium hydroxide–sucrose mixtures with an ionic strength about 0.1 at 18°. This is based on a value of K_w = approximately 10^{-14}, and is larger than the older value found for 25° by Madsen[9] from the rate of ethyl acetate hydrolysis in such mixtures at an ionic strength of 0.0245 and again based on K_w = 10^{-14}. Experiments under way in this Laboratory show that this constant is at least as high as 2.4 × 10^{-13} at μ = 0.1225; and smaller values lead to unreasonably high values for the molar catalysis constant of sucrose.

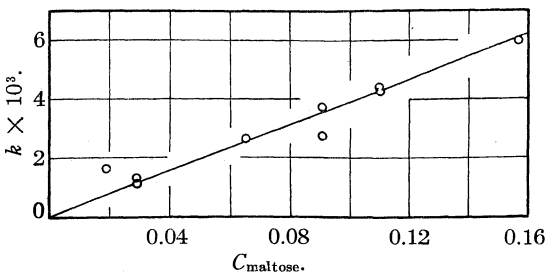


Fig. 5.—Catalysis by maltose.

TABLE VII

CATALYSIS BY SUCROSE: $C_{N_2(COO)_2^=}$ = 0.0075 *M*, μ = 0.1225, 24.9°, K_{HS} = 2.4 × 10^{-13}

Initial C_{NaOH}, *M*	Initial $C_{sucrose}$, *M*	C_{OH^-} *M*	C_{HS}, *M*	$k_{uni.}$	$k_{H_3O^+, H_2O}$	k_{HS}
0.03	0.05	0.0192	0.0392	0.00644	0.00587	0.00057
.03	.05	.0136	.0836	.01025	.00815	.00210
.03	.10	.0136	.0836	.01047	.00815	.00232
.03	.10	.0136	.0836	.01047	.00815	.00232
.03	.125	.0118	.1068	.01185	.00934	.00251
.03	.15	.0104	.1304	.01392	.01056	.00336
.03	.20	.0084	.1784	.01754	.01300	.00454
.03	.20	.0084	.1784	.01764	.01300	.00464
.02	.0373	.0138	.0311	.00891	.00804	.00087
.02	.0373	.0138	.0311	.00886	.00804	.00082
.04	.1616	.0133	.1349	.01097	.00833	.00264
.04	.1616	.0133	.1349	.01074	.00833	.00241
.05	.223	.0135	.1865	.01068	.00821	.00247
.05	.223	.0135	.1865	.01064	.00821	.00243
.05	.223	.0135	.1865	.01081	.00821	.00260
.06	.2716	.0141	.2257	.01049	.00787	.00262
.06	.2716	.0141	.2257	.01083	.00787	.00296
.06	.15	.0228	.1128	.00647	.00500	.00147
.06	.20	.0183	.1583	.00794	.00614	.00180

The catalysis constants are plotted in Fig. 6 *vs.* the unneutralized sucrose concentration. The molar catalysis is constant for each total base concentration, but is not constant at constant hydroxyl ion concentration, the actual catalytic

(8) Michaelis and Rona, *Biochem. Z.*, **49**, 232 (1913).

(9) Madsen, *Z. physik. Chem.*, **36**, 290 (1901); Scudder, *loc. cit.*

effect of sucrose seeming to approach a limiting upper value in series (b). A plot of the molar constants (slopes of solid and broken straight lines of Fig. 6) *vs.* the reciprocal of the sucrate ion concentration is not linear, and probably extrapolates to zero at infinite base concentration.

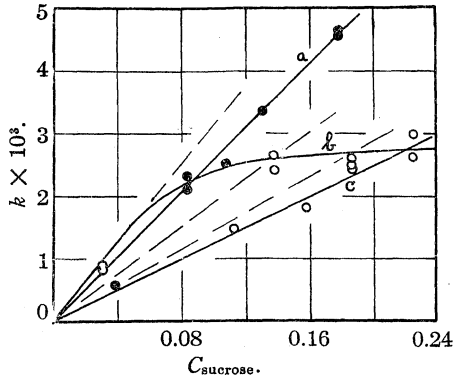


Fig. 6.—Catalysis by sucrose: (a) $C_{OH^-} + C_{S^-} = 0.03\ M$, (b) C_{OH^-} nearly constant, (c) $C_{OH^-} + C_{S^-} = 0.06\ M$.

The abnormalities of this catalysis are similar to those in the acid catalysis of diazoacetate ion decomposition[10] and in the nitramide decomposition in *m*-cresol.[11] Similar abnormalities would probably appear in the catalysis by maltose, acetoxime and the other acids if they were studied in more detail. Due to lack of accurate dissociation constants for these very weak acids and the relative inaccuracy of rate constant measurements, it seems impractical to make a more detailed study at this time.

For the present purpose we shall use as the molar catalytic constant for sucrose the value obtained with 0.06 *M* sodium hydroxide solutions, k_m (HS) = 0.0125.

Comparison of Rate Constants with Acid Strengths.—In Fig. 7 values of log k_m/p are plotted *vs.* log $(q/p\ K_A^0)$, where p and q are used as suggested by Pedersen and K_A^0 is the acid dissociation constant at zero ionic strength (where this is known) (see ref. 10). In this case p and q are always 1, except for acetic acid, where q is 2.

TABLE VIII

THE RELATION BETWEEN VELOCITY CONSTANTS AND ACID STRENGTH

Acid	k_m	K_A^0
H_3O^+	6.39×10^9	55.5
$HC_2H_3O_2$	1.9×10^5	1.75×10^{-5}
NH_4^+	7.4	5.5×10^{-5}
Maltose	3.8×10^{-2}	(1.4×10^{-12})
Acetoxime	2.3×10^{-2}	(6.0×10^{-13})
Sucrose	1.25×10^{-2}	(2.4×10^{-13})
H_2O	5.92×10^{-6}	1.80×10^{-16}

(10) King and Bolinger, THIS JOURNAL, **58**, 1533 (1936).

(11) Brönsted, Nicholson and Delbanco, *Z. physik. Chem.*, **A169**, 379 (1934).

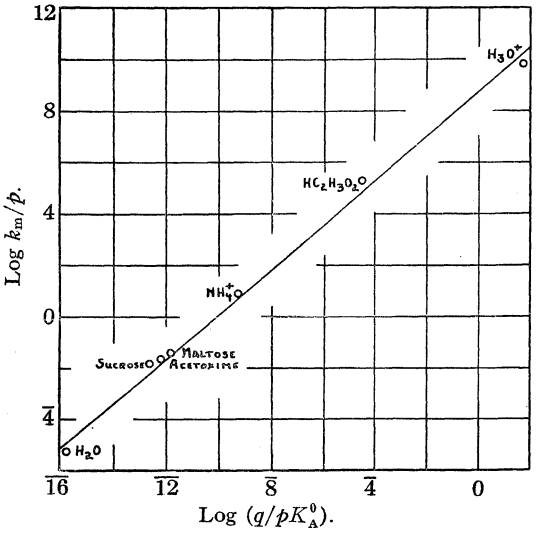


Fig. 7.—The relation between rate constants and acid dissociation constants.

The rates show satisfactory agreement with the Brönsted theory for general acid catalysis. Points on the straight line of Fig. 7 are represented by the equation

$$k_m/p = 7.40 \times 10^8 (q/pK_A^0)^{0.86}$$

Discussion.—This reaction is more sensitive to acid catalysis than any previously studied. The water catalysis is six times as great and the hydrogen ion catalysis eighteen times as great as in the diazoacetate ion catalysis.[10] The value of the constant G in the Brönsted equation (7.40×10^8) is thirty-nine times as great. On the other hand, the exponent, 0.86, is similar to the value found in several other cases.

This high sensitivity is probably largely due to the double negative charge of the azodicarbonate ion, which increases its ability to capture a proton from the catalyzing acid. While little definite evidence is available, one should expect the nitrogen–carbon bond of the azodicarbonate to be inherently more stable than that of the diazoacetate, from a comparison of the spacial relationships in the two ions, for example. The azodicarbonate is more thermostable: the diazoacetate explodes vigorously on heating or even with friction in the cold; the azodicarbonate decomposes less vigorously on heating to a somewhat higher temperature. Further, the diazoacetate poly-

merizes readily in solution, probably through rupture of a nitrogen–carbon bond, while this behavior is not shown by the azodicarbonate.

Consequently the actual increase in sensitivity to acid catalysis due to the double negative charge may well be much greater than shown by simple comparison of these two cases. It is significant that the positively charged hydrogen ion shows three times as great an increase in catalytic effect as the neutral water molecule. The effect of the charge of the catalyzing acid has been discussed in detail by Pedersen.[12]

The strength of azodicarbonic acid cannot be estimated easily, because of its instability and the nature of the decomposition products. It is almost certainly too strong to allow appreciable amounts of the acid ion or molecular acid to exist in the alkaline solutions used here. The general acid catalysis excludes spontaneous decomposition of traces of acid or acid ion as the mechanism of the reaction; but spontaneous decomposition of small amounts of equimolecular ion-acid compounds in equilibrium with the components would be indistinguishable from the bimolecular mechanism postulated. Neither mechanism accounts for the depressing effect of bases on the molar acid catalysis, found here for sucrose and in the diazoacetate decomposition for other acids.

(12) Pedersen, *J. Phys. Chem.*, **38**, 581 (1934).

The author is indebted to Mr. Lewis Appleton, who carried out some of the experimental work reported here.

Summary

The decomposition of azodicarbonate ion to give nitrogen, hydrazine and carbon dioxide or carbonate ion, has been found to be extremely sensitive to general acid catalysis. It is catalyzed by water, hydrogen ion and other acids in accordance with the equation $dx/dt = C_{N_2(COO)_2}(k_1C_{H_3O^+} + k_2C_{H_2O} + k_3C_{HA} + \ldots)$. That this equation does not completely explain the mechanism is shown by the fact that the molar catalysis by sucrose (and probably by other weak acids) is diminished by bases (hydroxyl ion, sucrate ion, etc.).

The molar catalysis constants as evaluated show good agreement with the Brönsted equation $k_m/p = G(q/pK_A^0)^x$ where $G = 7.40 \times 10^8$ and $x = 0.86$. This value of G is the highest yet found for acid catalysis; the value of x is similar to that found in several other cases.

WASHINGTON SQUARE COLLEGE
NEW YORK, N. Y. RECEIVED NOVEMBER 29, 1939

[CONTRIBUTION FROM THE WILLIAM H. CHANDLER CHEMISTRY LABORATORY OF LEHIGH UNIVERSITY]

The Photochemical Oxidation of Hydrogen[1]

BY HILTON A. SMITH AND A. NAPRAVNIK

There have been reported three earlier studies[2,3,4] of the photochemical oxidation of hydrogen by light of wave length 1719–1725 Å. The first of these papers dealt with the over-all temperature coefficient of the reaction, while the other two resulted from studies of the individual products obtained, and the quantum yields of these products at room temperatures. The present paper reports the quantum yields of the individual products at elevated temperatures as well as additional room temperature data.

Experimental

In the last of the papers mentioned above, it was demonstrated that the reaction products were ozone, hydrogen peroxide, and water. Analysis of this mixture was carried out by pumping the exit gases from the reaction cell through an analyzing bubbler, after which they were dried and returned to the cell. Three successive runs were made on each hydrogen–oxygen mixture. During the first run the bubbler contained titanium sulfate solution. The hydrogen peroxide formed was absorbed in this solution and determined colorimetrically. During the second run the bubbler contained neutral potassium iodide solution. This absorbed both hydrogen peroxide and ozone. The bubbler liquid subsequently was acidified and the liberated iodine titrated with sodium thiosulfate. The yield of ozone was calculated by subtracting from this result the yield of hydrogen peroxide determined in the first run. Finally, a much longer run was made, again using potassium

(1) Presented at the Boston meeting of the American Chemical Society, September 12, 1939.
(2) Kistiakowsky, *Proc. Nat. Acad. Sci.*, **15**, 194 (1929).
(3) Kistiakowsky, THIS JOURNAL, **52**, 1868 (1930).
(4) Smith and Kistiakowsky, *ibid.*, **57**, 835 (1935).

iodide in the bubbler. The pressure drop found during this run was corrected for ozone and hydrogen peroxide absorbed in the bubbler, and the water yields subsequently calculated.

A critical study of these procedures was undertaken. As a result it was possible to show that while either ozone or hydrogen peroxide may be determined individually by absorption in neutral potassium iodide, and subsequent titration of the iodine liberated in the acidified solution,[5] the two cannot be analyzed by simultaneous absorption in such a solution. In the presence of each other they are evidently catalytically decomposed.[6] It was shown that under conditions such that both ozone and hydrogen peroxide are formed in appreciable quantities, the apparent yield of ozone plus hydrogen peroxide was much less than that of hydrogen peroxide alone. For example, the yield of hydrogen peroxide obtained by passing a gas mixture of 50 mm. of oxygen and 710 mm. of hydrogen before the light source used in this research was 8.66×10^{-7} mole per minute. In this mixture the yield of ozone is approximately equal to that of peroxide. When the products obtained using this same mixture were passed through a bubbler containing neutral potassium iodide (2.5% solution), the yield of ozone plus hydrogen peroxide was only 1.95×10^{-7} mole per minute, a value less than one-fourth that of either product.

Further experiments established the fact that, if the mixture of ozone and peroxide were first passed through a bubbler containing titanium sulfate solution and then through neutral potassium iodide, the hydrogen peroxide was removed by the first bubbler, while the ozone was removed by the second. The passage of ozone through the titanium sulfate solution affects neither the ozone yields nor those of peroxide. This method of analysis was used in the work reported here.

The experimental set-up was similar to that previously employed.[4] The light source consisted of a condensed spark operating in a nitrogen atmosphere between two slowly revolving aluminum disks.[7,8] The gases to be illuminated were circulated at a velocity of 700 ml. per minute through a thin-walled quartz vessel of approximately 1 ml. volume (this time of light exposure was too short to cause photochemical decomposition of the products), and then through the two ice-cooled absorption bubblers. After the ozone and hydrogen peroxide had been removed, the gases were dried by means of a dehydrite tube, and returned to the cell through an all-glass circulating pump. This pump was a modification of the type described by Balsbaugh, Larsen, and Lyon.[9] It had two barrels, and the solenoids around these barrels were connected in quarter phase to the same motor. Thus, pumping action occurred four times per cycle. The pump operated at a speed of 80 cycles per minute. A section of capillary tubing between the pump and the cell evened out the gas flow so that it was quite regular when exposed to the light source. The whole circulating system was connected through a capillary tube to a constant-volume manometer.

The oxygen and hydrogen used were generated by the electrolysis of a solution of sodium hydroxide. Air or tank nitrogen was used in experiments dealing with nitrogen–oxygen mixtures.

The procedure employed in making a run was as follows. After the system was filled with the desired pressures of hydrogen and oxygen, the circulating pump was allowed to run for about fifteen minutes in order to assure temperature equilibrium with the surroundings. The pressure and temperature of the system were then taken. The pump was again allowed to run for a few minutes, and pressure readings repeated. This was continued until constant readings were obtained. Next, the gases passing through the reaction cell were exposed to the light source for a definite length of time, generally thirty minutes. After the illumination, the temperature was adjusted to its pre-run value, and pressure readings taken as before. The two bubblers were subsequently removed from the system, and ozone and peroxide yields determined. The pressure drop occurring during the run was corrected for the amounts of these products formed, and the water yield then calculated.

For runs at elevated temperatures, the thin-faced quartz cell was equipped with a thermocouple well which entered the cell from the gas-entrance side to a point just before that at which the reaction took place. Preceding the cell, and connected to it by a quartz to pyrex graded seal, was a short grill made from approximately four feet of pyrex tubing. The grill and cell were enclosed in a pyrex jacket to which was attached a long side arm, allowing entrance of the nitrogen into the cell jacket at a point behind the grill. The nitrogen emerged from the cell jacket through a round hole slightly less than one centimeter in diameter, this opening being directly between the thin face of the reaction cell and the spark. The cell jacket was insulated by placing it in a box packed with loose asbestos fibers, the front of the jacket emerging from the box for a distance of about one centimeter.

The side arm through which the nitrogen entered the cell jacket was wound with nichrome resistance wire. Heated nitrogen was blown over the pyrex grill at a rate of eight liters per minute, thus heating the gases passing into the reaction cell. Temperature equilibrium was established in the heat exchanger, and the temperature of the gases just before exposure to the light source was read by means of a copper–constantan thermocouple connected

(5) *Cf.* Treadwell and Hall, "Analytical Chemistry," John Wiley and Sons, Inc., New York, N. Y., 8th edition, Vol. II, p. 573, and p. 576.

(6) *Cf.* Bray, THIS JOURNAL, **60**, 82 (1938).

(7) Wiig and Kistiakowsky, *ibid.*, **54**, 1807 (1932).

(8) The authors are greatly indebted to Prof. G. B. Kistiakowsky for his generous loan of the sparker used in this research.

(9) Balsbaugh, Larsen and Lyon, *Ind. Eng. Chem.*, **28**, 682 (1936).

to a Leeds and Northrup potentiometer. During a run the temperature was kept constant to ±1°. Runs were made in the same manner as those performed at room conditions.

At the highest temperatures a number of experiments were tried without exposure to the light source. No dark reaction was detected.

As in earlier research,[4] each run with hydrogen–oxygen mixtures was preceded and followed by control runs made with air at atmospheric pressure in the system. The amounts of all products obtained were reduced to constant incident light intensity by means of these control runs. Since for experiments at elevated temperatures it was not feasible to cool the cell to room temperatures for the air runs, these were made under the same conditions as those of the corresponding hydrogen–oxygen runs.

A series of measurements of ozone yields in air at one atmosphere pressure and varying temperatures was made in order to study the effect of increased temperature on the yields of ozone. The results are given in Table I. They indicate clearly that in the mixture under consideration the amount of ozone formed is constant over the temperature range studied, and thus, that the control runs could be used without correction. This result is expected, since under the conditions of the runs, sufficient oxygen is present to absorb all of the light entering the cell. (Lyman[10] states that an air column one centimeter long completely absorbs the strong aluminum spark lines in the neighborhood of 1720 Å.)

Results

The quantum yields of the several products of each run were calculated by dividing such yields by the yield of ozone found in a mixture of nitrogen and oxygen containing the same partial pressure of oxygen as that of the hydrogen–oxygen run, and multiplying the resultant figure by two.[11] It has been demonstrated previously that neither reduction of total pressure nor dilution with nitrogen affects the quantum yield of ozone in the nitrogen–oxygen mixtures.[4] Table I indicates that the temperatures used in this research do not seriously alter its value.

TABLE I

EFFECT OF TEMPERATURE ON OZONE YIELDS IN AIR

T, °C.	Yields O_3 moles/min. × 10^6
25	3.14
100	2.95
150	3.16
200	2.97
240	3.13
280	2.98

Quantum yields of ozone, hydrogen peroxide and water obtained at room temperatures using hydrogen–oxygen mixtures of total pressures varying from 1140 to 95 millimeters are given in the first five figures. In the case of runs made at 95 mm. pressure, it was difficult to obtain reproducible results, but the general trend of the curves is certainly correct.

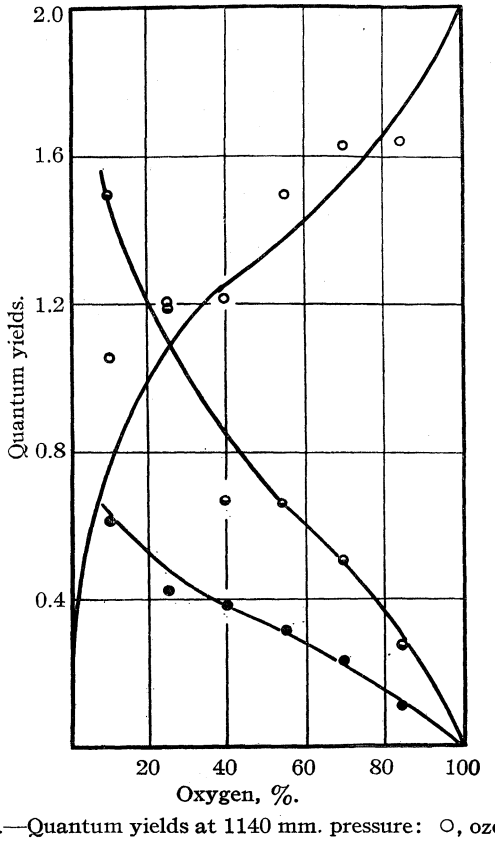


Fig. 1.—Quantum yields at 1140 mm. pressure: ○, ozone; ⊖, water; ●, hydrogen peroxide.

The quantum yields were not corrected for reaction due to absorbed light of wave lengths 1854–1862 Å., these corrections having been shown to be small in the case of a cell of the type used in this research.[4] This is particularly true at low pressures.

An examination of the figures shows the following:

1. With increasing oxygen content, the quantum yields of ozone increase, rapidly at first, and then more slowly, to a maximum value of two. The yields of water and hydrogen peroxide decrease quite regularly, the water yields always being greater than those of peroxide.

2. Pressure change from 1140 to 380 mm. has the following effect on the quantum yields of the three reaction products. The yields of both water and hydrogen peroxide increase, while that of ozone is decreased. These changes are minor

(10) Lyman, "The Spectroscopy of the Extreme Ultra-violet," Longmans, Green and Co., London, 1928.

(11) *Cf.* Vaughan and Noyes, THIS JOURNAL, 52, 559 (1930).

at high pressures, but become more pronounced at low pressures, as the results at 190 and 95 mm. total pressure indicate. The increase in water yields is much greater than that of peroxide yields, values as great as 14 having been found for water at 95 mm.

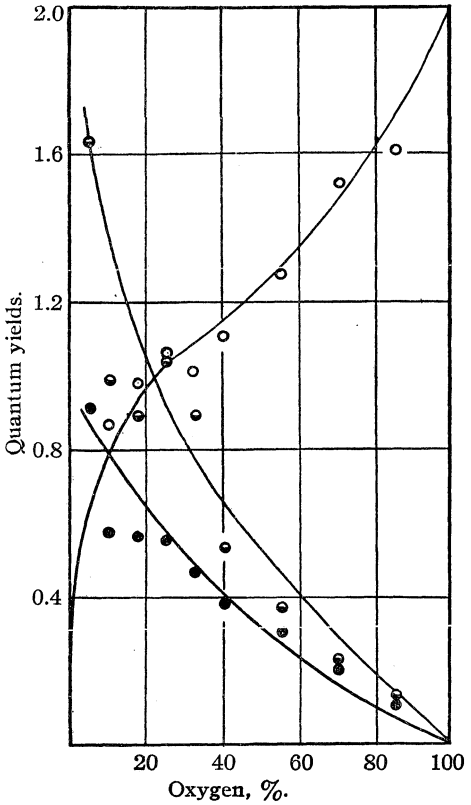


Fig. 2.—Quantum yields at 760 mm. pressure: ○, ozone; ◒, water; ●, hydrogen peroxide.

The results found using hydrogen–oxygen mixtures of 190 mm. total pressure and temperatures from 25 to 280° are given in Figs. 6, 7, and 8. They indicate that the quantum yields of ozone fall off with increasing temperature until this product becomes undetectable at temperatures as low as 150° for mixtures containing 10% oxygen, and higher temperatures for mixtures containing larger percentages.

In the case of water and hydrogen peroxide, the quantum yields are greatly increased with rise in temperature, the increase being relatively small at first, but subsequently becoming very rapid. The hydrogen peroxide yields are always much smaller than those of water, but the changes in the curves parallel each other very closely.

Similar results were obtained at higher total pressures, although the region of rapid rise in the quantum yields of water and peroxide was not found in the temperature range studied.

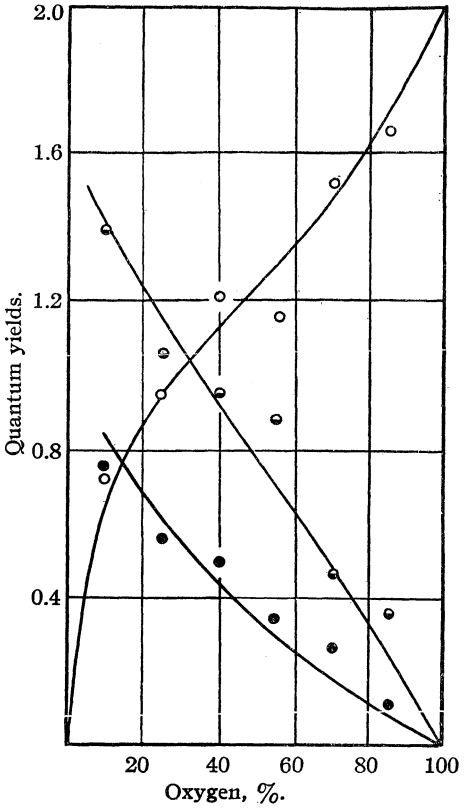


Fig. 3.—Quantum yields at 380 mm. pressure: ○, ozone ◒, water; ●, hydrogen peroxide.

Discussion

In general, the above results are explainable through a rather simple mechanism. The primary reaction is unquestionably that of rupture of an oxygen molecule to form two oxygen atoms.[12]

$$O_2 + h\nu \longrightarrow 2O \qquad 2I_{abs.} \quad (1)$$

This is followed by interaction of the atoms formed with molecules of oxygen and hydrogen. There is good evidence[13] that the oxygen atom will react with oxygen molecules to form ozone on triple collisions only.

$$O + O_2 + M \longrightarrow O_3 + M \qquad k_2 \quad (2)$$

As to its reaction with hydrogen, two possibilities exist. The first is that the oxygen atom may combine with hydrogen in a triple collision to form water.

$$O + H_2 + M \longrightarrow H_2O + M \qquad (3a)$$

In order to explain the experimental results it is

(12) Herzberg, *Z. physik. Chem.*, **4B**, 223 (1929).
(13) *Cf.* Schumacher, THIS JOURNAL, **52**, 2377 (1930).

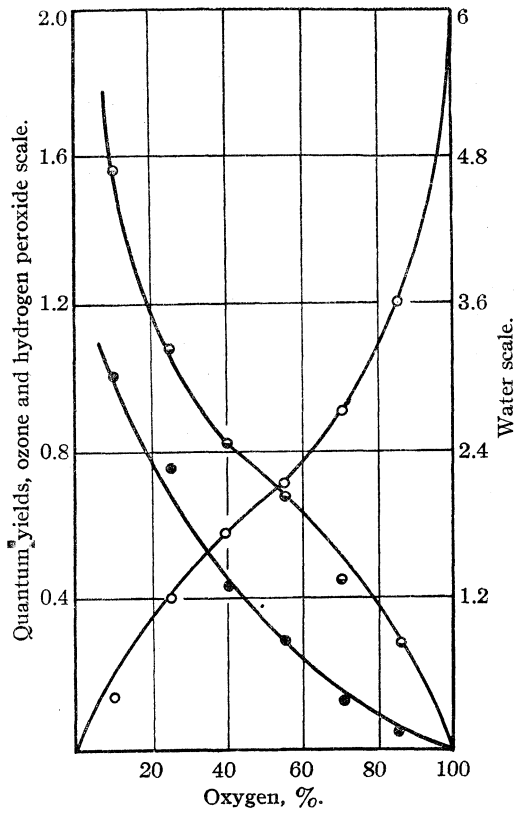


Fig. 4.—Quantum yields at 190 mm. pressure: ○, ozone; ◒, water; ●, hydrogen peroxide.

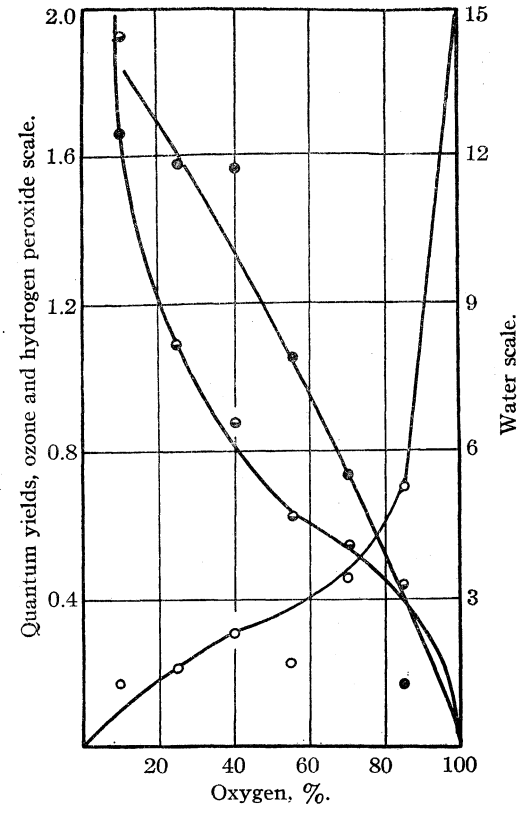


Fig. 5.—Quantum yields at 95 mm. pressure: ○, ozone; ◒, water; ●, hydrogen peroxide.

necessary to assume that in this reaction the third body is an oxygen molecule rather than a hydrogen molecule. However, it will be pointed out farther on that the possibility of hydrogen as the third body is not excluded.

$$O + H_2 + O_2 \longrightarrow H_2O + O_2 \qquad k_3 \quad (3)$$

The oxygen atoms may also react with the hydrogen molecules through a bimolecular collision.

$$O + H_2 \longrightarrow OH + H \qquad k_4 \quad (4)$$

The probability of this reaction is low,[14,15] but because other reactions require three-body collisions, the reaction is important, particularly at low pressures. The only logical fate of the OH radical is a reaction with hydrogen to form water and a hydrogen atom.

$$OH + H_2 \longrightarrow H_2O + H \qquad (5)$$

Finally, there is rather conclusive evidence that the sole result of the action of hydrogen atoms on a mixture of hydrogen and oxygen at room temperature and ordinary pressures is the formation of hydrogen peroxide.[16,17] The first step is the formation of the complex HO_2, which must take place by a triple collision mechanism.[18]

$$H + O_2 + M \longrightarrow HO_2 + M \qquad (6)$$

In order to explain the results of the mercury-sensitized reaction, Bates[19] postulated that HO_2 may react with hydrogen to form hydrogen peroxide and hydrogen atoms.

$$HO_2 + H_2 \longrightarrow H_2O_2 + H \qquad (7a)$$

This reaction is, however, energetically improbable at room temperatures. The logical fate of this radical is its reaction with another HO_2 either in the gas phase or on the walls to form hydrogen peroxide and oxygen; such a reaction was proposed by Bray[6] for the reaction in solution, and was also included in Bates' mechanism.

$$HO_2 + HO_2 \longrightarrow H_2O_2 + O_2 \qquad (7)$$

It should be noted, however, that the particular method by which hydrogen atoms react with the

(14) Harteck and Kopsch, *Z. physik. Chem.*, **B12**, 327 (1931).
(15) Rodebush, Wende, and Campbell, THIS JOURNAL, **59**, 1924 (1937).
(16) Bates and Salley, THIS JOURNAL, **55**, 110 (1933).
(17) Bonhoeffer and Bohm, *Z. physik. Chem.*, **119**, 385 (1926).
(18) Cook and Bates, THIS JOURNAL, **57**, 1775 (1935). See also von Elbe and Lewis, *J. Chem. Phys.*, **7**, 710 (1939).
(19) Bates, THIS JOURNAL, **55**, 426 (1933).

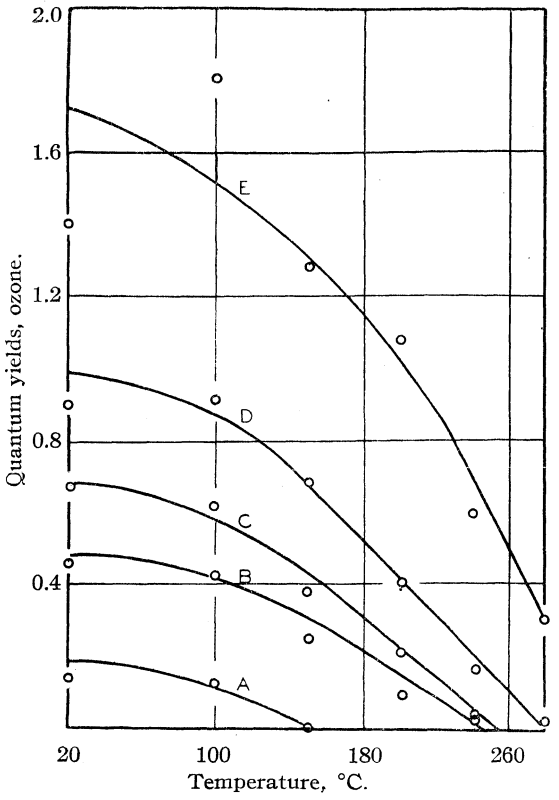


Fig. 6.—Quantum yields of ozone as a function of temperature, total pressure $H_2 + O_2 = 190$ mm.: A, 10% O_2; B, 30% O_2; C, 50% O_2; D, 70% O_2; E, 90% O_2.

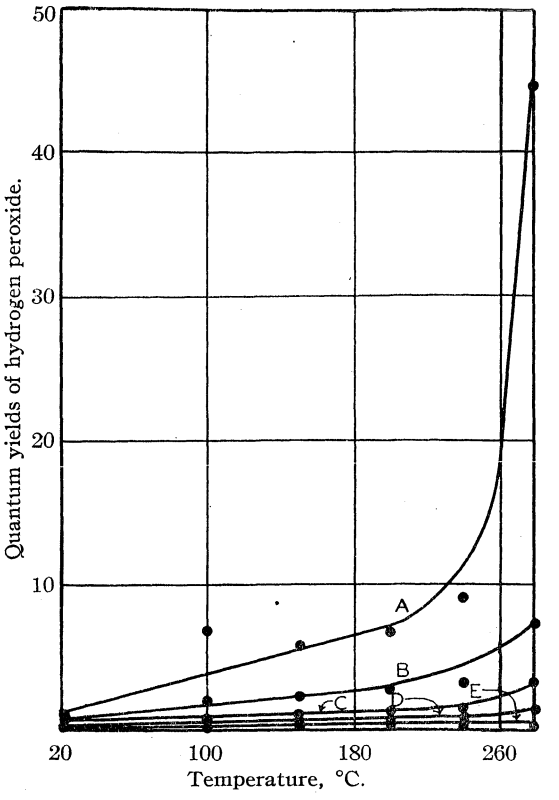


Fig. 7.—Quantum yields of hydrogen peroxide as a function of temperature, total pressure $H_2 + O_2 = 190$ mm.: A, 10% O_2; B, 30% O_2; C, 50% O_2; D, 70% O_2; E, 90% O_2.

gas mixture to form hydrogen peroxide may be altered without seriously affecting the resulting calculations.

Expressions for the quantum yields of the three products as calculated from the reaction mechanism given above are as follows

$$\Phi_{O_3} = \frac{2}{1 + k_3(H_2)/k_2(M) + k_4(H_2)/k_3(O_2)(M)}$$

$$\Phi_{H_2O_2} = \frac{2}{1 + k_3(O_2)/k_4 + k_2(O_2)(M)/k_4(H_2)}$$

$$\Phi_{H_2O} = \frac{8(O_2)/(M) + 2}{1 + k_3(O_2)/k_4 + k_2(O_2)(M)/k_4(H_2)}$$

Assuming that at one atmosphere total pressure $k_2 = k_3$ and $k_3(M) = 4k_4$, the above equations become

$$\Phi_{O_3} = \frac{2}{1 + (H_2)/(M) + (H_2)/4(O_2)}$$

$$\Phi_{H_2O_2} = \frac{2}{1 + 4(O_2)/(M) + 4(O_2)/(H_2)}$$

$$\Phi_{H_2O} = \frac{8(O_2)/(M) + 2}{1 + 4(O_2)/(M) + 4(O_2)/(H_2)}$$

Corresponding equations are easily derived for quantum yields at other pressures by introducing the appropriate factor into the ratio $k_4/k_3(M)$.

The values obtained from such equations fit the experimental results quite well, except in the case of water at low pressures. Here it is clear that the high quantum yields can be accounted for only by the introduction of a chain mechanism which is negligible at higher pressures. In the preceding mechanism, the only reasonable change which will result in such increased water yields is a change in the reactions representing the formation of hydrogen peroxide from hydrogen atoms. One might suspect that the reaction

$$H + O_2 \longrightarrow OH + O \qquad (8)$$

is responsible for the low pressure results were it not for its high activation energy, and also for the fact that if it were sufficiently prominent to cause the increased water yields, the quantum yields of both ozone and hydrogen peroxide should be much larger than those actually observed.

Another possibility is the reaction

$$HO_2 + H_2 \longrightarrow H_2O + OH \qquad (9)$$

which might well compete with (7) at low pressures since it involves the reaction of HO_2 with a

primary material rather than with another HO_2. This reaction followed by (5) and (6) readily accounts for increased water yields without affecting the yields of ozone or hydrogen peroxide, since the reaction of HO_2 by the chain of (9), (5), and (6) results in the formation of two molecules of water plus another HO_2 complex, and does not involve oxygen atoms. The chain would be broken by the formation of hydrogen peroxide.

Evidently there is some activation energy associated with (4), thus accounting for its probability of only 10^{-7} or 10^{-8}. As the temperature is increased, more molecules become sufficiently activated to react by (4), and this uses up oxygen atoms at the expense of (2) and also probably (3). While the yields of water and hydrogen peroxide do increase some as the ozone yields decrease, the sudden rapid rise in the formation of these two does not occur until a temperature considerably greater than that corresponding to the disappearance of ozone is reached. For instance, in a 10% H_2–90% O_2 mixture the formation of ozone is undetectable at 150°. The rapid rise in the water and peroxide yields does not occur until a temperature of some 220° is reached. Clearly, the disappearance of ozone is in no way connected with the appearance of long chains leading to water formation. Until the sudden rise in the water and hydrogen peroxide formation occurs, the course of the reaction is reasonably well described by the mechanism already outlined.

These sudden increases are probably due to the fact that the activation energy of (8) is overcome, allowing it to compete with (6). The result of the operation of this reaction is to cause a branching of the chain, forming two new chains of the type postulated in the room temperature mechanism. The new chains thus formed will be broken by the formation of hydrogen peroxide, and thus the simultaneous increase in water and peroxide yields is accounted for. Since the temperature at which chain branching becomes prominent is well above that at which (2) becomes negligible, no difficulty is offered by the fact that (8) does not cause increased ozone formation.

In order to check experimentally the fact that the results observed at elevated temperatures are caused by primary reactions rather than by the interaction of hydrogen and ozone, a run was made under the following conditions. A grill fashioned from 15 inches (38 cm.) of 6-mm. pyrex

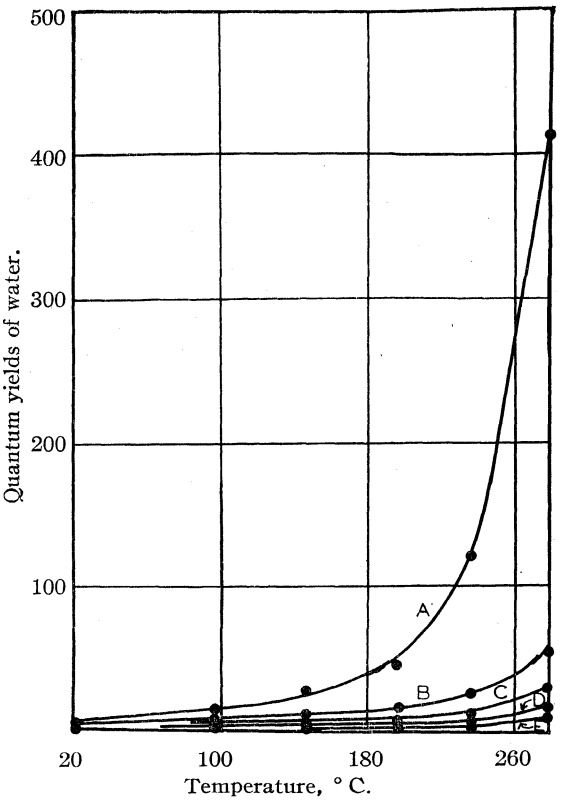


Fig. 8.—Quantum yields of water as a function of temperature, total pressure $H_2 + O_2 = 190$ mm.: A, 10% O_2; B, 30% O_2; C, 50% O_2; D, 70% O_2; E, 90% O_2.

tubing and surrounded by a pyrex jacket was placed between the reaction cell and the absorption bubblers. A resistance wound side arm allowed admission into the jacket of air at any desired temperature. The grill was equipped with a thermocouple well for measuring the temperature attained by the reaction gases after passing through two-thirds of the pyrex tubing. The volume between the thermocouple and the gas exit approximated that of the reaction cell between the light source and the exit of the gases from the heated jacket.

A 30–70 oxygen–hydrogen mixture at 190 mm. total pressure was exposed to the light source. The quartz cell was kept at room conditions while the air passing around the grill between the reaction cell and the absorption bubblers was maintained at such a temperature that the thermocouple reading corresponded to 260°. Thus the reaction products were kept at a temperature above 260° for as long a period as in a regular run. Under these conditions in the regular cell, no ozone was found, while quantum yields of approximately 5 and 40 were found for hydrogen

peroxide and water, respectively. On the other hand, in the room temperature runs the quantum yields were as follows: ozone, 0.5; hydrogen peroxide, 0.6; water, 2.8. The approximate quantum yields found with the cell at room conditions and the grill at 260° were: ozone, 0.1; hydrogen peroxide, 0.1; water, 3.5.

In order to bring the gas inside the grill to 260° the reaction products were necessarily exposed to more and hotter surface than in the regular runs. As a result, one would naturally expect some decomposition of the ozone and hydrogen peroxide on the walls of the grill. This accounts for the reduced yields of these products. The slight increase in the water yields is also readily attributed to decomposition of the peroxide. The fact that some ozone is still found after this treatment, while water and peroxide formation in no way compares to that found when the quartz cell was heated, indicates quite clearly that the reaction of hydrogen and ozone does not account for the results already presented.

Three objections may be raised to the proposed mechanism. The first of these lies in the fact that when the third body in (2) is a hydrogen molecule, reactions (2) and (3) involve identical reactants. If (2) takes place on nearly every triple collision as stated by Schumacher,[13] reaction (3) also must do so since $k_2 = k_3$. Accordingly, the theoretical yields of ozone must be decreased by an amount equal to the yields of water formed by (3). On the other hand, if only a small fraction of the triple collisions indicated by (2) are effective, this objection disappears. The probability of reaction (4) is estimated by Harteck and Kopsch[14] as 10^{-7}, and by Rodebush, Wende, and Campbell as 10^{-8}.[15] If these estimates are correct, reaction (2) cannot take place on nearly every triple collision, or else (4) could not compete with it, and no peroxide would be found.

A second objection results from the apparent exclusion of the hydrogen molecule as stabilizer in reaction (3). Actually this possibility is included in the proposed mechanism. If one combines (4) and (5) the result is

$$O + H_2 + H_2 \longrightarrow H_2O + H + H \qquad (10)$$

Since the reaction of an oxygen atom with a hydrogen molecule to form water is exothermic by some 117 kcal., while the heat of dissociation of the hydrogen molecule is only 102 kcal., it is readily understandable that reaction (10) might occur when a hydrogen molecule is the stabilizing body in the formation of water.

Finally, the absorption of light in the 1720 Å. region should produce a normal (^3P) and an excited (^1D) oxygen atom. No differentiation has been made between the two. Since the fastest possible reaction is evidently a three-body affair, it seems highly probable that collisional deactivation of the excited atom will take place before chemical reaction occurs.

Relation to the Mercury Sensitized Reaction.—The temperature coefficient of the mercury sensitized hydrogen–oxygen reaction was studied by Taylor and Salley.[20] These authors compared their results with those obtained for the direct photochemical reaction (2), and concluded as follows:

"The temperature coefficients of the mercury sensitized and the direct photochemical reactions of hydrogen and oxygen are shown to be comparable over the whole temperature range. It is suggested that the chain mechanism is the same whether initiated by atomic oxygen or atomic hydrogen."

The mechanism here proposed for the direct photochemical reaction would lead one to expect the complete similarity to the mercury sensitized reaction found by Taylor and Salley. The reaction responsible in both cases for the sudden rise in the temperature coefficient occurring at about 500° and approximately atmospheric pressure is reaction (8) which leads to chain branching.

Relation to the Explosion Reaction.—There is probably little doubt that the chains giving rise to large water yields in the photochemical reaction are the same as those involved in the explosion of oxy-hydrogen mixtures. For this reason it is of interest to examine mechanisms which have been presented in explaining the latter.

A rather satisfactory explanation of the explosive reaction is that proposed by Kassel and Storch[21] and modified by Lewis and von Elbe.[22] The present work would indicate that the explosion should follow reactions (4), (5), (6), and (9) for simple chain carrying reactions. However, (6) may result in chain breaking whenever (7) is more predominant than (9). Chain branching occurs by (8). The reaction as outlined by Kassel[23] includes four of the five equa-

(20) Taylor and Salley, THIS JOURNAL, **55**, 96 (1933).
(21) Kassel and Storch, *ibid.*, **57**, 672 (1935).
(22) Von Elbe and Lewis, *ibid.*, **59**, 656 (1937).
(23) Kassel, *Chem. Rev.*, **21**, 331 (1937).

tions given above. In place of (9), however, he gives the reaction (7a). The arguments given by Kassel seem to apply equally well if (9) is substituted. If (7a) were important at elevated temperatures, the yields of hydrogen peroxide should not parallel the water yields as was found for the photochemical reaction, but should depend primarily on the activation energy of (7a).

The modification proposed by von Elbe and Lewis[22] is identical with that proposed here, except that it admits the possibility of (7a) as well as (9), and also includes a reaction

$$H + O_2 + H_2 \longrightarrow H_2O_2 + H \qquad (11)$$

in order to explain the explosion limits. The present work gives no indication that such a reaction is of importance.

Acknowledgment.—The authors are grateful to the Roy R. Hornor Fund of Lehigh University for financial aid.

Summary

The photochemical oxidation of hydrogen has been studied by exposing mixtures of hydrogen and oxygen at room temperature to light of wave length 1719–1725 Å. The total pressure of the reaction mixture was varied from 1140 to 95 mm.

In general, with increasing oxygen content, the quantum yields of ozone increase while those of hydrogen peroxide and water decrease. Lowering of the total pressure tends to increase the water and peroxide yields, apparently at the expense of the ozone. At pressures of 190 mm. and less, the formation of water shows chain characteristics.

The temperature coefficients for the formation of the individual products have also been studied over the range 25 to 280°. The formation of ozone has a negative temperature coefficient while those of water and hydrogen peroxide are positive. At total pressures of 190 millimeters and in a 10–90% oxygen–hydrogen mixture, the temperature coefficients of water and hydrogen peroxide formation increase with great rapidity at temperatures above 230°.

A mechanism has been offered which explains satisfactorily the experimental results.

The relation of the direct photochemical reaction to the mercury sensitized and the explosive reactions has been discussed.

BETHLEHEM, PENNSYLVANIA
RECEIVED DECEMBER 14, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

Thermodynamic Properties of Substances. III. Vapor Volumes as Functions of Reduced Temperature Alone

BY HAROLD A. FALES AND CLARA S. SHAPIRO

In a previous article[1] we have shown that vapor volumes of chemically different substances can be expressed as a function of liquid volume and reduced temperature:

$$V_g = V_l e^{k(1-\tau^2)^m/\tau^n} \qquad (1)$$

The same type of function was found to give correct values for vapor pressures of thirty liquids, including water, the parameters k', m', n', being very close in value to those of the above equation.[2,3]

$$P_s = P_{cr}\, e^{-k'(1-\tau^2)^{m'}/\tau^{n'}} \qquad (2)$$

An attempt was made[3] further to express vapor volumes as a function of reduced temperature alone by an analogous equation

$$V_g = V_{cr} e^{k''(1-\tau^2)^{m''}/\tau^{n''}} \qquad (3)$$

This equation was applied to water vapor and was found to hold for almost the entire saturation line (60–360°) with an average deviation under 0.2 volume per cent.

In view of the fact that equations (1), (2) and (3) represent the behavior of water and equations (1) and (2) apply to the various other substances as well, it seems reasonable to presuppose that equation (3) would also apply to the other substances; actual tests confirm this supposition in every one of the cases, as will be shown in detail in the following pages.[4]

(1) H. A. Fales and C. S. Shapiro, THIS JOURNAL, **58**, 2418 (1936).
(2) H. A. Fales and C. S. Shapiro, *ibid.*, **60**, 794 (1938).
(3) H. A. Fales and C. S. Shapiro, *ibid.*, **60**, 784 (1938).

(4) After completing the test of equation (3) on all the various substances, we tried out (on water) the more general form

$$V_g/V_{cr} = \exp.\ k''[(1+\tau)^{s''}(1-\tau)^{m''}/\tau^{n''}] \qquad (4)$$

as was done previously for the vapor pressure of water.[3] This was done in the hope that it would improve the agreement at both extremes of the saturation line, namely, near the melting point and near the critical point. We found that both forms (4) and (3) fit water volumes equally well at every point in the interval 60–360°,

The substances selected for the present study are the same as before, except that argon has been replaced by krypton. The latter was chosen because its densities were recently measured by the Leiden Laboratories and checked by them up to highest coexistence temperatures against their new, very accurate mean diameter equation.[5]

In accordance with our earlier procedure, we have first made a graphical intercomparison of the observed vapor volume curves, which enabled us to answer two separate questions: (a) what is the shape and relative order of vapor volume curves of different liquids? (b) how are the three thermodynamic properties (vapor volume, vapor pressure and volume ratio) of any single substance related among themselves in the coördinate system?

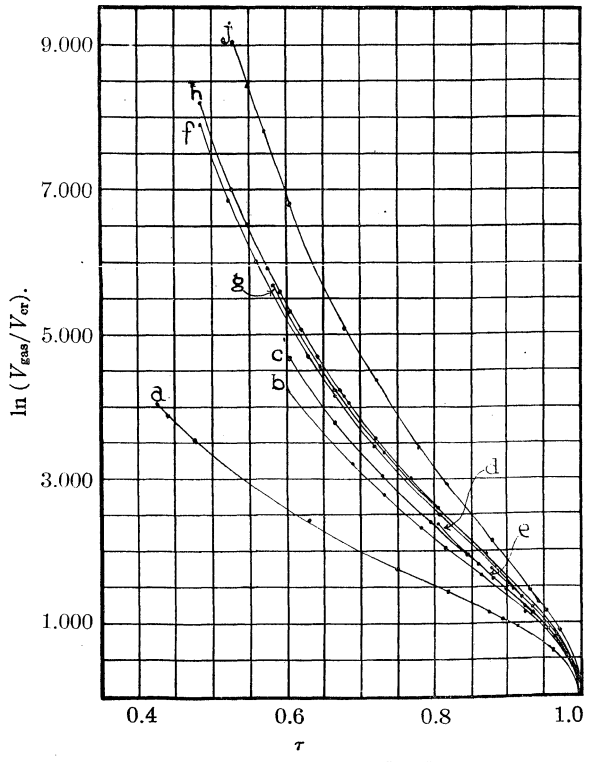


Fig. 1.—ln $(V_g/V_{cr}) = k''(1 - \tau^2)^{m''}/\tau^{n''}$: a, helium; b, krypton; c, ethane; d, acetylene; e, carbon monoxide; f, benzene; g, *n*-pentane; h, ammonia; j, ethyl alcohol.

the average deviation being: ΔV_g = 0.18 and 0.17%, respectively. At lower temperatures (0–40°) equation (4) deviates a trifle more than eq. (3).

As to the parameters, we find that both forms have practically equal values of k'', m'', n''; moreover, the constant s'' of eq. (4) is almost identical with its constant m'' (0.4708 and 0.4713). Since equation (4) did not show any appreciable improvement over eq. (3) in the case of water, there did not seem to be sufficient reason for investigating it any further.

(5) Literature on the new Leiden equation and on krypton densities is given below in Table V (bibliography).

For this purpose we have plotted the values ln V_g/V_{cr} obsd. against reduced temperature and have compared the ordinates of different curves at $\tau = 0.6000$ with each other as well as with the corresponding ordinates ln P_{cr}/P_s obsd., and ln V_g/V_{liq} obsd. of each substance.

We find here, as in the previous studies, that the ln of reduced vapor volume is represented by a family of curves, each of a form similar to that given earlier for water,[3] and very similar in shape to the curves ln V_g/V_{liq}. We see further that the order of the vapor volume curves, which is given herewith, is very close to that of the vapor pressures and is almost identical with the sequence of volume ratios[2,1]

1 Helium	16 Benzene
2 Hydrogen	17 *i*-Pentane
3 Neon	18 *n*-Pentane
4 Krypton	19 Ammonia
5 Oxygen	20 Monofluorobenzene
6 Carbon monoxide	21 Methyl formate
7 Nitrogen	22 Ethyl ether
8 Ethylene	23 *n*-Hexane
9 Ethane	24 Water
10 Hydrogen chloride	25 Acetic acid
11 Nitrous oxide	26 Ethyl propionate
12 Acetylene	27 Sulfur trioxide
13 Methyl ether	28 Methyl alcohol
14 Carbon dioxide	29 Ethyl alcohol
15 Carbon tetrachloride	30 Nitrogen tetroxide

As to the relative position of the above thermodynamic properties, we find that for every substance listed here their ascending order is the same as that shown for water:[3] ln P_{cr}/P_s; ln V_g/V_{cr}; ln V_g/V_{liq}.

An illustration of interrelation of different vapor volume curves is shown in Fig. 1, in which nine representative substances are plotted

(a) Helium	(f) Benzene
(b) Krypton	(g) *n*-Pentane
(c) Ethane	(h) Ammonia
(d) Acetylene	(j) Ethyl alcohol
(e) Carbon dioxide	

For graphical comparison of different properties of a single substance the reader is referred to the article on water.[3]

Accuracy of the Proposed Equation.—The tolerance of the vapor volume equation for water was estimated earlier.[3,1] It was found to be affected by two sources of error: (a) errors in T_{cr} and (b) errors in vapor volume. The deviations in the critical volume were assumed negligible due to the precise method of extrapolation used by Keyes and his collaborators.[6] Hence the total accuracy of equation (3) for water was found

(6) For corresponding literature see Table V below.

exactly equal to that of the volume ratio equation (1). In applying eq. (3) to other substances for which the critical densities are less accurately known, we can no longer neglect the effect of deviations in d_{cr} because for the majority of them the critical density is uncertain by at least 1–2% and for some liquids it may be in error by as much as 5–10%.[1]

The question of errors in critical density was discussed recently by Mathias and Crommelin of Leiden in connection with their new four-term diameter equation[5]

$$d_m = a + bT + cT^2 + dT^3 \qquad (5)$$

These authors have shown that the critical densities of krypton and carbon monoxide calculated from eq. (5) are about 1% higher than the d_{cr} values obtained from the rectilinear diameter formula

$$d_m = a + bt \qquad (6)$$

It seems to follow that many other substances for which the critical densities were extrapolated from the linear eq. (6) will be in error by about 1–2%.

Such will be the case with noble and permanent gases as well as with some organic and inorganic compounds. As to the reduced mean density formulas used by the "Int. Crit. Tables"

$$d_m = d_{cr}[1 + \gamma(1 - \tau) + \kappa(1 - \tau)^2] \qquad (7)$$

$$d_m = d_{cr}[1 + \gamma(1 - \tau)] \qquad (8)$$

it is obvious that they are less accurate than eq. (5) above, hence the critical densities given in Vol. III of these Tables may also deviate from true values by several per cent.

This situation raises a question: to what extent does an error of 1–5% in the critical density affect the total accuracy of the vapor volume equation?

To test this influence we have taken an actual case (carbon monoxide) and have made two sets of calculations using first the new and then the old d_{cr} values. In both sets of calculations the same reference points were used for evaluating the constants k'', m'', n''. A careful comparison of the results showed that, although the two sets of parameters I and II are different, the respective values of d_{gas} calcd. I and II are equal to each other at every temperature. In other words, a difference of 1% in d_{cr} produced no change in the calculations. Three other substances were tested similarly; these are krypton, ethyl ether, and ethane, with errors in d_{cr}, respectively, of 1, 1 and 5%. In each case we have found the two sets of calculated densities to be identical within 0.05%, which is a further proof that errors in d_{cr} of 1–5% have no effect whatsoever on the accuracy of the proposed equation.

In Table I we give the details of our calculations on carbon monoxide. This substance was chosen because of its long coexistence range (0.5–1.0 T_{cr}), and because its vapor densities are very accurately measured up to within 2° from the critical temperature. This affords an opportunity to test the proposed equation in the critical region (0.97–1.0 T_{cr}).

Table I is divided in two parts: the upper illustrates the agreement between experiment and the proposed equation. The lower part shows the effect of change in d_{cr} on the calculated values of d_{gas}. Here the calculations are given in detail for several temperatures and will be discussed first.

In columns 2 and 3 of the bottom part are given the two sets of observed ln V_g/V_{cr} data, the respective values of d_{cr} being 0.305 and 0.301. In columns 4 and 5 are given the corresponding sets of calculated ln V_g/V_{cr} values. In column 6 are shown the differences in per cent. between the observed ln values ($\Delta \ln$ % obsd. I–II); in column 7 are given the corresponding differences between the two sets of calculated ln values ($\Delta \ln$ % calcd. I–II). Examination of columns 6 and 7 shows clearly that at every temperature $\Delta \ln$ % obsd. I–II is equal to $\Delta \ln$ % calcd. I–II. From this fact it obviously follows that at each temperature the difference between observed and calculated ln values is the same for each set. This is very clearly demonstrated in the last two columns of the bottom part which contain the deviations $\Delta \ln$ % obsd. − calcd. I and $\Delta \ln$ % obsd. − calcd. II. We see that these are practically equal at every point both in sign and in value, averaging $\Delta \ln \phi = 0.62\%$ and 0.64%, respectively.

In the upper half of Table I are given: the Leiden data for vapor densities of carbon monoxide together with the two sets of calculated d_{gas} values I and II. At the very top of the table are given the corresponding two sets of parameters k'', m'', n''. In the last three columns are shown the two sets of deviations Δd_g % I and II, together with the corresponding deviations of the Leiden mean diameter equation (5). In examining this part of Table I we see again that the deviations Δd_g % obsd. − calcd. I and II are nearly identical at all temperatures. This shows that correct values for vapor densities can be obtained

from the proposed equation even when the critical density is only approximately known.

As to the agreement between experiment and calculation, we see that it is quite satisfactory. The estimated tolerance of equation (3) for carbon monoxide is $\Delta \ln$ est. $= 0.95\%$ while the average deviation actually found is $\Delta \ln \phi = 0.62\%$. Considering the volumes themselves we see that the deviations $\Delta d_g\,\%$ are rather small and regularly distributed even in the critical range where the maximum is $\Delta d_g = 1.2\%$ at $\tau = 0.988$ (0.5° below T_{cr}). Here, as in the case of water,[3] we see that in the critical neighborhood (0.97–1.0 T_{cr}) the vapor densities deviate much less than

TABLE I

INFLUENCE OF ERRORS IN CRITICAL DENSITY ON THE ACCURACY OF THE PROPOSED EQUATION

$$\ln V_g/V_{cr} = k''\frac{(1-\tau^2)^{m''}}{\tau^{n''}}$$ Carbon monoxide

	d_{cr}	k''	m''	n''
I	0.305	2.5061	0.46404	1.5229
II	.301	2.5135	.47192	1.5182
	$\Delta d_{cr} = 1.3\%$	$\Delta k = 0.3\%$	$\Delta m = 2.0\%$	$\Delta n = 0.3\%$

T, °K.	τ	d_g, g./cc. obsd. data[a]	d_g, g./cc. proposed equation $d_{cr} = 0.305$ I	d_g, g./cc. proposed equation $d_{cr} = 0.301$ II	Δd_g, % proposed equation $d_{cr} = 0.305$ I	Δd_g, % Obsd. − calcd. proposed equation $d_{cr} = 0.301$ II	Δd_g, % Obsd. − calcd. Leiden equation[b] $d_{cr} = 0.305$
68.13	0.512603	(0.00080)	0.00074	0.000743	+ 7.5	+ 7.5	
73.56	.553457	(.00171)	.00167	.001673	+ 2.2	+ 2.2	
78.03[c]	.587089	(.00296)	.00296	.00296	0[c]	0[c]	
82.25	.618840	(.00477)	.00476	.004758	+ 0.2	+ 0.25	
87.15	.655707	(.00774)	.00776	.007752	− 0.25	− .15	
90.28	.679257	(.01019)	.010289	.010283	− 1.0	− .95	
94.16	.708449	(.01422)	.014220	.014214	0.00	+ .04	
100.93	.759386	.02389	.023638	.023633	+ 1.0	+ 1.02	
103.50[c]	.778723	.02824	.02824	.02824	0[c]	0[c]	
107.61	.809646	.03681	.037050	.037061	− 0.65	− 0.68	
109.05	.820480	.04014	.040624	.040639	− 1.20	− 1.24	
120.90	.909638	[.08202]	.084715	.084822	−(3.2)	−(3.34)	−(4.1)
125.60	.945001	.11607	.115829	.115960	+ 0.2	+ 0.1	+ 1.0
127.82	.961704	.13601	.137029	.137360	− .75	− .98	+ 0.15
129.81[c]	.976676	.16357	.16357	.16357	0[c]	0[c]	− .25
130.56	.982319	.17767	.177058	.176951	+ .3	+ .37	− .10
130.86	.984576	.18462	.183348	.183190	+ .7	+ .78	+ .6
131.39	.988564	.19392	.19630	.19600	− 1.2	− 1.05	+ .3
132.91	1.000000	(.305, new)	.305	.301	0.0	0.0	.0
		(.301, old)		Av. diff. ΔV_g =	.9%	.9%	.34%
				range τ (0.55 − 1.0 T_{cr})		(0.9–1.0 T_{cr})	

[a] d_{gas} in parentheses are calculated from the Leiden eq. of state. d_{gas} at T°K. = 120.90 is uncertain according to Leiden. [b] The mean density equation (5) was used to evaluate d_{gas} at very high T°. [c] Indicates reference points.

T, °K.	$\ln V_g/V_{cr}$ Obsd. $d_{cr} = 0.305$ I	$\ln V_g/V_{cr}$ Obsd. $d_{cr} = 0.301$ II	$\ln V_g/V_{cr}$ Calcd. $d_{cr} = 0.305$ I	$\ln V_g/V_{cr}$ Calcd. $d_{cr} = 0.301$ II	$\Delta \ln$ % Obsd. I–II	$\Delta \ln$ % Calcd. I–II	$\Delta \ln$ % Obsd. − Calcd. I	$\Delta \ln$ % Obsd. − Calcd. II
68.13	5.94347	5.93027	6.01912	6.00376	+0.2	+0.2	−1.2	−1.3
73.56	5.18383	5.17063	5.20650	5.19257	+ .25	+ .25	−0.4	−0.4
78.03[c]	4.63514[c]	4.62193[c]	4.63514[c]	4.62193[c]	+ .3[c]	+ .3[c]	0[c]	0[c]
87.15	3.67392	3.66072	3.67168	3.65907	+ .35	+ .33	+ .06	+ .04
90.28	3.39891	3.38571	3.38918	3.37658	+ .4	+ .38	+ .27	+ .25
103.50[c]	2.37957[c]	2.36637[c]	2.37957[c]	2.36637[c]	+ .5[c]	+ .5[c]	0[c]	0[c]
107.61	2.11455	2.10134	2.10805	2.09454	+ .63	+ .65	+ .30	+ .32
120.90	[1.31335]	[1.30015]	[1.28101]	[1.26656]	[+1.0]	[+1.1]	[+2.5]	[+2.6]
125.60	0.96612	0.95292	0.96820	0.95385	+1.4	+1.5	−0.2	−0.1
129.81[c]	.62307	.60987[c]	.62307[c]	.60987[c]	+2.0[c]	+2.0[c]	0[c]	0[c]
130.86	.50201	.48882	.50894	.49658	+2.6	+2.4	−1.4	−1.6
131.39	.45286	.43967	.44067	.42897	+3.0	+2.7	+2.7	+2.4
132.91	.0	.0	.0	.0	....	....	....	....
							0.62	0.64
							I	II
							average $\Delta \ln$ % (0.55–0.96 T_{cr})	

Comparison of equations

Average differences:
Tolerance of equations (1) and (3), $\Delta \ln$ % est. = 0.95%
Average deviation of equation (3), $\Delta \ln V_g/V_{cr} = 0.62\%$
Average deviation of equation (1), $\Delta \ln V_g/V_{liq} = 0.58\%$

do the corresponding logs; this fact makes the equation applicable at these extreme temperatures.

In order to see how the proposed equation compares with other test equations, we have checked the above results against the Leiden eq. (5), which at very high temperatures can be used for evaluating vapor densities. We see that in the interval 0.9–0.98 T_{cr} the individual deviations are of the same order of magnitude for both eqs. (3) and (5), but at still higher temperatures the Leiden formula fits experimental data much better. On the whole we find that the proposed equation is valid in a long range 0.55–1.0 T_{cr} with an average accuracy $\Delta V_g = 0.9\%$. The Leiden eq. (5) applies to a short interval 0.9–1.0 T_{cr} within $\Delta V_g = 0.35\%$.

We have next proceeded to test other substances in a manner entirely similar to that described above. In each case we have compared the proposed equation with other vapor volume formulas. The intercomparison was done by a graphical method. For every substance the deviations of each equation from one and the same set of experimental data were calculated and plotted to the same scale so that the regional distribution and the average value of each set of deviations could be compared among themselves.

In Table II, which is similar in construction to Tables II of earlier articles,[1,2] we give the results of our calculations for the same nine typical substances portrayed in Fig. 1. The deviations are given up to the highest volumes known and are recorded in volume per cent. Average deviations are also given. In examining Table II we find certain points of interest with regard to individual substances which will be mentioned briefly.

Helium.—Its densities between 0.45–0.75 T_{cr} were evaluated from the latest form of the Leiden eq. of state[6]; the densities between 0.85–0.90 T_{cr} have been measured directly, while the value at 0.96 T_{cr} evidently has been calculated from the rectilinear diameter equation (6).[5] Examining our calculations we see that the proposed equation is in agreement with both the observed and calculated Leiden data, except at 0.96 T_{cr}. The average deviation $\Delta V_g = 0.5\%$ (0.45–0.92 T_{cr}) is much smaller than could be expected, as is evident from the fact that the tolerance for helium is Δ ln % estd. = 4.0%,[1] while the actually found deviation is $\Delta \ln \phi = 0.3\%$.

Contrasting the proposed equation with other formulas, we find that the volume ratio equation (1), when recalculated on the basis of the latest density data,[6] gives excellent agreement. At every point it runs parallel to the proposed equation and its average deviation is exactly the same as for the latter: $\Delta V_g = 0.5\%$. (In evaluating the averages the large discrepancies at 0.96 T_{cr} were omitted.) We have further checked our results against the standard Clapeyron equation for helium (available only between melting and boiling points) and against Meyers' equation (given for helium only at the high temperatures 0.8–0.9 T_{cr}).

Meyers' equation was discussed previously.[1,7] It is in good agreement with observed data of many liquids in the range melting point to 0.9 T_{cr}. At higher temperatures it is not valid. For helium its average deviation is $\Delta V_g = 1\%$ (0.8–0.9 T_{cr}). The Clapeyron equation has an equivalent accuracy at lower temperatures. We conclude from above that both the proposed and the volume ratio functions represent the helium data more closely and in a longer range than either the Clapeyron or Meyers' equation, the shortcoming of the former undoubtedly being due to inaccuracies in the data for latent heat of helium.

Krypton.—Its densities have been measured at Leiden up to 1° of T_{cr}. One value, however, for $\tau = 0.6000$, was calculated by them from their equation of state.[6] Contrary to the case of helium, we find that for this particular value the proposed and the volume ratio equations deviate enormously from the Leiden equation of state, while they fit remarkably well the other (observed) data for this substance. Both equations average $\Delta V_g = 0.23\%$ between 0.65–0.98 T_{cr}. The mean density equation (5) is equivalent to the other two between 0.85–0.98 T_{cr} ($\Delta V_g = 0.21\%$ on the average). In the immediate vicinity of the critical point the latter is definitely superior (average $\Delta V_g = 0.9\%$ as against 3.0% and 2.8%).

Ethane.—Its vapor densities between 0.65–0.90 T_{cr} are taken from the "Int. Crit. Tables" and are based on the experiments of Porter. The data at high temperatures (0.90–0.995 T_{cr}), as well as the critical constants, are from the new measurements of Sage, Webster and Lacey.[6] In our calculations the first two reference points were taken from the "Int. Crit. Tables" data and the third one from the data of Sage and co-workers. This was done purposely in order to test the consistency of the two sets of measurements. In fact we find exceptionally close agreement between the proposed equation and the experimental values of Porter and of Sage. With the exception of one value at 0.9 T_{cr}, the deviations in the range 0.65–0.96 T_{cr} are all under 0.2% and average 0.09 volume per cent. Even in the critical region (0.96–1.0 T_{cr}) the average $\Delta V_g = 0.6\%$. Comparing these results with the reduced diameter eq. (7), used by "Int. Crit. Tables," we see that the latter is much inferior, since its average is $\Delta V_g = 0.7\%$ (0.8–1.0 T_{cr}).[8]

As to the volume ratio equation, we find that calculations based on the new data of Sage, Webster and Lacey are less accurate than those based on the "Int. Crit. Tables" values alone. The average deviation is $\Delta V_g = 0.8\%$, as compared with 0.5% obtained previously.[1,9]

The only explanation seems to be that the liquid densi-

(7) C. H. Meyers, *Bur. Standards J. Research*, **11**, 691 (1933).

(8) We also notice that the "Int. Crit. Tables" diameter eq. (7), leads to a d_{cr} value which is 5% higher than that obtained by Sage and co-workers, or that selected by Pickering (see table of best critical data: "Int. Crit. Tables," Vol. III, 248 (1928)).

(9) Through oversight the critical temperature, the estimated tolerance and the actual and per cent. log deviations of the volume ratio eq. (1) for ethane were incorrectly given in the article on Orthobaric Densities.[1] These should be: $T_{cr} = 305.3°$ K.; Δ ln % estd. = 0.5%; $\Delta \ln \rho = 0.0045$ (actual) = 0.25%.

ties of Sage and collaborators are not quite consistent with the measurements of earlier observers recorded in the "Int. Crit. Tables." However, we find that the parameters of the recalculated volume ratio equation are of the same order of magnitude as before[1,9]: $K_{cr} = 3.638$ (Sage's critical data); $k = 3.681$; $m = 0.4175$; $n = 1.199$.

Acetylene.—In the case of this substance the question arises as to the correct value of the critical temperature. The different observed values range from 37.05° by Ansdell (1879) and by Mathias (1909) to 35.4° by Cardozo and Baumé (1912). In the "Int. Crit. Tables" the value 36.0° is used as the best average of the above. The vapor densities of acetylene are given in the "Int. Crit. Tables" to two significant figures only. The data for high temperatures are based on the experiments of Mathias (Leiden). The values at lower temperatures are evidently calculated from the reduced rectilinear diameter eq. (8). This equation is in agreement with Mathias' observed densities between −23° and +29° and leads to his value of d_{cr}, but in the interval +29° to +36.0° the discrepancy amounts to 2–3%. Remembering that the diameter equation is usually quite accurate in the critical region, one may ask whether the value 36.0° accepted as T_{cr} by "Int. Crit. Tables," might not be in error. In order to investigate this point we have turned to the original paper of Mathias.[6] It appears that his density values are much more consistent with the value $T_{cr} = 37.05°$, since the equation $d_m = a + bt°$ referred to this temperature agrees with his observations within 0.5% up to the highest temperatures.

In Table II we have applied the proposed equation both to the "Int. Crit. Tables" data and to Mathias' data for acetylene. For comparison we give the diameter equations (8), and (6), used by "Int. Crit. Tables" and Mathias, respectively. Examining the respective four sets of deviations, we notice that the densities of the "Int. Crit. Tables" cannot be represented by the proposed equation. The discrepancies amount to several volume per cent. and are especially large between 0.85–0.95 T_{cr}, which indicates the possibility of an error in T_{cr} greater than 0.5°.[1]

On the other hand, when referred to $T_{cr} = 37.05°$ and compared with the original d_{gas} values of Mathias, the proposed equation gives very good agreement. In the interval 0.9–0.98 T_{cr} it is slightly superior to Mathias' diameter eq. (6), ($\Delta V_g = 0.3\%$ against 0.5%). In the critical interval the reverse is true, the respective differences being $\Delta V_g = 1.5\%$ and 0.6%. We might add that the constants k'', m'', n'', obtained from Mathias' data, are quite in line with those of other substances.

Carbon Dioxide.—For this substance two sets of measurements are available, both in the short interval 0.9–1.0 T_{cr}. Those of Lowry and Ericson are checked against the cubic vapor density equation originally suggested by Jüptner.[6,12] The more recent measurements of Michels, Blaisse and Michels[6] are checked against the rectilinear diameter eq. (6). These authors have also given new critical constants for carbon dioxide, which are in good agreement with those of other observers. In our calculations we have used the critical data of Michels and collaborators, but the reference points were taken from the d_{gas} values of Lowry and Ericson, since we were interested in the numerical test of the cubic density equation. Our results show that both the proposed and the volume ratio equations deviate by less than 1% from the experimental densities of either observer, thereby indicating the high consistency of the two sets of measurements. On the other hand both equations are quite comparable to the cubic formula, the respective average deviations being $\Delta V_g = 0.8\%$, 0.8%, and 0.7% (0.9–0.99 T_{cr}). The rectilinear diameter eq. is much more accurate in this interval (average $\Delta V_g = 0.25\%$).

The remaining four substances: benzene, *n*-pentane, ammonia and ethyl alcohol are all checked in Table II against Meyers' equation discussed above. We find that **ammonia** shows excellent agreement both with the proposed and with Meyers' equations, the latter being superior at very low temperatures. In our calculations the three reference points were taken from the Bureau of Standards data. The deviations from these data are very small, averaging $\Delta V_g = 0.15\%$ and 0.04%, respectively (0.5–0.8 T_{cr}). The deviations from the d_{gas} values obtained from the Beattie and Lawrence equation of state[6] are larger: $\Delta V_g = 0.3$ and 0.4% on the average (0.8–0.9 T_{cr}). As to ***n*-pentane,** we see that Meyers' equation excels over the proposed equation at low and moderately high temperatures. ($\Delta V_g = 0.4\%$ as against 0.8% between 0.65–0.97 T_{cr}.) In the critical neighborhood Meyers' equation is not expected to hold and, accordingly, we find its deviation to rise to 15% at $\tau = 0.995$, where the proposed equation differs as little as 0.6% from observed value.

Ethyl alcohol is represented much more accurately by the proposed equation than by that of Meyers. We see that the former follows Young's data all along the line with an average $\Delta V_g = 0.5\%$ (0.6–0.96 T_{cr}). The latter deviates unevenly at different temperatures, averaging $\Delta V_g = 1.5\%$ between 0.5–0.8 T_{cr} and $\Delta V_g = 3\%$ between 0.8–0.99 T_{cr}. Substitution of the vapor densities evaluated by the Bureau of Standards (0–130°)[6] makes the agreement definitely worse for either formula, which suggests a lack of consistency between the two sets of d_{gas} data. **Benzene** shows a similar lack of consistency between Young's measured densities and those calculated by the Bureau of Standards from the latent heat (0–130°).[6] Since Young's values are extrapolated at low temperatures, we have used the Bureau of Standards values for the first reference point. We find that the proposed equation deviates from the calculations of the Bureau of Standards by $\Delta V_g = 1.5\%$ (0.6–0.8 T_{cr}). On the contrary, the densities measured by Young are in close agreement with our calculations, the deviations averaging $\Delta V_g = 0.5\%$ (0.8–0.97 T_{cr}). The equation of Meyers shows a reverse picture: it fits the Bureau of Standards values within $\Delta V_g = 0.1\%$ and differs from those of Young by $\Delta V_g = 2\%$ on the average.

The inspection of the foregoing nine typical substances shows that the proposed equation expresses vapor densities of different liquids very accurately (within one volume per cent. or less) in the range boiling point to 0.97 T_{cr}. Near the critical temperature the majority of substances show larger differences, but only a few give as much as 5–6% deviation even at those very high

temperatures. When compared with other formulas, the proposed equation is found equivalent to the volume ratio function, as regards precision. It is also found comparable and in some cases superior to other vapor volume equations recorded in the literature. Only in the critical region it is less accurate than the mean density formulas (5)–(8) of Cailletet and Mathias.

TABLE II

COMPARISON OF THE PROPOSED EQUATION WITH OTHER VAPOR VOLUME EQUATIONS, AS SHOWN BY THE DIFFERENCES: ΔV_g % OBSD. − CALCD.

Substances:	(a) Helium			(b) Krypton			(c) Ethane			(d) Acetylene			
Equations:	Proposed	Volume ratio	Clapeyron and Meyers	Proposed	Volume ratio	Diameter eq. (6)	Proposed	Volume ratio	Diameter eq. (7)	Proposed	Diameter eq. (6)	Proposed	Diameter eq. (8)
τ	ΔV_g %			ΔV_g %			ΔV_g %			ΔV_g %			
0.400	...	...	...										
.450	0.9[a]	0.5[a]	1.5[c]										
.500	.1	.08	...										
.550	.25	.22	...	....	....	....							
.600	.42	.38	...	(27.0)[a]	(28.0)[a]		....	...	...			...	
.650	.40	.38	1.3	0.08[b]	0.22[b]		0.1[f]	1.2[f]				1.6[f]	
.700	.20	.20	...	.28	.50		.1	1.5				0.9	
.750	.00	.00	0.7	.22	.20		.03	0.9		...	...	0.22	
.800	.00[b]	1.00[b]	1.5[d]	.02	.10		.01	0.2		0.00[i]	5.00[i]	1.0	
.850	.95	1.2	1.25	.12	.08	0.20[b]	.06	1.5	0.9[f]	...	...	4.0	1.3[j]
.900	.18	0.5	0.85	.30	.15	.09	.8	4.2	0.4	.10	1.00	3.5	0.8
.910	.05	0.2	...	.45	.35	.12	....	...	...	.04	0.20	3.4	.75
.920	...	...	...	.58	.50	.15	....	...	...	.06	0.6	3.4	.65
.930	...	...	...	.60	.55	.15	....	...	...	.25	0.9	2.7	.5
.940	...	...	...	.45	.30	.18	....	...	...	.4	1.0	2.2	.4
.950	...	...	...	.35	.15	.20	.2[g]	0.25[g]	...	.3	0.6	1.7	.2
.960	(4.0)[e]	(8.0)[e]	...	.15	.03	.25	.1	0.2	2.0[g]	.9	.6	...	...
.970	...	...	...	.10	.07	.25	.5	1.4	0.5	.3	.6	...	...
.980	...	...	...	.30	.13	.20	.5	1.7	0.7	.00	.00	0.00	.10
.990	...	...	...	....	....	....	.7	0.7	1.0	1.5	.6	...	...
.995	...	...	...	3.2	2.8	0.90	.6	...	...	...	...	...	...
.999	...	...	...	....	....	....	....	...	...	...	...	...	...
1.000	0.00	0.00	7.00[d]	0.00	0.00	0.00	0.00	0.00	5.00[h]	0.00	0.00	0.00	0.00
Av. ΔV_g =	0.5%	0.5%	1.0%	0.23%	0.23%	0.21%	0.09%	0.8%	0.7%	0.3%	0.5%	1.6%	0.6%

Substances:	(e) Carbon dioxide				(f) Benzene		(g) *n*-Pentane		(h) Ammonia		(j) Ethyl alcohol	
Equations:	Proposed	Volume ratio	Jüptner's cubic eq.	Diameter eq. (6)	Proposed	Meyers' eq.	Proposed	Meyers' eq.	Proposed	Meyers' eq.	Proposed	Meyers' eq.
τ	ΔV_g %				ΔV_g %		ΔV_g %		ΔV_g %		ΔV_g %	
0.450					....	....			....	....		
.500					20.0[n]	....			2.7[q]	0.01[q]	...	...
.550					5.0	0.1[n]	...	...	.7	.02	8.2[s]	1.0[s]
.600					1.9	0.1	(1.4)[p]	...	.07	.02	0.4	1.1
.650					0.9	0.05	0.2[o]	0.4[o]	.08	.05	.52	1.3
.700					1.9	0.35	.7	.08	.08	.07	.7	1.2
.750					1.7[o]	1.4[o]	.5	.3	.12	.08	.5	1.6
.800					0.25	2.5	.05	.6	.25[r]	.05[r]	.30	2.2
.850		...	...	....	0.08	2.5	.28	.18	.4	.5	.7	3.3
.900		0.4[k]	0.55[k]	0.4[k]	0.6	2.4	1.6	.4	.55	.9	.55	3.9
.910		0.9[l]	1.0[l]	1.1	0.00[l]	....	....	...	...	....	....	...
.920		2.2[k]	2.5[k]	1.9	.10	....	....	2.4	.2	....	....	...
.930		1.0[l]	1.2[l]	1.0	.15	....	....	...	...	....	....	.3
.940		0.4[k]	0.4[k]	0.5	.18	....	....	...	...	....	....	...
.950		1.0[k]	1.0[k]	.07	.19	0.55	2.4	1.2	.75	....	....	.05
.960		1.2[l]	1.6[l]	.10	.20	0.2	2.3	0.85	0.9	....	....	1.0
.970		0.4[k]	0.7[k]	.30	.20	0.1	2.2	.4	...	....	....	2.0
.980		0.4[l]	0.6[l]	...	.20	1.8	2.2	.1	...	....	....	3.0
.990		0.6	0.45	...	.00	2.5	2.1	.6	...	....	....	...
.995		2.0	1.4	...	1.2	....	....	...	15.0	....	....	6.0
.999		3.4	3.4	...	0.8	....	....	...	...	....	....	...
1.000		0.00	0.00	0.3[m]	0.00	0.00	19.0	0.00	17.0	0.00	not given	0.00
Av. ΔV_g =		0.8%	0.8%	0.7%	0.25%	1.0%	1.2%	.8%	0.4%	0.25%	0.15%	0.5%

[a] d_g values (0.45 − 0.75 T_{cr}) taken from Leiden equation of state. [b] d_g (0.80 − 0.91 T_{cr}) taken from Leiden measurements. [c] ΔV_g % by Clapeyron equation (0.45 − 0.75 T_{cr}). [d] ΔV_g % by Meyers' equation (0.80 − 1.00 T_{cr}). [e] d_g (0.96 T_{cr}) taken from diameter equation (6). [f] d_g (0.65 − 0.90 T_{cr}) taken from "Int. Crit. Tables." [g] d_g (0.95 − 1.00 T_{cr}) obsd. by Sage, Webster and Lacey. [h] Equation (7) leads to ΔV_{cr} = 5%. [i] All values of d_g obsd. by Mathias, t_{cr} = 37.05°. [j] All values of d_g from "Int. Crit. Tables," t_{cr} = 36.0°. [k] d_g obsd. by Lowry and Ericson at various points (0.90 − 0.97 T_{cr}). [l] d_g obsd. by Michels, Blaisse and Michels at various points (0.91 − 1.00 T_{cr}). [m] The cubic equation leads to ΔV_{cr} = 0.3%. [n] d_g taken from Bureau of Standards calculations (0.50 − 0.70 T_{cr}). [o] d_g obsd. by Young (0.75 − 1.00 T_{cr})(0.65 − 1.00 T_{cr}). [p] d_g extrapolated by Young (0.60 T_{cr}). [q] d_g taken from Bureau of Standards observations. [r] d_g values taken from Beattie and Lawrence equation of state (0.80 − 0.90 T_{cr}). [s] All values of d_g from Young's data only.

In Table III we give, as in previous papers, a brief summary of our calculations on thirty liquids. The table is constructed in the same way as before.[1,2] The arrangement of liquids is in the order of ascending ln V_g/V_{cr} values at $\tau = 0.6000$.

In part 1, column 3 of this table we give numbers to literature references, which are listed in Table V below. The fourth column gives values of critical densities which in all cases, except that of ethyl ether, were obtained by extrapolation from mean density equations. The critical density of ethyl ether was obtained by direct measurement (Schröer[6]). In column 5 are given the observed values of ln V_g/V_{cr} which were read directly from the graph at $\tau = 0.6000$. In the last three columns we compare the average deviations of the proposed equation ($\Delta \ln \phi$ %) with the estimated tolerances ($\Delta \ln$ % estd.) and with the corresponding average deviations of the volume ratio equation ($\Delta \ln \rho$ %). The figures in the columns ($\Delta \ln$ % estd. and $\Delta \ln \rho$ %) are the same as in the article on orthobaric densities[1] with few corrections, namely: two new substances, krypton and carbon dioxide, have been added and three old ones, helium, ethane and acetylene, have been recalculated on the basis of more reliable data.

TABLE III

SUMMARY OF RESULTS

Substances in the table are arranged in the ascending order of curves

	Substances	Literature[a]	$d_{crit.}$[b] g./cc.	ln V_g/V_{cr} Obsd. $\tau = 0.6000$	Average per cent. differences[c]: $\Delta \ln \phi$ % found	$\Delta \ln \rho$ % found	$\Delta \ln$ % estd.
1	Helium	2, 1, 10	0.06930	2.60	0.3	0.26[d]	4.0
2	Hydrogen	2, 1	.03102	3.29	.21	.54	0.9
3	Neon	2, 1, 10	.4835	4.07	.86	.61	1.0
4	Krypton	2, 1	.9191	4.22	.15	.09	1.0
5	Oxygen	2, 1	.4299	4.32	.55	.54	1.0
6	Carbon monoxide	2, 1	.305	4.42	.62	.58	1.0
7	Nitrogen	2, 1	.311	4.42	.63	.37	1.0
8	Ethylene	2, 1	.21597	4.60	.57	.52	0.7
9	Ethane	3	.21216	4.70	.07	.35[d]	.5
10	Hydrogen chloride	5	.424	4.78	.48	.32	.7
11	Nitrous oxide	5	.451	4.85	.35	.40	.7
12	Acetylene	2	.230	below triple pt.	.20	.16[d]	1.0[e]
13	Methyl ether	5	.2714	5.09 extrap.	.63	.50	0.5
14	Carbon dioxide	4	.467	..	.74	.56[d]	.7[e]
15	Carbon tetrachloride	6	.5576	5.13	.35	.14	.5
16	Benzene	6, 10	.3045	5.22	.25	.18[f]	.5
17	*i*-Pentane	6	.2343	5.23	.07	.06	.5
18	*n*-Pentane	6, 10	.2323	5.35	.53	.40	.5
19	Ammonia	7, 10	.23635	5.35	.10	.05[f]	.25
20	Monofluorobenzene	6	.3541	5.35	.10	.10	.5
21	Methyl formate	6	.3489	5.42	.34	.18	.5
22	Ethyl ether	6	.265	5.48	.24	.24	.5
23	*n*-Hexane	6, 10	.2344	5.52	.38	.07	.5
24	Water	8, 10	.31274	5.75	.09	.26	.25
25	Acetic acid	6	.3506	5.75	.37	.11	.5
26	Ethyl propionate	6	.2965	6.00	.13	.05	.5
27	Sulfur trioxide	5	.630	6.20 extrap.	.25	.73	.5
28	Methyl alcohol	6, 10	.2722	6.70	.19	.08	.5
29	Ethyl alcohol	6, 10	.2755	6.95	.20	.20	.5
30	Nitrogen tetroxide	9	.570	7.00 extrap.	.20	.20	.5

[a] The numbers in column 3 indicate the corresponding references on observed vapor densities and critical densities listed in Table V. [b] The critical densities are all extrapolated from corresponding equations, except that of ethyl ether which is the value actually measured by Schröer. [c] The per cent. deviations given in the last three columns refer to the range of reliable densities (0.6–0.95 T_{cr}) with the following exceptions: helium, hydrogen, ethylene (0.45–0.95); oxygen and sulfur trioxide (0.75–0.95); acetylene and carbon dioxide (0.90–0.99); and nitrogen tetroxide (0.65–0.75). [d] The average deviations of the volume ratio equation, $\Delta \ln \rho$ %, for helium, ethane, carbon dioxide and acetylene are recalculated in accordance with the new data for these substances (see Tables II and V for details). [e] The tolerances of the proposed equation, $\Delta \ln$ % estd., for acetylene and carbon dioxide refer to the range 0.9–0.95 T_{cr} and are evaluated according to the method given in the article on orthobaric densities.[1] [f] The average deviations $\Delta \ln \rho$ % for benzene and ammonia were evaluated from Young's, respectively, Bureau of Standards data only.

TABLE III (*Concluded*)

Proposed equation: $\ln V_g/V_{cr} = k''(1 - \tau^2)^{m''}/\tau^{n''}$ V_g = vapor volume (cc./g.)

	Substances	K_{cr}[a]	k''[b]	m''	n''	Average differences ΔV_g %[c] Proposed equation	Volume ratio eq.	Meyers' eq.	Diameter eq.
1	Helium	3.264	(1.8967)	(0.43255)	(0.98753)	0.5	0.5	1.0	1.8
2	Hydrogen	3.273	2.3567	.51218	1.0880	.6	1.4	...	0.6
3	Neon	3.245	2.3301	.44312	1.4955	1.5	1.9	1.4	1.7
4	Krypton	3.480	2.5458	.46526	1.4115	0.23	0.23	...	0.21
5	Oxygen	3.421	(2.2973)	(.40623)	(1.5792)	(.7)	(1.0)	...	(.5)
6	Carbon monoxide	3.440	2.5061	.46404	1.5229	.6	1.6	...	.3
7	Nitrogen	3.426	2.5798	.44696	1.4428	1.0	1.2	...	2.8
8	Ethylene	3.527	(2.6454)	(.46750)	(1.4949)	0.9	2.0	...	2.6
9	Ethane	3.638	2.8023	.48283	1.4300	.09	0.8	...	0.7
10	Hydrogen chloride	3.801	2.8032	.46448	1.4569	1.0	1.0	...	1.1
11	Nitrous oxide	3.630	2.8326	.48209	1.4808	0.8	1.0	...	0.86
12	Acetylene	3.647	(2.8785)	(.49507)	(1.4520)	.3	0.35	...	.5
13	Methyl ether	3.719	(2.7887)	(.45821)	(1.6070)	1.4	1.7	...	.8
14	Carbon dioxide	3.639	(2.9412)	(.46665)	(1.1753)	0.8	0.8	0.7[d]	.25
15	Carbon tetrachloride	3.680	2.8831	.46394	1.5088	.7	.5	...	.52
16	Benzene	3.755	2.9982	.47406	1.4850	1.0	.8	1.2	1.4
17	*i*-Pentane	3.735	2.9148	.47063	1.5466	0.25	.2	...	0.23
18	*n*-Pentane	3.766	2.9233	.46216	1.5727	.8	.4	0.4	.4
19	Ammonia	4.125	(3.1678)	(.49408)	(1.4770)	.25	.4	.15	..
20	Monofluorobenzene	3.796	2.8669	.45069	1.6231	.2	.4	...	.5
21	Methyl formate	3.922	2.9612	.45990	1.5872	.7	.5	...	.5
22	Ethyl ether	3.878	2.9216	.45221	1.6219	.5	1.0	...	1.9
23	*n*-Hexane	3.830	3.0092	.46273	1.5946	.8	0.6	1.0	1.0
24	Water	4.234	3.2813	.47169	1.5190	.17	1.7	0.1	0.03[e]
25	Acetic acid	4.991	3.1956	.47403	1.5677	1.3	0.6	...	.7
26	Ethyl propionate	3.923	3.1312	.46283	1.6627	0.6	.4	...	.35
27	Sulfur trioxide	3.805	(4.1556)	(.55677)	(0.8308)	.6	1.7	...	.25
28	Methyl alcohol	4.559	3.5527	.46455	1.6338	1.0	0.4	1.2	1.2
29	Ethyl alcohol	4.026	3.5420	.48701	1.7438	0.5	1.0	2.1	1.0
30	Nitrogen tetroxide	4.385	(4.3281)	(.52971)	(1.3151)	.9	1.0	...	..

[a] The critical coefficient $K_{cr} = (RT_{cr})/(P_{cr}V_{cr})$ is given for comparison. The values are the same as in the previous papers, except those of ethane, carbon dioxide, acetylene, ethyl ether. For these substances K_{cr} was recalculated in accordance with the new values for the critical constants (see Table V). [b] The values of k'', m'', n'', in brackets are not reliable, the range of known densities being too short, or the data at the reference points being uncertain. [c] The average deviations for the proposed equation and the volume ratio equation refer in general to the range: 0.6–0.97 T_{cr}. Exceptions: see footnote *c* in the first half of Table III. The average deviations for Meyers' equation refer to the range 0.6–0.9 T_{cr}. Exceptions: helium (0.8–0.92 T_{cr}); water (0.42–0.95 T_{cr}); ammonia (0.5–0.9 T_{cr}); benzene (0.7–0.95 T_{cr}); methyl and ethyl alcohols (0.55–0.97 T_{cr}). The average deviations for the mean density equation refer in general to the range: 0.85–1.0 T_{cr}. Exceptions: helium, ethyl ether, *n*-hexane, methyl formate (0.75–1.0 T_{cr}); hydrogen, ethane, hydrogen chloride, benzene (0.7–1.0 T_{cr}); neon; nitrous oxide, methyl ether (0.6–1.0 T_{cr}); Acetylene and carbon dioxide (0.9–1.0 T_{cr}) (for literature see Table V). [d] The equation for carbon dioxide in column 9 is that of Jüptner and used by Lowry and Ericson (0.9–0.97 T_{cr}). [e] The equation for water in column 10 is that by Keyes, Smith and Gerry (0.45–0.95 T_{cr}).

Examining the three sets of deviations, we see that in all cases, except that of carbon dioxide, the $\Delta \ln \phi$ % of the proposed equation are smaller than the estimated tolerances and are very close to the $\Delta \ln \rho$ % of the volume ratios.

We conclude that the proposed equation holds with required accuracy in twenty-nine cases out of thirty and that it has the same reliability as the volume ratio equation.

In part 2 of Table III we give the constants k'', m'', n'' of the proposed equation together with the critical coefficients (for the purpose of comparison). The latter values are the same as given before, except a few new data: the K_{cr} of ethane, carbon dioxide, acetylene and ethyl ether. In the last four columns the precision of the proposed equation is compared with the precision of other vapor volume functions, the deviations V_g obsd. $- V_g$ calcd. being in volume per cent.[10] The literature references on the different equations are given under individual substances in Table V below.

(10) The ΔV_g % of the volume ratio equation are taken from the article on orthobaric densities; ref. 1, Table III$_2$, column 6. To obtain the volume per cent. deviations the actual log differences were multiplied by 100.

In examining individual liquids with regard to the accuracy of the proposed equation, we notice, as in the case of pressures, that the best agreement with experiment is found for those substances recently measured, the average deviations being between 0.09–0.6%. These are: water, ammonia, krypton, carbon dioxide, helium and ethane. Of the substances measured by Young, *i*-pentane, monofluorobenzene, ethyl ether, ethyl propionate and ethyl alcohol fall in the same category, while *n*-pentane, *n*-hexane, carbon tetrachloride, methyl formate, methyl alcohol, acetic acid and benzene deviate from experiment by about 1% on the average. Of the substances listed in the "Int. Crit. Tables," only one, acetylene, has a set of adjusted vapor densities less consistent than the original data (of Mathias). In all other instances, methyl ether, hydrogen chloride, sulfur trioxide and nitrous oxide, the adjusted vapor densities of "Int. Crit. Tables" were found in close agreement with the proposed equation, the average deviations ranging between 0.5–1.0 volume per cent., while the original data of the respective observers were found inconsistent with both the "Int. Crit. Tables" data and with our calculations.[11]

Comparison of the Constants k'', m'', n'' of the Proposed Vapor Volume Equation.—These constants possess the same general characteristics as the corresponding parameters for vapor pressures and for volume ratios.[2,1] Thus we find that helium and nitrogen tetroxide have extreme values of k'', m'' and n''. We also notice that the parameters change but little from substance to substance, the limits being: k'', from 1.89 (He) to 4.32 (N_2O_4); m'', from 0.4062 (O_2) to 0.5568 (SO_3); and n'', from 0.8809 (SO_3) to 1.744 (C_2H_5OH). Where two substances are located on adjacent curves, their parameters become very close, as was found for other properties. For instance: ethyl ether and *n*-hexane have $k'' =$ 2.9216 and 3.0012; $m'' =$ 0.4522 and 0.4627; $n'' =$ 1.622 and 1.595; similarly water and acetic acid have $k'' =$ 3.281 and 3.196; $m'' =$ 0.4717 and 0.4740; and $n'' =$ 1.519 and 1.568; etc.

We notice further (as before) that the constant k'' varies more than m'' or n''. The increase of the constant k'' from substance to substance is parallel to the rise of the critical coefficient and to the order of curves $\ln V_g/V_{cr}$. For each substance it stands in almost constant ratio to its critical coefficient, the values K_{cr}/k'' lying within narrow limits, 1.14–1.39. Since the same parallelism was observed with regard to the curves $\ln P_{cr}/P_s$ and $\ln V_g/V_{liq.}$, we conclude that the critical coefficients exert a directing influence on the arrangement of the above three thermodynamic properties. To what extent this influence is alike for all of them can be seen by comparing Table III of the present paper with Tables III of the earlier articles.[1,2] We find that the first eighteen and last three of the vapor volume curves (helium to *n*-pentane and methyl alcohol to nitrogen tetroxide) have identical positions with the volume ratio curves. Carbon dioxide is placed just below carbon tetrachloride, which is different from its position in the pressure table; this, however, is provisional inasmuch as accurate measurements of its densities at low temperatures are not available. Krypton is placed just below oxygen in all three tables. The nine remaining substances exhibit slight shifts in their position: for instance, monofluorobenzene is removed from benzene even further than in the volume ratio table, ammonia entering between it and *n*-pentane. Acetic acid, ethyl propionate and sulfur trioxide follow each other as in the volume ratio table. Water, on the contrary, occupies the same place as in the pressure table, just above *n*-hexane.

In summarizing we can say that the three properties, vapor pressures, vapor volumes and volume ratios of different substances show almost identical behavior for the equilibrium liquid–vapor, as demonstrated by the relative succession of their curves and by the close correspondence of their k and n parameters. As appropriate examples we can cite in addition to that of water[3] two other substances, nitrogen tetroxide and carbon monoxide. The former has respective k values 5.4, 4.33, 4.0, while its n values are 1.24, 1.31, 1.22; the latter has k values 2.77, 2.51, 3.25, and n values 1.48, 1.52, 1.32.

(11) The case of nitrous oxide is typical in this regard. Its densities and critical data have been measured many times, but with little concordance. Only recently Quinn and Wernimont[6] have carried out new measurements over a long temperature range. On checking these data against the cubic equation of Jüptner (same as used for carbon dioxide by Lowry and Ericson), they have found complete lack of agreement, the deviations ranging from 2–50% and averaging 17%.[6] The proposed equation fits their values much closer than that of Jüptner, since the average deviation is only 5.5%; however, this cannot be considered a satisfactory agreement, especially since the constants of k'', m'', n'' acquire abnormal values. The agreement of the proposed equation with the adjusted vapor densities of nitrous oxide and with the "Int. Crit. Tables" diameter equation is within $\Delta V_g = 0.8\%$ in the range 0.6–0.97 T_{cr}. Accordingly, the parameter values obtained are in line with those of other substances, suggesting high consistence of the "Int. Crit. Tables" d_{gas} data for nitrous oxide.

TABLE IV

Ratio average		Per cent. deviations number of substances: 0%		0.2–5.0%		6–10%		11–15%		20–100%	
		Δa	Δu	Δa	Δu	Δa	Δu	Δa	Δu	Δa	Δu
k'/k''	1.076	0	0	25	7	0	15	3	3	1	4
m'/m''	2.087	0	0	21	20	5	6	1	0	2	3
n'/n''	0.9816	0	0	26	25	0	1	1	1	2	2

In closing this discussion we wish to point out that the parameters k'' and n'' for vapor volume are in no instance exactly equal to the constants k' and n' for pressure, although at first sight the ratios k'/k'' and n'/n'' appear to be close to unity. Similarly, the ratios m'/m'' are never exactly equal to the integer 2. In order to make this clear, we have computed the averages for the ratios k'/k'', m'/m'', n'/n'', on the basis of all the liquids studied, except those with bracketed parameters. In Table IV we show how many substances deviate from those averages (Δa), as well as from the integral ratio values (Δu). On the top of the table we mark per cent. deviations divided into groups. In the vertical columns marked Δa and Δu we give the number of substances contained in each one of these groups:

Table IV shows that the deviation from unity or from 2 is never zero, but for the majority of substances the difference is small. It is also clear that for nearly all thirty liquids the constant k' for pressure is slightly larger than k'' for volume; the reverse is true for the constant n, with but few exceptions; the constant m'' for volume is almost half that of pressure. This regularity is followed by the majority of liquids within 5% or less.

It must be added that of thirty substances only one, sulfur trioxide, has very abnormal ratios k'/k'', m'/m'', and n'/n'' which equal 0.657, 1.54 and 2.67, respectively. The cause of this abnormality lies in the pressure constants which form a very peculiar set of values.[2] The volume parameters of sulfur trioxide are quite within the range of normal values.

Intercomparison of Different Vapor Volume Equations.—Historically there appear to be only four original attempts to express vapor density as function of temperature alone. Cailletet and Mathias observed many years ago that at high temperatures the densities of nitrous oxide, sulfur dioxide and other substances can be expressed by a parabolic equation, which in ordinary and in reduced units is[6,12]

$$d_{gas} = a - bt - c\sqrt{t_{cr} - t} = d_{cr}[1 + B(1 - \tau) - C\sqrt{1 - \tau}] \text{ range: 0.8–1.0 } T_{cr} \quad (9)$$

Later van Laar and also Jüptner developed on the basis of respective theoretical considerations the relationships

$$d_{gas} = f(-\sqrt{1 - \tau}) = d_{cr}[1 - \alpha(1 - \tau)^{0.5} + \gamma(1 - \tau) - \phi(1 - \tau)^{1.5} + \kappa(1 - \tau)^{2.0} - \nu(1 - \tau)^{2.5} + \ldots] \quad (10)$$

$$d_{gas} = F(-\sqrt[3]{1 - \tau};\ 1 + \tau) = d_{cr}[1 - \omega(1 - \tau)^{1/3} + \beta(1 - \tau)^{2/3} - \left(\frac{\delta}{1 + \epsilon\tau} - 1\right)(1 - \tau)] \quad (11)$$

These were found, however, to be in complete disagreement with experiment.[12]

Finally, Jüptner offered an empirical cubic equation, which was considered by van Laar an artificial relationship,[12] yet was found to give good results at high temperatures[6,12]

$$d_{gas} = d_{cr} + b'(t_{cr} - t) - c'\sqrt[3]{t_{cr} - t} = d_{cr}[1 + B'(1 - \tau) - C'\sqrt[3]{1 - \tau}] \text{ range: 0.8–0.95 } T_{cr} \quad (12)$$

In this equation the constants B' and C' are characteristic for each substance.

All other vapor density formulas recorded in the literature and used here for comparison, express d_{gas} in terms of two or more variables. To the category $d_{gas} = f(d_{liq}, t)$ belong, besides the volume ratio eq. (1), the different modifications of the mean density equation (5)–(8). Recently two formulas of the type: $V_{gas} = f(p, t)$ were

(12) We give the literature on variation of vapor density with temperature: (a) parabolic d_{gas} equations, Cailletet and Mathias, *J. phys.*, **5**, 549 (1886). Further elaboration of same: Mathias, *ibid.*, **1**, 53 (1892). (b) Van Laar's equation of state and the function: $d_{gas} = f(-\sqrt{1 - \tau})$; expansion of it into series and numerical tests, showing disagreement: van Laar; "Die Zustandgleichung," Leipzig, 1924, pp. 132–139, 327–328, 332–333, 344–345. (c) Jüptner's vapor pressure equation and the function: $d_{gas} = F(-\sqrt[3]{1 - \tau}, 1 + \tau)$ also numerical test on fluorobenzene (Young's data), showing poor results: Jüptner, *Z. physik. Chem.*, **63**, 355, 360 (1908); **73**, 173 (1910). (d) Cubic d_{gas} equation: Jüptner, *ibid.*, **80**, 299, 307–311 (1912); numerical test on fluorobenzene showing poor agreement when $C' = 2$ is a universal constant: *ibid.*, pp. 309–310; discussion of the cubic equation (assuming B' and C' to be characteristic constants), van Laar, "Die Zustandgleichung," pp. 345–348; numerical tests on carbon dioxide showing good results when equation is applied to high temperatures only and the constants have characteristic values: Lowry and Ericson, THIS JOURNAL, **49**, 2729 (1927). Numerical tests on nitrous oxide showing disagreement when equation is applied to the whole saturation line: Quinn and Wernimont, *ibid.*, **51**, 2002 (1929). (e) Modification of the cubic equation, assuming the coefficient $C' = f(1 - \tau)$; also numerical test on fluorobenzene, showing no improvement over $C' = 2$: Jüptner, *Z. physik. Chem.*, **80**, 299, 309 (1912). Further modification of cubic equation, assuming the first term, unity, to be replaced by T/T_{cr} and the constants B' and C' to be equal to each other: $d_{gas} = d_{cr}[B''(1 - \tau) - B''(1 - \tau)^{1/3} + \tau]$; no direct numerical tests are given here, Jüptner, *Z. physik. Chem.*, **85**, 1, 55–57 (1913).

TABLE V

BIBLIOGRAPHY ON EXPERIMENTAL DATA FOR VAPOR VOLUMES AND CRITICAL PROPERTIES; INCLUDING EMPIRICAL TEST EQUATIONS USED BY DIFFERENT OBSERVERS

(1) The new scale of temperature: (Absolute zero = −273.144°C.); improved equation for mean diameter (in ordinary and reduced units); corrected critical temperatures, critical densities and critical coefficients for: helium, hydrogen, neon, oxygen, nitrogen, carbon monoxide, and ethylene (Mathias and Crommelin, *Ann. phys.*, **5**, 137, 143, 144 (1936)); for krypton (Mathias, Crommelin and Meihuizen, *ibid.*, **8**, 467 (1937)); improved equation of state (Leiden), "Leiden Lab. Comm. No. 234e."

(2) Substances observed at the Leiden Laboratories: Helium and carbon monoxide; vapor densities calcd. (eq. of state) and observed; also the corresponding mean diameter equations, *Ann. phys.*, **5**, 137, 143 (1936).

Helium: vapor density at 5°K. (0.96 T_{cr}), also Clapeyron eq. (melting to boiling point), "Leiden Lab. Comm. No. 179c."

Hydrogen, oxygen, nitrogen: vapor densities calcd. (eq. of state) and observed; also corresponding rectilinear diameter equations, *Ann. phys.*, **17**, 416 (1922).

Neon: same, *ibid.*, **19**, 231 (1923).

Ethylene: same, *ibid.*, **11**, 344 (1929).

Krypton: vapor densities calcd. (eq. of state) and observed: *ibid.*, **8**, 467 (1937).

Acetylene: vapor densities observed (−23.75° to t_{cr}); t_{cr} = 37°.05; also the rectilinear diameter equation, Mathias, *Compt. rend.*, **148**, 1102 (1909). Critical density: "International Critical Tables," Vol. III, 230 (1928). Adjusted vapor densities (normal b. p. to t_{cr}); t_{cr} = 36.0°; also the reduced rectilinear diameter equation: *ibid.*, "Int. Crit. Tables," III, 230 (1928).

(3) Ethane: adjusted vapor densities (from Porter) between: normal b. p. and +10° also at +20 and +30°, together with the reduced mean diameter equation of second degree: "Int. Crit. Tables," Vol. III, 230 (1928); observed vapor densities (from isotherms) between +17.6° and t_{cr}; also all critical data, Sage, Webster and Lacey, *Ind. Eng. Chem.*, **29**, 658 (1937).

(4) Carbon dioxide: vapor densities observed (−5.8 to +22.9°); also the cubic equation for d_{gas} as function of temperature alone: Lowry and Ericson, THIS JOURNAL, **49**, 2729 (1927). Vapor densities (from isotherms) between +2.8° and t_{cr}; also all critical data and the rectilinear diameter equation: Michels, Blaisse and Michels, *Proc. Roy. Soc.*, **A160**, 358 (1937).

(5) Substances recorded in the "International Critical Tables" (1928). Hydrogen chloride, methyl ether, sulfur trioxide: adjusted vapor densities (normal b. p. to t_{cr}); all critical data; mean diameter eq.; *ibid.*, Vol. III, p. 228–236. Nitrous oxide: adjusted vapor densities (normal b. p. to t_{cr}); reduced rectilinear diameter equation; all critical data, "International Critical Tables," Vol. III, p. 228 (1928). Original observed vapor densities; corresponding T_{cr} values and test equations: (a) Cailletet and Mathias, *J. phys. radium*, **5**, 549 (1886); (b) Villard, *Compt. rend.*, **118**, 1096 (1894); (c) Quinn and Wernimont, THIS JOURNAL, **51**, 2002 (1929).

(6) Substances observed by Young: *n*-hexane, carbon tetrachloride, monofluorobenzene, methyl formate, ethyl propionate, acetic acid, ethyl alcohol, methyl alcohol: vapor densities observed (0° to t_{cr}); also all critical data and corresponding mean density equations; Young, *Proc. Roy. Dublin Soc.*, **12**, 374 (1910). The cubic equation applied to fluorobenzene; Jüptner, *Z. physik. Chem.*, **80**, 309, 310 (1912).

Ethyl and methyl alcohols: vapor densities calculated from the Clapeyron equation (0–130°); *Bur. Standards J. Research*, **6**, 881 (1931).

Benzene: vapor densities calculated from the Clapeyron equation between 0 and +130°; Fiock, Ginnings and Holton, *Bur. Standards J. Research*, **6**, 881 (1931). Vapor densities observed between +140° and t_{cr}; also all critical data and mean diameter equation of second degree: Young, *Proc. Roy. Dublin Soc.*, **12**, 374 (1910).

i-Pentane and *n*-pentane: vapor densities observed (0° − t_{cr}); also all critical data; Young, *Proc. Roy. Dublin Soc.*, **12**, 374 (1910). Mean density equations of second degree (same range): Timmermans, *ibid.*, **13**, 310 (1912).

Ethyl ether: vapor densities observed (0° − t_{cr}); also t_{cr}; P_{cr}; and the mean diameter eq. of second degree; Young, *ibid.*, **12**, 374 (1910). Critical density (observed): Schröer, *Z. physik. Chem.*, **129**, 79 (1927); **140**, 241 (1929).

(7) Ammonia: vapor volumes observed between −77.5 and +60°; also all critical data and an empirical test equation: (a) Circular Bur. Standards, No. 142, (1923); and (b) the ammonia table in the article by Meyers, *Bur. Standards J. Research*, **11**, 699 (1933). Vapor densities calculated from the eq. of state of Beattie and Lawrence between +60° and +95.6°; ammonia table in the article of Meyers, *ibid.*; equation of state; Beattie and Lawrence, THIS JOURNAL, **52**, 6 (1930). (Vapor densities calculated from the Clapeyron equation between −50 and +50°: *Bur. Standards* Sci. Papers, No. 18, 707 (1923).)

(8) Water: vapor volumes calculated from the empirical equation for water at saturation between 0–340°: Keyes, Smith and Gerry, *Proc. Am. Acad. Arts and Sci.*, **70**, 319 (1936). Vapor volumes between 340° − t_{cr}, calculated by the Clapeyron equation (Bureau of Standards data) *ibid.*, table of saturated volumes. Values of T_{cr} and d_{cr}: Smith and Keyes, *ibid.*, **69**, 285 (1934). Vapor volumes calculated from the Clapeyron eq. between 0–360° (details). Preliminary report, *Bur. Standards;* Osborn, Stimson and Fiock, *Mech. Eng.*, **57**, 162 (1935).

(9) Nitrogen tetroxide: vapor densities observed between +3 and +55°: Mittasch, Kuss and Schleuter, *Z. anorg. Chem.*, **159**, 29 (1927). Vapor densities observed between +60° − t_{cr}; also T_{cr} and d_{cr}; (also mean rectilinear diameter eq. in this interval): Bennewitz and Windish, *Z. physik. Chem.*, **A166**, 401 (1933).

(10) Meyers' equation: C. H. Meyers, *Bur. Standards J. Research*, **11**, 691 (1933).

suggested for water and ammonia by Keyes and collaborators and by the Bureau of Standards, respectively. The Clapeyron equation gives vapor volume as a function of V_{liq}, dp/dT and T; while Meyers' equation

$$\log_{10}(1 - pv_{gas}/RT)(1 - pv_{liq}/RT) = A \log_{10} p/p_{cr} \; 2.718 \text{ (range: } 0.5\text{–}0.9\ T_{cr}) \quad (13)$$

expresses vapor volume in terms of V_{liq}, P_{sat} and T.

In the last two columns of Table III are given the summarized results on intercomparison of the proposed equation with the several volume functions listed above. For every one of the thirty substances the average deviations of each equation were evaluated (in volume per cent.) by a graphical method, as described under Table II.

Examining the equations (9)–(12) of the type $d_{gas} = f(\tau)$, we see that only two, the first and the last, have any applicability, and this over a limited range. The proposed equation was found to be superior to each of them, inasmuch as it expresses correctly the whole saturation line rather than a portion of it, with an accuracy equal to or better than that of equations (9) or (12).

Comparing the deviations of the proposed equation with those of the volume ratios, we find that twenty-three out of thirty liquids have smaller or equal average deviations. The seven substances which show inferior results are: *n*-pentane, *n*-hexane, carbon tetrachloride, ethyl propionate, methyl formate, acetic acid and methyl alcohol. As to the distribution of deviations, they run for most liquids parallel in both equations. Water, sulfur trioxide, hydrogen and a few organic liquids are exceptions, but here the difference is not so great as to be of importance. On the whole we feel justified to conclude that the proposed and the volume ratio equations are entirely equivalent as regards accuracy, range of validity and extent of applicability to different substances.

Considering the different modifications of the mean density equation, we see that they are of no practical value at lower temperatures, but in the region 0.9–1.0 T_{cr} they are invariably superior to the proposed equation (ethane and methyl alcohol being the only exceptions so far encountered).

The functions $V_{gas} = f(p, T)$ of Keyes and coworkers and of the Bureau of Standards are extremely accurate (V_{gas} = 0.03% and 0.1%). On the other hand, they are very cumbersome in form (7 or 8 constants), and seem to be of specific rather than general applicability.

Meyers' equation was tested on eight liquids. At low and moderate temperatures it was found equivalent or slightly better than the proposed equation in all cases except that of ethyl alcohol. The fact that it does not hold above 0.9 T_{cr}, as well as the large number of independent variables necessary for its evaluation make this relationship inferior to the proposed equation. However, at temperatures below the boiling point it is most reliable.

Clapeyron's equation was contrasted with the proposed equation on ammonia, water[3] and helium. Both equations apply about equally well to the first two substances (ΔV_g = 0.1–0.2%). The inferior accuracy of the Clapeyron equation for helium is subject to revision, pending more accurate data for the latent heat of helium.

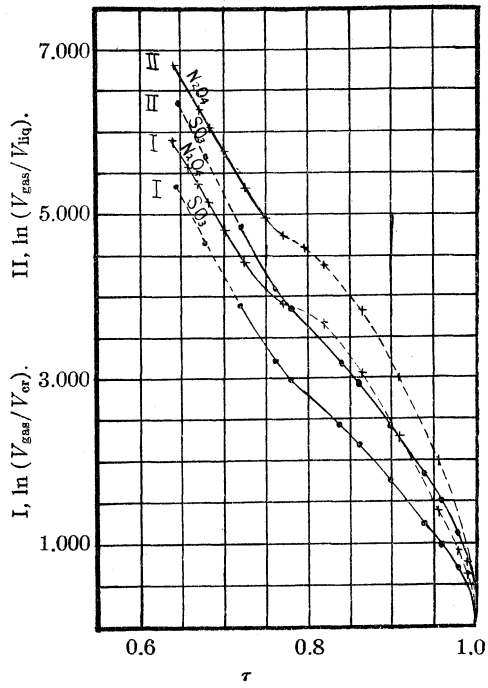


Fig. 2.—Curves I give ln (V_g/V_{cr}), obsd. Curves II give ln (V_g/V_{liq}), obsd. ———— Parts of experimental curves I and II which follow the equations; - - - - - - - - - parts of experimental curves I and II which deviate from the equations. ●, SO_3; +, N_2O_5.

As the result of the above comparative study of equations, we can say that both the proposed and the volume ratio functions have a definite advantage over the other vapor volume expressions here discussed, because, having equivalent or, sometimes, better accuracy, they fit a larger variety of liquids over a longer temperature interval than any of the others. In addition, we see

that the proposed equation is the only rather satisfactory attempt to express V_{gas} in terms of a single independent variable, reduced temperature.

Before leaving the subject we wish to add a few words regarding sulfur trioxide and nitrogen tetroxide. Both were previously found to have abnormally shaped experimental curves ln V_{gas}/V_{liq}.[1] The deviating portion of either curve was found in disagreement with the volume ratio equation, while the portion regularly shaped was found to follow this equation within expected limits. A corresponding behavior is to be noted for the vapor volume curves of these substances. In Fig. 2, the observed curves ln V_g/V_{cr} of SO_3 and N_2O_4 are plotted alongside the observed values of their ratios, ln V_g/V_{liq}. We see that for either substance the two functions have deviating portions (dotted lines) very similar both in direction and in length of temperature interval. As to the proposed equation, we find that it follows the experiment in the normal region of the vapor volume curves ($\Delta V_g = 0.6\%$ and 1.0% for SO_3 and N_2O_4, respectively). On the other hand, in the abnormal section of these curves the vapor volume equation deviates enormously from observed data, and this behavior is in accordance with that observed for the volume ratio.[1]

Summary

1. The reduced vapor volume of chemically different substances is found to be an exponential function of reduced temperature alone. The form of this function is identical with those for vapor pressure and for volume ratio

$$\ln V_g/V_{cr} = k''(1 - \tau^2)^{m''}/\tau^{n''} = x \qquad (14)$$

$$V_{gas} = V_{cr} \cdot e^x \qquad (15)$$

2. The accuracy of this equation is well within experimental limits; it is in good agreement with vapor volume equations of other investigators.

3. When compared with the volume ratio equation it is found to give analogous results as regards average and regional accuracy and range of application. Its advantage lies in the fact that V_{gas} is expressed as a function of one independent variable only.

4. The parameters k'', m'', n'' of this equation have the same characteristics as the constants of the vapor pressure and of the volume ratio equations; they vary only slightly with chemical properties of substances; the constant k'' increases in the same order as the critical coefficient and the heights of ordinates ln V_g/V_{cr}, but there is no simple mathematical relationship between K_{cr} and k''.

5. The three properties, vapor pressure, vapor volume and volume ratio, exhibit striking similarity along the whole saturation line, since not only the mathematical expressions of these functions are identical, but the respective parameters are of the same order of magnitude; further, the geometrical shape of the curves ln P_{cr}/P_s, ln V_g/V_{cr}, ln V_g/V_{liq} is similar and their relative order to each other is identical for every substance here studied; finally, for each one of these properties the successive order of liquids in the coördinate system is the same with but few exceptions.

6. The constants k'' and n'' for vapor volume are nearly equal to the respective constants for pressure and the constants m'' are nearly half the others. However, in no case have the ratios k'/k'', n'/n'', m'/m'' assumed the integral values 1, or 2. Their averages for 30 liquids are respectively: 1.08; 0.98; and 2.09.

NEW YORK, N. Y. RECEIVED AUGUST 23, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, NEW YORK UNIVERSITY]

An Empirical Relation between Solubility of Slightly Soluble Electrolytes and Dielectric Constant of the Solvent

BY J. E. RICCI AND T. W. DAVIS

The solubilities of an electrolyte in two media of different dielectric constant are related, on the basis of the Born theory of ion–solvent interaction,[1] and ignoring ion–ion interactions, by the equation[2]

$$\log S_2 = \log S_1 - C\frac{z_+z_-}{2r}\left(\frac{1}{D_2} - \frac{1}{D_1}\right) \qquad (1)$$

If the interionic effects are taken into account, by introducing the Debye–Hückel expression for the mean ionic activity coefficients of the electrolyte in each medium, the solubility being sufficiently low in each, the equation is modified as follows

$$\log S_2 = \log S_1 - C\frac{z_+z_-}{2r}\left(\frac{1}{D_2} - \frac{1}{D_1}\right) + \frac{\frac{B}{D_1^{3/2}} z_+z_- \sqrt{\mu_1}}{1 + \frac{A}{D_1^{1/2}} a\sqrt{\mu_1}} - \frac{\frac{B}{D_2^{3/2}} z_+z_- \sqrt{\mu_2}}{1 + \frac{A}{D_2^{1/2}} a\sqrt{\mu_2}} \qquad (2)$$

where A, B and C are constants at any given temperature, S the solubility, D the dielectric constant, the z's represent ionic valences, both considered as positive numbers, μ the ionic strength, r the ionic radius in the Born sense, and a the distance of closest approach of the ions in the Debye–Hückel sense. The subscripts refer to the two different media.[3] Equations 1 and 2, both, require previous knowledge of the ion size a, and in the absence of such information the equations cannot be used.

In connection with studies of the solubilities of salts in dioxane–water mixtures,[2] we have noted that the activity coefficient of an electrolyte in saturated solution is in many cases practically constant and independent of the nature of the solvent. Several examples of this empirical regularity are found in the literature although no especial significance has hitherto been laid upon it. Thus Walden[4] reported tetraethylammonium iodide to be about 48% dissociated in saturated solution in many solvents. The quantity $-\log f_\pm$, for thallous iodate, calculated from its solubility in alcohol–water solvents, on the basis of the limiting law of Debye and Hückel, by La Mer and Goldman,[5] is practically a constant. The mean activity coefficient, $f_\pm$, of a number of uni-univalent electrolytes in pure methanol was determined by Brönsted, Delbanco and Volqvartz,[6] on the basis of solvent effects of added salts, and was noted to be practically the same as that in saturated aqueous solutions; although this fact was specifically mentioned by these authors, no further notice was taken of it, or of any possibility of applying the relation.

From the measurements of Brönsted and Williams[7] on the solubility of complex cobalt ammines in the presence of added salts, the activity coefficient of croceo tetranitro-diammino cobaltiate (a uni-univalent electrolyte) is calculated to be 0.981 at saturation both in pure water (D = 81.1) and in water saturated with ether (D = 74.5), at 18°; and that of the luteo salt (a 3:1 type), 0.916 and 0.907, respectively, in the same solvents. Similar measurements by Hansen and Williams[8] give the following values for $f_\pm$ at saturation, for the croceo cobaltiate at 25°

(a) in water (D = 78.5), 0.978
(b) in 20 mole % ethanol (D = 54.0), 0.969
(c) in 40 mole % ethanol (D = 41.4), 0.969
(d) in 60 mole % ethanol (D = 33.8), 0.974

The values for the croceo sulfate (a 1:2 salt) are 0.805, 0.929 and 0.952 in (a), (b) and (c), respectively, and for the luteo iodate (3:1), 0.537, 0.756 and 0.857, respectively, in the same solvents. We see here a substantial constancy at least in the case of the simpler types.

Table I shows the mean activity coefficients for silver acetate in its pure saturated solutions in various solvents, as determined by the usual method of solvent salt effects. The approximate constancy of f is evident.

(1) M. Born, *Z. Physik*, **1**, 45 (1920).

(2) T. W. Davis and J. E. Ricci with C. G. Sauter, THIS JOURNAL, **61**, 3274 (1939).

(3) While "a" and "$2r$" are both ionic diameters, they apply to different processes and might have quite distinct values for a given salt. We have regarded this as a minor question, however, in this paper, and hereafter equate "a" and "$2r$" at least as a first approximation.

(4) P. Walden, *Z. physik. Chem.*, **55**, 683 (1906).

(5) V. K. La Mer and F. H. Goldman, THIS JOURNAL, **53**, 473 (1931).

(6) J. N. Brönsted, A. Delbanco and K. Volqvartz, *Z. physik. Chem.*, **162A**, 128 (1932).

(7) J. N. Brönsted and J. W. Williams, THIS JOURNAL, **50**, 1338 (1928).

(8) L. A. Hansen and J. W. Williams, *ibid.*, **52**, 2759 (1930).

TABLE I

ACTIVITY COEFFICIENT OF SILVER ACETATE IN PURE SATURATED SOLUTION, AT 25°

Solvent	Dielectric constant	$f_\pm$
Water[9]	78.55	0.800
Alcohol[9] 10%	72.9	.797
20%	67.1	.803
30%	61.2	.802
Acetone[10] 10%	73.0	.804
20%	67.0	.805
30%	61.0	.798
Dioxane[2] 10%	69.7	.786
20%	60.8	.771

If this observation should be found to apply generally even though approximately, it offers a simple way of predicting solubilities in any medium from a knowledge of the value in one, inasmuch as the logarithm of the activity coefficient at saturation is related directly to the ionic strength (and hence to the saturation concentration for a pure solution if complete dissociation is assumed), by means of the familiar Debye–Hückel equations.

If the activity coefficient of an electrolyte, at saturation, is a constant, independent of the dielectric constant of the medium, the solubilities in two media will be related, where the Debye–Hückel limiting law holds, by the equations:

$$-\log f_1 = -\log f_2 \qquad (3)$$

$$\frac{1.8123 \times 10^6 (z_+z_-)^{3/2}\nu^{1/2}\sqrt{S_1}}{D_1^{3/2}\,T^{3/2}\sqrt{2}} = \frac{1.8123 \times 10^6 (z_+z_-)^{3/2}\nu^{1/2}\sqrt{S_2}}{D_2^{3/2}\,T^{3/2}\sqrt{2}} \qquad (4)$$

where T is the temperature and ν is the total number of ions formed by the complete ionization of one molecule of the electrolyte, and the other symbols have the meanings previously noted.

If the Debye–Hückel expression for the activity coefficient is modified to take into account the effect of the ionic size, then the equation takes the form

$$\frac{\frac{B}{D_1^{3/2}\,T^{3/2}}\sqrt{S_1}}{1+\frac{A}{D_1^{1/2}\,T^{1/2}}a\sqrt{S_1}} = \frac{\frac{B}{D_2^{3/2}\,T^{3/2}}\sqrt{S_2}}{1+\frac{A}{D_2^{1/2}\,T^{1/2}}a\sqrt{S_2}} \qquad (5)$$

where $B = 1.8123 \times 10^6 (z_+z_-)^{3/2}\nu^{1/2}/\sqrt{2}$, and $A = 50.288 (z_+z_-)^{1/2}\nu^{1/2}\sqrt{2}$, a being in Ångström units.

In either case the solubility in any dielectric can be calculated from that in any one reference medium. In equation 4 the variation of the solubility with D is seen to be independent of the valence type of the electrolyte since the valence factors cancel out of the equation. In equation 5, the valence factors again cancel except those involved in the definition of the ionic strength in the denominators, so that the effect of the valence type is only very slight.

Neglecting effects of ionic size, and using, therefore, equation 4, the solubility in the second medium is related to that in the first or reference medium at the same temperature, by the equation

$$S_1^{1/2}/D_1^{3/2} = S_2^{1/2}/D_2^{3/2} \qquad (6)$$

or

$$\log S_2 = \log S_1 + 3(\log D_2 - \log D_1) \qquad (7)$$

so that a plot of the logarithm of the solubility against the logarithm of D would give a straight line with a slope of 3. The solubility according to equation 5 can be written in the form

$$\log S_2 = \log\left(\frac{2K^2}{\nu z_+z_-}\right) + \log D_2 + \log T - 2\log\left[\frac{1.8123 \times 10^6 z_+z_-}{D\,T} - 50.288\,K\,a\right] \qquad (8)$$

where K is the negative logarithm of the activity coefficient in the first medium.

In order to determine the extent to which this empirical rule of constant activity coefficient may be applicable, and to test its possible usefulness in correlating known solubilities and hence in predicting unknown solubilities, we have examined much of the published data on solubilities of slightly soluble electrolytes in non-aqueous solvents and in mixtures of water and organic liquids. For comparison between the calculated and the observed solubilities ($S_{\text{obsd.}}$), the calculations were made, from the solubility in water, according to the various principles: thus, S_f represents the solubility calculated by means of the simplest equation, namely, eq. 7; S_{fa}, that according to equation 8; and S_{Born}, according to equation 1. The latter two calculations of course could be made only where suitable values of the ion diameters could be found. The values of a used in the various cases were taken from reports in the literature on aqueous solutions, some determined by solubilities, some by e. m. f.'s. The dielectric constants for the various solvents were taken from the literature, principally from the data of Åkerlöf.[11]

(9) F. H. MacDougall and C. E. Bartsch, *J. Phys. Chem.*, **40**, 649 (1936).

(10) F. H. MacDougall and W. D. Larson, *ibid.*, **41**, 417 (1937).

(11) G. Åkerlöf, THIS JOURNAL, **54**, 4125 (1932); G. Åkerlöf and O. A. Short, *ibid.*, **58**, 1241 (1936).

As an example and to facilitate comparison, the data and calculations for the solubility of barium iodate monohydrate in dioxane–water solvents,[2] presented in Table II, are shown graphically also in Fig. 1, where log S has been plotted against log D. The predictions of the constant activity coefficient rule, as can be seen both from the table and from the curves, are at least in moderate agreement with the observed values over the whole range, while the Born equation very quickly predicts much too small solubility. Since S_{fa} differs so little from S_f in this case, values of S_{fa} have not been calculated for the other salts reported, even where values of a were available.

TABLE II

SOLUBILITY OF BARIUM IODATE MONOHYDRATE IN DIOXANE–WATER SOLVENTS, AT 25°; a = 2.34 Å.[2]

Wt. % dioxane	Soly. observed, $M\left(\frac{P_{H_2O}}{P^{\circ}_{H_2O}}\right)\times 10^4$	S_f calcd. $\times 10^4$	S_{fa} calcd. $\times 10^4$	S_{Born} calcd. $\times 10^4$	$S_f/S_{obsd.}$
0	8.145				
10	4.687	5.66	5.60	3.78	1.2
20	2.407	3.76	3.68	1.39	1.6
30	1.167	2.34	2.27	0.363	2.0
40	0.5198	1.33	1.28	.054	2.6
50	.2550	0.673	0.643	.00324	2.6
60	.1247	.289	.274	.000035	2.3
70	.0933	.0926	.0872	.0872	1.0
80	.0170	.0206	.0192	.01518	1.2
90	.0029	.00295	.00275	.03351	1.0
100	.0000	.00016	.00014	.0959	

The degree of usefulness of the principle of constant activity coefficient at saturation, in predicting at least the order of magnitude for solubilities in organic solvents from the known solubility in water, is best judged by means of the ratio, $S_f/S_{obsd.}$, especially if this is compared with the same ratio for the solubility calculated from the Born equation. Thus in the case of barium iodate monohydrate, the ratio, $S_f/S_{obsd.}$, is correct throughout as far as the order of magnitude is concerned, within a maximum factor of only 2.6, while the ratio $S_{Born}/S_{obsd.}$, becomes extremely low especially in the high dioxane mixtures.

The results of the comparison of observed and calculated solubilities for a number of uni-univalent electrolytes in various solvents are shown in Tables III, IV and V. Table III lists the results for silver acetate in dioxane–water solvents; here the ratio, $S_f/S_{obsd.}$, is, throughout the very wide range of D covered, again satisfactory in respect to the order of magnitude of the calculated solubility, the factor being $^1/_6$ at worst. Table

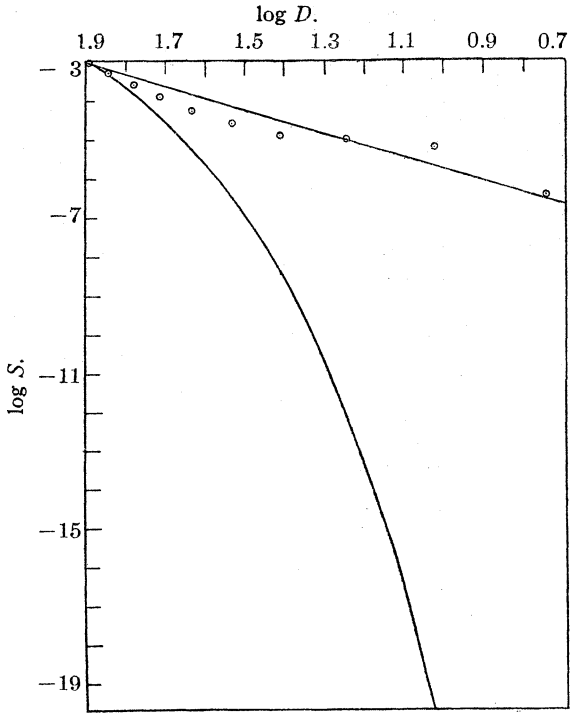


Fig. 1.—Solubility of $Ba(IO_3)_2 \cdot H_2O$ in dioxane–water mixtures: the straight line, as predicted on constant activity coefficient; the curve, as predicted by the Born equation; the points, as observed, ⊙.

IV gives the ratio, $S_f/S_{obsd.}$, for a number of 1:1 electrolytes in mixtures of water with various organic substances. The value of the ratio is seen to be such, throughout, as to predict at least roughly the solubility in the various media. The dielectric constants represented in this group vary from 112.4 in the case of silver chloride in glycine solutions, to that of ethanol at 40°, 22.2; a variation of temperature, between 14 and 40°, is also included, in the data for the perchlorates in ethanol–water mixtures. Table V gives

TABLE III

SOLUBILITY OF SILVER ACETATE IN DIOXANE–WATER SOLVENTS AT 25°; a = 3.99 Å.[2]

Wt. % dioxane	$S_{obsd.}$ $\times 10^2$ moles/l.	$S_f \times 10^2$	$S_{Born} \times 10^2$	$S_f/S_{obsd.}$
0	66.63			
10	50.35	46.3	53.2	0.9
20	36.38	30.7	39.7	.8
30	24.52	19.1	26.8	.8
40	15.17	10.9	15.5	.7
50	8.564	5.5	6.71	.7
60	4.23	2.36	1.80	.6
70	1.74	0.758	0.148	.4
80	0.611	.168	.0389	.3
90	.154	.024	.0866	.2
100	.000	.0013	.0265	

the data and calculations for the same three insoluble alkali perchlorates, $KClO_4$, $RbClO_4$ and $CsClO_4$, in a number of pure solvents.[12] The ratio $S_f/S_{obsd.}$ again shows that the solubility can be predicted at least roughly throughout.

TABLE IV

APPLICATION OF EQUATION 7 TO SOLUBILITY OF SOME UNI-UNIVALENT ELECTROLYTES IN VARIOUS MIXTURES OF WATER AND ORGANIC SUBSTANCES

Salt	Solvent	Temp., °C.	D, range	Ratio $S_f/S_{obsd.}$ Average	Extremes	Ref.
AgCl	Urea	25	78.5–95.1	0.7	0.6–0.8	13
AgCl	Glycine	25	78.5–112.4	0.9	0.8–1.1	13
$AgC_2H_3O_2$	Ethanol	25	78.5–49.8	1.2	1.1–1.4	9
$AgC_2H_3O_2$	Acetone	25	78.5–61.0	1.2	1.1–1.5	10
$KClO_4$	Ethanol	14	82.5–28.1	1.4	0.9–3.3	14
$KClO_4$	Ethanol	25	78.5–24.3	1.9	0.9–4.5	15, 16
$KClO_4$	Ethanol	40	73.1–36.3	1.1	1.1–1.2	17
$RbClO_4$	Ethanol	25	78.5–39.5	0.8	0.8–0.8	16
$RbClO_4$	Ethanol	40	73.1–36.3	.8	.8–.8	17
$CsClO_4$	Ethanol	25	78.5–39.5	.7	.7–.7	16
$CsClO_4$	Ethanol	40	73.1–36.3	.8	.7–.8	17
$TlIO_3$	Ethanol	25	78.5–52.9	3.3	1.2–6.7	5
Croceo salt[a]	Ethanol	25	78.5–33.8	0.6	0.5–0.8	8
Croceo salt	Ether	18	81.1–74.5	0.9		7
$AgBrO_3$	*i*-propanol	25	78.5–25.4	1.9	1.6–2.1	18

[a] Croceo tetranitrodiammino cobaltiate.

TABLE V

SOLUBILITY OF ALKALI PERCHLORATES IN SOME PURE ORGANIC SOLVENTS, AT 25°; I = $KClO_4$; II = $RbClO_4$; III = $CsClO_4$

Solvent	D	Salt	$S_{obsd.} \times 10^3$	$S_f \times 10^3$	$S_f/S_{obsd.}$
Water	78.5	I	145		
		II	71.8		
		III	84.4		
Methanol	31.5	I	6.0	8.2	1.4
		II	2.5	4.0	1.6
		III	3.2	4.7	1.5
Ethanol	24.2	I	7.0[a]	4.5	0.6
		II	0.4	2.1	5.2
		III	.4	2.5	6.2
n-Propanol	20.2	I	.6	2.5	4.2
		II	.3	1.2	4
		III	.2	1.4	7
Acetone	19.1	I	8.5	2.1	0.25
		II	4.0	1.0	.25
		III	5.1	1.2	.24
n-Butanol	17.8	I	0.3	1.7	6
		II	.1	0.8	8
		III	.2	1.0	5
i-Butanol	16.0	I	0.4	1.2	3
		II	.2	0.6	3
		III	.2	.7	3.5
Ethyl acetate	6.2	I	.1	.07	0.7
		II	.1	.04	.4
		III	"insol."	.04	
Ethyl ether	4.3	I	"insol."	.02	
		II	"insol."	.01	
		III	"insol."	.01	

[a] A very different value (0.565×10^{-3}) for this solubility is given by R. P. Seward and W. C. Schumb, THIS JOURNAL, **52**, 3692 (1930).

Some results on higher type electrolytes are given in Tables VI and VII. The ratio $S_f/S_{obsd.}$ for silver sulfate in dioxane–water solvents (Table VI) again shows that the order of magnitude of the solubility can be predicted down to 90% dioxane ($D = 5.6$), in great contrast to the calculation based on the Born equation. From the ratios obtained for the salts listed in Table VII it is again seen that the solubility is predicted, roughly in most cases, at least in respect to the order of magnitude. Only one experimental point has been omitted in the preparation of this table, namely, the solubility of potassium chloroplatinate

TABLE VI

SOLUBILITY OF SILVER SULFATE IN DIOXANE–WATER SOLVENTS, AT 25°; $a = 2.43$ Å.[2]

Wt. % dioxane	$S_{obsd.} \times 10^4$	S_f	S_{Born}	$S_f/S_{obsd.}$
0	268.4			
10	155.0	187	127.4	1.2
20	83.1	124	48.9	1.5
30	40.2	77.0	13.4	1.9
40	17.0	43.8	2.14	2.6
50	6.02	22.2	0.164	3.7
60	1.80	9.52	.00183	5.3
70	0.63	3.05	.0651	4.8
80	.23	0.68	.01324	3.0
90	.063	.097	.03030	1.5
100	.000	.0051	.0892	

TABLE VII

APPLICATION OF EQUATION 7 TO SOLUBILITIES OF SOME HIGHER TYPE ELECTROLYTES IN VARIOUS MIXTURES OF WATER AND ORGANIC SUBSTANCES

Salt	Solvent	Temp., °C.	D, range	Ratio $S_f/S_{obsd.}$ Average	Extremes	Ref.
$PbCl_2$	Urea	25	78.5–91.1	0.8	0.6–0.9	13
$PbCl_2$	Glycine	25	78.5–96.6	0.7	0.6–0.8	13
$PbCl_2$	Ethanol	25	78.5–67.7	1.2	1.0–1.4	18
K_2PtCl_4	Ethanol	14	82.5–28.1	4.6	1.8–9.0	14
K_2SiF_6	Ethanol	14	82.5–28.1	3.8	1.6–5.7	14
$K_3Co(NO_2)_6$. $3/2H_2O$	Ethanol	14	82.5–28.1	3.6	2.0–6.0	14
Croceo sulfate	Ethanol	25	78.5–41.4	12.4	7.0–17.8	8
Luteo iodate	Ethanol	25	78.5–41.4	24.5	11.0–38	8
Luteo[a] salt	Ether	18	81.1–74.5	0.9		7

[a] Luteo tetranitrodiammino cobaltiate.

(12) H. H. Willard and G. F. Smith, THIS JOURNAL, **45**, 286 (1923).
(13) W. J. Dunning and W. J. Shutt, *Trans. Faraday Soc.*, **34**, 1192 (1938).
(14) M. Pierrat, *Compt. rend.*, **172**, 1041 (1921).
(15) R. G. Thin and A. C. Cumming, *J. Chem. Soc.*, **107**, 361 (1915).
(16) R. Flatt and A. Jordan, *Helv. Chim. Acta*, **16**, 37 (1937).
(17) "International Critical Tables," Vol. IV, 1936.
(18) P. Gross, P. Kuzmany and M. Wald, THIS JOURNAL, **59**, 2692 (1937).

in 95% ethanol at 14°; for this point, the ratio $S_f/S_{obsd.}$ was 19.

The solubility according to the Born equation, S_{Born}, also was calculated for several of the salts reported in Tables IV and VII, such as silver chloride, silver acetate and lead chloride. On the whole the calculated S_{Born} was in poorer agreement with the observed than the calculated S_f, except in the case of lead chloride, where it was just slightly better throughout. Although, therefore, the solubility according to the Born equation (where dependable values of a are available) is occasionally better than that predicted by the simpler calculation on the basis of the constant activity coefficient, the latter is on the whole at least as good as the Born calculation; the Born calculation, moreover, fails completely in the high dioxane range, while the correct order of solubility is still given by the constant activity coefficient rule.

The solubilities for the three potassium compounds in Table VII are interesting from the point of view of analytical chemistry, inasmuch as the simple rule of constant activity coefficient has at least a rough degree of usefulness in predicting the order of magnitude of the solubilities in various mixtures of alcohol and water; and in the absence of knowledge of the ionic diameter, no other estimate of the solubilities would be possible.

The solubilities of a series of complex cobalt ammines, in water and in pure methanol (at 20°), were determined by Brönsted, Delbanco and Volqvartz.[6] On calculating the solubility in methanol according to the rule of constant activity coefficient, from the observed solubility in water, S_w, the ratio of the calculated to the observed solubility in methanol, or S_f/S_M, was found to be 0.3 to 7.6 (averaging 1.9) for twenty-two 1:1 electrolytes (the croceo iodate and the croceo iodoacetate being exceptions, with ratios of 22 and 19, respectively); for seventeen cases of 2:1 electrolytes the agreement between calculated and observed solubilities was much poorer, the average ratio being 12. It is to be pointed out, however, that the application of Born's equation to this same series of forty-one electrolytes cannot be expected to give better agreement than this. If we assume a value of a approximately the same for all these very similar electrolytes, then the ratio of S_w to S_M at 20° (substituting an average value of 2.5 Å. for a in Born's equation) should be $10^{\frac{246}{2.5}\left(\frac{1}{31}-\frac{1}{81.3}\right)}$, or about 89.6, for the 1:1 electrolytes. The actual ratio for this group however, varies from about 5 to about 400, which would correspond to a change in the Born parameter from 7 to 1.8 Å. We may say that the calculation on the simple idea of a constant activity coefficient is at least as useful as the Born calculation and can be used to predict roughly approximate solubilities in different media.

TABLE VIII

SOLUBILITY OF TETRANITRO-DIAMMINO-COBALTIATE, $[Co(NH_3)_4(NO_2)_2]^+[Co(NH_3)_2(NO_2)_4]^-$

Solvent	D	$S_{obsd.}$	S_f	$S_f/S_{obsd.}$
A. The Flavo Salt, in Various Organic Solvents, at 20°				
Formamide·$2H_2O$	84.7	0.068	0.00368	0.05
Water	81.3	.00325		
Furfural	41.3	.00356	.000438	.12
Nitromethane	38.5	.000085	.000172	2.0
Acetonitrile	37.0	.000525	.000307	0.58
Nitrobenzene	35.7	.0000003	.000276	920
Methanol	31.2	.000192	.000185	0.96
Ethanol	25.0	.0000054	.0000945	17.5
Epichlorhydrin	22.7	.0000236	.000071	3.0
Acetone	20.8	.000302	.0000547	0.18
B. The Croceo Salt, in Sugar Solutions, at 18°				
Water	81.1	0.0003130		
0.585 *M* Sugar	75.1	.0003519	0.000249	0.7
.877	73.1	.0003694	.000229	.6
1.140	71.3	.0003797	.000213	.6

Table VIII (part A) lists certain interesting measurements by K. Volqvartz[6] on the solubility of the uni-univalent electrolyte, flavo tetranitrodiammino cobaltiate, in various pure solvents with dielectric constants varying from 20.8 (for acetone) to 84.7 (for formamide); part B of this table gives the solubility of the croceo salt in sugar solutions, determined by Brönsted and Williams.[7] The ratio of calculated to observed solubility (the calculated being on the basis of the water solubility as reference) shows considerable scattering. The important point, however, is that the observed variation of solubility in this group of measurements is of such a nature that no simple theory, obviously, can account for them. The solubility of the croceo salt in sugar solution, for example, rises as D decreases. The same is true for the solubility of the luteo tetranitrodiammino cobaltiate (3:1 type) in 0.877 *M* sugar solution,[7] and for the nitro-rhodanotetrammine picrate in methanol,[6] as compared to the solubility in water. Moreover, taking the solubility in water as reference, the solubility of the flavo salt in two media such as acetonitrile and nitrobenzene with almost identical dielectric constants, *viz.*, 35.7 and 37.0, respectively, should

be the same, as long as there is attributed to the electrolyte in question an ionic diameter characteristic of the electrolyte itself. There are obviously, in other words, factors of a highly specific nature entering here, so that uniform theories based on physical variables such as ionic radii and dielectric properties (which are the only variables in the Debye–Hückel, the Born and the Bjerrum ion association[19] theories) cannot be expected to work satisfactorily throughout. The Debye effect[20] of non-uniform distribution of solvents around the charged ions, moreover, depending as it does on a designation of definite molecular weight to the solvent, may be significant, but the molecular weight, of course, remains in doubt. Finally, also, the ions may be differently solvated in the various media, but this may be regarded as just another way of referring to the Debye dielectric distribution effect.

Conclusion

Inasmuch as the observed solubilities can be interrelated, for different media, about as well, with the simple rule of constant activity coefficient, as on the basis of the Born equation utilizing the elusive parameter, the "ionic diameter," it is interesting to speculate as to any possible theoretical foundation that can be suggested for the validity of the assumption of at least an approximately constant activity coefficient at saturation. Consideration of the Born equation, modified for interionic effects according to the Debye–Hückel theory, *i. e.*, eq. 2, shows that the activity coefficients for a given electrolyte at saturation in two media of different D will be equal at a given temperature for certain values of a relative to D.

Although the two activity coefficient terms in equation 2 are small and generally negligible compared to the Born term itself, so that the difference between them, $\log f_2 - \log f_1$, will be expected in general to be close to zero, it does not follow that we can in general expect the ratio, $\log f_2/\log f_1$, to equal unity, especially when the activity coefficients are themselves close to one. The principle on which the present calculations are made, that $\log f_2/\log f_1 = 1$, remains then essentially an assumption, and we can only examine the general equation to determine under what conditions the principle can be expected to apply.

For a uni-univalent electrolyte, for which $z_+z_- = 1$, and for which the ionic strength, μ, = the solubility, S, the solubility S_M compared with the solubility in water, S_{H_2O}, is given approximately, at 25°, by

$$\log S_M = \log S_{H_2O} - \frac{242}{a}\left(\frac{1}{D_M} - \frac{1}{D_{H_2O}}\right) \qquad (9)$$

Now substituting in the familiar Debye–Hückel limiting expression for $\log f$ the above value of S_M for μ_M and S_{H_2O} for μ_{H_2O}, we find by setting the two $\log f$ terms equal to each other, that

$$\frac{342.6}{D_M^{3/2}}\sqrt{S_{H_2O} \times 10^{(-242/a)[(1/D_M) - (1/D_{H_2O})]}} = \frac{342.6}{D_{H_2O}^{3/2}}\sqrt{S_{H_2O}} \qquad (10)$$

and the condition for equality is

$$a = \frac{3.083 - (242/D_M)}{3 \log D_M - 5.684} \qquad (11)$$

Table IX shows corresponding values of a and D, satisfying equation 11. This table shows the value of D at which an electrolyte having one of the a values listed in the first column would exhibit an activity coefficient at saturation equal to that of its saturated aqueous solution.

TABLE IX

a	D	a	D
2.10	100	3.38	40
2.32	80	3.98	30
All values	78.5	5.06	20
2.51	70	7.87	10
2.75	60	12.6	5
2.99	50		

The divergence from equality, for an electrolyte, for example with an a equal to 2.75 Å., would increase on both sides of $D = 60$, but while the divergence would increase continuously in lower D, it would disappear with increasing D to give equality, of course, again at $D = 78.5$. Since the a for many electrolytes appears to fall in the range 2 to 3 Å., we might expect, therefore, an approximate equality of $\log f$'s in solutions with dielectric constants between 80 and 40.

If these arguments are repeated on the basis of the more extended form of the Debye–Hückel expression for the activity coefficient, as shown in eq. 2, it is found that the range over which agreement may be expected is somewhat but almost negligibly widened.

In conclusion, we may say that whether or not there is any theoretical meaning in the principle, the assumption of a constant mean ionic activity coefficient for an electrolyte at saturation,

(19) R. M. Fuoss and C. A. Kraus, THIS JOURNAL, **55**, 1019 (1933).
(20) P. Debye, *Z. physik. Chem.*, Cohen Festband 56 (1927).

independent of dielectric, is useful in at least an approximate way to predict solubilities in other media from the known solubility in water, without knowledge of the parameter a required for the Born equation. And some of these predictions may be of practical value in analytical and preparative chemistry requiring recrystallizations.

Summary

1. The activity coefficient of a salt in saturated solution has been noted in many cases to be practically constant and independent of the dielectric constant of the medium.

2. This observation leads to an empirical relation between the solubility of a slightly soluble electrolyte and the dielectric constant of the solvent which makes it possible to predict the solubility of a salt in other media from the solubility in water without knowledge of ionic diameters.

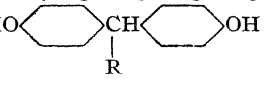
3. Calculated and observed solubilities are compared; the agreement is found in general to be satisfactory at least as to the order of magnitude and to be on the whole as good as that obtained by the Born equation where ionic diameters have been estimated.

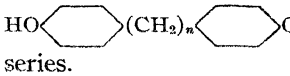
New York, N. Y. Received December 11, 1939

[Contribution from the Chemistry Laboratory of Johns Hopkins University]

α,ω-Di-p-hydroxyphenyl Alkanes

By Edwin M. Richardson[1] and E. Emmet Reid

It has been observed that introduction of alkyl groups into phenols increases their bactericidal power and decreases their toxicity. Harden and Reid[2] showed that rather potent bactericides are produced by joining two phenols through a carbon having a side chain of varying length, giving compounds of the type  where R is H or an alkyl group.

This paper reports the preparation of a series of α,ω-di-p-hydroxyphenyl alkanes  paralleling the above series.

The solubilities in oil and in water of the compounds are given in Table I along with the partition coefficients calculated from them. The solubilities are plotted in Fig. 1. There is a marked alternation with increasing chain length. The partition coefficients and the maximum killing dilution are plotted in Fig. 2; both increase rapidly with the length of the intervening carbon chain. The two curves show a definite similarity. Unfortunately the low solubility of these compounds made extensive testing impossible. All tests were run in 20% alcohol using 20% alcohol as control. The organism used was *Staphylococcus aureus* strain #209 and the technique was a modified F. D. A. We are greatly indebted to Hynson, Westcott and Dunning for their kindness in carrying out these tests. The α,ω-derivatives here described are much less soluble than the corresponding α,α-derivatives described by Harden and Reid[2]; however, the maximum killing dilu-

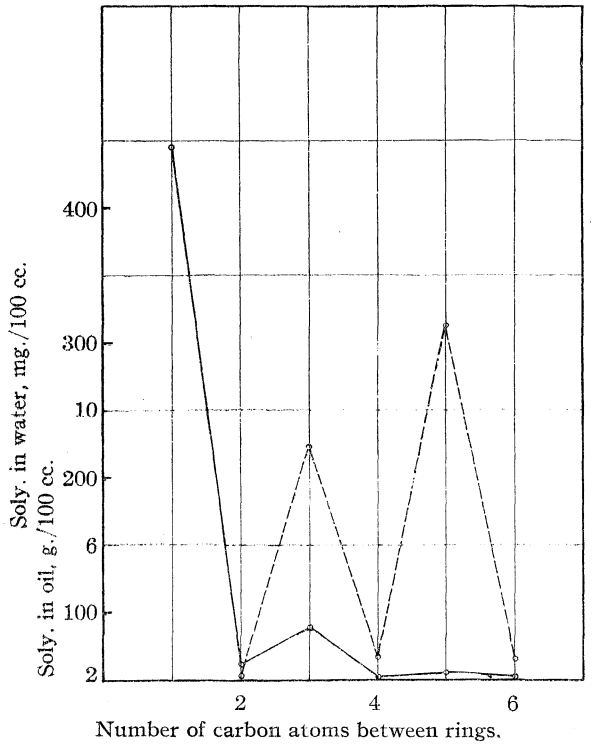


Fig. 1.—Solubility in oil and water: ———, soly. in water; — — —, soly. in oil.

(1) From a part of a Ph.D. dissertation, Johns Hopkins University, 1938.

(2) Harden and Reid, This Journal, **54**, 4325 (1932).

TABLE I

No.	Compd.	Soly., g./100 cc. H_2O	Soly., g./100 cc. Oil	Partition coeff.	Max. killing diln.
1	4,4′-$HOC_6H_4CH_2C_6H_4OH$-	0.3950	..	....	300
2	4,4′-$HOC_6H_4(CH_2)_2C_6H_4OH$	.0116	0.10	8.62	1000
3	4,4′-$HOC_6H_4(CH_2)_3C_6H_4OH$	.0381	6.88	180	2000
4	4,4′-$HOC_6H_4(CH_2)_4C_6H_4OH$	.0024	0.67	280	5000
5	4,4′-$HOC_6H_4(CH_2)_5H_6C_4OH$	.0044	10.47	2400	
6	4,4′-$HOC_6H_4(CH_2)_6C_6H_4OH$	insol.	0.62		
7	4,4′-$HOC_6H_4(CH_2)_{10}C_6H_4OH$	insol.	.09		

TABLE II

Compd.	% yield	M. p., °C.	Analyses C Calcd.	C Found	H Calcd.	H Found
4,4′-$CH_3OC_6H_4(CH_2)_2C_6H_4OCH_3$	72	125.5–127				
4,4′-$HOC_6H_4(CH_2)_2C_6H_4OH$	94	198–199				
4,4′-$CH_3OC_6H_4CH{=}CHCOC_6H_4OCH_3$	95	100–101				
4,4′-$CH_3OC_6H_4(CH_2)_3C_6H_4OCH_3$	81	45–46	79.63	79.70	7.86	7.82
4,4′-$HOC_6H_4(CH_2)_3C_6H_4OH$		107–108	78.90	78.67	7.07	7.04
4,4′-$CH_3OC_6H_4(CH_2)_3COOH$	55					
4,4′-$CH_3OC_6H_4(CH_2)_4C_6H_4OCH_3$	53	78–79	79.96	79.66	8.20	8.30
4,4′-$HOC_6H_4(CH_2)_4C_6H_4OH$	62	158–159	79.31	79.30	7.49	7.49
$(4\text{-}CH_3OC_6H_4CH{=}CH)_2CO$	92					
$(4\text{-}CH_3OC_6H_4CH_2CH_2)_2CO$		55–55.2				
4,4′-$CH_3OC_6H_4(CH_2)_5C_6H_4OCH_3$	63					
4,4′-$HOC_6H_4(CH_2)_5C_6H_4OCH_3$	92	104–105				
4,4′-$CH_3OC_6H_4CO(CH_2)_4COC_6H_4OCH_3$	85	145–146	73.60	73.40	6.80	6.75
4,4′-$CH_3OC_6H_4(CH_2)_6C_6H_4OCH_3$	62	70–71	80.49	80.35	8.78	8.74
4,4′-$HOC_6H_4(CH_2)_6C_6H_4OH$	90	144.5–145.5	79.96	79.79	8.20	8.14
4,4′-$CH_3OC_6H_4CO(CH_2)_8COC_6H_4OCH_3$	90	119–119.5	75.36	74.86	7.91	7.85
4,4′-$CH_3OC_6H_4(CH_2)_{10}C_6H_4OCH_3$	58	69–70	81.31	81.11	9.67	9.59
4,4′-$HOC_6H_4(CH_2)_{10}C_6H_4OH$	74	138.5–139.5	80.93	80.89	9.26	9.16

tions are nearly the same, 1000 compared to 1200 for the ethane derivatives, 2000 to 1500 for the propane and 5000 to 3500 for the butane derivatives.

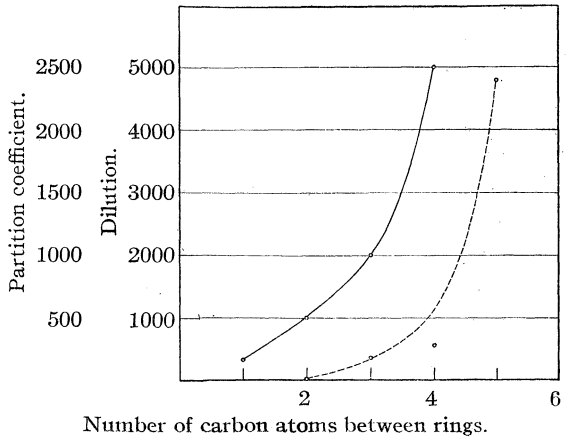


Fig. 2.—Maximum killing dilution ——— and partition coefficient — — —.

The melting points of the phenols and their methyl ethers are plotted in Fig. 3. The two curves are remarkably similar and both show marked alternation.

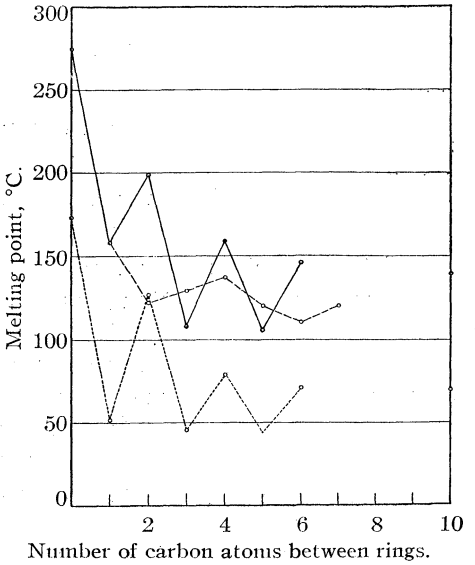


Fig. 3.—Melting points of α,ω-di-*p*-hydroxyalkanes ———, α,ω-di-*p*-methoxyalkanes, – – – – –, α,α-di-*p*-hydroxyalkanes — — —.

Experimental

Hydrogenation of ethylenic double bonds was carried out using the Adams[3] PtO_2 catalyst. Ketones were re-

(3) Adams, Voorhees and Shriner, *Org. Syntheses*, Vol. VIII, 1928, p. 92.

duced in all cases by the Clemmensen reduction or Martin's[4] modification of it. Demethylation was accomplished in all cases by refluxing 0.1 mole with a mixture of 130 g. of glacial acetic acid and 50 g. of constant boiling hydrobromic acid.

1,2-Di-*p*-hydroxyphenylethane.—Anisoin was reduced by the Martin modification of the Clemmensen reduction giving 1,2-dianisylethane which on demethylation gave 1,2-di-*p*-hydroxyphenylethane.

1,3-Di-*p*-hydroxyphenylpropane.—*p*-Acetylanisole prepared according to Baranger[5] was condensed with anisaldehyde to give 1-anisyl-2-anisoylethylene. This on reduction and demethylation gave 1,3-di-*p*-hydroxyphenylpropane.

1,4-Di-*p*-hydroxyphenylbutane.—γ-Anisylbutyric acid was prepared by reduction of the *p*-anisoylpropionic acid obtained by condensing succinic anhydride and anisole according to Rosenmund and Shapiro.[6] The acid chloride prepared using thionyl chloride was condensed with anisole and the crude ketone obtained was reduced and demethylated to give 1,4-di-*p*-hydroxyphenylbutane.

1,5-Di-*p*-hydroxyphenylpentane.—Dianisalacetone prepared from anisaldehyde and acetone by the method of Conard and Dolliver[7] was reduced and demethylated to give 1,5-di-*p*-hydroxyphenylpentane, previously prepared by Borsche.[8]

1,6-Di-*p*-hydroxyphenylhexane.—One mole of adipoyl chloride was condensed with two moles of anisole using 2.25 moles of anhydrous aluminum chloride in 500 cc. of carbon disulfide. The diketone was reduced and demethylated to give 1,6-di-*p*-hydroxyphenylhexane. Oxidation of the diketone with alkaline potassium permanganate gave *p*-anisic acid, showing that condensation took place *para* to the methoxyl group.

1,10-Di-*p*-hydroxyphenyldecane.—Sebacoyl chloride and anisole were condensed as in the case of adipoyl chloride, and the diketone reduced and demethylated to give 1,10-di-*p*-hydroxyphenyldecane.

The solubilities in water were determined by the usual method. Solubilities in olive oil were determined by the method of Dunning, Dunning and Reid.[9]

(4) Martin, THIS JOURNAL, **58**, 1438 (1936).
(5) Baranger, *Bull. soc. chim.*, [4] **49**, 213–222 (1931).
(6) Rosenmund and Shapiro, *Arch. Pharm.*, **272**, 313–323 (1934).
(7) Conard and Dolliver, *Org. Syntheses*, Vol. XII, 1932, p. 22.
(8) Borsche, *Ber.*, **52**, 2079 (1919).
(9) Dunning, Dunning and Reid, THIS JOURNAL, **58**, 1565 (1936).

BALTIMORE, MD. RECEIVED DECEMBER 1, 1939

Summary

1. A series of α,ω-di-*p*-hydroxyphenyl alkanes has been prepared having 2, 3, 4, 5, 6 and 10 methylene groups between the benzene rings.

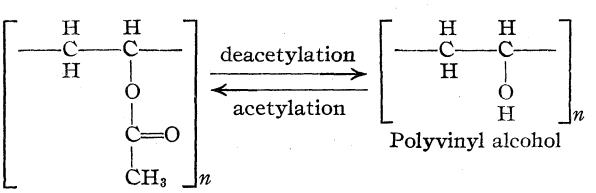
2. The lower members of the series have decided bactericidal properties but are too insoluble in water to prove useful as antiseptics.

[COMMUNICATION NO. 741 FROM THE KODAK RESEARCH LABORATORIES]

Some Relationships between Polyvinyl Acetates and Polyvinyl Alcohols*

BY W. H. MCDOWELL AND W. O. KENYON

By analogy to the simple organic esters such as ethyl acetate, polyvinyl acetate would be expected to yield the corresponding polyvinyl alcohol by deacetylation and, conversely, polyvinyl acetate would be expected from the acetylation of polyvinyl alcohol as indicated in the formulas:



Polyvinyl acetate — Polyvinyl alcohol

These reactions have been described by Staudinger and his co-workers,[1,2] by Herrmann and Haehnel[3] and by others.

The present investigations were undertaken to determine whether polyvinyl acetates could be transformed into polyvinyl alcohols and whether the alcohols could be reacetylated to produce polyvinyl acetates which are similar to the original acetates. Because of the polymeric nature of the polyvinyl alcohols and acetates, comparisons are made on the basis of the degree of polymerization as determined by viscosity measurements.

Experimental

Two different series of polyvinyl acetates of various viscosities were used. One series, composed of commercial samples, was used without further purification. The second series was prepared by the following method.

Monomeric vinyl acetate (practical grade) was distilled in an all-glass apparatus and the fraction boiling between 72.2 and 72.8° used for polymerization. Samples of the monomer were placed in all-glass reflux apparatus with the amounts of benzoyl peroxide catalyst (Eastman grade) shown in Table I and heated overnight on steam-baths.

* Presented before the Paint and Varnish Division of the American Chemical Society at the Boston Meeting, September 11–15, 1939.
(1) Staudinger, *Ber.*, **59**, 3019 (1926).
(2) Staudinger and Schwalbach, *Ann.*, **488**, 8–56 (1931).
(3) Herrmann and Haehnel, *Ber.*, **60**, 1658–1663 (1927).

The polymers obtained were dispersed in acetone, and the dopes were poured into water. The cakes of precipitated resins were steamed to remove excess monomer and decomposition products of the catalyst, cut into small pieces, and dried between 80 and 100° *in vacuo*. The specific viscosities of the polyvinyl acetates obtained are given in Table I.

TABLE I

Experiment	Benzoyl peroxide, % by weight	Specific viscosity in acetone
I	2	0.050
II	1	.090
III	0.75	.115
IV	.30	.209

acetates were measured in acetone and the polyvinyl alcohols in water. The average degrees of polymerization were calculated from the relationship

$$\text{Average degree of polymerization } (D.\ P.) = \frac{\eta_{sp}}{K_m}$$

where η_{sp} is the determined specific viscosity and K_m is the Staudinger constant. The degrees of polymerization of the polyvinyl alcohols and acetates were calculated,[4] using a value of $K_m = 2.6 \times 10^{-4}$.

Average molecular weight polyvinyl alcohol = $D.\ P. \times 44$
Average molecular weight polyvinyl acetate = $D.\ P. \times 86$

In Table II the properties of the various polyvinyl acetates and alcohols are tabulated and compared.

TABLE II

	Original polyvinyl acetate			Polyvinyl alcohol by deacetylation			Polyvinyl acetate by reacetylation		
Expt.	Sp. visc.	Degree of polym.	Mol. wt.	Sp. visc.	Degree of polym.	Mol. wt.	Sp. visc.	Degree of polym.	Mol. wt.
I	0.050	192	16,500	0.043	165	7,250	0.042	162	13,900
II	.090	346	29,800	.056	216	9,500	.056	216	18,600
III	.115	442	38,000	.063	242	10,600	.060	230	19,800
IV	.209	804	69,200	.080	308	13,500	.080	308	26,500
				Commerical Samples					
V	0.021	81	6,970	0.027	104	4,580	.015	58	5,000
VI	.048	188	16,200	.048	185	8,140	.026	100	8,600
VII	.069	262	22,500	.063	242	10,600	.033	127	10,900
VIII	.086	330	28,400	.077	296	13,000	.042	161	13,800
IX	.108	415	35,700	.087	335	14,700	.047	181	15,600
X	.126	485	41,700	.090	346	15,200	.049	188	16,200
XI	.223	857	73,700	.322[a]	1240	54,600	.147[b]	565	48,600

[a] Determined in formic acid, 0.1 g. of resin/100 cc. of solution. [b] Determined in benzene, 0.1 g. of resin/100 cc. of solution. The specific viscosities in benzene are comparable with those determined in acetone.

The polyvinyl acetates were converted to polyvinyl alcohols by the following method. Samples of resins were dissolved in methanol (about 6 cc. of solvent per gram of resin), and 4% of the theoretical amount of alcoholic potassium hydroxide necessary to react with the acetyl groups was added. On standing overnight at room temperature, a practically colorless, tough gel of polyvinyl alcohol formed. A liquid phase of excess methanol, methyl acetate, potassium acetate, and possibly acetic acid separated by syneresis. This was decanted and the polyvinyl alcohol was dispersed in water. When the aqueous dispersion was stirred into acetone, the white, fibrous polyvinyl alcohol separated. It was soaked in acetone with occasional agitation, separated and freed from acetone *in vacuo*.

The polyvinyl alcohols were reacetylated by the following method. One part of the alcohol was heated on the steam-bath for four hours with ten parts of a 2:1 (vol.) mixture of pyridine and acetic anhydride. The resulting polyvinyl acetate dissolved in the reaction mixture to form a homogeneous dope. The ester was precipitated in water, washed with water, and dried at 80 to 100° *in vacuo*. Acetyl determinations of representative samples indicated that the reacetylated materials possessed acetyl contents equal to those of the original acetates. Specific viscosities were determined in an Ostwald viscometer at 25°, using a solution of 0.1 g. of resin in 100 cc. of solution. Unless otherwise specified, the polyvinyl

Because of the decrease in molecular weight observed when polyvinyl acetates were deacetylated and reacetylated, a sample of polyvinyl acetate prepared in the laboratory was carried through two of these cycles to ascertain whether or not a further decrease would be observed in the second cycle. The results are shown in Table III.

TABLE III

Polymer	Specific viscosity	Degree of polymerization	Mol. wt.
(1) Original polyvinyl acetate	0.295	1135	97,600
(2) Polyvinyl alcohol from (1)	.175[a]	672	29,600
(3) Polyvinyl acetate by reacetylation of (2)	.086	330	28,400
(4) Polyvinyl alcohol from (3)	.180[a]	691	30,400
(5) Polyvinyl acetate by reacetylation of (4)	.090	346	29,800

[a] These specific viscosities were determined in formic acid solution, using 0.1 g. of resin per 100 cc. of solution.

The results indicate that a decrease in the degree of polymerization occurred in the first cycle but not in the second, since the values for acetates 3 and 5 are in good agreement. The *D. P.* values

(4) We wish to thank Dr. Newsome and Mr. Wagner of these Laboratories for these measurements.

for the alcohols 2 and 4 in formic acid corroborate this but are twice as great as expected. The use of a K_m value of 5.2×10^{-4} when calculating the *D. P.* values from measurements in formic acid solution would have given values for the alcohols in agreement with those of the corresponding acetates.

The polyvinyl acetates prepared in the laboratory (I to IV, Table II) underwent degradation during de-esterification to produce polyvinyl alcohols with average chain lengths about one half as great as those of the original acetates. The corresponding acetates produced by reacetylation possessed the same chain lengths, within experimental error, as those of the corresponding alcohols. Experiments with commercial polyvinyl acetates (V to X, Table II) yielded opposite results. The change in the degree of polymerization occurred principally during reacetylation, and the degrees of polymerization of the resulting acetates were about one-half those of the corresponding alcohols. There appeared to be some decrease during deacetylation, especially with the acetates of higher viscosities, though the decrease was slight when compared to that which occurred during reacetylation. The specific viscosity of the polyvinyl alcohol of experiment XI (Table II) was determined in formic acid and cannot be employed in such comparisons.

As indicated by the structural formulas previously given, polyvinyl acetate and polyvinyl alcohol are usually assumed to consist of chains of carbon atoms having hydrogen atoms, acetoxy groups and hydroxyl groups attached. The average chain lengths or degrees of polymerization as calculated from specific viscosity measurements are assumed to be proportional to the number of monomeric units comprising the chains. The conditions of deacetylation and reacetylation are mild and would not be expected to rupture the carbon chains since they do not cause breakage of carbon to carbon linkages of simpler esters. However, if it is assumed that these conditions are sufficient to rupture the carbon chains of high molecular weight compounds, a further rupture might be expected when a reacetylated ester is carried through a second cycle, for the reacetylated compounds still possess large molecular weights (Table II). A sample of polyvinyl acetate prepared in the laboratory was carried through two cycles without decrease of the degree of polymerization during the second cycle (Table III). This suggests that the viscosity decrease is not due to rupture of the carbon chains but is caused by the presence of other, less stable, linkages in the chain which are broken under the experimental conditions. If a limited number of such less stable links are present in the original esters and are broken during the first cycle, no further change would be expected in the second cycle.

While no conclusions concerning the nature of such unstable linkages can be drawn from the present data, we wish to suggest the possibility of oxygen atoms from peroxide catalyst or acetaldehyde from the vinyl acetate entering into the polymer to produce a small number of such linkages. This concept of the inclusion of oxygen in the linear chain of a polymer is not novel. Staudinger and Schwalbach[2] suggest attachment of oxygen to a vinyl acetate molecule to produce an activated addition product from which chain growth proceeds. However, it appears that the effect of such linkages on the properties of the polymers has not been considered previously. An examination of other resins produced by polymerization of ethylenic bonds in the presence of peroxide catalysts might throw additional light on this question.[5]

Summary

1. Polyvinyl acetates of various degrees of polymerization have been deacetylated to polyvinyl alcohols and the latter reacetylated to polyvinyl acetates.

2. The polyvinyl acetates obtained by reacetylation possessed degrees of polymerization, as calculated from specific viscosity measurements, which were less than those of the corresponding original polyvinyl acetates.

3. It is suggested that this decrease of the average chain lengths may be due to rupture of unstable linkages present in the linear molecule.

ROCHESTER, NEW YORK RECEIVED OCTOBER 13, 1939

(5) The authors wish to thank Mr. L. M. Minsk and Mr. W. T. W. Pepper for certain of the samples of resins used in this work.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE JOHNS HOPKINS UNIVERSITY]

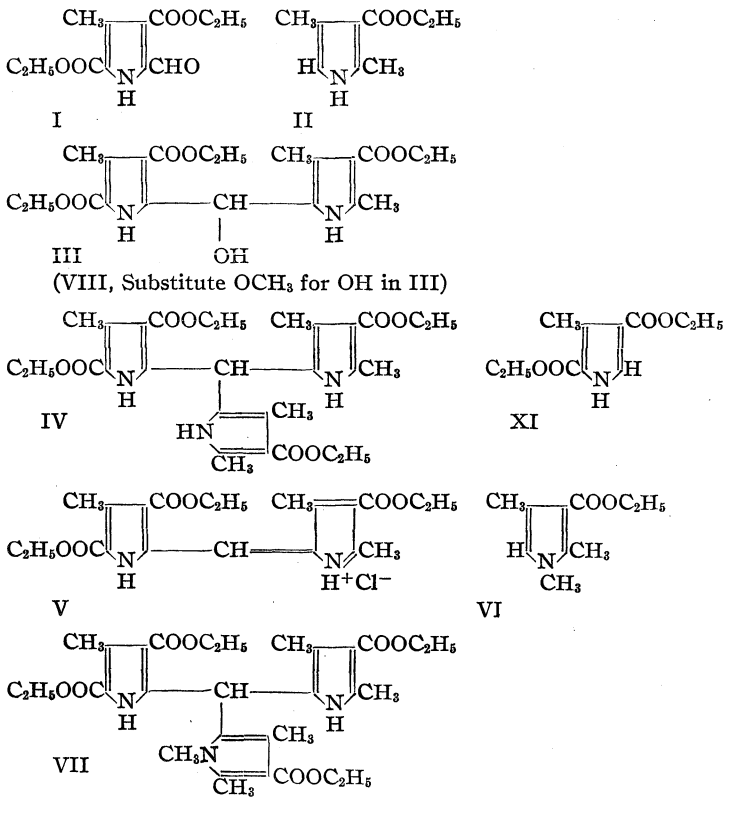
Studies in the Pyrrole Series. IV. A Dipyrrylmethene which is a True Intermediate in its own Formation[1]

BY JOSEPH H. PADEN,[2] ALSOPH H. CORWIN AND WILLIAM A. BAILEY, JR.[3]

In the preceding communication[4a] it was demonstrated that a stepwise synthesis of 3,5,4′-tricarbethoxy-4,3′,5′-trimethyldipyrrylmethene hydrochloride (compound V, Chart I) could be achieved in which a tripyrrylmethane (compound IV) was an intermediate if two moles of the alpha-free pyrrole II were used to one mole of the pyrryl aldehyde I and the resulting tripyrrylmethane cleaved subsequently by the addition of another mole of aldehyde as in scheme (1):

$$\text{I} + 2\text{II} \longrightarrow \text{IV};\ \text{IV} + \text{I} + 2\text{HCl} \longrightarrow 2\text{V} \qquad (1)$$

CHART I



The data then current did not permit a decision as to the course of the reaction when equimolar quantities of the pyrrole II and the aldehyde I were used. As an alternative to the tripyrrylmethane mechanism given in scheme (1), direct formation of methene from carbinol may be formulated:

$$\text{I} + \text{II} \longrightarrow \text{III} + \text{HCl} \longrightarrow \text{V} \qquad (2)$$

The present paper summarizes a group of experiments on the relative velocities of the reactions concerned which permits a decision between these possibilities.

In previous communications on the mechanism of the aldehyde synthesis of dipyrrylmethenes, it has been assumed arbitrarily that dipyrrylcarbinols are intermediates in the various cleavages.[4b,5] While it still seems necessary to retain the assumption of a carbinol as the first reaction product of aldehyde and alpha-free pyrrole, it is now unnecessary to assume any chemical intermediate between tripyrrylmethanes and dipyrrylmethenes, either in cleavage or in recombination, since it can be demonstrated that the methenes themselves are capable of combining with alpha-free pyrroles to form tripyrrylmethanes. This new condensation bears a superficial resemblance to the Diels–Alder reaction. In certain cases the tendency to reaction is so strong that the free base of the methene condenses spontaneously with the alpha-free pyrrole; in other cases it is necessary to use acid catalysts such as potassium acid sulfate or hydrogen chloride or to use the hydrochloride of the methene as one of the reagents. With the aid of this reaction it is possible to make the direct measurements of velocity necessary to an understanding of the course of the methene synthesis.

By the application of this new condensation, direct confirmation of our conclusion[4b] with respect to the hindering influence of an N-methyl group upon condensation is now available and is obtained by a comparison of the following two reactions:

$$\text{V (base)} + \text{II} \longrightarrow \text{IV} \qquad (3)$$
$$\text{V (base)} + \text{VI} \longrightarrow \text{VII} \qquad (4)$$

(1) Presented at the Milwaukee meeting of the American Chemical Society, September, 1938.

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(4) (a) Corwin and Andrews, THIS JOURNAL, **59**, 1974 (1937); (b) **59**, 1975 (1937); (c) **59**, 1979 (1937); (d) **59**, 1976 (1937).

(5) Corwin and Andrews, *ibid.*, **58**, 1987 (1936).

In the absence of added catalyst, reaction (3) is complete in fifty seconds. Under the same conditions reaction (4) has not proceeded appreciably after one hundred minutes. In the presence of potassium acid sulfate reaction (4) is incomplete after one minute but complete in three and one-half minutes. Reaction (3) is complete in thirty seconds. Thus the N-methyl group on an alpha-free pyrrole decreases its speed of combination with a methene.

A close scrutiny of the course of the reaction between a carbinol methyl ether (compound VIII) and an alpha-free pyrrole, or alternatively between a methene base (IV free base) and an alpha-free pyrrole, both reactions in the presence of hydrogen chloride, leads to the conclusion that the reaction to form methene hydrochloride (reaction a, scheme (5) and that to form tripyrrylmethane (reaction b) are not competing reactions but are consecutive as in reaction c.[6]

$$\begin{array}{l} \text{VIII (or V base)} + \text{II} + \text{HCl} \xrightarrow{a} \text{V} + \text{II} \\ \qquad\qquad\qquad\quad \downarrow b \qquad\quad \downarrow c \\ \qquad\qquad\qquad\quad \text{IV} + \text{HCl} \end{array} \qquad (5)$$

When the mixture of carbinol–ether VIII and pyrrole II in ether or dioxane is treated with hydrogen chloride, a transient precipitate of methene hydrochloride V is formed. This immediately reacts with the pyrrole to give tripyrrylmethane IV. When the pyrrole is added after the precipitation, the reaction follows the same course. It thus becomes necessary to assume that the salt of the methene is itself able to react with alpha-free pyrroles to form tripyrrylmethanes. In the case of the N-methyl alpha-free pyrrole VI, the reaction is slow enough to permit the simultaneous isolation of methene salt V and tripyrrylmethane VII although the amount of the methene salt decreases with increasing reaction time. These observations show that the methene hydrochloride is an intermediate in the formation of tripyrrylmethane from carbinol methyl ether in the presence of hydrogen chloride and from them it is inferred that the *methene hydrochloride is an intermediate in the formation of tripyrrylmethane from free carbinol*, a material which has so far resisted all our attempts at isolation.[7]

(6) It may possibly be more accurate to say that carbinol-ether, methene base and methene hydrochloride are all equally capable of forming the same kinetic intermediate under the conditions of the various reactions. Decision upon this point would have to await a more precise and detailed kinetic analysis.

(7) Superficially, it might appear that the formation of N-methyl tripyrrylmethane VII from methene hydrochloride V and pyrrole VI (reaction 4), mentioned in the preceding paragraph, and the reverse of this reaction, namely, the cleavage of the same tripyrrylmethane to form methene hydrochloride V, reported in the preceding paper,[4b] were mutually contradictory experiments. These experiments appear to show that each side of the reaction is more stable than the other side. The apparent contradiction disappears, however, when it is remembered that hydrogen chloride is a reagent in this reaction as well as a catalyst. Presence of excess hydrogen chloride reverses the condensation reaction and causes cleavage of the tripyrrylmethane.

In the preceding paper[4a] it was stated that a decision as to whether or not tripyrrylmethane IV is an intermediate in the synthesis of methene V depends upon the determination of the relative velocities of formation of tripyrrylmethane and dipyrrylmethene.

$$\begin{array}{l} \text{I} + \text{II} + \text{V} + \text{HCl} \xrightarrow{d} 2\text{V} \\ \qquad\qquad\quad \downarrow e \qquad\quad \uparrow f \\ \qquad\qquad\quad \text{IV} + \text{I} + 2\text{HCl} \end{array} \qquad (6)$$

If aldehyde I reacts with pyrrole II faster than methene V reacts with the pyrrole (that is, if reaction d, scheme 6, is faster than reaction e), tripyrrylmethane will not be formed in appreciable quantity because of the removal of one of the reagents essential to its formation. If, on the other hand, methene V reacts with pyrrole II faster than aldehyde I reacts with it (that is, if reaction e is faster than reaction d), tripyrrylmethane formation will remove the pyrrole from the solution preferentially, and methene formation will finally take place only after subsequent cleavage of tripyrrylmethane IV by aldehyde I, a reaction demonstrated in the preceding paper.

The determination of these relative velocities has now been accomplished. In order to slow down all velocities to a measurable rate, potassium acid sulfate was used as a catalyst instead of hydrogen chloride.

$$\text{I} + \text{II} \xrightarrow{g} \text{V (base)} \qquad \text{V (base)} + \text{II} \xrightarrow{h} \text{IV}$$

$$\text{IV} + \text{I} \xrightarrow{j} 2\,\text{V(base)} \qquad (7)$$

Under these conditions the reaction of the free base of methene V with pyrrole II (reaction h, scheme 7) is complete in fifteen seconds while that of aldehyde I (reaction g) is not complete in an hour. Under the same conditions no appreciable cleavage of tripyrrylmethane IV by aldehyde I (reaction j) took place even when the mixture was refluxed for half an hour. This demonstrates that reaction g is faster than reaction j. A qualitative confirmation of these velocity relationships may be obtained from the minimum acid strength necessary to initiate the various reactions. Reaction h proceeds in the absence of

added catalyst; reaction g proceeds only when potassium acid sulfate is added; reaction f proceeds only when hydrogen chloride is added. It must be pointed out, however, that the addition of hydrogen chloride stabilizes the forward direction of reaction f by its mass action effect, so these relationships are not uncomplicated velocity relationships.

The most convincing confirmation that the relative velocities in the presence of hydrogen chloride, the standard reaction conditions for methene formation, are the same as those in the presence of potassium acid sulfate is obtained by the following experiment: as the solution of aldehyde I and pyrrole II used for the synthesis of methene V in the presence of hydrogen chloride becomes increasingly dilute the time of initial appearance of a precipitate of the methene is progressively delayed, as is the time required for obtaining the maximum yield. Under these conditions it is possible to stop the reaction well before the appearance of methene and to isolate the chemical intermediates in the reaction. When equimolar quantities of aldehyde and pyrrole are used, the intermediates isolated are equivalent quantities of unreacted aldehyde I and tripyrrylmethane IV. *This demonstrates that the tripyrrylmethane is an intermediate in the formation of the methene hydrochloride.* Since the methene hydrochloride is an intermediate in the formation of tripyrrylmethane from carbinol, which is the most probable primary product of the condensation of aldehyde and pyrrole, it follows that *the methene hydrochloride is an intermediate in its own formation.* These relationships are summarized in scheme (8).

$$2I + 2II + 2HCl \longrightarrow III + I + II + 2HCl \longrightarrow V + I + II + HCl + H_2O \longrightarrow IV + I + 2HCl + H_2O \longrightarrow 2V + 2H_2O \quad (8)$$

A number of "stable" tripyrrylmethanes of the type of methane IV have been prepared.[8] Their apparent stability would have constituted a strong argument against the adoption of a condensation to tripyrrylmethanes as a general scheme for the synthesis of methenes from aldehydes. This objection has now been removed by the proof that the case which appears to be the most unfavorable to the tripyrrylmethane mechanism is one in which the demonstration of the reality of this mechanism is relatively simple. The reaction in which a satisfactory experimental determination of mechanism will be most difficult is that in which cleavage of the tripyrrylmethane is rapid.

It is of interest to inquire into the mechanism of the last step of scheme (8). One possibility is that tripyrrylmethane IV and aldehyde I combine to form a compound which cleaves to give methene V. All our attempts to prepare such a compound have met with failure. A second possibility is that cleavage to give methene V does not take place until a molecule of aldehyde I and methane IV collide in a preferred orientation or with a sufficiently activated collision. This possibility might be explored by suitable kinetic measurements. There exists the further possibility that the reaction of formation of the tripyrrylmethane is reversible[9] and that the formation of methene is due to the slow displacement of the process toward a more stable product. In the preceding paper[4a] considerable evidence was presented to show that the reaction is actually reversible. For this reason we incline to the third scheme for the course of the cleavage. According to this scheme the rate determining step in the reaction is the combination of aldehyde I with pyrrole II. This slow step intervenes twice, the first time in the presence of excess pyrrole II which favors the reaction by its mass action effect, the second time in the presence of traces of the pyrrole, formed by cleavage of tripyrrylmethane IV. It is the slowness of this reaction combined with the rapidity of the recombination of pyrrole II with methene V which permits the isolation of tripyrrylmethane IV as an intermediate.

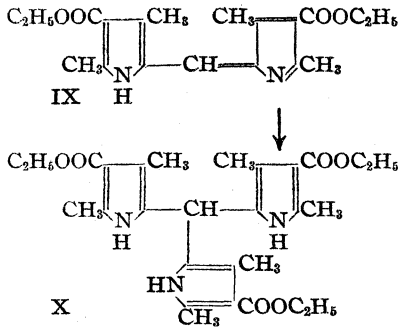
A corollary consistent with the preceding argument would be that the formation of readily cleavable tripyrrylmethanes from methenes and alpha-free pyrroles should be a slower process than the formation of "stable" tripyrrylmethanes. This argument already has been explored, scheme (5), for a case in which the methene remains constant and the pyrrole is varied and was found to be true in that case. The complementary case is now reported (Chart II).

Methene IX combines with pyrrole II in the presence of potassium acid sulfate to form tripyrrylmethane X. This reaction is slower in the

(8) Fischer and Ernst, *Ann.*, **447**, 139 (1926).

(9) The word *reversible* is used here in the usual sense of the organic chemist to signify a process proceeding in both directions. It does not imply that the process is energetically reversible in the thermodynamic sense. In fact, if one were to devise an electrode system to measure the free energy of such a reaction, the electrode behavior would undoubtedly be erratic and the physical chemist would say that he was dealing with an irreversible system.

CHART II



presence of the catalyst than the reaction with the free base of methene V is without any catalyst. These observations are consistent with the assumption that the ready cleavage of tripyrrylmethane X is due essentially to the slowness of the reverse reaction of formation of the tripyrrylmethane. This assumption is also consistent with the course of the cleavages of N-methyl tripyrrylmethanes in which the effect of the N-methyl group has been shown to be due to hindrance of the condensation to tripyrrylmethane. Thus again we are led to regard the reactions involved in the formation of dipyrrylmethenes as a complex series of reversible reactions in which all possible cleavages and condensations take place. One is not justified in regarding these reactions as equilibria, however. The velocities of the competing reactions vary over a sufficiently wide range that products obtained after the usual reaction times allowed in organic work may not be the products thermodynamically most stable and, furthermore, the products obtained after a very short time may be different from those obtained in the normal time.

As a further illustration of the time dependence of these reactions, we may cite the cleavage of tripyrrylmethane IV in the presence of hydrogen chloride. A dry ether solution of this "stable" tripyrrylmethane becomes colored within a few hours after adding dry hydrogen chloride. The color deepens during the course of several weeks and crystals are slowly deposited upon the walls of the reaction vessel. These crystals were identified as the hydrochloride of methene IX, presumably resulting from the reaction shown in scheme (9).

$$\text{IV} + \text{HCl} \longrightarrow \text{XI (Chart I)} + \text{IX (Chart II)} \qquad (9)$$

The possibility of this reaction was discussed in our previous paper.[4d] Unfortunately, it has not been possible to isolate pyrrole XI from the reaction. This experiment lends support to the view that cleavage takes place at all bonds in tripyrrylmethane IV, the chief factor differentiating it from less stable tripyrrylmethanes being the rates of the reactions involved.

One of us, J. H. P., wishes to acknowledge his indebtedness to the Chemical Foundation for a post-doctoral stipend which made this investigation possible. The authors also wish to acknowledge the courtesy of the Carbide and Carbon Chemicals Corporation in furnishing the acetoacetic ester used in this work.

Experimental Part

Condensations of 3,5,4′-Tricarbethoxy-4,3′,5′-trimethyldipyrrylmethene (Methene V Base) with 2,4-Dimethyl-3-carbethoxy-pyrrole (Pyrrole II).—Four-tenths gram (0.001 mole) of the free base of methene V was dissolved in 20 cc. of pure dioxane, dried over 40% sodium amalgam and freshly distilled from sodium; 0.184 g. (0.0011 mole) of pyrrole II was dissolved in 5 cc. of dioxane, purified identically. The solution of pyrrole II was poured into the methene solution, which was shaken quickly. The empty flask was rinsed with 5 cc. of dioxane. The reaction flask was shaken for fifty seconds after the addition of the main portion of the pyrrole and was then poured into 200 cc. of ice and water. A colorless precipitate was formed with no evidence of methene. The product was filtered off, washed well with water and dried by suction in the dark. It was then dissolved in 15 cc. of 95% ethanol and diluted with water until the oil would come out immediately upon removing the flask from the hot-plate. A tiny crystal was added as a seed, and induced crystallization immediately; yield, 0.54 g. (95%) of tripyrrylmethane III, m. p. 190.5–191.5°.

The distillation of the dioxane is important. The methene color remains unchanged for at least fifteen minutes in dioxane decanted from sodium amalgam. The reaction was made to go with an experiment similar to that above except that the dioxane was decanted from sodium amalgam and 0.01 g. of powdered potassium bisulfate was added; yield, 98% of a material melting at 190–192°. A similar experiment was performed using distilled dioxane and potassium bisulfate. Fifteen seconds after mixing, the contents of the flask were poured into 200 cc. of ice and water containing 0.5 g. of sodium carbonate. The tripyrrylmethane was isolated and purified as described above; yield, 94%, m. p. 190–192°. The reaction follows a similar course in redistilled absolute ether: 0.4 g. of the methene was dissolved in 75 cc. of absolute ether, distilled from sodium into the flask. The alpha-free pyrrole was dissolved in 25 cc. of absolute ether, distilled into another flask. The solutions were protected from air by soda lime tubes. Upon mixing, the methene color faded to a light yellow within twenty seconds and this yellow color had disappeared within forty seconds more. The ether was distilled off on a steam-bath and the residue recrystallized as described above; yield, 0.540 g. (95%); m. p. 191–192°. Thus a single recrystallization gave a very pure product which also showed less tendency to darken in the air than most others.

Condensations of 3,5,4′-Tricarbethoxy-4,3′,5′-trimethyldipyrrylmethene (Methene V Base) with 1,2,4-Trimethyl-3-carbethoxy-pyrrole (Pyrrole VI).—Four-tenths of a gram (0.001 mole) of the free base of methene V and 0.199 g. (0.0011 mole) of the pyrrole VI were dissolved in 40 cc. of absolute dioxane, freshly distilled from sodium, and 0.01 g. of potassium bisulfate was added. The color faded to a light yellow and the mixture was poured into ice and water after three and one-half minutes. The product was a pale yellow solid with no evidence of unreacted methene. The suspension was seeded with a tiny crystal and allowed to stand overnight in the icebox before filtering. For the isolation of tripyrrylmethane VII, the following procedure was used. After filtering it was dried in air, warmed with 10 cc. of hexane, cooled and filtered; yield, 0.530 g. or 91%. This crude product melts at 151–153°. The m. p. may be raised by recrystallization from dilute methanol to 155–156°. A similar experiment was performed but the mixture was poured into ice and water after one minute. The original methene was isolated as described in the first experiment; yield, 40%.

A reaction mixture not containing potassium bisulfate was allowed to stand for one hundred minutes. There was no apparent change in color and no tripyrrylmethane could be isolated. A similar experiment was then allowed to stand for over two hours in direct sunlight and then overnight in the laboratory. There was no appreciable change in color in this time.

Preparation of 3,5,4′-Tricarbethoxy-4,3′,5′-trimethyldipyrrylmethene Hydrochloride (Methene V) from its Free Base and from its Carbinol-methyl-ether (Compound VIII).—Two-tenths gram (0.0005 mole) of chromatographically purified methene base V was dissolved in 75 cc. of absolute ether. The solution was cooled in an ice-bath and a stream of dry hydrogen chloride was passed in. As soon as the gas reached the solution a precipitate was formed. Hydrogen chloride was passed in for one minute and the flask was shaken for another minute. The product was filtered off rapidly; yield, of methene V, 96%. The experiment was repeated using an equivalent quantity (0.217 g.) of carbinol methyl ether VIII. This was dissolved in 50 cc. of ether and the methene precipitated without cooling; yield, 93%. In this experiment, as in the preceding, the precipitation of the methene salt was instantaneous.

Condensations of 3,5,4′-Tricarbethoxy-4,3′,5′-trimethyldipyrrylmethene Hydrochloride (Methene V) with 2,4-Dimethyl-3-carbethoxypyrrole (Pyrrole II).—Four-tenths gram of the free base of methene V was dissolved in 75 cc. of absolute ether distilled from sodium; 50 cc. of similar ether was cooled in ice while a strong stream of dry hydrogen chloride was passed in for twenty minutes; 0.167 g. of pyrrole II was dissolved in this solution and then poured rapidly with shaking into the methene solution. A copious precipitate formed which all redissolved within five seconds. The flask was shaken for two minutes and then the contents were poured into 150 cc. of cold 5% sodium hydroxide in a separatory funnel. The ether solution was washed with a second 150-cc. portion of cold sodium hydroxide and with two 100-cc. portions of cold dilute sodium chloride. (The salt was added to facilitate separation of layers.) The ethereal layer was evaporated and the residue recrystallized from dilute ethanol; yield of tripyrrylmethane IV, 0.52 g. or 91.5%, m. p. 191–192°.

The experiment above was repeated with the variation that the ethereal solution of hydrogen chloride was added to the methene free base before the addition of pyrrole II. A copious orange precipitate of the methene hydrochloride V separated immediately but practically all of it redissolved within ten seconds. After three minutes the pyrrole II was added in the solid state. After standing four minutes the solution was poured into sodium hydroxide and the tripyrrylmethane was isolated as described above; yield, 95% of a product melting at 187–188°.

The experiment may be performed with dry dioxane, using only 16 cc. as the solvent. The reaction is complete after fifteen seconds; yield of tripyrrylmethane IV after two recrystallizations from ethanol, 90%, m. p. 191–192°. When either dioxane or ether is used which is decanted from sodium or sodium amalgam, no reaction takes place until the addition of the hydrogen chloride. The yield in ethereal solution may be increased to 97.5% by bubbling in the hydrogen chloride for only five seconds and then evaporating the ether on the steam-bath.

Condensations of 3,5,4′-Tricarbethoxy-4,3′,5′-trimethyldipyrrylmethene Hydrochloride (Methene V) with 1,2,4-Trimethyl-3-carbethoxypyrrole (Pyrrole VI).—Four-tenths gram of the free base of methene V was dissolved in 100 cc. of absolute ether; 0.181 g. of pyrrole VI was added to the solution. It dissolved rapidly. Hydrogen chloride gas was passed into the solution without cooling for two minutes. As soon as the gas reached the solution a precipitate formed but after the first fifteen seconds apparently no more was formed. The flask was shaken at room temperature for three minutes after the addition of the hydrogen chloride and the solution was filtered; 5 mg. of the methene salt V was obtained, corresponding to a recovery of 1.1%. The filtrate was shaken for five minutes more without the formation of more precipitate, showing that the methene salt was not formed from the tripyrrylmethane VII which was present in the solution. The tripyrrylmethane was then isolated in a manner similar to that used for the isolation of tripyrrylmethane IV from hydrogen chloride solution; yield, 0.51 g. or 88%; m. p. 150–152°. Recrystallization from dilute methanol raised the melting point one degree.

When it was desired to isolate the reaction product after a shorter time, the reagents were dissolved in part of the ether and the other part was saturated with hydrogen chloride and then added all at once. An orange-colored precipitate formed immediately. In a typical experiment, the flask was shaken for two minutes after the addition of the hydrogen chloride and then filtered rapidly; yield of methene salt V, 11%; yield of tripyrrylmethane VII, isolated as above, 72%; m. p. 150–152°.

In a similar experiment, carbinol methyl ether VIII was substituted for methene base V, and 40 cc. of hexane was used as solvent. The methene salt was filtered off after two minutes; yield, 73%. The filtrate was practically colorless. On drawing air over it for a few minutes a solid separated, which was allowed to stand overnight, filtered and dried; yield, 24% of tripyrrylmethane VII. It is thus evident that hexane is less well adapted to the production of tripyrrylmethane than is ether, probably

because of the insolubility of the methene salt in hexane. When the experiment was varied by adding only one bubble of hydrogen chloride to prevent the formation of a large amount of methene salt, only a small amount of methene salt precipitated out and it was accompanied by tripyrrylmethane.

Isolation of Intermediates from the Reaction of 2-Formyl-3,5-dicarbethoxy-4-methyl-pyrrole (Aldehyde I) and 2,4-Dimethyl-3-carbethoxy-pyrrole (Pyrrole II).—Five hundred and six milligrams (0.002 mole) of aldehyde I and 334 mg. (0.002 mole) of pyrrole II were dissolved in 20 cc. of absolute ether freshly distilled from sodium. The solution was cooled to 5° in an ice-bath and dry hydrogen chloride was passed in for three minutes. The solution, which was originally colorless, slowly deepened to a light tan. It was poured into 200 cc. of cold 5% sodium hydroxide solution. The flask was rinsed with 20 cc. of ether. The ether and sodium hydroxide solutions were carefully but vigorously shaken for thirty seconds. The ether solution was washed rapidly with two 100-cc. portions of cold 5% sodium hydroxide and finally with two 100-cc. portions of dilute sodium chloride. The sodium hydroxide and sodium chloride solutions were run into an excess of cold dilute hydrochloric acid solution, precipitating the unchanged aldehyde II. This was thoroughly cooled in ice, filtered, and the colorless solid dried in air; recovery, 0.225 g. or 44.5% of a product melting at 124–125° without recrystallization; mixed m. p. with pure aldehyde I (m. p. 127°), 126–127°. One crystallization from dilute ethanol raised the m. p. to 125–126°.

The ether was evaporated on a steam-bath, leaving a sticky yellow residue, partly crystalline. This was recrystallized from dilute ethanol; yield, 0.535 g. or 47% of a yellowish solid, m. p. 191–192°; mixed m. p. with pure tripyrrylmethane IV (m. p. 191–192°) 191–192°.

To duplicate as closely as possible our postulated mechanism for the methene reaction, the following experiment was performed: 434 mg. (0.001 mole) of carbinol ether VIII, 254 mg. (0.001 mole) of aldehyde I and 167 mg. (0.001 mole) of pyrrole II were dissolved in 100 cc. of absolute ether and the solution treated as in the preceding experiment; recovery of aldehyde I, 215 mg. or 85%; yield of tripyrrylmethane IV, 490 mg. or 86%.

Further Examination of the Course of the Condensation of Aldehyde I and Pyrrole II. (a) In Concentrated Solution.—Five grams of aldehyde I and 3.34 g. of pyrrole II were dissolved by warming in 350 cc. of anhydrous ether and then cooled in an ice-bath. A moderate stream of dry hydrogen chloride was passed in. The first precipitation of methene salt V took place after two minutes. The gas was passed in for fifteen minutes and the flask was allowed to stand in the ice-bath for twenty minutes more. The precipitate was filtered and washed with 50 cc. of hexane; yield, 6.8 g. or 78.5%. After standing in the icebox overnight, 0.1 g. additional methene salt was obtained; total yield, 79.8%.

(b) In Dilute Solution.—Two hundred fifty-three milligrams of aldehyde I (0.001 mole) and 167 mg. of pyrrole II (0.001 mole) were dissolved in 100 cc. of absolute ether and treated as in the foregoing experiment. No change in color was visible for four minutes and the first precipitation of methene salt took place after fourteen minutes. The salt was filtered off after twenty-five minutes; yield, 0.270 g. or 61.5%. The filtrate was placed in the icebox for another hour and yielded 70 mg. or 16% additional methene salt. On standing another hour, 20 mg. or 4.5% additional methene salt was obtained. On further standing no more methene was obtained and the solution turned purple; total time, one hundred forty-five minutes; total yield, 82%.

(c) With Potassium Bisulfate.—One hundred twenty-seven milligrams (0.0005 mole) of aldehyde I and 167 mg. (0.001 mole) of pyrrole II were dissolved in 10 cc. of anhydrous dioxane and 0.01 g. of potassium bisulfate was added. The solution was allowed to stand in the dark with occasional shaking for an hour. It was then poured into 100 cc. of ice and water containing 0.5 g. of sodium carbonate and the tripyrrylmethane isolated as described in the first experiment; yield, 0.170 g. or 60% of tripyrrylmethane III, m. p. 190–191°. This experiment fails when commercial dioxane is used.

One hundred forty-two milligrams of tripyrrylmethane IV (0.00025 mole) and 64 mg. of aldehyde I (0.00025 mole) were dissolved by warming in 20 cc. of absolute dioxane and 10 mg. of potassium bisulfate was added. The solution turned an orange color. It was refluxed for thirty minutes and then poured into 200 cc. of ice and water containing 2 g. of sodium carbonate. A colorless solid precipitated which was filtered, washed and recrystallized from dilute ethanol; recovery, 0.130 g. or 91.5% of the tripyrrylmethane IV. The filtrate was acidified and cooled in ice. A colorless solid precipitated; recovery, 52 mg. or 81% of aldehyde I.

(d) Cleavage of Tripyrrylmethane IV by Aldehyde I in Dilute Solution for Comparison with (b).—Two hundred eighty-four milligrams (0.0005 mole) of tripyrrylmethane IV and 127 mg. (0.0005 mole) of aldehyde I[10] were dissolved in 100 cc. of absolute ether by shaking. The conduct of the experiment was as described in (b). The first precipitate appeared after twelve and one-half minutes; yields: after twenty-five minutes, 54.8%; after eighty-five minutes, 15% additional; after one hundred forty-five minutes, 7% additional; total reaction time, one hundred forty-five minutes; total yield, 77%.

Condensations of 3,5,3′5′-Tetramethyl-4,4′-dicarbethoxydipyrrylmethene (Methene IX) and 2,4-Dimethyl-3-carbethoxy-pyrrole (Pyrrole II).—Two hundred fifty milligrams (0.00073 mole) of methene IX and 134 mg. (0.0008 mole) of pyrrole II were dissolved in 20 cc. of absolute dioxane by warming and the solution was then cooled to room temperature; 10 mg. of potassium bisulfate was added and the solution shaken for several minutes. The red color had faded to a light yellow in twenty minutes. The reaction was allowed to stand for a total time of one hundred fifty-five minutes and then poured into ice and water. The yellow solid was filtered off, dried in air and recrystallized from dilute ethanol; yield, 340 mg. or 91% of tripyrrylmethane X, m. p. 193–194°. A similar experiment was performed with the variation that the solution was refluxed for five minutes and then poured immediately into ice and water; yield, 96% of tripyrrylmethane X, m. p. 188–190°. Extraction of the product

(10) It should be noted that 0.0005 mole of these reagents is equivalent to 0.001 mole of the reagents in (b).

with toluene–hexane followed by repeated recrystallization from dilute ethanol raised the m. p. to 205–208°.

The experiment was repeated using ether as a solvent. This is not satisfactory because of the low solubility of the methene in ether. With no added catalyst the reaction proceeded slowly. Tripyrrylmethane X began to separate from the solution after forty minutes. The ether was evaporated on a steam-bath; yield, 97%, m. p. 191–192°.

With dioxane as solvent but with the substitution of hydrogen chloride for potassium bisulfate, only the hydrochloride of methene IX could be isolated; yield, 100% of a product melting with decomposition at 206°. This exactly parallels the cleavage of the tripyrrylmethane X which gave a copious precipitate of the salt of methene IX after five seconds and a quantitative yield when filtered after one minute.

An attempted condensation of 2,4-dimethyl-3-carbethoxy-5-formylpyrrole with 2,4-dimethyl-3-carbethoxy-pyrrole to give tripyrrylmethane X in dioxane with potassium bisulfate as catalyst was unsuccessful under the conditions which succeeded in giving tripyrrylmethane IV from the corresponding aldehyde.

Cleavage of Tripyrrylmethane IV with Hydrogen Chloride.—One and one-tenth grams of tripyrrylmethane IV was suspended in 185 cc. of dry ether and cooled in an ice-bath. Dry hydrogen chloride was passed in for ten minutes. The tripyrrylmethane dissolved with a light yellow color which rapidly gave way to orange. After two hours the solution was cherry-red. It was allowed to stand in an icebox and was wrapped with a towel to protect it from light. After two days it was deep violet but no crystals had appeared. After one month crystals had begun to appear on the walls of the vessel. The mixture was then allowed to warm up to room temperature and to stand for one year. The mother liquor was drained off and neutralized with calcium hydroxide and then chromatographed over alumina using carbon tetrachloride as solvent. The colorless fore-runs contained a dissolved oil but no crystalline derivative was obtained from it.

The crystals on the wall of the vessel were dissolved in chloroform and chromatographed over calcium hydroxide to prepare the free base of the methene. The methene solution was evaporated to dryness and taken up in a mixture of 25% chloroform and 75% carbon tetrachloride (both solvents freshly treated with lime to remove acidic decomposition products). The methene layer developed below a much darker layer on the chromatogram and was separated and eluted with purified chloroform. The solution was evaporated in a weighed flask; yield, 0.223 g. or 33%. It was identified as methene IX by its decomposition point, 187°, and by hydrogenation to 3,5,3′,5′-tetramethyl-4,4′-dicarbethoxy-dipyrrylmethane, m. p. 229°.

Summary

1. It has been discovered that dipyrrylmethenes react with pyrroles with free alpha positions to form tripyrrylmethanes.

2. Application of this reaction permits direct velocity comparisons which make it possible to study the mechanism of the formation of dipyrrylmethenes.

3. It has been demonstrated by actual isolation that a tripyrrylmethane is an intermediate in a "normal" dipyrrylmethene synthesis.

4. It is inferred from comparisons of velocity that this dipyrrylmethene is an intermediate in the formation of the tripyrrylmethane and is, therefore, an intermediate in its own formation.

5. Cleavage of a "stable" tripyrrylmethane by hydrogen chloride alone has been demonstrated.

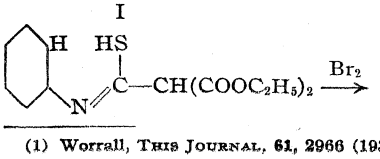
BALTIMORE, MARYLAND RECEIVED OCTOBER 23, 1939

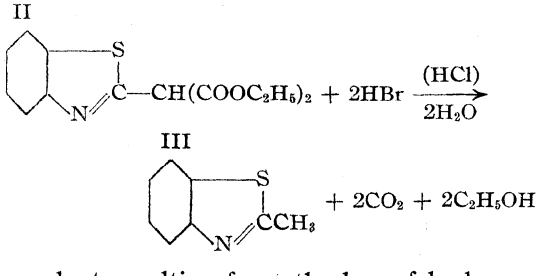
[CONTRIBUTION FROM THE PEARSON MEMORIAL LABORATORY OF TUFTS COLLEGE]

The Action of Bromine on Certain Thioamides

BY DAVID E. WORRALL AND ARTHUR W. PHILLIPS

The thioamide obtained by the action of two equivalents of *p*-tolyl isothiocyanate on ethyl acetonedicarboxylate reacts spontaneously with bromine.[1] In order to present a structural interpretation of the product formed here, a study of the action of bromine on the addition product of malonic ester and phenyl isothiocyanate is here reported. The course of the reactions involved can be outlined as follows





The product resulting from the loss of hydrogen bromide, and cyclization, forms a salt with alcoholic potassium hydroxide and also acts enolic toward a Grignard reagent. With hydrochloric acid, it undergoes hydrolysis and decarboxylation, to yield the well-known 1-methylbenzothiazole.

(1) Worrall, THIS JOURNAL, 61, 2966 (1939).

Experimental

Benzothiazole-1-diethyl Malonate.—To 10 g. of I, prepared from malonic ester and phenyl isothiocyanate dissolved in glacial acetic acid, was added slowly the molar equivalent of bromine in acetic acid. The mixture, which became turbid from the separation of small amounts of sulfur and other decomposition products, was immediately poured into water. After three crystallizations from alcohol, the new product was obtained in small needles, m. p. 138–139°; yield approximately 5 g.

Anal. Calcd. for $C_{14}H_{15}NO_4S$: C, 57.3; H, 5.1. Found: C, 56.9; H, 5.1.

II was soluble in cold concd. hydrochloric acid, separating unchanged on dilution with water. It changed into a powder in the presence of alcoholic potassium hydroxide, which was soluble in water and which was changed by hydrochloric acid into the original substance. A precipitate was formed and bubbles of gas escaped when an ether solution of the thiazole was mixed with methylmagnesium iodide from which the same thiazole was recovered on the addition of water.

1-Methylbenzothiazole from II.—Ten grams of II was heated for two hours with concd. hydrochloric acid, the mixture was diluted with water, filtered and steam distilled until the distillate was clear. Then an excess of alkali was added and steam distillation resumed. A colorless oil with a strong pyridine-like odor resulted. Its identity with an authentic sample of 1-methylbenzothiazole was confirmed by a boiling point determination, and an analysis.

1-Benzothiazoylacetylacetone.—The thiazole prepared from acetylacetone and phenyl isothiocyanate separated from ligroin in silky needles, m. p. 155°. It was rapidly changed by hot alkali, more slowly by acid, into methyl benzothiazole.

Anal. Calcd. for $C_{12}H_{11}NO_2S$: C, 61.8; H, 4.7. Found: C, 62.1; H, 4.5.

Summary

It has been shown that bromine converts the monothioanilide of carbethoxyethylmalonate into benzothiazoylmalonic ester, which is changed by hydrolysis into methylbenzothiazole.

MEDFORD, MASS. RECEIVED OCTOBER 9, 1939

[CONTRIBUTION FROM THE BURROUGHS WELLCOME & CO. U. S. A. EXPERIMENTAL RESEARCH LABORATORIES]

3-Methyl-3,4-dihydroisoquinolines and 3-Methyl-1,2,3,4-tetrahydroisoquinolines[1]

BY WALTER S. IDE AND JOHANNES S. BUCK

Work in progress on the pharmacological effects of various substituting groups in the isoquinoline nucleus necessitated the preparation of a series of 3-methyl-3,4-dihydroisoquinolines and 3-methyl-1,2,3,4-tetrahydroisoquinolines (analogous to norhydrastinine and dihydronorhydrastinine). There are a number of scattered isoquinoline compounds with a 3-methyl group in the literature, but the methods of preparation vary widely and in many cases essential details are lacking. Most of the compounds are also substituted in the 1-position.

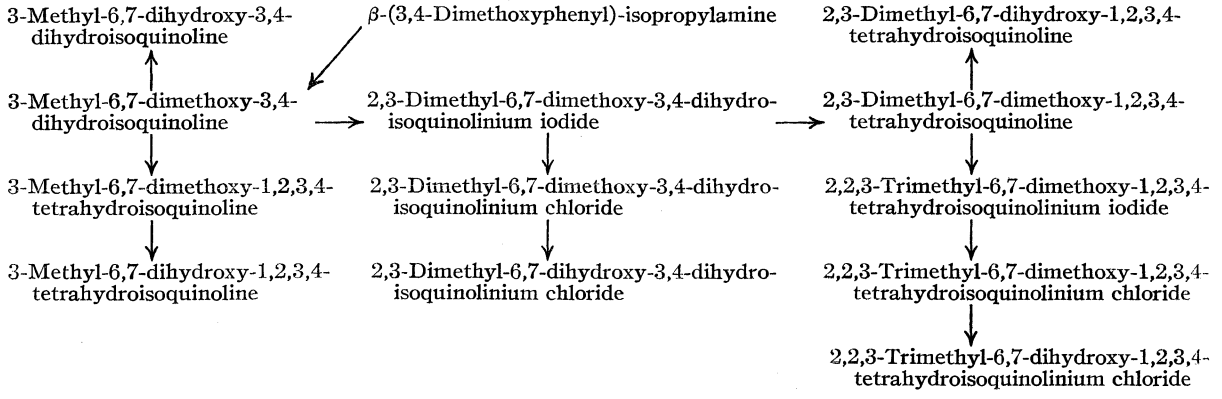
The authors therefore set out to devise a series of general reactions for the preparation of the desired 3-methylisoquinoline derivatives. By the method selected three series of compounds, containing as substituents 6,7-dimethoxyl, 6,7-methylenedioxyl and 6,7-dihydroxyl, were prepared and other series doubtless could be made in a similar way. The isoquinolines were prepared by cyclizing formyl-β-phenylisopropylamines (Bischler–Napieralski reaction). This required fairly large amounts of β-phenylisopropylamines. The methods of Mannich and Jacobsohn[2] and of Merck[3] for the preparation of these amines were not investigated since they depend on naturally-occurring materials and are therefore not general. The nitropropenyl method of Alles[4] also was not investigated. The most feasible route appeared to be a series of reactions similar to those used for phenethylamines[5,6] but attempts to prepare disubstituted α-methylcinnamic acids by the method of Bogert and Davidson[7] failed, the condensation of disubstituted benzaldehydes with methyl ethyl ketone not proceeding in the desired way. Recourse therefore was had to the Reformatsky reaction and the required α-methylcinnamic acids were prepared by condensing ethyl α-bromopropionate with the aldehyde, followed by the dehydration and saponification of the product. An alternative method used was the Claisen condensation of the aldehyde with ethyl propionate, followed by saponification. The α-methylcin-

(1) This work is part of a joint research being carried out in collaboration with a pharmacological group at the above laboratories.

(2) Mannich and Jacobsohn, *Ber.*, **43**, 189 (1910).
(3) German Patent 274,350.
(4) United States Patent 1,879,003.
(5) Buck, THIS JOURNAL, **54**, 3661 (1932).
(6) Woodruff and Conger, *ibid.*, **60**, 465 (1938).
(7) Bogert and Davidson, *ibid.*, **54**, 334 (1932).

namic acid was reduced, the product amidated and the amine obtained by a Hofmann reaction.

The production of the various isoquinoline types from the substituted β-phenylisopropylamines can be best illustrated by the chart below (for the case of the 6,7-dimethoxy compounds). The reactions are all convenient and the yields at each stage are good, for the cases examined.



Experimental

α-Methyl-3,4-dimethoxycinnamic Acid. (a) **Claisen Method.**—17.3 g. (1.25 atoms) of sodium was "atomized" (not too finely) under toluene, and the toluene decanted. To the sodium was added, in one lot, a solution of 100 g. (1 mol) of veratric aldehyde in 350 cc. (5 mols) of ethyl propionate. The reaction was carried out in a large flask fitted with an efficient reflux condenser, and provision was made for water cooling the flask. A violent reaction took place and was controlled by cooling. After the reaction had subsided, the flask was allowed to stand for two hours, and water then added under a coal-gas atmosphere; 76 cc. (1.25 mol) of concd. hydrochloric acid was added to the aqueous solution and the excess of ethyl propionate removed by steam distillation. The residual oil was extracted with ether and the ether evaporated. The crude ester was saponified by 67 g. (2 mols) of potassium hydroxide dissolved in methyl alcohol; the alcohol was then evaporated and the acid precipitated by hydrochloric acid.

The corresponding 3,4-methylenedioxy acid was prepared similarly but occasionally almost explosive carbonization took place (possibly due to the sodium being too finely atomized) and extreme caution is therefore necessary.

(b) Reformatsky Method.[8,9]—Eighty-three grams (0.5 mole) of veratric aldehyde and 91 g. (0.50 mole) of ethyl α-bromopropionate were dissolved in 300 cc. of benzene and 35 g. of zinc (Baker 80-mesh, granular) added. The whole was refluxed gently for about one hour, then cooled and the benzene solution decanted from the zinc. After washing with dilute sulfuric acid, the benzene solution was dried over calcium chloride, and about one-half the benzene evaporated. After cooling, 40 cc. of phosphorus oxychloride was added cautiously in portions and the whole then heated on the bath for twenty to thirty minutes. After cooling, the purple solution was washed with ice water, then with 10% sodium hydroxide, and the benzene evaporated. Saponification of the residue (methyl alcoholic potassium hydroxide) followed by removal of the alcohol and acidification gave the acid as a pasty solid.

The crude acid, fractionated from benzene, gave two compounds, about 20% being the higher-melting one. The lower-melting compound, recrystallized from alcohol, forms white needles, melting at 144°.[10]

Anal. Calcd. for $C_{12}H_{14}O_4$: C, 64.83; H, 6.35. Found: C, 65.03; H, 6.57.

The higher-melting compound from alcohol, consists of a white, granular powder, melting at 232°. It is probably the *trans* isomer.

Anal. Calcd. for $C_{12}H_{14}O_4$: C, 64.83; H, 6.35. Found: C, 64.94; H, 6.49.

α-Methyl-3,4-methylenedioxycinnamic Acid.[11]—This acid was prepared by either of the foregoing methods. Recrystallized from benzene it forms light yellow glittering needles, melting at 200°.

Anal. Calcd. for $C_{11}H_{10}O_4$: C, 64.05; H, 4.89. Found: C, 64.07; H, 5.11.

α-Methyl-3,4-dimethoxyphenylpropionic Acid.—This acid was prepared by a sodium amalgam reduction. The properties agreed with those described in the literature.[10]

α-Methyl-3,4-methylenedioxyphenylpropionic Acid.—This was also prepared by a sodium amalgam reduction and the properties agreed with those recorded.[11]

α-Methyl-3,4-dimethoxyphenylpropionamide.—The amide was prepared (a) by heating the ammonium salt in a stream of ammonia, for two hours at 220°, and (b) by running the acid chloride (thionyl chloride method) into aqueous ammonia containing sodium hydroxide. Recrystallized from benzene, it forms white flakes, melting at 109°.

Anal. Calcd. for $C_{12}H_{17}O_3N$: C, 64.54; H, 7.68. Found: C, 64.77; H, 7.64.

α-Methyl-3,4-methylenedioxyphenylpropionamide.—The preparation was carried out as in the foregoing case,

(8) *Cf.* Lindenbaum, *Ber.*, **50**, 1270 (1917).

(9) *Cf.* Woodruff and Pierson, THIS JOURNAL, **60**, 1075 (1938).

(10) Tiemann and Kraaz, *Ber.*, **15**, 2070 (1882), by another method.

(11) *Cf.* Wallach and Evans, *Ann.*, **357**, 77 (1907); Lorenz, *Ber.*, **13**, 756 (1880).

TABLE I

DIHYDRO- AND TETRAHYDROISOQUINOLINE DERIVATIVES

3-Methyl-6,7-	M. p., °C.	Formula	Analyses: Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
Dimethoxy-3,4-dihydroisoquinoline hydrochloride[a,e,m]	189	$C_{12}H_{16}O_2NCl$	59.60	59.52	6.68	6.67
Methylenedioxy-3,4-dihydroisoquinoline hydrochloride[d,f,m,u]	198	$C_{11}H_{12}O_2NCl$	58.52	58.82	5.36	5.56
Dihydroxy-3,4-dihydroisoquinoline hydrochloride[a,f,h,n]	297	$C_{10}H_{12}O_2NCl$	56.19	56.14	5.64	5.64
Dimethoxy-1,2,3,4-tetrahydroisoquinoline hydrochloride[c,e,o,v]	245	$C_{12}H_{18}O_2NCl$	59.11	59.29	7.45	7.64
Methylenedioxy-1,2,3,4-tetrahydroisoquinoline hydrochloride[d,e,o]	238	$C_{11}H_{14}O_2NCl$	58.01	58.24	6.20	6.46
Dihydroxy-1,2,3,4-tetrahydroisoquinoline hydrochloride[c,g,i,n]	270	$C_{10}H_{14}O_2NCl$	55.67	55.51	6.55	6.80
2,3-Dimethyl-6,7-						
Dimethoxy-3,4-dihydroisoquinolinium iodide[a,e,p]	156	$C_{13}H_{18}O_2NI$	44.95	45.05	5.23	5.41
Dimethoxy-3,4-dihydroisoquinolinium chloride[a,e,t]	125–128	$C_{13}H_{18}O_2NCl$	61.03	61.06	7.09	7.44
Methylenedioxy-3,4-dihydroisoquinolinium iodide[b,e,i,p]	213	$C_{12}H_{14}O_2NI$	43.50	43.66	4.26	4.37
Methylenedioxy-3,4-dihydroisoquinolinium chloride[d,e,t]	212	$C_{12}H_{14}O_2NCl$	60.11	60.27	5.87	6.02
Dihydroxy-3,4-dihydroisoquinolinium chloride[a,e,n]	199	$C_{11}H_{14}O_2NCl$	58.01	58.27	6.20	6.35
Dimethoxy-1,2,3,4-tetrahydroisoquinoline hydrochloride[c,e,q]	232	$C_{13}H_{20}O_2NCl$	60.56	60.73	7.82	7.98
Dimethoxy-1,2,3,4-tetrahydroisoquinoline[c,g,r]	100	$C_{13}H_{19}O_2N$	70.54	70.70	8.66	8.93
Methylenedioxy-1,2,3,4-tetrahydroisoquinoline hydrochloride[c,g,q,w]	228–229	$C_{12}H_{16}O_2NCl$	59.61	59.81	6.67	6.88
Methylenedioxy-1,2,3,4-tetrahydroisoquinoline[d,e,r,x]	88	$C_{12}H_{15}O_2N$	70.20	70.19	7.37	7.38
Dihydroxy-1,2,3,4-tetrahydroisoquinoline hydrochloride[d,e,k,n]	266	$C_{11}H_{16}O_2NCl$	57.50	57.73	7.02	6.99
2,2,3-Trimethyl-6,7-						
Dimethoxy-1,2,3,4-tetrahydroisoquinolinium iodide[c,e,s]	232	$C_{14}H_{22}O_2NI$	46.27	46.48	6.11	6.29
Dimethoxy-1,2,3,4-tetrahydroisoquinolinium chloride[c,e,t]	239	$C_{14}H_{22}O_2NCl$	61.85	62.12	8.16	8.24
Methylenedioxy-1,2,3,4-tetrahydroisoquinolinium iodide[a,g,l,s]	242	$C_{13}H_{18}O_2NI$	44.95	45.26	5.23	5.22
Methylenedioxy-1,2,3,4-tetrahydroisoquinolinium chloride[c,e,t]	248–250	$C_{13}H_{18}O_2NCl$	61.03	61.18	7.09	7.40
Dihydroxy-1,2,3,4-tetrahydroisoquinolinium chloride[c,e,k,n]	258	$C_{12}H_{18}O_2NCl$	59.11	59.35	7.45	7.33

[a] Yellow. [b] Brown yellow. [c] White or almost white. [d] Light ivory to light tan. [e] Prisms. [f] Plates. [g] Crystalline powder. [h] Recryst. dil. HCl. [i] Recryst. aq. alcohol. [k] Recryst. methanol–ethanol. [l] Recryst. water. [m] Prepared by cyclizing the formyl amine by the method of Buck and Ide, THIS JOURNAL, **60**, 2101 (1938). [n] By demethylation of the corresponding methoxy compound with hydrochloric acid at 170° (*cf.* Buck and Ide, *loc. cit.*). [o] The dihydroisoquinoline hydrochloride was reduced hot with zinc and dilute sulfuric acid, and the product isolated via the base. [p] The 3-methyldihydroisoquinoline base, in cold benzene solution, was treated with methyl iodide. [q] By reduction (zinc and hot dilute sulfuric acid) of the 2,3-dimethyldihydroisoquinolinium iodide. [r] From the hydrochloride with aqueous potassium hydroxide. Recrystallized from hexane. [s] By the action of methyl iodide on the 2,3-dimethyltetrahydroisoquinoline in cold benzene solution. [t] Iodides were converted into chlorides in cold aqueous solution by fresh silver chloride. [u] German Patent 279,194 describes base only. [v] Prepared by different methods, German Patent 336,153 gives m. p. 232°; German Patent 280,502 gives m. p. 238° and German Patent 320,480 gives base m. p. 65–67°. [w] Prepared by different methods, German Patent 336,153 gives m. p. 230–232° and German Patent 320,480 gives m. p. 230°. [x] German Patent 320,480 gives m. p. 86°.

the chloride method being preferred. After recrystallization from benzene, the amide forms white flakes, m. p. 122°.

Anal. Calcd. for $C_{11}H_{13}O_3N$: C, 63.73; H, 6.33. Found: C, 64.00; H, 6.33.

β-(3,4-Dimethoxyphenyl)-isopropylamine.—The Hofmann reaction on the corresponding amide was carried out as usual, with 1.1 mol of sodium hypochlorite. The amide may be added dissolved in dioxane. After two distillations the amine forms a colorless, refractile liquid, with a sweet, musty odor. It boils at 154° (9 mm.) and has n_D 1.5347, d^{25}_4 1.0624. The yield was 53%.

Anal. Calcd. for $C_{11}H_{17}O_2N$: C, 67.64; H, 8.78. Found: C, 67.79; H, 8.66.

The amine has been prepared by other methods[2,3,12] and is mentioned (no details) by Gunn, *et al.*[13]

The **hydrochloride,** recrystallized from alcohol forms a bulky white mass of ill-defined prisms, melting at 150°. Merck[3] gives m. p. 150–151°.

Anal. Calcd. for $C_{11}H_{18}O_2NCl$: C, 56.99; H, 7.83. Found: C, 56.93; H, 7.77.

(12) German Patent 247,906.

(13) Gunn, Gurd and Sachs, *J. Physiol.*, **95**, 485 (1939).

β-(3,4-Methylenedioxyphenyl)-isopropylamine.—The preparation is similar to that of the foregoing amine. After two distillations, the amine forms a slightly viscous, colorless liquid, with a faint, sweet, musty odor, boiling at 143–145° (11 mm.) and having n_D 1.5394 and d^{25}_4 1.1277. The yield was 40%.

Anal. Calcd. for $C_{10}H_{13}O_2N$: C, 67.00; H, 7.31. Found: C, 67.00; H, 7.00.

Other methods of preparation have been described,[2,3] and it has been mentioned by Gunn, *et al.*[13]

The **hydrochloride** forms bulky white aggregates of small rhombs when crystallized from alcohol. The melting point is 188° (*cf.* ref. 3, m. p. 183–185°).

Anal. Calcd. for $C_{10}H_{14}O_2NCl$: C, 55.67; H, 6.54. Found: C, 55.66; H, 6.60.

The salts described below were recrystallized until pure from absolute alcohol, with the addition of ether or ethyl acetate or both, unless otherwise noted. The solubilities are all very similar, the compounds being in general soluble in methyl and ethyl alcohols, very soluble in water, sparingly soluble in ethyl acetate, and practically insoluble in non-polar solvents. The melting points are corrected.

Summary

A number of 3-methyl-3,4-dihydroisoquinoline and 3-methyl-1,2,3,4-tetrahydroisoquinoline derivatives are described. The substituents are 6,7-dimethoxyl, 6,7-methylenedioxyl and 6,7-dihydroxyl. The compounds are closely related to norhydrastinine and dihydronorhydrastinine. A series of general reactions for their preparation is given.

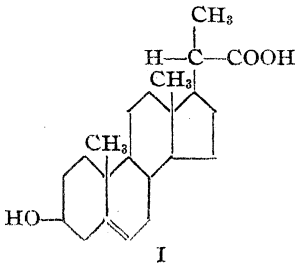
TUCKAHOE, NEW YORK RECEIVED NOVEMBER 13, 1939

[CONTRIBUTION FROM THE SQUIBB INSTITUTE FOR MEDICAL RESEARCH, DIVISION OF ORGANIC CHEMISTRY]

Brassicasterol. II. Degradation by Ozone

BY ERHARD FERNHOLZ AND HOMER E. STAVELY

In a previous communication[1] it was shown that completely hydrogenated brassicasterol, brassicastanol, is not identical with stigmastanol, the common hydrogenated derivative of the phytosterols stigmasterol, β-sitosterol, and α-spinasterol. This was somewhat unexpected since our analytical data favored an empirical formula with 29 carbon atoms, rather than one with 28 carbon atoms as originally proposed by Windaus and Welsch.[2] Analyses reported[1] for brassicasteryl *m*-dinitrobenzoate fitted almost equally well for a C_{28} or a C_{29} sterol but analyses for brassicastyl *m*-dinitrobenzoate definitely favored a C_{29} sterol. In spite of this, on the basis of ozonization experiments we are now forced to conclude that brassicasterol contains only 28 carbon atoms.



I

After addition of one mole of bromine to the nuclear double bond of brassicasteryl acetate, treatment with ozone and subsequent debromination, β-3-hydroxy-bisnorcholenic acid (I) was isolated, the same acid obtained by similar treatment of stigmasteryl acetate.[3] This degradation product accounts for the largest part of the molecule and leaves no doubt as to the position of the two double bonds and the hydroxyl group. Another sample of brassicasterol was ozonized under conditions favorable for the isolation of a volatile aldehyde, the other molecular fragment. A crystalline semicarbazone of the aldehyde was obtained which analyzed for six carbon atoms from the aldehyde. It is therefore conclusively proved that the empirical formula of brassicasterol is $C_{28}H_{46}O$.

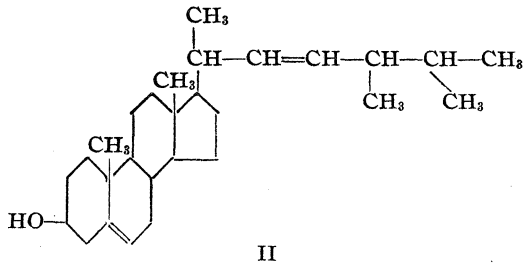
A comparison of the properties of the aldehyde semicarbazones obtained by ozonizing ergosterol,[4] stigmasterol[5] and brassicasterol seems to indicate that the aldehyde from brassicasterol is slightly racemized 1-methylisopropylacetaldehyde, as shown in Table I. A mixed sample of the semicarbazone from brassicasterol with the semicarbazone of 1-methylisopropylacetaldehyde from ergosterol (m. p. 128) melted at 120–122°, showing no depression.

TABLE I

	Ethylisopropylacetaldehyde semicarbazone (from stigmasterol)	Methylisopropylacetaldehyde semicarbazone (from ergosterol)	Semicarbazone from brassicasterol
M. p., °C.	128	128	119
$[\alpha]D$	+9°	−52°	−40°
C, %	56.14	53.46	53.65
H, %	9.95	9.62	9.70
N, %	24.58	26.74	26.76

This is noteworthy because all precautions were taken to prevent racemization and in a trial run with ergosterol no racemization occurred. The assumption that brassicasterol contains a certain amount of an isomer with the opposite configuration on C_{24} seems to offer an attractive explanation for this observation, although it is also possible that brassicasterol contains a closely related isomeric sterol with a structurally differing side chain. Our degradation experiments leave, however, little doubt that formula II must be assigned to brassicasterol, which could be called 7,8-dihydroergosterol.

(1) Fernholz and Stavely, THIS JOURNAL, **61**, 142 (1939).
(2) *Ber.*, **42**, 612 (1909).
(3) Fernholz, *Ann.*, **507** 128 (193
(4) Guiteras, Nokamiya and Inhoffen, *Ann.*, **494**, 119 (1932).
(5) Guiteras, *Z. physiol. Chem.*, **214**, 89 (1933).



II

The difficulty of obtaining a pure sample of brassicasterol is also illustrated by a marked difference in the rotation of its hydrogenation product and pure ergostanol and their derivatives, except the *m*-dinitrobenzoate as shown in Table II.

TABLE II

	M. p., °C.	$[\alpha]^{25}D$
Brassicastanol	142	+24
Brassicastyl acetate	143	+15
Brassicastyl *m*-dinitrobenzoate	202	+14
Ergostanol	144	+15
Ergostyl acetate	145	+ 6
Ergostyl *m*-dinitrobenzoate	203	+13

In view of these discrepancies it was not possible to assume their identity in spite of the absence of mixed melting point depressions throughout the series without the more convincing evidence obtained by ozone degradation of brassicasterol.

The great structural similarity of stigmasterol and brassicasterol has led us to apply the partial debromination reaction recently described by us[6] for stigmasteryl acetate tetrabromide also to the brassicasterol derivative. A 22,23-dibromobrassicasteryl acetate of m. p. 236–238° was obtained.

Experimental

Ergostyl *m*-Dinitrobenzoate.—Five and one-half grams of ergostanol, 5 g. of *m*-dinitrobenzoyl chloride and 70 cc. of pyridine were heated for one-half hour on the steam-bath, then diluted with water, filtered, and recrystallized from ethanol–chloroform, m. p. 202–203°; $[\alpha]^{24}D$ +14° (12.7 mg. in 2.0 cc. chloroform, $\alpha^{24}D$ +0.09°, 1 dm. tube).

Anal.[7] Calcd. for $C_{35}H_{52}O_6N_2$: C, 70.43; H, 8.78. Found: C, 70.18; H, 8.66.

β-3-Hydroxy-bisnorcholenic Acid.—Brassicasteryl acetate (3.82 g.) was dissolved in chloroform and 1.34 g. of bromine (1 mole) in chloroform was added dropwise. After twice the theoretical amount of ozone had been passed through the solution it was evaporated *in vacuo* below 30°, and the residue debrominated with zinc and acetic acid. Water was added and the mixture extracted with ether, the ether washed with water and an excess of 2 *N* sodium hydroxide. A precipitate, which appeared between the ether and an aqueous layer, was washed with 2 *N* sodium hydroxide and ether, then acidified with dilute acid and extracted with ether. The ether was evaporated and the residue refluxed with alcoholic potassium hydroxide for two hours, water was then added and the mixture extracted with a large amount of ether. The ether residue was recrystallized from acetic acid, m. p. (dec.) 293°

Anal. Calcd. for $C_{22}H_{34}O_3$: C, 76.23; H, 9.91. Found: C, 76.15; H, 10.10. Mixed m. p. with an authentic sample of β-3-hydroxy-bisnorcholenic acid showed no depression.

β-3-Hydroxy-bisnorcholenic Acid Methyl Ester.—The methyl ester was prepared from 160 mg. of β-3-hydroxy-bisnorcholenic acid by means of diazomethane; recryst. from aqueous methanol, m. p. 139–140°.

Anal. Calcd. for $C_{23}H_{36}O_3$: C, 76.58; H, 10.10. Found: C, 75.45; H, 9.96.

A mixed m. p. with an authentic sample of the methyl ester of β-3-hydroxy-bisnorcholenic acid showed no depression.

β-3-Acetoxy-bisnorcholenic Acid Methyl Ester.—Seventy milligrams of β-3-hydroxy-bisnorcholenic acid methyl ester stood overnight in a solution of 0.3 cc. of acetic anhydride in 3 cc. of pyridine. The solvent was evaporated *in vacuo* and the residue crystallized from methanol, m. p. 138°.

Anal. Calcd. for $C_{25}H_{38}O_4$: C, 74.59; H, 9.54. Found: C, 74.77, 74.82; H, 9.47, 9.49.

A mixed m. p. with an authentic sample of β-3-acetoxy-bisnorcholenic acid methyl ester showed no depression.

Ozonization of Brassicasteryl Acetate.—Two grams of brassicasteryl acetate was suspended in 20 cc. of glacial acetic acid and an excess of ozone passed through the suspension. It was poured immediately into 100 cc. of water and distilled until no more oil drops distilled over. The distillate was neutralized with sodium bicarbonate, 200 mg. of semicarbazide hydrochloride was added, and more sodium bicarbonate to slight alkalinity. The semicarbazone crystallized on shaking. It was filtered, washed with water, and recrystallized from petroleum ether. The melting point could not be raised above 119° by recrystallization or sublimation; $[\alpha]^{23}D$ −39.4 ± 2.0 (8.65 mg. in 2.0 cc. of ethanol, $\alpha^{23}D$ −0.17, 1 dm. tube).

Anal. Calcd. for $C_7H_{15}ON_3$: C, 53.46; H, 9.62; N, 26.74. Calcd. for $C_8H_{17}ON_3$: C, 56.14; H, 9.95; N, 24.58. Found: C, 53.65; H, 9.70; N, 26.76.

A mixed m. p. with the semicarbazone of 1-methylisopropylacetaldehyde from ergosterol (m. p. 128) melted at 120–122°.

Brassicasteryl Acetate-22,23-dibromide.—Brassicasteryl acetate tetrabromide (180 mg.) was debrominated with sodium iodide by the method used for stigmasteryl acetate tetrabromide.[6] The product was crystallized from ethanol–benzene, m. p. 236–238°.

Anal. Calcd. for $C_{30}H_{48}O_2Br_4$: Br, 42.1. Calcd. for $C_{30}H_{48}O_2Br_2$: Br, 26.7. Found: Br, 27.9.

Summary

On ozonizing brassicasteryl acetate, a C_{22} acid,

(6) THIS JOURNAL, **61**, 2956 (1939).

(7) Analyses herein reported are by Mr. J. F. Alicino, Fordham University.

β-3-hydroxy-bisnorcholenic acid, and a C_6 aldehyde are obtained. The empirical formula of brassicasterol is therefore $C_{28}H_{46}O$.

The C_6 aldehyde appears to be a partially racemized 1-methylisopropyl-acetaldehyde, which is a degradation product of ergosterol.

The structural formula of 7,8-dihydroergosterol is proposed for brassicasterol.

NEW BRUNSWICK, NEW JERSEY
RECEIVED NOVEMBER 27, 1939

[CONTRIBUTION FROM THE SQUIBB INSTITUTE FOR MEDICAL RESEARCH, DIVISION OF ORGANIC CHEMISTRY]

The Vitamin K Activity of Naphthoquinones

BY ERHARD FERNHOLZ, S. ANSBACHER AND H. B. MACPHILLAMY

Soon after McKee, *et al.*,[1] reported that vitamins K_1 and K_2 have a quinoid structure, publications from various laboratories appeared on the vitamin K activity of naphthoquinones. Because of its outstanding potency 2-methyl-1,4-naphthoquinone and its derivatives have been investigated most thoroughly. A discussion of the pertinent literature concerning this compound has been presented in a foregoing publication.[2] A suggestion also has been made to use 2-methyl-1,4-naphthoquinone as a basic standard for the assay of vitamin K;[3] under the conditions used in our laboratory one milligram contains 2000 units.

The following summarizes our assay results with other naphthoquinones: inactive, 1,2-naphthoquinone; weakly active in a dose of one milligram, 2,6-dimethyl, 2-allyl-, 2,3-diallyl-, 2-*n*-hexadecyl-,2-*n*-octadecyl-1,4-naphthoquinone; one unit per milligram, 1,4-naphthoquinone, 2-ethyl-, 2-propyl-, and 2-methyl-3-*n*-octadecyl-1,4-naphthoquinone; 20 units per milligram, 2,3-dimethyl-1,4-naphthoquinone; 70 units per milligram, 2-methyl-3-phytyl-1,4-naphthoquinone(vitamin K_1).

Thayer, *et al.*,[4] reported that 1,2-naphthoquinone is inactive whereas 1,4-naphthoquinone is active in a dose of 1 mg.; our results confirm this report. Almquist and Klose,[5] however, stated that they had obtained entirely negative results with the latter compound. The interesting contrast between the comparatively active 2,3-dimethyl-1,4-naphthoquinone and the rather weakly active 2,6-dimethyl-1,4-naphthoquinone[6] has been reported also by Tishler and Sampson.[7] There is some uncertainty concerning the activity of 2-ethyl-1,4-naphthoquinone. Thayer, *et al.*,[4] state that it is fully active at a level of 125 γ, and according to Tishler and Sampson it shows activity above 200 γ. In our experience the compound is not nearly as active as reported by Thayer, *et al.*, since 1 mg. was found to be necessary to give a unit response. The propyl derivative has been assayed and found inactive at a level of 0.4 mg.;[7] we found it active in a dose of 1 mg. Fieser, *et al.*,[8] originally reported that 2-allyl-1,4-naphthoquinone is very active but Thayer, *et al.*,[4] stated in the same issue of THIS JOURNAL that the compound was inactive in a dose of 2 mg. In a later paper Fieser, *et al.*,[9] agreed with Thayer. We also found that 2-allyl-1,4-naphthoquinone and 2,3-diallyl-1,4-naphthoquinone have little, if any, activity at a level of 1 mg. We have prepared and assayed the *n*-hexadecyl, *n*-octadecyl, and 2-methyl-3-octadecyl-1,4-naphthoquinones. These compounds have shown rather low potencies.[10] The last of the three, containing the methyl group in the 2-position, is definitely more active than the two others.

The long-chain naphthoquinones were prepared by chromic acid oxidation of the corresponding hydrocarbons. With the exception of the *n*-octadecyl compound, substitution of the naphthalene nucleus in the β-position was ensured by using the method of Barbot[11] for the production of β-substituted tetralin ketones. The ketones were reduced by the Clemmensen

(1) McKee, Binkley, MacCorquodale, Thayer and Doisy, THIS JOURNAL, **61**, 1295 (1939).

(2) Ansbacher, Fernholz and Dolliver, THIS JOURNAL, **62**, 155 (1940).

(3) Thayer, Binkley, MacCorquodale, Doisy, Emmet, Brown and Bird, *ibid.*, **61**, 2563 (1939).

(4) Thayer, Cheney, Binkley, MacCorquodale and Doisy, THIS JOURNAL, **61**, 1932 (1939).

(5) *Ibid.*, **61**, 2557 (1939).

(6) We are indebted to Professor Fieser for sending us samples of these two substances as well as of allyl-naphthoquinone and diallyl-naphthoquinone.

(7) *Ibid.*, **61**, 2563 (1939).

(8) Fieser, Bowen, Campbell, Fry and Gates, *ibid.*, **61**, 1926 (1939).

(9) Fieser, Campbell and Fry, THIS JOURNAL, **61**, 2206 (1939).

(10) After this paper had been submitted a paper by Fieser [THIS JOURNAL, **61**, 3467 (1939)] appeared wherein it is postulated that vitamin K activity begins to appear as the alkyl groups are increased in size. Obviously our results do not support this idea.

(11) Barbot, *Bull. soc. chim.*, [4] **47**, 1314 (1930).

method and the resulting hydrocarbons dehydrogenated with sulfur to give the desired alkylnaphthalenes. In the case of the *n*-octadecyl derivative, naphthalene was substituted directly and the mixture of α- and β-naphthalene ketones separated according to the directions of Seidel and Engelfried.[12]

The starting material used in the preparation of the 2-methyl-3-octadecyl derivative was prepared by the catalytic hydrogenation of 2-methylnaphthalene to the corresponding tetralin derivative. That the product thus obtained is 2-methyl-5,6,7,8-tetrahydronaphthalene has been shown by Schroeter[13] and by Fieser and Jones.[14] Since condensation of this substance with stearyl chloride would lead to substitution only in the 3-position, experiments to prove the structure of this compound were not carried out.

We reported recently[15] that the minimum effective dose of vitamin K_1 depends much more on the assay period than does that of 2-methyl-1,4-naphthoquinone or of alfalfa concentrates prepared and investigated by us. While 15 γ of vitamin K_1 is required in our six-hour assay, only 1γ is needed if the test period is prolonged to eighteen hours. In similar fashion it is possible, therefore, that the activity of the long-chain naphthoquinones may be greater if an eighteen hour or longer test period is used. Although the number of naphthoquinones which could be tested for vitamin K activity could be greatly increased, from the present investigation it does not appear likely that the preparation of such compounds would lead to the discovery of a substance surpassing in activity 2-methyl-1,4-naphthoquinone.

Experimental Part

2-*n*-Pentadecyl-5,6,7,8-tetrahydronaphthyl Ketone.—The acid chloride[16] from 15 g. of palmitic acid was decanted into 100 cc. of carbon disulfide containing 8 g. of tetralin. Gradually 8 g. of anhydrous aluminum chloride was added and the reaction mixture allowed to stand overnight. After evaporating the carbon disulfide, the residue was decomposed with ice water and extracted with ether. The ether extract was washed with dilute alkali and dried over anhydrous sodium sulfate. The ether was removed and the remaining oil was distilled at 130–140° (about 1 mm.). The distillate solidified on cooling and was recrystallized from acetone. The yield was 12 g. (56%) of white crystals melting at 44–45°.

Anal. Calculated for $C_{26}H_{42}O$: C, 84.3; H, 11.4. Found: C, 84.2; H, 11.2.

2-*n*-Hexadecyl-5,6,7,8-tetrahydronaphthalene.—Ten grams of the above ketone was reduced according to the modification of the Clemmensen method described by Mikeska, *et al.*[16] The final product was distilled at 210–215° (about 1 mm.), yield 6 g. (63%) of hydrocarbon.

Anal. Calculated for $C_{26}H_{44}$: C, 87.6; H, 12.4. Found: C, 88.0; H, 12.1.

2-*n*-Hexadecylnaphthalene.—The above hydrocarbon was subjected to sulfur dehydrogenation according to the directions of Barbot.[11] Five grams of the tetralin derivative and 3 g. of sulfur were heated to 200–210° for five hours. The product was extracted with ether and the ethereal solution washed with dilute alkali. On evaporation of the dried solution an oil remained which distilled *in vacuo* at about 200° (1 mm.). The distillate solidified on cooling and was recrystallized from ether–methanol mixture giving about 1 g. (20%) of material melting at 45–46°.

Anal. Calculated for $C_{26}H_{40}$: C, 88.56; H, 11.44. Found: C, 88.24; H, 11.68.

2-*n*-Hexadecyl-1,4-naphthoquinone.—A solution of 1.5 g. of chromic acid in 3 cc. of 50% acetic acid was added dropwise to a suspension of 0.5 g. of 2-*n*-hexadecylnaphthalene in 10 cc. of glacial acetic acid. The reaction mixture was stirred rapidly during the addition. The temperature was then raised to 60° and the agitation continued for 1.5 hours at this temperature. The reaction mixture was then diluted with water and extracted with ether. The ethereal solution was washed with dilute alkali and dried over anhydrous sodium sulfate. After removal of the ether the solid yellow residue was crystallized from a small amount of ether yielding 0.2 g. (37%) of quinone melting at 80–81°.

Anal. Calculated for $C_{26}H_{38}O_2$: C, 81.6; H, 10.0. Found: C, 81.6; H, 10.3.

2-*n*-Octadecyl-1,4-naphthoquinone.—The compound was prepared as described for the above quinone. Four grams of 2-*n*-octadecylnaphthalene[16] (m. p. 58–59°) upon oxidation with 10 g. of chromic acid gave 1 g. (23%) of quinone melting at 84–85°.

Anal. Calculated for $C_{28}H_{42}O_2$: C, 81.9; H, 10.3. Found: C, 81.7; H, 10.4.

Methyl-3-*n*-heptadecyl-5,6,7,8-tetrahydronaphthyl Ketone.—This substance was prepared from 2-methyl-5,6,7,8-tetralin and stearyl chloride as described in the preparation of 2-pentadecyl tetrahydronaphthyl ketone. A yield of 5.0 g. (36%) of the ketone was obtained from 2.5 g. of 2-methyl tetralin and 5 g. of stearic acid. The material was crystallized from acetone, m. p. 64–65°.

Anal. Calculated for $C_{29}H_{48}O$: C, 84.4; H, 11.7. Found: C, 84.6; H, 11.6.

2-Methyl-3-*n*-octadecyl-5,6,7,8-tetrahydronaphthalene.—The above ketone was reduced as described for the preparation of 2-octadecylnaphthalene; 3.5 g. of ketone yielded 2.5 g. (72%) of hydrocarbon. The final product after recrystallization from ether–methanol mixture melted at 60–61°.

Anal. Calculated for $C_{29}H_{50}$: C, 87.4; H, 12.6. Found: C, 87.3; H, 12.8.

(12) Seidel and Engelfried, *Ber.*, **69**, 2584 (1936).
(13) Schroeter, *Ber.*, **54**, 2247 (1921).
(14) Fieser and Jones, THIS JOURNAL, **60**, 1940 (1938).
(15) Ansbacher, Fernholz and MacPhillamy, *Proc. Soc. Exp. Biol. Med.*, **42**, 655 (1939).
(16) Mikeska, Smith and Lieber, *J. Org. Chem.*, **2**, 449 (1938).

2-Methyl-3-*n*-octadecylnaphthalene.—Two grams of the above hydrocarbon was subjected to sulfur dehydrogenation as already described for the preparation of 2-hexadecylnaphthalene. After crystallization from acetone 0.7 g. (35%) of a product was obtained melting at 47–48°.

Anal. Calculated for $C_{29}H_{46}$: C, 88.25; H, 11.75. Found: C, 88.60; H, 11.30.

2-Methyl-3-*n*-octadecyl-1,4-naphthoquinone.—The oxidation of 0.5 g. of the above hydrocarbon with chromic acid gave 0.2 g. (37%) of quinone which melted at 95–97° after recrystallization from ether.

Anal. Calculated for $C_{29}H_{44}O_2$: C, 82.0; H, 10.4. Found: C, 81.7; H, 10.2.

Summary

The preparation and vitamin K activity of a number of naphthoquinones is described. None of these compounds surpasses or even approaches 2-methyl-1,4-naphthoquinone in activity.

NEW BRUNSWICK, NEW JERSEY
RECEIVED DECEMBER 13, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

o-Halide Synthesis of 10-Methyl-1′,9-methylene-1,2-benzanthracene

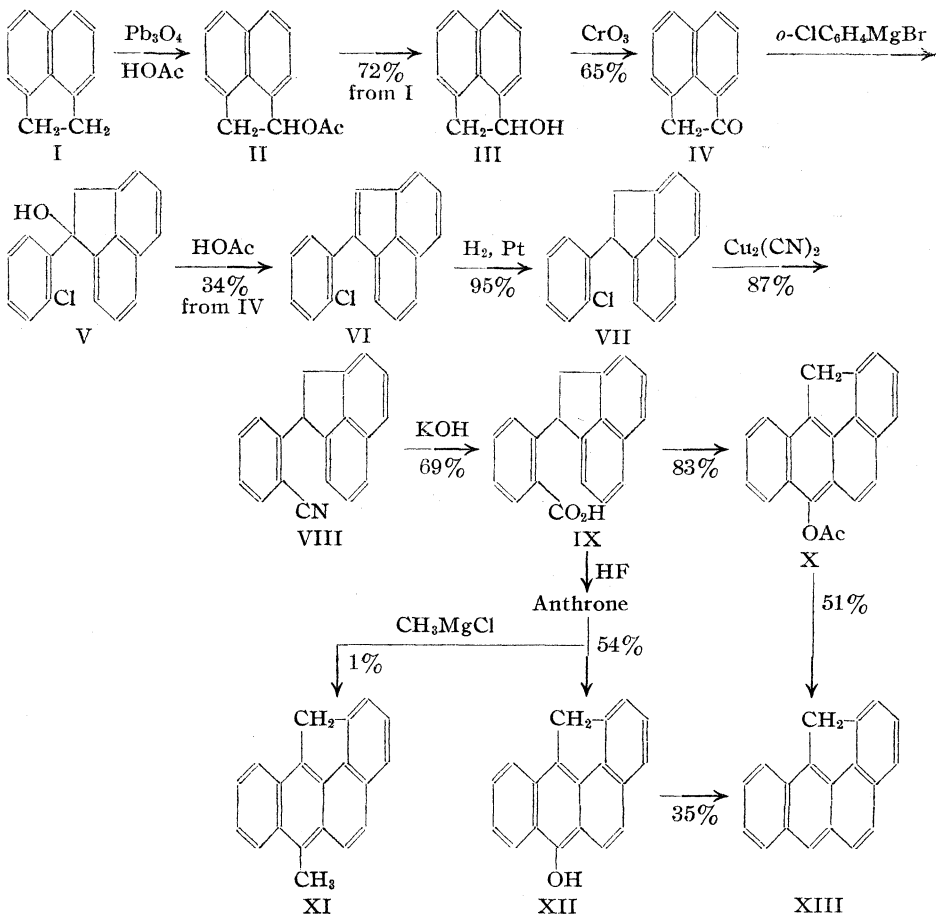
BY LOUIS F. FIESER AND JAMES CASON[1]

Since attempts to introduce methyl or hydroxyl groups into the interesting and reactive 1′,9-methylene-1,2-benzanthracene[2] (XIII) by direct substitution offered little promise of success a second synthesis was investigated which affords a route not only to the parent hydrocarbon but to various 10-substituted derivatives. The method embodies the general scheme of synthesis of anthracene derivatives introduced by one of us and Seligman.[3] This involves the preparation, through a Grignard reaction and reduction, of a suitable *o*-halide of a diphenylmethane, conversion through the nitrile to the acid and ring closure. The halogen may be introduced in various sequences into either aromatic ring, giving considerable flexibility to the method.

For the present application of the *o*-halide synthesis 7-acenaphthenone (IV) was required as starting material, and as the ketone heretofore has been accessible only by quite laborious processes,[4] a new method was sought. Marquis[5] observed that the corresponding alcohol is produced in low yield in the form of the acetate by the oxidation of acenaphthene with lead dioxide in acetic acid, and in connection with a study of the action of lead tetraacetate on other hydrocarbons[6] Dr. E. B. Hershberg noted that 7-acenaphthenyl acetate can be obtained more smoothly with the use of this reagent.[7] M. E. Gross then worked out a practical procedure for conducting the oxidation and this was employed initially in the present investigation. The experience of treating quantities of red lead with acetic acid for the preparation of a reagent for use in this solvent suggested that the operation might be dispensed with, and indeed it was found that acenaphthene can be converted smoothly and easily into the 7-acetoxy compound with red lead and acetic acid. The yield is equal to that obtained with purified lead tetraacetate, and considerable time is saved. The acetate is a liquid and is not easily freed from traces of acenaphthene and acenaphthenone, but pure crystalline 7-acenaphthenol is readily obtained in good over-all yield on saponification. Under the most favorable conditions found, oxidation with chromic acid and steam distillation of the product gave the pure ketone in reasonably good yield, and by this sequence of reactions 7-acenaphthenone is obtainable in quantity from the hydrocarbon in 47% over-all yield.

The further stages of the synthesis are indicated in the chart. The carbinol (V) resulting from the action of *o*-chlorophenylmagnesium bromide on 7-acenaphthenone was obtained in a crystalline condition only with considerable loss; the dehydration of the crude reaction product with acetic acid proceeded smoothly enough but in rather low over-all yield. The unsaturated compound VI crystallizes in brilliant orange prisms, while its dihydride VII is a colorless solid of lower

(1) Research Fellow on funds from the National Cancer Institute.
(2) Fieser and Cason, THIS JOURNAL, **61**, 1740 (1939).
(3) Fieser and Seligman, *ibid.*, **61**, 136 (1939).
(4) Ewan and Cohen, *J. Chem. Soc.*, **55**, 580 (1889); Graebe and Gfeller, *Ann.*, **276**, 12 (1893); Graebe and Jequier, *ibid.*, **290**, 197 (1896); Badische Anilin u. Soda-Fabrik, German Patent 230,237 (1910); Ghigi, *Gazz. chim. ital.*, **68**, 184 (1938).
(5) Marquis, *Compt. rend.*, **182**, 1227 (1926).
(6) Fieser and Hershberg, THIS JOURNAL, **60**, 1893, 2542 (1938).
(7) Our results appear to be at variance with the observations reported by Monti, *C. A.*, **33**, 9316 (1939).



melting point. Conversion to the nitrile VIII proceeded well, and saponification of this rather hindered derivative was accomplished satisfactorily by refluxing with alcoholic alkali for a prolonged period (ten days). Decomposition occurred at higher temperatures, and other methods of hydrolysis were tried without success. The acid IX was cyclized in good yield to 10-acetoxy-1′,9-methylene-1,2-benzanthracene (X) by the zinc chloride–acetic acid–anhydride procedure,[8] and the acetate on reduction with zinc and alkali afforded 1′,9-methylene-1,2-benzanthracene (XIII), identical with the material previously described.[2] The over-all yield from acenaphthene in ten steps is 3.8%, as compared with 3.4% by the previous five-step synthesis.[2]

For the preparation of the 10-methyl compound XI it was desirable to effect cyclization of the acid IX under conditions most favorable for retaining the product in the anthrone form and avoiding enolization. The hydrogen fluoride method[9] appears superior to any other and has given good service in the synthesis of simpler 10-alkyl-1,2-benzanthracenes (56% yield), while the introduction of 9-alkyl groups is beset by greater difficulties and the yields are lower (14–35%[10]). The present case seems to be the most unfavorable yet encountered, for in a number of experiments under varying conditions cyclization of IX with hydrogen fluoride and treatment of the crude or crystallized product with methyl Grignard reagent afforded the hydrocarbon XI in no better than 1.2% yield, the bulk of the material being recovered as the crystalline anthranol XII. The anthranol is a sensitive substance and the yield on reduction to the parent hydrocarbon is lower than when the more stable acetate X is employed. By using adequate amounts of materials, a small supply of pure, pale orange 10-methyl-1′,9-methylene-1,2-benzanthracene (XI), m. p. 181–181.4°, was obtained and the hydrocarbon is being tested for carcinogenic activity, along with the 10-hydroxy compound XII.

(8) Fieser and Hershberg, THIS JOURNAL, **59**, 1028 (1937).
(9) Fieser and Hershberg, *ibid.*, **61**, 1272 (1939).
(10) Fieser and Hershberg, *ibid.*, **62**, 49 (1940).

The new hydrocarbon is of special interest because of its structural relationship to the potently carcinogenic 9,10-dimethyl-1,2-benzanthracene.[11]

Experimental Part[12]

7-Acenaphthenol (With M. E. Gross).—The "95% acenaphthene" (m. p. 92.5–93.5°) supplied by the Reilly Tar and Chemical Co. proved to be just as satisfactory for the preparation as recrystallized material (m. p. 93–93.5°) or a purer commercial grade (m. p. 93–93.5°). A solution of 154 g. of the crude hydrocarbon in 1.1 l. of glacial acetic acid (distilled over permanganate) was stirred mechanically at a temperature of 60–70° (maintained throughout the reaction) and treated with 820 g. of red lead (85–90%), added in 50-g. portions in the course of about forty minutes, a fresh addition being made on discharge of the red coloration. Very shortly after the addition of the oxidizing agent the test for lead tetraacetate with moistened starch–iodide paper was negative and the dark red, viscous solution was thereupon poured into 2 liters of water. The precipitated oil was extracted with 350 cc. of ether and then with 250 cc. of this solvent, and the washed extract was shaken with saturated sodium chloride solution and filtered through a layer of anhydrous sodium sulfate. After removal of the solvent, the **7-acenaphthenyl acetate** was distilled at 5 mm., b. p. 166–168° from a bath at 180–185°; the yield of material (containing small amounts of acenaphthene and acenaphthenone) was 170–175 g. The result was the same using lead tetraacetate.

For hydrolysis the acetate was refluxed with 40 g. of sodium hydroxide in 400 cc. of water and 275 cc. of methanol for two hours. Crystalline acenaphthenol began to separate almost immediately and the liquor acquired a dark violet color probably due to the presence of acenaphthenone. After cooling to 20° the product was collected, washed well with water, dried and recrystallized from benzene, using 2 liters of solvent, and after clarification with Norite concentrated to a volume of 1 liter. The first crop amounted to 117–121 g. of pure acenaphthenol in the form of colorless needles, m. p. 144.5–145.5°, unchanged on further crystallization from benzene or alcohol, and the mother liquor afforded 3–5 g. of pure material; yield 70.5–74% (from acenaphthene). The melting points 146°[13] and 148°[5] have been reported.

7-Acenaphthenone (With M. E. Gross).—A suspension of 100 g. of acenaphthenol in 300 cc. of glacial acetic acid was stirred mechanically and treated with a solution prepared by dissolving 43 g. of chromic anhydride in the minimum amount of water and diluting with 240 g. of acetic acid. The solution was added in the course of fifty minutes while maintaining a reaction temperature of 28–32° by external cooling. The acenaphthenol dissolved giving a green solution and, after stirring for an additional hour at the same temperature, this was poured into 6 liters of ice water and the precipitated ketone collected on a large Büchner funnel and washed well with water. As purification by direct crystallization or by vacuum distillation proved unsatisfactory, the moist product was distilled with steam, a method which proved very satisfactory. The distillate (35 liters) was cooled below 20° and the practically colorless ketone collected and dried. The acenaphthenone thus obtained melted at 118.5–120.5° and was satisfactory for the synthesis; the average yield in three runs was 64.5 g. (65%). Recrystallization from benzene–hexane (1:4) gave colorless needles, m. p. 121–121.5°.

7-(*o*-Chlorophenyl)-acenaphthylene (VI).—After trying numerous variations the following procedure was adopted as the most satisfactory. A solution of 45 g. of acenaphthenone in 125 cc. of benzene and 70 cc. of ether was added in fifteen minutes to the Grignard reagent from 7.8 g. of magnesium, 67.6 g. of *o*-bromochlorobenzene and 250 cc. of ether. After refluxing and stirring for forty-five minutes longer, the complex was decomposed with 55 cc. of saturated ammonium chloride solution and the benzene–ether layer was decanted from the pasty salt mass. By distilling most of the solvent and triturating the residue with hexane, crude **7-(*o*-chlorophenyl)-acenaphthenol-7** (V) was obtained as an almost colorless powder. By recrystallization from benzene the carbinol was obtained as colorless, elongated prisms, m. p. 216–218° with decomposition to the orange acenaphthylene derivative, but the yield of crystalline product was only 15–20% and the material was not analytically pure. For the best over-all yield it was found expedient to dehydrate the crude product of the Grignard reaction. For this purpose the initial benzene–ether extract was concentrated on the steam cone and the solvent removed by heating to 70° at the water-pump. The reddish-orange oil remaining was refluxed with 225 cc. of glacial acetic acid for one hour and the dark solution poured into 500 cc. of water and extracted with benzene. After washing the extract free of acid it was filtered through anhydrous sodium sulfate, concentrated and passed through a 2.5 × 13-inch tower of activated alumina and Supercel (1:1). The column was washed with benzene until the dark orange zone due to the unsaturated chloro compound (which migrates rapidly) had passed into the filtrate. The column must be large enough to retain a more strongly adsorbed substance forming a broad yellow zone. The benzene in the filtrate was replaced by methanol and the product crystallized from a volume of about 350 cc. with seeding and slow cooling. This gave 20.5–22.5 g. of orange elongated prisms, m. p. 100–102° (softening at about 96°). No further crystalline material was obtained from the mother liquor on concentration, but on removing the solvent and distilling the residue at 2 mm. a red oil was obtained which yielded 3 g. of satisfactory product, m. p. 98–102°; the total yield of material suitable for the hydrogenation was 33–36%. When the total crude reaction product was distilled directly the yield fell to 15%, and attempted crystallization of material dehydrated with acetic acid but not purified by chromatographic adsorption proved difficult and unsatisfactory.

For analysis a sample of distilled material was crystallized three times from methanol and obtained as yellow-orange cubic or elongated prisms, m. p. 104–104.4°.

(11) Bachmann and Chemerda, THIS JOURNAL., **60**, 1023 (1938); Newman, *ibid.*, **60**, 1141 (1938).

(12) All melting points are corrected. Microanalyses by Lyon Southworth except as indicated.

(13) V. Braun and Bayer, *Ber.*, **59** 920 (1926).

Anal.[14] Calcd. for $C_{18}H_{11}Cl$: C, 82.25; H, 4.24; Cl, 13.52. Found: C, 82.15; H, 4.31; Cl, 13.33.

7-(*o*-Chlorophenyl)-acenaphthene (VII).—A solution of 32 g. of VI in 155 cc. of purified glacial acetic acid and 15 cc. of absolute ether was shaken with hydrogen at atmospheric pressure in the presence of 0.8 g. of Adams catalyst. The reaction was stopped after the absorption of one mole of hydrogen (three and one-half hours), for after saturation of the external double bond the aromatic nucleus is hydrogenated rather rapidly. After filtering and removing the solvent, the product distilled at 190–192° at 2 mm. (bath at 208–212°) as a light yellow oil which crystallized rapidly; yield 30.6 g. (95%). This material, m. p. 68–74°, was satisfactory for the next step. After three crystallizations from methanol a sample formed colorless elongated prisms melting constantly at 81–82°.

Anal.[15] Calcd. for $C_{18}H_{13}Cl$: Cl, 13.42. Found: Cl, 13.64.

***o*-(7-Acenaphthyl)-benzonitrile (VIII).**—A mixture of 35.6 g. of the chloro compound VII, 11.5 g. of cuprous cyanide (dried in vacuum at 100°), 3 cc. of acetonitrile and 31 cc. of pyridine was heated in an autoclave under nitrogen (initial pressure, 800 pounds) at 243–245° for twenty-five hours. (Longer heating lowers the yield: thirty-five hours, 74.5%; forty-eight hours, 66.5%; a run conducted for sixty hours at 255° gave a 20% yield of a very poor product). The reaction mixture was shaken with dilute ammonia solution and benzene and after filtering the two-phase system with suction, the benzene layer was separated, washed with ammonia solution, water and dilute hydrochloric acid, filtered by suction, and washed free of acid. The residue from the benzene solution was distilled at 3 mm., the nitrile passing over as a reddish oil at 208–212° (bath, 220–230°); yield 25.9 g. (87%). The sample for analysis was passed through a tower of alumina in benzene solution and crystallized three times from hexane. It formed small, colorless needles, m. p. 79.7–80.5°. Impure samples often melt at higher temperatures.

Anal.[15] Calcd. for $C_{19}H_{13}N$: N, 5.49. Found: N, 5.55.

***o*-(7-Acenaphthyl)-benzoic Acid (IX).**—A solution of 25.9 g. of distilled nitrile and 164 g. of potassium hydroxide in 1050 cc. of alcohol and 590 cc. of water was refluxed for 250 hours in a copper flask. The alcohol was expelled by distillation, water being added to maintain a volume of about 1200 cc., and the resulting hot aqueous solution was treated with Norite. The dark filtrate was acidified and cooled and the crude acid which separated was dried, refluxed in benzene with Norite and crystallized twice from benzene–hexane (1/1), giving 18 g. of acid crystallizing in soft, snow-white needles, m. p. 194–195°. The final mother liquor afforded 0.9 g. of pure product; total yield 69%. An additional crystallization from benzene–hexane gave a sample of constant m. p. 195–195.5°.

Anal. Calcd. for $C_{19}H_{14}O_2$: C, 83.18; H, 5.14. Found: C, 82.94; H, 5.29.

Attempts to shorten the reaction time by conducting the hydrolysis under pressure at higher temperatures resulted in extensive decomposition. After seventeen hours at 120° only 5% of acid could be isolated from the tarry product, and on heating for sixty-five hours at 100° extensive decomposition was evident and only 40% of the acid could be isolated. On one occasion the nitrile was saponified as described, but for only one hundred hours; an oil separated after distillation of the alcohol and this crystallized on prolonged scratching. Crystallization from benzene–hexane (Norite) afforded ***o*-(7-acenaphthyl)-benzamide, m. p. 177–180°,** in 32.5% yield. Three crystallizations from benzene gave nearly colorless blades, m. p. 182–182.8°.

Anal.[15] Calcd. for $C_{19}H_{15}ON$: N, 5.13. Found: N, 4.98.

The alkaline filtrate from the amide on suitable working afforded the acid in 40.5% yield. Treatment of the amide with amyl nitrite in acetic acid solution gave only a non-acidic, amorphous red material.

10-Acetoxy-1′,9-methylene-1,2-benzanthracene (X).—A mixture of 0.5 g. of the acenaphthylbenzoic acid IX, 3 cc. of glacial acetic acid, 2.5 cc. of acetic anhydride and a trace of zinc chloride was refluxed for one hour and water was added by drops to the hot solution until crystallization commenced. The acetoxy compound separated in fluffy, dull yellow plates, m. p. 171–178°; yield 0.45 g. (83%). Boiling with acetic acid caused decomposition, but alcohol proved satisfactory for recrystallization. A sample crystallized four times from this solvent formed fine, straw-colored needles, m. p. 175–179°, with softening at 171°. Further recrystallization did not give a product of sharp m. p.

Anal. Calcd. for $C_{21}H_{14}O_2$: C, 84.54; H, 4.73. Found: C, 84.66; H, 4.89.

1′,9-Methylene-1,2-benzanthracene.[2]—The acetate X (60 mg.) was reduced with zinc and alkali according to Martin[16] and the fluorescent toluene layer passed through a tower of alumina and Supercel. The material recovered from the filtrate on crystallization from alcohol afforded 15 mg. of 1′,9-methylene-1,2-benzanthracene, m. p. 122.5–123°, and 10 mg., m. p. 120–122° (51.5%). The pure sample showed no depression when mixed with the hydrocarbon prepared by the Elbs reaction.[2] Like the previous sample, the hydrocarbon appears colorless in artificial light and is a fluorescent greenish-yellow in daylight.

10-Methyl-1′,9-methylene-1,2-benzanthracene (XI).—Five grams of *o*-(7-acenaphthyl)-benzoic acid was cyclized by standing in 100 g. of anhydrous hydrogen fluoride for fifteen minutes. The dark red solution was poured onto ice and the yellow precipitate was collected, washed and dried in vacuum. Attempted crystallization of the moist product from aqueous acetone was unpromising, for although some crystals were obtained, considerable tarry material resulted. For the Grignard reaction it was found best to use the crude dried product. This was added in half-gram lots with good stirring to 5 equivalents of methylmagnesium chloride in 150 cc. of ether; after refluxing for forty-five minutes and decomposing with dilute acid, the washed ether layer was concentrated until most of the ether had been removed and taken up in about 30 cc. of hot benzene. On cooling, 2–2.5 g. (43–54%) of **1′,9-methylene-1,2-benz-10-anthranol** crystallized in slender, buff-

(14) Analysis by the Arlington Laboratories. Both this substance and its hydrogenation product are difficultly combustible.

(15) Analysis by H. S. Wight.

(16) Martin, THIS JOURNAL, **58**, 1438 (1936).

colored needles, m. p. 160–164° dec. (see below). The filtrate was taken to dryness and the residue heated briefly on the hot-plate to effect dehydration and put through an alumina–Supercel tower in benzene solution. The hydrocarbon collected from the highly fluorescent filtrate was clarified with Norite in alcohol and crystallized from about 15 cc. of this solvent, giving 50–90 mg. (1.1–1.9%) of material melting at 174–177.5°. Three further crystallizations gave a product of the constant m. p. 181–181.4°; the first crop formed fine, pale orange needles (26–47 mg.) and the mother liquors gave 10 mg. more of good material; yield of pure hydrocarbon, 0.8–1.2%.

Anal. Calcd. for $C_{20}H_{14}$: C, 94.45; H, 5.55. Found: C, 94.25; H, 5.77.

The **trinitrobenzene derivative** when prepared from pure hydrocarbon crystallized from alcohol in bright orange-red needles, m. p. 182.5–183.2°.

Anal. Calcd. for $C_{26}H_{17}O_6N_3$: N, 8.99. Found: N, 9.13.

This derivative is not suitable for use in purifying the hydrocarbon, for when the crude reaction product from the tower was treated with trinitrobenzene the complex was brown-black and melted at about 162° and was not improved on repeated crystallization. The dark red picrate is too unstable to be useful as a derivative.

Many variations were tried in the procedure of conducting the Grignard reaction. In boiling benzene or toluene, in cold benzene, or in ether at −70°, the yield was either as reported or lower. Lithium methyl in ether gave the same yield as the Grignard reagent, and the addition of the crude cyclization product in benzene rather than as a solid lowered the yield. The low yield even under the most favorable conditions seems to be due to extensive and rapid isomerization to the anthranol.

1′,9-Methylene-1,2-benz-10-anthranol (XII).—The material separated from the Grignard reaction mixture by crystallization from benzene proved to be the anthranol in an essentially pure condition. The substance is quite sensitive and rapidly turns red in boiling benzene or in cold dioxane. It is moderately soluble in ether or ligroin (b. p. 80–90°) and on three crystallizations from this solvent-pair formed pale yellow, fibrous needles, m. p. 160–164° with charring. The sample retained ligroin tenaciously and gave a satisfactory analysis only after drying for fifteen hours in high vacuum at 70°.

Anal. Calcd. for $C_{19}H_{12}O$: C, 89.03; H, 4.72. Found: C, 89.08; H, 4.85.

The substance is highly fluorescent in dilute alcoholic solution, and the addition of ferric chloride produces an orange-red coloration. Extensive decomposition occurred on attempted acetylation. The Bucherer reaction was tried at 140, 155, and 180° but gave only water-soluble products. On reduction of the anthranol with zinc and alkali, 1′,9-methylene-1,2-benzanthracene was obtained in 35% yield, and the result was the same using the crude cyclization product. That the yield was lower than from the acetate X is probably because of the great sensitivity of the anthranol and anthrone.

Summary

A synthesis has been developed for 1′,9-methylene-1,2-benzanthracene and its hitherto undescribed 10-methyl and 10-hydroxy derivatives starting with the reaction between *o*-chlorophenylmagnesium bromide and 7-acenaphthenone. A new method was found whereby the ketonic starting material can be produced readily in quantity. This consists in the oxidation of acenaphthene with red lead in acetic acid solution, saponification of the resulting 7-acetoxy compound and oxidation of 7-acenaphthenol to 7-acenaphthenone.

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RECEIVED DECEMBER 18, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF MERCK & CO., INC.]

Erythrina Alkaloids. VII. Isolation and Characterization of the New Alkaloids, Erythraline and Erythratine

BY KARL FOLKERS AND FRANK KONIUSZY

The isolation of erythramine from the seeds of *Erythrina sandwicensis* Deg. and *Erythrina subumbrans* (Hassk.) Merr. was described recently.[1] It was stated in that paper that erythramine had been isolated from other species of *Erythrina*, but that it was found associated with another alkaloid of such similar properties that its isolation was more difficult. This other new alkaloid has been named erythraline.

By fractional crystallization of the hydriodides from the crude free alkaloids of *Erythrina glauca* Willd., with particular observance of the optical rotations, pure erythraline hydriodide was isolated as the major alkaloid and pure erythramine hydriodide as a minor alkaloid. A second minor alkaloid was also isolated as the hydriodide, and since it has been also characterized as new, it has been named erythratine. It was discovered later that pure erythratine base could be easily obtained directly by crystallization of the crude bases from ethanol, and the yield was twice that

(1) Folkers and Koniuszy, THIS JOURNAL, **61**, 1232 (1939).

obtained by fractional crystallization of the hydriodides. Erythraline and erythramine hydriodides have similar solubilities in ethanol and although prepared in this solvent their separation from it was not satisfactory. However, erythraline hydriodide was less soluble in water than the erythramine and erythratine hydriodides and their separation was satisfactory. The fact that erythraline hydriodide is the least soluble, and therefore the easiest to obtain pure, signifies that this alkaloid would probably be the only one isolated in those cases where only semi-micro quantities of the crude free alkaloid bases were available. It has been desirable to restrict these studies to authentic samples of seeds[2] and, since such samples are generally small, often only semi-micro quantities of bases are available for examination. On this basis, erythraline was isolated as the hydriodide from the seeds of *Erythrina variegata* L. var. *orientalis* (L.) Merr., *Erythrina Folkersii* Kruk. and Mold., *Erythrina velutina* Willd., and *Erythrina macrophylla* DC. The isolation of erythramine and erythratine as minor alkaloids from *Erythrina glauca* was facilitated by the large quantities of seeds of this species which were available.

Because of the close botanical relationship of *Erythrina velutina* forma *aurantiaca* (Ridl.) Kruk. and *Erythrina Grisebachii* Urb. to *Erythrina velutina*, it was considered that erythraline exists also in these, although the hydriodides were not prepared and crystallized after the amount of the free bases present in the seeds was determined.

Erythraline was isolated also from the seeds of *Erythrina fusca* Lour. as the pure free base directly from the crude free alkaloidal fraction. This direct isolation of the free base was considered a manifestation of the freedom of erythraline from its closely related alkaloids in this species and the distinct character of *Erythrina fusca*. In contrast to this was the failure to isolate pure erythraline base directly from the crude free alkaloidal fraction of *Erythrina velutina*. It has been preferred generally to isolate these alkaloids as the hydriodides.

It is to be emphasized from these studies (and others, as yet unpublished) on new *Erythrina* alkaloids that melting points alone of bases and salts (decomposition point for the latter) are unreliable as proof of homogeneity or identity. Mixtures frequently melt at the same temperature as one component. Microanalyses of mixtures of these alkaloids with identical or closely related empirical formulas may be confusing. The optical rotations after crystallizations are the best guide. Consequently, the identity of an individual alkaloid is established best by the combined data of melting points, optical rotations, analyses, and other derivatives if possible.

The results of the microanalyses of the free base, the hydriodide, and the hydrobromide have established the empirical formula of erythraline as $C_{18}H_{19}NO_3$; thus, it differs from erythramine, $C_{18}H_{21}NO_3$, by only two hydrogen atoms.

The microanalyses of the free base hemihydrate, the hydriodide, and the hydrobromide were all in agreement with the empirical formula $C_{18}H_{21}NO_4$ for erythratine.

The initial studies on the constitution of erythramine have been published[3] and their continuance will be described in a forthcoming paper and with new experiments concerning the structure of erythraline.

Hypaphorine was newly isolated from the seeds of *Erythrina glauca*, *Erythrina Folkersii*, *Erythrina fusca*, *Erythrina velutina*, and *Erythrina macrophylla*, and it undoubtedly exists in *Erythrina Grisebachii* and *Erythrina velutina* forma *aurantiaca*. Hypaphorine was re-isolated from *Erythrina variegata* var. *orientalis*.[4]

The relative pharmacological potencies of these *Erythrina* alkaloids are of interest. The threshold dose of erythramine hydrobromide for curare-like paralyzation of frogs was 7 mg./kg., injected intralymphatically.[3] Dr. Klaus Unna of the Merck Institute of Therapeutic Research has reported after preliminary tests that the threshold dose of erythraline hydrobromide was 8 mg./kg. frog, and that of erythratine hydrobromide was 75 mg./kg. frog.

The species names used in this paper are in accord with the recent taxonomic revision of *Erythrina* by Mr. B. A. Krukoff.[5,6]

Experimental Part

Isolation of Erythraline and Hypaphorine

Erythrina fusca **Lour. (Tamesis 9345).**—The 980 g. of seed powder was extracted first with 1500 ml. of petroleum

(2) The identity of the *Erythrina* seeds used in these studies was established either by accompanying herbarium material, which was determined by Mr. B. A. Krukoff at the New York Botanical Garden, or by other evidence which left no doubt regarding the identity.

(3) Folkers and Koniuszy, THIS JOURNAL, **61**, 3053 (1939).

(4) Maranon and Santos, *Philippine J. Sci.*, **48**, 563 (1932).

(5) Krukoff, *Brittonia*, **3**, No. 2, 205 (1939).

(6) Krukoff, *J. Arnold Arboretum*, **20**, 225 (1939).

ether for six hours in a Soxhlet. After distillation of the solvent, the yield of the yellow fat fraction was 77 g. (7.8%). The extraction of the seed powder was then continued for thirty-six hours with two 1500 ml. portions of methanol. This extract was concentrated by distillation and finally pumped out at 30° and 18 mm. to remove the last of the methanol. The 150 g. (15.8%) of gum-like residue was dissolved in 700 ml. of water, treated with 14 ml. of concentrated hydrochloric acid, and freed of residual emulsified oil droplets by extracting first with petroleum ether, then with chloroform. The clear aqueous solution was made just alkaline with sodium bicarbonate and extracted with ten 100 ml. portions of chloroform. The yield of crude erythraline, after complete solvent removal at 30° and 18 mm., was 1.829 g. (0.19%).

The hypaphorine may be isolated by treating the alkaline aqueous solution with hydrochloric acid, etc., as described for its isolation from *Erythrina sandwicensis*.[1] Data on hypaphorine from *Erythrina fusca* are in Table III.

Erythraline Base.—The 1.829 g. of crude alkaloids was recrystallized from absolute ethanol. The first crystallization yielded 1.348 g. of gummy crystals, the second yielded crystals of m. p. 55–65° and the third yielded crystals of m. p. 106–107°. Subsequent crystallizations did not alter the melting point; it remained constant at 106–107°. The yield was 0.6731 g. (0.068%). These white crystals of pure erythraline showed $(\alpha)^{27}D$ + 211.8, C = 0.944, absolute ethanol. They were dried at 60° and 2 mm. for thirty minutes before analysis.

Anal. Calcd. for $C_{18}H_{19}NO_3$: C, 72.70; H, 6.44; N, 4.71. Found: C, 72.55; H, 6.33; N, 4.88.

Erythraline base was much more stable than erythramine base and was stored in a black vial at ordinary temperatures and pressures.

Mixed melting points of erythraline (m. p. 106–107°) and erythramine (m. p. 103–104°) were as follows: 10 parts and 1 part, respectively, m. p. 88–94°; 5 parts and 5 parts, m. p. 90–96°; 1 part, and 10 parts, m. p. 93–97°

Erythraline Hydriodide.—A quantity of 94.4 mg. of analytically pure erythraline base was dissolved in 2 ml. of absolute ethanol and 47.5 mg. of sodium iodide was added. The solution was acidified with the calculated amount of glacial acetic acid. Yellow crystals of the hydriodide formed at 25°. They melted at 252–253° with decomposition and this constant was not changed by further recrystallizations. This melting or decomposition point varies somewhat with the rate of heating the bath. In the same bath, pure erythramine hydriodide melted at 245–245.5°, and the mixed salts melted at 247–249°, each with decomposition. Erythraline hydriodide showed $[\alpha]^{31}D$ + 177°, C = 0.322, water. A sample was dried at 25° and 2 mm. before analysis.

Anal. Calcd. for $C_{18}H_{19}NO_3 \cdot HI$: C, 50.83; H, 4.74; N, 3.29. Found: C, 51.01; H, 4.78; N, 3.38.

Erythraline Hydrobromide.—A quantity of 100 mg. of analytically pure erythraline was dissolved in 3 ml. of absolute methanol, acidified with 40% hydrobromic acid, and brought to the crystallization point with anhydrous ether. After twelve hours at 10°, white, granular crystals formed. They melted at 243° and showed $[\alpha]^{27}D$ +216.6, C = 0.500, water. The salt was dried at 25° and 30 mm. before analysis.

Anal. Calcd. for $C_{18}H_{19}NO_3 \cdot HBr$: C, 57.15; H, 5.32. Found: C, 57.30; H, 5.28.

Isolation of Erythraline, Erythramine and Erythratine

Erythrina glauca Willd. (Wortley 9242.)—A 10-kg. quantity of powdered seeds was extracted. The fourteen hours of extraction with petroleum ether yielded 940 g. (9.4%) of the fatty fraction. The thirty-three hour extraction with methanol yielded 1660 g. (16.6%) of a thick green gum. This gum was dissolved in 6 liters of water, made just acid to congo red with 100 ml. of concentrated hydrochloric acid, and clarified first with petroleum ether and then chloroform. Five liters of the clear solution was made alkaline with sodium bicarbonate at 10–15° and then extracted continuously with chloroform for five hours. The chloroform residue, which was pumped out at 30° and 2 mm. for four hours, weighed 19.3 g. (0.15%).

The 19.3 g. of crude alkaloidal bases was dissolved in 40 ml. of absolute ethanol and treated with 9.65 g. of sodium iodide and 3.86 g. of glacial acetic acid. After standing at 10° for twelve hours, 9.31 g. of mixed yellow hydriodides were obtained. Recrystallization of these hydriodides from 95% ethanol gave the following results: first crop, Fraction A, 5.45 g., m. p. 242–244.5°; $[\alpha]^{27}D$ +196.4; second crop, Fraction B, obtained by concentrating the mother liquor to one-half the volume, 0.341 g., m. p. 241–243°; $[\alpha]^{27}D$ +200.8; third crop, Fraction C, obtained by concentrating the mother liquor to one-half the volume, 0.99 g., m. p. 242°; $[\alpha]^{26}D$ +119°. The third crop or Fraction C was not only markedly different in optical rotation, but was white in color whereas the first two crops were yellow-orange in color. Table I contains the data on the fractional crystallization of 238.3 mg. of Fraction A.

TABLE I

CRYSTALLIZATIONS ON FRACTION A

Crystallization from water	Starting amt., mg.	Amt. recov., mg.	$[\alpha]^{25-28}D$, water	M. p., °C.	Fraction
First	238.3	188.0	+191.3	242	
	2nd Crop	13.8	+221	242	D
Second	168.0	132.0	+187.9	245	
Third	106.0	102.0	+176.9	249	E
Fourth	73.0	70.0	+177	249	F

Fraction D was shown by the physical constants to be pure erythramine hydriodide.[1] Larger amounts of erythramine hydriodide were obtained from the balance of Fraction A. A yield of 0.003% was obtained (based on seed powder).

Fractions E and F were shown by the physical constants to be pure erythraline hydriodide. A yield of 0.03% was obtained. A sample for analysis was dried at 25° and 2 mm.

Anal. Calcd. for $C_{18}H_{19}NO_3 \cdot HI$: C, 50.83; H, 4.74; N, 3.29. Found: C, 50.68; H, 4.77; N, 3.16.

Fraction B was found to be a mixture of erythraline and erythramine hydriodides.

The data on Fraction C are in Table II.

Erythratine Hydriodide.—Fraction G of Table II, which had constant properties, was recognized as a new

TABLE II

CRYSTALLIZATIONS ON FRACTION C

Solvent	Starting amt., mg.	Amt. recov., mg.	$[\alpha]^{25-28}D$, water	M. p., °C.	Fraction
95% ethanol	99.0	79.2	+110.2	242–242.5	
Water	75.2	61.0	+108.4	242–242.5	
Water	56.1	47.9	+109.0	242–242.5	G

alkaloid and the base was named erythratine. A yield of 0.007% was obtained.

Anal. Calcd. for $C_{18}H_{21}NO_4 \cdot HI$: C, 48.66; H, 4.99; N, 3.15. Found: C, 48.67; H, 5.10; N, 3.13.

Direct Isolation of Erythratine Base.—It was discovered later that when the crude free alkaloidal fraction of *Erythrina glauca* (Wortley 9242) was dissolved in 95% ethanol, and allowed to stand, the erythratine base crystallized in a fairly pure condition. The 23.7 g. of crude alkaloidal bases from 12 kg. of seeds was dissolved in 72 ml. of 95% ethanol. On standing, crystals formed; yield, 2.7542 g. of m. p. 167.5–168° and $[\alpha]_D$ +138.6, absolute ethanol. They were recrystallized twice by dissolving in 20 ml. of absolute ethanol, distilling to 8 ml., and adding petroleum ether to incipient crystallization. The final yield of pure erythratine hemihydrate base was 2.16 g. (0.018%); m. p. (and mixed with base derived from the isolated hydriodide) 170°; $[\alpha]^{28}D$ +145.5, C = 0.371, absolute ethanol. The sample was dried at 100° and 0.01 mm. for twenty minutes for analysis.

Anal. Calcd. for $C_{18}H_{21}NO_4 \cdot {}^1/_2H_2O$: C, 66.66; H, 6.83. Found: C, 66.46; H, 7.02.

Erythratine hemihydrate base was more stable than either erythramine or erythraline, the crystals remaining pure on standing for over six months.

Erythratine Hemihydrate Base.—A sample of 296.9 mg. of pure erythratine hydriodide was converted to the free base by dissolving in water, adding sodium bicarbonate, and extracting with chloroform. Experiments with the *Erythrina* free bases are best done with bases so obtained. The pumped out base (210.6 mg.) was a clear gum. It was dissolved in 30 ml. of anhydrous ether and 10 ml. of petroleum ether was added. Flocculent material was filtered, and after concentration to 10 ml., white crystals formed. They melted at 168–169° and through four recrystallizations from anhydrous ether the constant value, m. p. 170–170.5°, was obtained. The crystals were dried at 25° and 2 mm. for analyses, $[\alpha]^{25}D$ +144.9, C = 0.159, absolute ethanol.

Anal. Calcd. for $C_{18}H_{21}NO_4 \cdot {}^1/_2H_2O$: C, 66.66; H, 6.83; N, 4.31. Found: C, 66.21; H, 6.61; N, 4.53.

The erythratine hemihydrate could not be converted to the anhydrous base by drying at 140° and 0.01 mm. for four hours. Less drastic conditions did not materially dehydrate the hemihydrate.

A sample of the pure erythratine hemihydrate was converted back to the hydriodide, and the properties were the same as those of the starting hydriodide; $[\alpha]^{26}D$ +113.3.

Anal. Calcd. for $C_{18}H_{21}NO_4 \cdot HI$: C, 48.66; H, 4.99; I, 28.65. Found: C, 48.49; H, 5.08; I, 28.82.

Erythratine Hydrobromide.—A sample of 50 mg. of pure erythratine hemihydrate was dissolved in 1 ml. of absolute ethanol and the solution was acidified with two drops of concentrated hydrobromic acid. The yield of hydrobromide was 39 mg., m. p. 241°. Recrystallization yielded 21.4 mg. of m. p. 241° also, $[\alpha]^{25}D$ +158.7, C = 0.258, water. The salt was dried at 25° and 30 mm. for analysis.

Anal. Calcd. for $C_{18}H_{21}NO_4 \cdot HBr$: C, 54.56; H, 5.59;

TABLE III

DATA ON THE ISOLATION OF ALKALOIDS FROM SPECIES OF *Erythrina*

Plant	Collectors' names, specimens, numbers and source	Seeds, g.	Fatty fraction, %	Alcohol residue, %	Hypaphorine hydrochloride, %	Crude free alkaloid fraction,[a] %	Identity and authenticity of alkaloids
E. glauca Willd.	Haigh 9170 (Ceylon)	200.0	13.3	14.0[b]	0.16	0.40[c]	*d*
E. glauca Willd.	P. Campos Porto 9199 (Brazil)	9.4	8.8	18.2[e]	..	.33[f]	..
E. glauca Willd.	A. Dugand 9203 (Colombia)	50.7	9.9	15.9[e]	0.9	.38[c]	..
E. glauca Willd.	Wortley 9242 (Trinidad)	10 kg.	9.4	16.6[e]	..	.19[f]	*g*
E. glauca Willd.	Wortley 9242 (Trinidad)	12 kg.	7.7	19.7[e]	..	.19[f]	..
E. glauca Willd.	Wortley 9242 (Trinidad)	5 kg.	8.6	..	..	.25[f]	..
E. Folkersii Kruk. and Mold.	Kinloch 9163 (British Honduras)	63.0	15.0	10.3[b]	1.3	..	..
E. Folkersii Kruk. and Mold.	Kinloch 9167 (British Honduras)	200.0	15.3	12.0[b]	2.2	..	..
E. Folkersii Kruk. and Mold	Kinloch 9167 (British Honduras)	650.0	15.4	16.3[e]	..	.074[f]	*h*
E. variegata L. var. *orientalis* (L.) Merr.	Otero 9131 (Puerto Rico)	100.0	12.4	6.4[b]	2.2	.04[c]	*i*
E. variegata L. var. *orientalis* (L.) Merr.	Canicoza 9152 (Philippine Is.)	586.2	10.9	4.8[b]	1.3	.009[c]	*i*
E. variegata L. var. *orientalis* (L.) Merr.	H. Smith 9176 (Tahiti)	370.0	*k*	15.4	..	*k*	..
E. variegata L. var. *orientalis* (L.) Merr.	*j*	700.0	13.4	17.4[e]	..	0.035	*l*
E. fusca Lour.	Philippine Forest Service 9153	150.0	6.8	8.1[b]	0.94	.071[f]	..
E. fusca Lour.	Tamesis 9345 (Philippine Is.)	980.0	7.8	15.8[e]	..	.19[f]	*g*
E. velutina Willd.	Vasconcellos Sobrinho 9263 (Brazil)	650.0	9.2	20.0[e]	2.0	.321[f]	*m*
E. velutina Willd.		650.0	14.4	16.3[e]	..	.290[f]	*n*
E. velutina Willd.	Gomez Parente 9169 (Brazil)	50.0	9.6	13.0[b]	1.72	.195[c]	..
E. velutina forma *aurantiaca* (Ridl.) Kruk.	Rocha 9272 (Brazil)	50.0	15.2	22.4[e]	..	.255[f]	*o*
E. Grisebachii Urb.	Walsingham 9316 (Cuba)	50.0	12.0	12.6[e]	..	.195[f]	*o*
E. macrophylla DC.	Armstrong 9442/52, 53	800.0	12.2	24.0[e]	3.5	.225[f]	*p*

[a] It is recommended that the crude free alkaloid fraction be extracted before the hypaphorine hydrochloride is removed exactly as described in detail for *E. fusca* and *E. glauca*. This method is called the "preferred procedure" and the percentage figure obtained for the crude free alkaloid fraction expresses quite accurately the amount actually present. The

"alternative procedure," which consisted of the removal of the hypaphorine hydrochloride before the extraction of the crude free alkaloids, gives a slightly high value for the percentage of the crude free alkaloids because of the introduction of other substances. [b] Extracted with 95% ethanol. [c] By the "alternative procedure." See note *a*. [d] Erythraline hydriodide; m. p. 247°; $[\alpha]^{28}D$ +179.2, water. *Anal.* Calcd. for $C_{18}H_{19}NO_3 \cdot HI$: C, 50.83; H, 4.74. Found: C, 50.72; H, 5.18. Thus, the alkaloid in the seeds from Ceylon does not differ from the alkaloid in the seeds from Trinidad. The mother liquors from erythraline hydriodide were not examined further because of the small amount available. [e] Extracted with absolute methanol. It is generally preferred because of greater extracting power. [f] By the "preferred procedure." See note *a*. [g] See Expt. Part. [h] The 481.2 mg. of crude free alkaloids was dissolved in 0.4 ml. of absolute ethanol and treated with 240 mg. of sodium iodide and 94 mg. of glacial acetic acid. The 80.1 mg. of mixed hydriodides containing a little sodium acetate was recrystallized; yield, 20 mg., m. p. 239.5–241°, $[\alpha]^{28}D$ +197.2. *Anal.* Calcd. for $C_{18}H_{19}NO_3 \cdot HI$: C, 50.83; H, 4.74. Calcd. for $C_{18}H_{21}NO_3 \cdot HI$: C, 50.60; H, 5.15. Found: C, 51.01; H, 5.38. These properties are those of mixed erythraline and erythramine hydriodides. Two more recrystallizations from water yielded pure erythraline hydriodide, $[\alpha]^{26}D$ +178. The first mother liquor from the 20 mg. yielded crude erythramine hydriodide of $[\alpha]^{26}D$ +211.1. The accepted value is $[\alpha]D$ +220. The material was now exhausted. [i] A crystalline hydriodide was not obtained from the 40 mg. of crude free alkaloid. [j] The following three samples were combined: 363 g., Belaev 9220, Philippine Islands; 164 g., Haigh 9172, Ceylon; 211 g. Acuna 9164, Cuba. A sample of 700 g. was used after grinding. [k] The fatty fraction and the alcohol extractives were removed together by extracting for twenty-eight hours with methanol. The alcohol residue was dissolved in 300 ml. of water, made acid with hydrochloric acid, and extracted fifteen times with petroleum ether for removal of the fatty fraction. However, after making alkaline with sodium bicarbonate and extracting with chloroform, it was found that the expected semi-micro quantity of alkaloids was badly contaminated with extraneous material. This extraction experiment demonstrated that the "preferred procedure" described for *E. fusca* should be followed when semi-micro quantities of alkaloids are being extracted, and that chloroform extraction should follow the petroleum ether in the clarification step. [l] The 247.8 mg. of crude bases yielded 70.2 mg. of crude hydriodides, m. p. 234–238°. One recrystallization yielded 35.6 mg., m. p. 242–243°, $[\alpha]^{28}D$ +212.4. Two more recrystallizations yielded pure erythraline hydriodide, m. p. (and mixed) 249–250°, $[\alpha]D$ +177.4, 0.0035% yield. *Anal.* Calcd. for $C_{18}H_{19}NO_3 \cdot HI$: C, 50.83; H, 4.74. Found: C, 50.98; H, 5.06. The last 1 mg. of mother liquor hydriodides showed $[\alpha]D$ +238.5°. [m] The 2.087 g. of crude bases yielded 0.9784 g. of mixed hydriodides, m. p. 234–235°. Recrystallization yielded 0.744 g., m. p. 243–244°, $[\alpha]D$ +189.6°. One more recrystallization from water yielded pure erythraline hydriodide, m. p. (and mixed) 249°, $[\alpha]D$ +176.0, 0.056% yield. [n] An attempt was made to crystallize the crude free bases from ethanol as was done for the crude bases from *E. fusca*. However, pure erythraline could not be obtained because it could not be crystallized away from the accompanying alkaloids. The inseparable mixture showed m. p. 101–102°, $[\alpha]^{25}D$ +213 whereas pure erythraline showed m. p. 106–107° and $[\alpha]D$ +211. There was no depression in mixed melting points when this impure erythraline was mixed with pure erythramine or erythraline. [o] See discussion in the introduction of this paper. [p] The 1.8298 g. crude bases yielded 1.5928 g. mixed hydriodides, m. p. 229–230°, $[\alpha]D$ +148.3. After fractional crystallizations, only pure erythraline hydriodide was obtained as the major free alkaloid, although related alkaloids were present. It showed m. p. 249–250°, $[\alpha]D$ +176.6, 0.06% yield. *Anal.* Calcd. for $C_{18}H_{19}NO_3 \cdot HI$: C, 50.83; H, 4.74; N, 3.29; I, 29.86. Found: C, 50.54; H, 4.91; N, 3.13; I, 29.99.

N, 3.53; Br, 20.17. Found: C, 54.53; H, 5.31; N, 3.55; Br, 20.21.

Isolation of Alkaloids from Other Species of *Erythrina*.—The technique of fractional crystallization of the hydriodides of erythraline, erythramine, and erythratine from the seeds of *Erythrina glauca* has been described in detail. The significant data on the alkaloids as isolated from other species of *Erythrina* are summarized in Table III. In general, the amount of the crude free alkaloidal fraction was 0.2–0.4% for all of the species of *Erythrina* mentioned in Table III with the exception of *Erythrina variegata* var. *orientalis* and *Erythrina Folkersii*. These two species contained only traces of this alkaloid fraction. The 0.2–0.4% amount of this fraction was also true for *Erythrina sandwicensis* and *Erythrina subumbrans*.

Acknowledgments.—We are especially indebted to Mr. B. A. Krukoff for the task of obtaining the plant materials, for the determinations of plants, and for his suggestions and advice on botanical matters. We are greatly appreciative of the efforts of the many people who have aided materially in the collection of seed samples. The coöperation of Messrs. Douglass Hayman and Wilhelm Reiss on microanalyses was very valuable.

Summary

Erythramine and two new alkaloids, named erythraline and erythratine, have been isolated from the seeds of *Erythrina glauca* Willd. Erythraline was also isolated from the seeds of *Erythrina fusca* Lour., *Erythrina Folkersii* Kruk. and Mold., *Erythrina variegata* L. var. *orientalis* (L.) Merr., *Erythrina velutina* Willd., and *Erythrina macrophylla* DC.

Hypaphorine was isolated from all of the above mentioned species and all for the first time, with the exception of *Erythrina variegata* var. *orientalis* from which it had been previously isolated by others.

Erythraline and hypaphorine undoubtedly

exist also in *Erythrina velutina* forma *aurantiaca* (Ridl.) Kruk. and *Erythrina Grisebachii* Urb.

The crystalline erythraline and erythratine bases, their hydrobromides and hydriodides, have been described. Many microanalyses on several samples and from different species have shown that erythraline has the empirical composition, $C_{18}H_{19}NO_3$, and erythratine has the empirical composition $C_{18}H_{21}NO_4$.

Erythraline and erythramine were of comparable activity (7–8 mg./kg.) in causing a curare-like paralysis in frogs, whereas, erythratine had one-tenth of this activity.

RAHWAY, N. J. RECEIVED DECEMBER 5, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BRYN MAWR COLLEGE]

The Introduction of Substituted Vinyl Groups. V. A Rearrangement Involving the Migration of an Allyl Group in a Three-Carbon System[1]

BY ARTHUR C. COPE AND ELIZABETH M. HARDY[2]

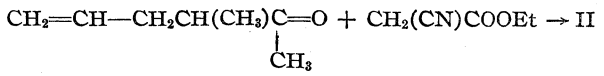
The (dialkylvinyl)-alkylcyanoacetic esters described recently[3] were stable compounds which were not altered in any way during purification. However, in the preparation of ethyl (1-methylpropenyl)-allylcyanoacetate, which was studied but not reported in the previous work, an unstable product was formed, which changed into a stable substance of higher boiling point after several distillations in vacuum. The structures of these compounds and the nature of the rearrangement have now been determined, and are reported in this paper.

The substance formed initially when the sodium derivative prepared from ethyl (1-methylpropylidene)-cyanoacetate was treated with allyl halides proved to be sufficiently stable to be isolated in a pure state if it was distilled at a pressure of 1 mm. Analysis and molecular refraction were in agreement with the structure of the normal alkylation product, ethyl (1-methylpropenyl)-allylcyanoacetate, I.

$$CH_3CH_2C(CH_3)=C(CN)COOEt \xrightarrow{NaOEt}$$

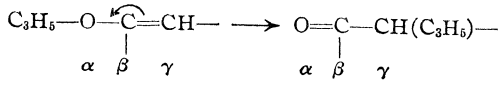
$$[CH_3CH=C(CH_3)C(CN)COOEt]^- Na^+ \xrightarrow{CH_2=CHCH_2X}$$

$$CH_3CH=C(CH_3)C(CN)COOEt$$
$$\quad\quad\quad

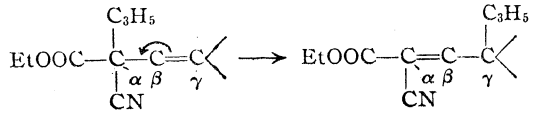


This appears to be the first case in which an allyl group has been observed to undergo a thermally induced α, γ shift in a three-carbon system. It seems probable, however, that this new rearrangement is similar in type to the Claisen rearrangement of allyl enol,[5,6] phenol[7,5,8] and vinyl[8b,9] ethers, and that it is motivated by similar forces.

In the Claisen rearrangement of ethers, an allyl group undergoes an α, γ shift from the electron attracting element oxygen to a carbon atom, and a carbonyl group is formed by migration of a double bond.

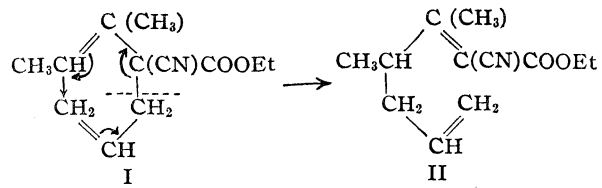


In the present case, an allyl group undergoes an α, γ shift from a carbon atom which is electron attracting by virtue of attachement to CN and COOEt groups to one which is less electron attracting. In the process the double bond which shifts becomes attached to the electron attracting carbon atom and conjugated with the CN and COOEt groups.

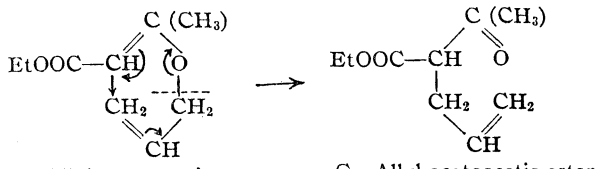


As in the thermal rearrangement of enol, phenol and vinyl ethers, the isomerization is dependent upon the presence of the allyl group. Three (1-methylpropenyl) alkylcyanoacetic esters, $CH_3CH{=}C(CH_3)C(R)(CN)COOEt$, in which R was methyl, propyl and butyl, were completely stable at much higher temperatures than are required to rearrange the allyl compound. Consequently a cyclic mechanism is regarded as probable.

If the mechanism postulated for the present rearrangement is correct, the isomerization is intramolecular and the allyl group is turned around during the shift. These points are being studied, as is the possibility that this type of rearrangement is general for appropriately substituted three carbon systems attached to allyl or substituted allyl groups.

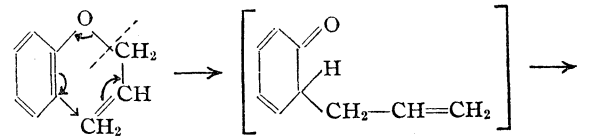


analogous to

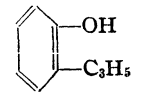


O—Allyl acetoacetic ester C—Allyl acetoacetic ester

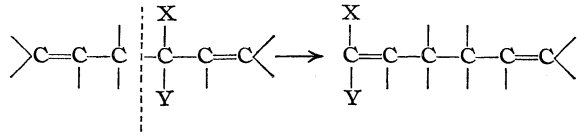
Vinyl allyl ether Allyl acetaldehyde



Allyl phenyl ether



o-allyl phenol



Experimental Part

Ethyl (1-Methylpropenyl)-allylcyanoacetate (Formula I).—One-half mole of ethyl (1-methylpropylidene)-cyanoacetate[10] was converted to the sodium enolate in absolute ethyl alcohol and alkylated with allyl bromide by the general procedure described previously.[3] The reaction mixture was refluxed until it became neutral (forty-five minutes), cooled, diluted with water and extracted with benzene in the usual manner. The residue obtained on concentration of the benzene extract was distilled at a low pressure and superheating was avoided in order to minimize rearrangement. The first distillation gave 67 g. of crude ester, b. p. 90–143° (1 mm.), and 29 g. of tarry residue. The distillate was purified by shaking with 200

(5) Summary by Claisen and Tietze, *Ber.*, **58**, 275 (1925).

(6) Lauer and Kilburn, THIS JOURNAL, **59**, 2586 (1937).

(7) Claisen, *Ber.*, **45**, 3157 (1912).

(8) References to important recent studies are made by: (a) Mumm and Möller, *ibid.*, **70**, 2215 (1937); (b) Hurd and Pollack, *J. Org. Chem.*, **3**, 550 (1939); (c) Lauer and Ungnade, THIS JOURNAL, **61**, 3047 (1939).

(9) Hurd and Pollack, *ibid.*, **60**, 1905 (1938).

(10) Prepared by condensing methyl ethyl ketone with ethyl cyanoacetate in the presence of piperidine acetate or ammonium acetate and acetic acid and removing the water formed by distilling benzene from the mixture. See Cope, THIS JOURNAL, **59**, 2327 (1937). The ester has been described by Scheiber and Meisel, *Ber.*, **48**, 259 (1915).

cc. of 20% sodium bisulfite solution for twelve hours and redistilling through a Widmer column. The yield of pure ester was 37 g. (34%); b. p. 94.5–96° (1 mm.); $n^{25}D$ 1.4609; d^{25}_{25} 0.9735; MD calcd. 58.10, found 58.54.

Anal. Calcd. for $C_{12}H_{17}O_2N$: N, 6.76. Found: N, 6.58.

The ester also was prepared by a similar alkylation using allyl chloride, but the yield was smaller (17%).

Ethyl (1,2-Dimethyl 4-Pentenylidene)-cyanoacetate (Formula II).—When the alkylation product prepared by the method described in the preceding section was purified by distillation at pressures of 15 to 20 mm., partial rearrangement occurred. A typical product had b. p. 141–148° (16 mm.); $n^{25}D$ 1.4683. This material was refractionated at 16 mm. several times in an effort to obtain a pure product, but each distillation resulted in a rise in both the boiling point and refractive index of each fraction. The various fractions were finally combined and refluxed for periods of one to five hours at pressures of 18 to 60 mm., and refractionated through a Widmer column after each period of refluxing until there was no further rise in refractive index or boiling point. The properties of the pure rearranged ester (Formula II) obtained in this way were: b. p. 147–148° (16 mm.); $n^{25}D$ 1.4780; d^{25}_{25} 0.9816; MD calcd. 58.10; found 59.63, exaltation +1.53.

Anal. Calcd. for $C_{12}H_{17}O_2N$: N, 6.76. Found: N, 6.50.

The rearrangement was practically complete after the ester I was refluxed for four hours at 18 mm., at which pressure the temperature of the refluxing liquid was 150–160°. There was little if any decomposition during the period of heating, and the yield of the rearrangement product (25–30%) differed from that of the normal alkylation product only by the amount to be expected because of the manipulative losses resulting from several distillations.

The rearrangement can be carried out more rapidly by refluxing the ester at atmospheric pressure (b. p. approximately 260°). A 12-g. sample of pure ethyl (1-methylpropenyl)-allylcyanoacetate (Formula I) was refluxed for twenty minutes at atmospheric pressure and then distilled in vacuum. The yield of the rearrangement product (Formula II, properties described above) was 8 g. Some high boiling material was formed at this temperature.

Thermal Stability of Other Ethyl (1-Methylpropenyl)-alkylcyanoacetates.—A 10-g. sample of ethyl (1-methylpropenyl)-propylcyanoacetate was refluxed for two hours at atmospheric pressure. There was only slight darkening of the liquid during heating, and on distillation in vacuum 9 g. of the pure ester was recovered, unchanged in boiling point and refractive index. Samples of ethyl (1-methylpropenyl)-ethylcyanoacetate and ethyl (1-methylpropenyl)-butylcyanoacetate[3] were also refluxed for two hours at atmospheric pressure. On distillation following the period of heating 80 to 90% of each of the pure esters was recovered.

Proof of the Structure of Ethyl (1-Methylpropenyl)-allylcyanoacetate (Formula I).—Several samples of the ester were hydrogenated in alcohol solution at room temperature, using a palladinized charcoal catalyst.[11] Complete reduction, which required two moles of hydrogen, was obtained only by several additions of catalyst, or preferably by purification of the partially reduced ester by distillation after the catalyst had become deactivated. The reduced ester (5.8 g. from the reduction of 7.1 g. of I) had b. p. 138–140° (25 mm.) and $n^{25}D$ 1.4358, in agreement with the properties of a known sample of ethyl (*s*-butyl)-propylcyanoacetate (see below).

The reduced ester described above was converted into a solid derivative by condensation with urea in the presence of alcoholic sodium ethoxide in the usual manner.[12] Hydrolysis of the intermediate iminobarbituric acid obtained from 5.8 g. of the ester gave a mixture of neutral and acidic material, from which the substituted barbituric acid was separated by extraction with dilute sodium hydroxide. The product obtained by acidification of the alkaline extract was purified by one crystallization from 50% alcohol. The yield of pure 5-propyl 5-*s*-butyl-barbituric acid,[13] m. p. 135–137°, was 0.6 g. (10%). The identity of this barbituric acid derivative was established by comparison with a known sample of 5-propyl-5-*s*-butyl-barbituric acid[14] prepared from the known ethyl (*s*-butyl)-propylcyanoacetate described below. The m. p. and mixed m. p. of the two samples were identical.

The known ethyl (*s*-butyl)-propylcyanoacetate referred to above was prepared from ethyl (1-methylpropylidene)-cyanoacetate.[10] Fifty grams of the alkylidene ester, 100 cc. of alcohol and 2 g. of palladinized charcoal catalyst were shaken with hydrogen at 15 to 30 lb. (1–2 atm.) pressure until reduction had become very slow and the theoretical amount of hydrogen had been absorbed (forty minutes). The catalyst was removed by filtration, the solvent distilled in vacuum, and the residue shaken with a 20% sodium bisulfite solution to remove any unreduced ester. The ester layer was combined with an ether extract of the sodium bisulfite solution, washed with dilute hydrochloric acid, and distilled through a Widmer column. The yield of pure ethyl (*s*-butyl)-cyanoacetate[15] was 37.5 g. (74%); b. p. 105–106° (11 mm.); $n^{25}D$ 1.4273; d^{25}_{25} 0.9617; MD calcd. 45.18, found 45.31.

Anal. Calcd. for $C_9H_{15}O_2N$: N, 8.28. Found: N, 8.28.

The ethyl (*s*-butyl)-cyanoacetate (30.3 g.) was converted into the sodium derivative by addition to a solution of sodium (4.14 g.) in 150 cc. of absolute alcohol. *n*-Propyl bromide (24.6 g.) was added and the solution refluxed for one and one-half hours. The reaction mixture was diluted with water and extracted with benzene. The benzene was distilled and the crude ester was purified by shaking with concd. ammonium hydroxide overnight to remove any remaining monoalkyl cyanoacetic ester. Distillation through a Widmer column gave 26.7 g. (73%) of ethyl (*s*-butyl)-propylcyanoacetate, b. p. 122.5–123.5° (11 mm.) $n^{25}D$ 1.4356; d^{25}_{25} 0.9378; MD calcd. 59.04, found 58.99.

(11) Hartung, THIS JOURNAL, **50**, 3372 (1928).

(12) *Cf.* Cope and Hancock, *ibid.*, **61**, 353 (1939).

(13) Shonle and Waldo, *ibid.*, **55**, 4649 (1933).

(14) The barbituric acid derivative identifies the ester obtained by reduction even though it was formed in low yield, for under the same conditions the ester of known structure also gave 5-propyl-5-*s*-butyl-barbituric acid in only 10% yield. Relatively large amounts of the same neutral by-product were formed from both samples of the ester.

(15) This ester has been described by Roger in French Patent 598,072, which records only b. p. 118° (17 mm.).

Anal. Calcd. for $C_{12}H_{21}O_2N$: N, 6.63. Found: N, 6.57.

Proof of the Structure of Ethyl (1,2-Dimethyl 4-Pentenylidene)-cyanoacetate (Formula II). Reduction.—Duplicate samples of the ester were reduced rapidly and quantitatively in alcohol solution at room temperature and pressure in the presence of palladinized charcoal, absorbing 105 and 107% of two molar equivalents of hydrogen. From the reduction of 5.8 g. of II, 3.0 g. of ethyl (1,2-dimethylpentyl)-cyanoacetate was obtained; b. p. 134–136° (12 mm.); $n^{25}D$ 1.4389.

Anal. Calcd. for $C_{12}H_{21}O_2N$: N, 6.63. Found: N, 6.50.

Condensation of the ethyl (1,2-dimethylpentyl)-cyanoacetate with urea, followed by hydrolysis, gave 5-(1,2-dimethylpentyl)-barbituric acid, m. p. 219.5–220.5°.

Anal. Calcd. for $C_{11}H_{18}O_3N_2$: N, 12.38. Found: N, 12.54.

Cleavage with Ammonia.—Seven grams of the rearranged ester (II) and 50 cc. of concd. aqueous ammonia were shaken for thirty hours. The ammonia was extracted twice with ether and the extract dried over potassium carbonate. Distillation gave 2.2 g. (60%) of *unsym*-methyl allyl acetone (3-methyl-5-hexene-2-one), b. p. 137–138°, $n^{25}D$ 1.4215. Evaporation of the ammonia solution left a crystalline residue which on recrystallization from alcohol gave 1.5 g. (54%) of cyanoacetamide, m. p. and mixed m. p. with a known sample 121–122°.

In order to be certain of the identity of the *unsym*-methyl allyl acetone produced by cleavage a known sample and solid derivatives were made. The ketone was prepared by the hydrolysis of ethyl allylmethylacetoacetate as described by Jacobi and Merling.[16] The ethyl allylmethylacetoacetate[17] was synthesized from ethyl allylacetoacetate.[18] The *unsym*-methyl allyl acetone had b. p. 137–138° (previously reported as 138–140°) and $n^{25}D$ 1.4218. Its semicarbazone (m. p. 84–85°) and 2,4-dinitrophenylhydrazone (m. p. 41–42°) were prepared by standard methods.

(16) Jacobi and Merling, *Ann.*, **278**, 11 (1894).
(17) James, *ibid.*, **226**, 207 (1884).
(18) Brühl, *J. prakt. Chem.*, **50**, 132 (1894).

Anal. of the semicarbazone. Calcd. for $C_8H_{15}ON_3$: N, 24.83. Found: N, 24.70. *Anal.* of the dinitrophenylhydrazone. Calcd. for $C_{13}H_{16}O_4N_4$: N, 19.17. Found: N, 19.35.

The semicarbazone and 2,4-dinitrophenylhydrazone prepared from the ketone isolated from the cleavage of II with ammonia were identical in m. p. and mixed m. p. with the derivatives prepared from the known ketone.

Synthesis of II from *unsym*-Methyl Allyl Acetone.—*unsym*-Methyl allyl acetone (9.3 g.), ethyl cyanoacetate (9.5 g.), ammonium acetate (0.8 g.), acetic acid (1.2 g.) and benzene (25 cc.) were refluxed under a constant water separator for one hour. The benzene solution was cooled, washed with water and distilled in vacuum. The reaction was incomplete, for 6 g. of ethyl cyanoacetate was recovered, but 5 g. (29%) of ethyl (1,2-dimethyl 4-pentenylidene)-cyanoacetate was obtained, b. p. 153–154° (23 mm.); $n^{25}D$ 1.4781. These properties are in good agreement with those of the ester II prepared by the thermal rearrangement of I.

Summary

Ethyl (1-methylpropenyl)-allylcyanoacetate rearranges readily on heating at temperatures between 150 and 260°, giving ethyl (1,2-dimethyl 4-pentenylidene)-cyanoacetate. In the rearrangement the allyl group migrates from the α to the γ carbon atom of a three carbon system, while the double bond in the latter shifts from the β, γ to the α, β position.

It appears probable that this rearrangement involving the migration of an allyl group in a three carbon system occurs for reasons similar to those responsible for the Claisen rearrangement of enol, phenol and vinyl ethers, and that the two types of rearrangement follow similar mechanisms.

BRYN MAWR, PA. RECEIVED DECEMBER 18, 1939

NOTES

A Method for Separating Para-hydrogen from Oxygen and Carbon Monoxide

By E. Bergmann, L. Farkas and L. Sandler

Para-hydrogen has often been used as a research tool for elucidating reaction mechanisms. In order to analyze the para–ortho ratio in the hydrogen, the hydrogen has to be separated from all gases taking part in, or formed by, the reaction, so that the ortho–para ratio is not changed by this process. In most cases satisfactory separation can be achieved by the use of liquid or solid air which freeze out most of the common gases. In two important cases, however, *viz.*, when oxygen or carbon monoxide is present, liquid hydrogen had to be used for the separation process. Since liquid hydrogen is not always available and its preparation is very expensive, we have tried to substitute a chemical method of separation for the physical one. For this purpose, solutions had to be found which absorb the above gases quantitatively without causing any appreciable para–ortho conversion during the absorption process.

Absorption of Oxygen.—To the quantitative absorption of oxygen a method was adapted which has been devised for the purification of nitrogen by Schlenk,[1] and which is based on the fast and complete reaction of triphenylmethylsodium solution[2] with gaseous oxygen. As diethyl ether as used by Schlenk and Marcus in their investigations, has a very high vapor pressure and dissolves the grease of the stopcocks, it was replaced by dibutyl ether, having a vapor pressure of a few mm. only at 20°. The solution prepared and filtered in the usual way was evaporated in a stream of pure nitrogen and dibutyl ether added gradually during this process.

The solution actually used was saturated with triphenylmethylsodium and contained an excess of this substance in solid form so as to render possible the uptake of a large amount of oxygen. The solution was kept in a shaking vessel, attached to the high vacuum apparatus by a glass spiral and remained in use for many months without renewal. The diffusion of the gas into the solution can be accelerated by cooling the solution and is completed within less than one minute.

The following two experiments characterize the above solution:

A lock system of 5 cc. capacity was connected through a very narrow capillary tube to a washing bottle containing about 20 cc. of the solution. It was found that when 130 cubic mm. (at S. T. P.) of oxygen passed through the capillary tube no measurable amount of oxygen (less than 0.005%) could be detected by a McLeod gage on the other side of the washing bottle.

In order to test whether any appreciable ortho–para conversion takes place in presence of the triphenylmethyl sodium solution, para-hydrogen was introduced into the shaking vessel (70 cc. capacity) containing the sodium compound (30 cc.). The half-life-time of the conversion under our conditions was two and one-half hours; thus, the conversion occurring during the short period of oxygen absorption is negligible. The conversion observed is most probably due to the presence of small quantities of free (paramagnetic) triphenylmethyl.

Absorption of Carbon Monoxide.—For the absorption of carbon monoxide the common cuprous oxide–ammonia solution was used. In the same arrangement as used in the case of oxygen, 500 cubic mm. (S. T. P.) of carbon monoxide (at an actual pressure of 70 mm.) were made to pass the capillary tube and again no trace (less than 0.005%) of the gas could be detected on the other side of the washing bottle.

The following experimental arrangement was used in an actual experiment, carried out at low pressure (10^{-2} mm.).[3] The gas mixture was collected in a bulb of 700 cc. to which a smaller vessel was attached, containing 40 cc. of the absorbing solution cooled, in order to accelerate the diffusion of the gas, and separated from the larger bulb by a stopcock. The gas mixture (40 cubic mm. at S. T. P.) was collected in the large bulb, the stopcock opened and the absorption vessel shaken for a few hours. A control experiment, carried out with a mixture of 20 cubic mm. of normal hydrogen and 200 cubic mm. of carbon monoxide showed that no carbon monoxide could be detected in a micro-conductivity cell after the process of absorption, indicating that the amount of carbon monoxide was reduced to at least 0.1%.

Under the conditions used, the half-life-time of the ortho–para conversion was found to be one hundred hours, although no special care had been taken to exclude from the cuprous oxide–ammonia solution divalent (paramagnetic) copper compounds which certainly are responsible for the greater part of the conversion observed. In any case the conversion during the period of absorption again is negligible.

It is obvious that the methods described may be useful in experiments with other hydrogen modifications, too, such as ortho-deuterium or mixtures of light and heavy hydrogen and hydrogen deuteride.

(1) Schlenk, Houben–Weyl's "Methoden der organischen Chemie," 1924, Vol. 4, pp. 959, 974.

(2) Schlenk and Marcus, *Ber.*, **47**, 1664 (1914).

(3) Farkas, Hirschberg and Sandler, This Journal, **61**, 3393 (1939).

Daniel Sieff Research Institute
Rehovoth, Palestine Received September 30, 1939

Solvolytic Reactions of Organic Halides

By Michael P. Balfe and Joseph Kenyon

While we cannot enter into the discussion of the kinetics of these reactions, which have been de-

scribed as unimolecular,[1] as bimolecular,[2,3] as either bimolecular or termolecular,[4] and as polymolecular,[5,6] the diversity of conclusions suggests, as indicated by Bartlett,[4] that the course of these reactions is not sufficiently simple to justify the application of the kinetic method.

Our present purpose is to comment on the mode of formulation of the solvated cation which is assumed as an intermediate in these reactions by Winstein.[6] In the hydrolysis of halides, Winstein's formulation $H_2O^+—C\lesssim$ leads to no difficulties, but is not generally applicable. The rearrangement of phenylmethylcarbinyl *p*-toluenesulfinate to *p*-tolyl-α-phenylethylsulfone,[7] a reaction which involves ionization in the same sense as the solvolytic reactions mentioned above, does not occur in solution in acetonitrile, but proceeds readily in solution in formic acid. The suggestion which seems best to explain this difference in behavior is that there is a difference between the solvating properties of the two solvents.

If solvation of the cation be assumed its formulation as $\begin{matrix}H\\HO\end{matrix}\!\!>C=O^+—C\lesssim$ would, in our opinion, imply that phenylmethylcarbinyl formate should be a major product of the reaction, whereas it is in fact a minor product. The alternative explanation, that by two successive solvolytic reactions the sulfinate is converted first into the formate and then into the sulfone, is not consistent with the stereochemical observations recorded in the communication referred to.[7]

We submit, therefore, that it is undesirable to assume that in these reactions there is solvation of carbonium cations by co-valency formation between solvent and cation.

(1) Bateman, Hughes and Ingold, THIS JOURNAL, **60**, 3080 (1938).
(2) Olson and Halford, *ibid.*, **59**, 2644 (1937).
(3) Taylor, *J. Chem. Soc.*, 1853 (1937).
(4) Bartlett, THIS JOURNAL, **61**, 1630 (1939).
(5) (a) Steigmann and Hammett, *ibid.*, **59**, 2358 (1937), (b) Farinacci and Hammett, *ibid.*, **59**, 2542 (1937).
(6) Winstein, *ibid.*, **61**, 1635 (1939).
(7) Arcus, Balfe and Kenyon, *J. Chem. Soc.*, 485 (1938).

CHEMISTRY DEPARTMENT
BATTERSEA POLYTECHNIC
LONDON S. W. 11, ENGLAND RECEIVED AUGUST 2, 1939

Organolithium Compounds of Pyridine and Quinoline

BY HENRY GILMAN AND S. M. SPATZ

The halogen–metal interconversion reaction observed with *m*- and *p*-bromodimethylanilines,[1] mono- and dibromo- and iodocarbazoles and bromoanilines[2] suggested that corresponding reactions might take place with bromo- and iodopyridines and quinolines. We have found this to be the case. For example, 3-bromoquinoline and *n*-butyllithium react promptly, and carbonation of the reaction mixture gives a 52% yield of 3-quinolinecarboxylic acid. Under corresponding conditions 3-bromopyridine gives a 70% yield of nicotinic acid.

Perhaps the first evidence for the formation of Grignard reagents from 3-bromopyridine and 2-iodopyridine is to be found in a study by Harris.[3] Later, Overhoff and Proost[4] prepared 2-pyridylmagnesium bromide in quantity and obtained from it and benzaldehyde, phenyl-2-pyridylcarbinol. The formation of organolithium compounds from nitrogen heterocycles by means of other RLi compounds is of interest because it appears to be generally applicable, and because it establishes the possibility of selecting conditions to reduce the tendency of addition of an organolithium compound to the anil linkage. Under ordinary conditions, RLi compounds add promptly to the anil linkage. The reaction undoubtedly can be extended to poly-substituted nitrogen heterocycles containing functional groups in addition to bromine and iodine. For example, *o*-bromobenzoic acid and *n*-butyllithium give the lithium salt of *o*-lithiobenzoic acid, which on carbonation (followed by hydrolysis) gives a 31% yield of phthalic acid.[5] Details on the preparation and some reactions of the organolithium compounds of various nitrogen heterocycles will be published later.

A solution of 14.6 g. (0.07 mole) of 3-bromoquinoline in 50 cc. of dry ether was added rapidly to an ether solution of a slight excess of *n*-butyllithium. The reaction was carried out at −35° for fifteen minutes, at the end of which time the transparent reddish solution was carbonated by dry-ice. On working up the reaction mixture in a customary manner, there was isolated a 52% yield of 3-quinolinecarboxylic acid. Identification was established by comparison with an authentic specimen of the acid (m. p. 270–272°); in addition, the method of mixed melting points was also used with the ethyl 3-quinolinecarboxylate (m. p., 69.5°), prepared from the 3-quinolinecarboxylic acid.

DEPARTMENT OF CHEMISTRY
IOWA STATE COLLEGE
AMES, IOWA RECEIVED DECEMBER 26, 1939

(1) Gilman and Banner, THIS JOURNAL, **62**, 344 (1940).
(2) Gilman, Langham and Willis, *ibid.*, **62**, 346 (1940).
(3) Harris, *Iowa State Coll. J. Sci.*, **6**, 425 (1932); [*C. A.*, **27**, 279 (1933)].
(4) Overhoff and Proost, *Rec. trav. chim.*, **57**, 179 (1938).
(5) Studies by C. E. Arntzen.

The Preparation of Ferric Mesoporphyrin Chloride

BY T. HARRISON DAVIES*

Ferric mesoporphyrin chloride is readily obtained from ferric protoporphyrin chloride by reduction of the latter with hydrogen and palladium charcoal in alkaline methyl alcohol solution. The method leads to higher yields with less labor than the procedure of Fischer and Pützer[1] and Fischer and Stängler,[2] in which ferric protoporphyrin chloride is first reduced to mesoporphyrin by the action of formic acid and colloidal palladium and the iron is then reintroduced in acetic acid solution. The yields are higher and the general procedure is less troublesome than the method of Fischer and Röse,[3] in which ferric mesoporphyrin is obtained directly by heating ferric protoporphyrin in pyridine–methyl alcohol or pyridine–potassium methyl alcoholate solution in a bomb at 225°.

Experimental

Ferric protoporphyrin chloride (4 g.), prepared and recrystallized by the usual methods, is dissolved in 450 ml. of methyl alcohol and 50 ml. of 0.5 *N* potassium hydroxide. Palladinized charcoal (2 g. of a preparation 12% in palladium) is added. The mixture is refluxed with hydrogen bubbling until a test drop in a few ml. of 0.5 *N* sodium cyanide solution gives no evidence of the absorption bands of cyanide ferrous protoporphyrin upon reduction with a little sodium dithionite. About eight hours is ordinarily required. The solution is cooled and filtered. The catalyst, after thorough washing, drying, and shaking with air, can be used again. The filtrate is treated with 1 *N* hydrochloric acid to precipitate the metalloporphyrin. The latter is collected on a filter, washed with a little water and dried *in vacuo* over sodium hydroxide. The semi-crystalline material is dissolved in 100 ml. of chloroform containing 4 g. of quinine. The chloroform solution is added dropwise to 150 ml. of glacial acetic acid saturated with sodium chloride and held above 90° on a water-bath. During the addition, air is bubbled through the acetic acid to assist in the removal of the chloroform. The solution is allowed to cool slowly. After a few hours the crystalline ferric mesoporphyrin chloride is collected on a hardened filter, washed with 50% acetic acid, then with water, and finally dried over potassium hydroxide: yield in one preparation 2.7 g., in a second 3.2 g.

The absorption spectra of cyanide ferrous mesoporphyrin and of ethanolamine ferrous mesoporphyrin from this preparation were identical with those of a preparation of ferric mesoporphyrin chloride made by the method of Fischer and Stängler from an authentic sample of mesoporphyrin hydrochloride.

(*) National Research Fellow in Medicine.

(1) Fischer and Pützer, *Z. physiol. Chem.*, **154**, 39 (1926).

(2) Fischer and Stängler, *Ann.*, **459**, 53 (1927).

(3) Fischer and Röse, *Z. physiol. Chem.*, **88**, 9 (1913).

ABSORPTION SPECTRA

Sample	In NaCN soln. + $Na_2S_2O_4$	In NH_2CH_2-CH_2OH soln. + $Na_2S_2O_4$
Ferric protoporphyrin chloride	531–541; 565–574	(525); 550–562
Ferric mesoporphyrin chloride from mesoporphyrin hydrochloride	527–535; 555–562	(515); 542–551
Ferric mesoporphyrin chloride by this procedure	526–536; 555–562	(516); 541–550

GATES AND CRELLIN LABORATORIES OF CHEMISTRY
CALIFORNIA INSTITUTE OF TECHNOLOGY
PASADENA, CALIFORNIA RECEIVED DECEMBER 28, 1939

Reaction of *bis*-β-Chloroethyl Ether with Ethylenediamine

BY M. E. HULTQUIST AND E. H. NORTHEY

The reaction of *bis*-β-chloroethyl ether with ammonia, aliphatic monoamines, and aromatic amines and diamines is well known.[1,2,3,4] We sought a simpler method for the preparation of 4-(β-aminoethyl)-morpholine than the reaction of N-(β-bromoethyl)-phthalimide with morpholine followed by hydrolysis and found one in the action of *bis*-β-chloroethyl ether with a large excess of ethylenediamine.

To 1.875 kg. of 57.5% ethylenediamine (18 moles anhydrous) in a 5-liter flask equipped with agitator, reflux condenser and dropping funnel, 863 g. (6 moles) of *bis*-β-chloroethyl ether was added during one hour. Thirty minutes later, 505 g. of flake sodium hydroxide was added cautiously. The mixture was cooled and the precipitated salt filtered. The liquor was dried over solid sodium hydroxide and then distilled through a 60 cm. × 50 mm. packed column. After distillation of excess ethylenediamine, 370 g. (47.5% of theoretical) of 4-(β-aminoethyl)-morpholine boiling at 121–123° (68 mm.), b. p. 204.5° (768 mm.), was obtained as a water-white liquid with a refractive index of 1.4742 (25°). These values were in agreement with those of 4-(β-aminoethyl)-morpholine prepared by the phthalimide process.

Anal. Calcd. for $C_6H_{14}N_2O$: N, 21.55. Found: N, 21.4.

On fractionation of the residues, the following cuts were obtained: 50 g. 123° (68 mm.) to 164° (30 mm.); 69 g. 164–166° (30 mm.); 8.5 g. 166–200° (30 mm.); 7.3 g. 200–203° (30 mm.); 5.5 g. 203° (30 mm.) to 220° (4 mm.).

Fraction 2 was mainly ethylenedi-(4-morpholine). It solidified to a light yellow solid. After two recrystallizations from hexane, it was obtained as colorless, coarse prisms; m. p. 70–73°, setting point 71.3°. It was converted to the dihydrochloride by dissolving in alcohol and adding concentrated hydrochloric acid, then twice recrystallizing from dilute alcohol.

(1) Axe and Freeman, THIS JOURNAL, **56**, 478 (1934).

(2) A. L. Wilson to Carbide & Carbon Chemical Corp., U. S. Patent, 2,096,441, October 19, 1937.

(3) A. L. Wilson to Carbide & Carbon Chemical Corp., U. S. Patents 2,105,828, January 18, 1938.

(4) Marion C. Reed to Goodrich Tire & Rubber Co., U. S. Patent, 2,001,584, May 14, 1935.

The dihydrochloride crystallized as colorless plates decomposing and subliming over 250°.

Anal. Calcd. for $C_{10}H_{22}O_2N_2Cl_2$: N, 10.3; Cl, 25.9. Found: N, 10.5; Cl, 25.7.

Fraction 4 was mainly *bis*-{2-[N-(β-aminoethyl)-amino]-ethyl} ether, a light yellow oil. It was converted to the tetrahydrochloride and recrystallized three times from methanol giving small, colorless, thin plates; m. p. 185–187°.

Anal. Calcd. for $C_8H_{26}ON_4Cl_4$: N, 16.7; Cl, 42.2. Found: N, 16.9; Cl, 41.6.

By increasing the proportions of ethylenediamine in the reaction to 6 moles to 1, a 58% yield of 4-(β-aminoethyl)-morpholine, based on *bis*-β-chloroethyl ether, was obtained.

LABORATORIES OF
CALCO CHEMICAL DIVISION
AMERICAN CYANAMID COMPANY
BOUND BROOK, N. J. RECEIVED DECEMBER 13, 1939

Precipitation of Barium Sulfate in the Presence of Ammonium Chloride

BY J. T. MCHENRY, G. A. AMPT AND E. HEYMANN

It has been known for a long time that the analytical errors involved in the precipitation of the sulfate radical as barium sulfate are due to the presence of foreign material in the precipitate. Several explanations for the mechanism of this inclusion of foreign material have been considered.[1]

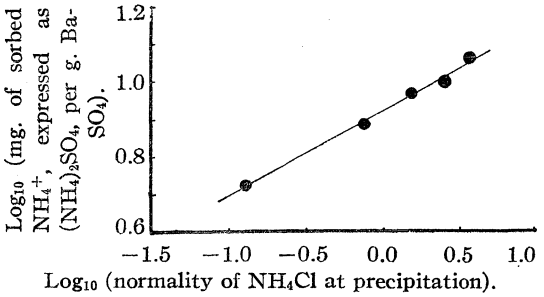


Fig. 1.

We performed a number of precipitations of barium sulfate by means of a barium chloride solution from sulfuric acid in the presence of ammonium chloride. To 200 ml. of boiling solution, containing 0.1859 equivalent of ammonium sulfate and varying amounts of ammonium chloride, 19.0 ml. of 1.96 *N* barium chloride solution was slowly added. Twenty hours after precipitation the precipitate was filtered, washed and dried in a vacuum desiccator.

The sorbed material was determined in two ways: (1) 1-g. aliquots were dissolved in 10 ml. of cold concentrated sulfuric acid, the solution poured into 200 ml. of boiling water, the liquid filtered, the precipitate washed and the filtrate made alkaline and distilled. The ammonia was collected in 0.1 *N* hydrochloric acid and the excess acid determined iodimetrically. Second extractions were carried out on the reprecipitated samples and the total extracted was regarded as the full amount of sorbed material, (2) one-gram aliquots were dissolved in 200 ml. of 50% sodium hydroxide by warming, the solution diluted to 500 ml. and then distilled. The ammonia was absorbed in 0.1 *N* hydrochloric acid. Both procedures gave results which did not differ by more than 4%.

Investigation of our precipitates, by a method first suggested by Hulett and Duschak,[2] showed that about 50% of the ammonia is present as sulfate.

Figure 1 shows that a linear relation exists between the logarithms of the amount sorbed and the ammonium chloride concentration (Freundlich's adsorption isotherm). It is, however, recognized that this empirical relation may also formally describe processes other than surface adsorption. Further it can be seen that barium sulfate, precipitated in the presence of *N* ammonium chloride contains 7.0 mg. of NH_4, expressed as ammonium sulfate, per 1 g. of barium sulfate.

The investigations of Kolthoff and MacNevin[3] and of Imre[4] indicate that the essential process in

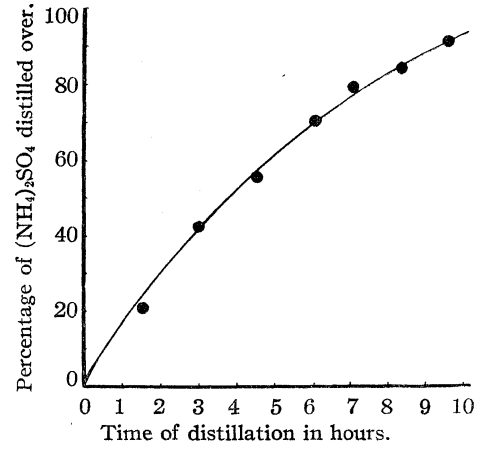


Fig. 2.

(1) E. F. Allen and J. Johnston, THIS JOURNAL, **32**, 588 (1910); J. Johnston and L. H. Adams, *ibid.*, **33**, 829 (1911); I. M. Kolthoff, *J. Phys. Chem.*, **36**, 860 (1932); Z. Karaoglanow, *Z. anal. Chem.*, **106**, 129 (1936); *Z. physik. Chem.*, **A178**, 143 (1937); D. Balarew and co-workers, *Kolloid-Beihefte*, **30**, 249 (1929); **32**, 304 (1930); *Kolloid-Z.*, **67**, 203 (1934); **83**, 319 (1938); *Z. anal. Chem.*, **101**, 161 (1935); *Z. Krist.*, **89**, 268 (1934); *Kolloid-Beihefte*, **50**, 1 (1939).

(2) G. A. Hulett and L. A. Duschak, *Z. anorg. Chem.*, **40**, 196 (1904); cf. Treadwell and Hall, "Analytical Chemistry," Vol. II, p. 402.

(3) I. M. Kolthoff and W. M. MacNevin, THIS JOURNAL, **58**, 725 (1936).

(4) L. Imre, *Kolloid-Z.*, **87**, 12 (1939).

the inclusion of foreign material in barium sulfate precipitates is a sorption on the initially formed primary crystallites. The growth of these will be such that most of the initially sorbed material does not find its way out of the internal "mosaic" structure of the macrocrystal (*cf.* also Darwin,[5] Smekal,[6] Balarew[1]).

This point is supported by our experiments in which the precipitates were treated by prolonged boiling with dilute sodium hydroxide (0.02–0.01 *N*). In Fig. 2 the percentage of ammonium salt distilled over as ammonia is plotted against the time of distillation. It is very significant that, in this case, ammonia distils over *very slowly, ten to fifteen hours being needed to expel most of it.* This is incompatible with adsorption on the external surface of the macrocrystals only. It can only be explained on the assumption that the contaminating salt is mainly present on an internal surface of the macrocrystal. The results of the distillation experiments would, moreover, be difficult to reconcile with the existence of secondary insoluble compounds (Karaoglanow[1]) or of solid solutions.[7] It is highly improbable that, in these cases, the total ammonia could be expelled by treatment with an alkali as dilute as 0.01 *N* sodium hydroxide.

It is not quite simple to visualize a satisfactory mechanism of the formation of macrocrystals which possess a mosaic structure. Kolthoff[1] suggests that the electrolyte, adsorbed on the primary nuclei, will influence crystallization in such a way that the lattice of the eventually formed macrocrystals will contain many imperfections. Another way of visualizing the formation of a mosaic structure would be found in the assumption that the primary crystallites will grow together on certain faces to irregular macrocrystals which possess a large internal surface.

(5) C. G. Darwin, *Phil. Mag.*, **27**, 315, 675 (1914); **43**, 800 (1922).
(6) A. Smekal, *Physik. Z.*, **27**, 837 (1926); *Ann. Phys.*, **93**, 1204 (1927).
(7) G. H. Walden, Jr., and M. U. Cohen, THIS JOURNAL, **57**, 2597 (1935); P. R. Averell and G. H. Walden, Jr., *ibid.*, **59**, 907 (1937).

CHEMISTRY DEPARTMENT
UNIVERSITY OF MELBOURNE
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Dissociation of Carbonic Acid in Ordinary and in Heavy Water

BY G. ALEXANDER MILLS

In general, acids are considerably weaker in heavy than in ordinary water. The ratio K^H/K^D, where K^H and K^D are the dissociation constants of the acid in H_2O and D_2O, increases with decreasing acid strength.[1] The ratio of the apparent first dissociation constants of proto- and deutero-carbonic acid has been accurately determined to be 2.68 at 25°.[2] This does not agree with the predicted value of 3.6 obtained from the function given by Rule and La Mer and recently confirmed by Martin and Butler. However, the acid strength should not be judged from the apparent dissociation constant.

In aqueous solution carbon dioxide is hydrated only to a small extent forming rather strong metacarbonic acid. The relationship between K_1, the hydration constant, K_t, the true first dissociation constant and K_a, the apparent first dissociation constant, is

$$\frac{(H^+)(HCO_3^-)}{(CO_2) + (H_2CO_3)} = K_a = \frac{K_tK_1}{1 + K_1}$$

If hydration of carbon dioxide is assumed to be the same in D_2O as in H_2O (the solubilities are very nearly identical) then $K^H{}_t/K^D{}_t = 2.68$. It has been possible to determine the total amount of carbonic acid in solution since carbon dioxide does not react immediately with water. In conjunction with conductivity data the true dissociation constant has been estimated therefore to be 4×10^{-4}.[3] From the smooth curve plot of $-\log K^H$ against[1] K^H/K^D the value of 2.9 is now obtained for the ratio. This compares more favorably with 2.68 than with 3.6, the value predicted on the basis of the apparent dissociation constant.

(1) Rule and La Mer, THIS JOURNAL, **60**, 1974 (1938); Martin and Butler, *J. Chem. Soc.*, 1366 (1939).
(2) Curry and Hazelton, THIS JOURNAL, **60**, 2773 (1938).
(3) Strohecker, *Z. Nahrungsm. Untersuch. Hyg. Warenkunde*, **31**, 121 (1916); Buytendyk, Brinkman and Mook, *Biochem. J.*, **21**, 576 (1927).

DEPARTMENT OF CHEMISTRY
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HANOVER, N. H. RECEIVED NOVEMBER 7, 1939

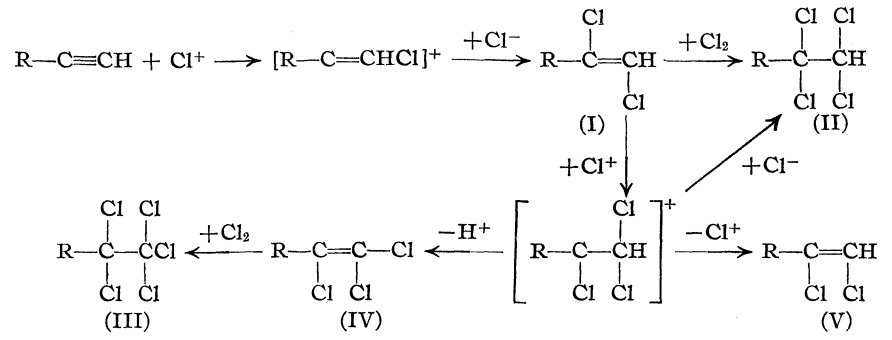
Chlorination of 1-Hexyne in Reactive Solvents. II[1]

BY R. O. NORRIS AND G. F. HENNION

Previous papers[2,3] from this Laboratory describe the chlorination of 1-hexyne in various

(1) Paper XXXVI on the chemistry of substituted acetylenes and their derivatives; previous paper, THIS JOURNAL, **61**, 2897 (1939). Also paper 5 on halogenation in reactive solvents; *cf.*, *ibid.*, **61**, 1460 (1939).
(2) Verbanc and Hennion, *ibid.*, **60**, 1711 (1938).
(3) Norris, Vogt and Hennion, *ibid.*, **61**, 1460 (1939).

oxygen-containing solvents. This work has now been continued, particularly to study the effect of high proton concentrations in the chlorination reaction. For this purpose 1-hexyne was chlorinated as an emulsion in concentrated hydrochloric acid, 30%[4] sulfuric acid and 30%[4] phosphoric acid and as a solution in methanol previously saturated with hydrogen chloride. The various experiments gave complex mixtures of hexyne chlorides as shown in Table I. Fortunately the individual substances boil sufficiently far apart to permit their separation by fractional distillation through an efficient column.



It is noteworthy that *cis*-1,2-dichloro-1-hexene (V) was obtained in each case as well as the anticipated *trans* isomer (I) and that oxygen-containing compounds were not isolated. In methanol[2] and in water,[3] to which acid has not been added, the *trans* dichloride is obtained as well as oxygen-containing products.

The trichloride (IV) listed in Table I previously was formulated[3] as 1,2,2-trichlorohexane. It appears now that this compound actually is 1,1,2-trichloro-1-hexene and is the precursor of the pentachloride (III). Attempts[5] to prepare 1,2,2-trichlorohexane from 1-hexyne have failed. Neither *cis*- nor *trans*-1,2-dichloro-1-hexene could be made to add hydrogen chloride.

Chlorination of 2-chloro-1-hexene in carbon tetrachloride also failed to give the anticipated trichlorohexane, but yielded rather *cis*-1,2-dichloro-1-hexene (V) and 1,1,2,2-tetrachlorohexane (II). The following mechanism explains satisfactorily the various products obtained in the present investigation.

(4) Concentration by volume.

(5) Unpublished work, Chas. Welsh and G. F. Hennion.

The experimental procedure and analyses and physical constants for the products have been cited previously[3] and need not be repeated. However, the product having b. p. 90–93° at 10 mm.; $n^{25}D$ 1.4760; d^{25} 1.225 now is reported as 1,1,2-trichloro-1-hexene rather than as 1,2,2-trichlorohexane.

TABLE I

WEIGHTS OF REAGENTS AND PRODUCTS IN THE CHLORINATION OF ONE MOLE OF 1-HEXYNE AT 40–50°

Reagents			Products, R is *n*-C_4H_9				
Solvent	Vol., ml.	Cl_2, g.	RCCl=CH	RCCl=CHCl	RCCl=CCl	RCCl—CHCl	RCCl—CCl
35% HCl–H_2O	300	176	23	26	25	11	14
30% H_2SO_4–H_2O	300	150	25	25	30	8	14
30% H_3PO_4–H_2O	300	115	24	30	36	10	17
22% HCl–MeOH	400	122	45	16	65	18	6

CHEMICAL LABORATORY
UNIVERSITY OF NOTRE DAME
NOTRE DAME, INDIANA RECEIVED NOVEMBER 20, 1939

Remarks on "A New Method for the Cleavage of Unsaturated Fatty Acids"

BY DONALD PRICE AND RICHARD GRIFFITH

Under the above title Chi-yi Hsing and Kou-jen Chang [THIS JOURNAL, **61**, 3589 (1939)] report the application of Criegee's[1] lead tetraacetate oxidation to polyhydroxy fatty acids, which are readily obtained from the corresponding unsaturated acids by oxidation with alkaline permanganate. They describe in detail the oxidation of 9,10-dihydroxyoctadecanoic acid, the cleavage products of which were found to be pelargonic aldehyde and the hemialdehyde of azelaic acid.

These authors seem to have overlooked the fact that Criegee's method previously was applied to the same as well as other acids by Nunn and Smedley-MacLean, *Biochem. J.*, **29**, 2742 (1935),

(1) Criegee, *Ber.*, **64**, 260 (1931); *Ann.*, **481**, 263 (1930); **507**, 159 (1933).

with the identical results obtained by them. It was also applied similarly by Raudnitz, Schindler and Petru, *Ber.*, **68,** 1675 (1935), to the determination of the structure of aleuritic acid. More recently Mr. Daniel Swern of the Bureau of Agricultural Chemistry and Engineering, U. S. Department of Agriculture read a paper at the Boston meeting of the American Chemical Society on Sept. 12, 1939, entitled, "Action of Lead Tetraacetate upon Hydroxylated Oils, Fats, Fatty Acids, and Related Compounds."

RESEARCH LABORATORY
NATIONAL OIL PRODUCTS COMPANY
HARRISON, N. J. RECEIVED DECEMBER 30, 1939

Hydrogen Fluoride as a Condensing Agent. IX.[1] Reactions of Di- and Triisobutylene with Phenol

BY J. H. SIMONS AND S. ARCHER

In connection with other work, it became necessary to determine whether or not highly branched aliphatic olefins would react with aromatic compounds to give normal or cleaved products. It is known that in the presence of large amounts of sulfuric acid, diisobutylene reacts with phenol to give cleaved products, but with small quantities of the acid the uncleaved product is obtained.[2] The same olefin reacts with toluene in liquid hydrogen fluoride to give mono and di-*t*-butyltoluene.[3]

We have found that under conditions similar to those employed by Calcott and co-workers, di- and triisobutylene both react to give *p*-*t*-butylphenol as the only monoalkylated phenol. However, by employing milder conditions it was possible to effect condensation without cleavage in the case of diisobutylene. By using a small amount of 70% hydrofluoric acid at 0°, *p*-*t*-octylphenol was isolated unaccompanied by any cleavage products. Under the same conditions dodecylphenol was not isolated when the twelve-carbon olefin was employed, although even this might be accomplished under even milder conditions.

The triisobutylene used was the so-called "lower isomer," which consists chiefly of dineopentylethylene and methylneopentyl-*t*-butylethylene. The diisobutylene was the usual commercial product, dried and redistilled, the fraction boiling at 100–103° being used.

(1) For previous paper of this series, see THIS JOURNAL, **61,** 1821 (1939).

(2) Ipatieff, Pines and Friedman, *ibid.*, **60,** 2495 (1938).

(3) Calcott, Tinker and Weinmayr, *ibid.*, **61,** 1010 (1939).

Experimental

Phenol and Diisobutylene

A. Large Quantities of Hydrogen Fluoride.—To 121 g. of hydrogen fluoride contained in a copper flask, was added a solution of 94 g. of phenol in 300 cc. of carbon tetrachloride. One mole of the olefin was dropped in with constant stirring, the reaction being kept at 0°. After twenty-four hours the reaction was stopped and then treated in the usual way. Distillation gave 88 g. of *t*-butylphenol, m. p. 97–98.5°, 14 g. of a fraction boiling at 165–185° (28 mm.), and a residue of 41 g. The higher boiling fraction did not solidify even after standing for some weeks.

B. Small Quantities of Hydrogen Fluoride.—A mixture of 20 g. of 70% hydrofluoric acid, 56 g. of the olefin, and 47 g. of phenol was kept at 0° for forty-eight hours. After the usual treatment, distillation gave 35 g. of *p*-*t*-octylphenol, m. p. 82–83°, and recovered phenol. When mixed with an authentic specimen there was no depression in melting point.

Phenol and Triisobutylene

A. Large Quantities of Hydrogen Fluoride.—One mole of phenol was dissolved in 300 cc. of carbon tetrachloride and added to 122 g. of hydrogen fluoride maintained at 0°. To this mixture one mole of the olefin was added slowly. After being stirred for twenty-four hours, the reaction was stopped. Removal of the solvent left a residue of 206 g. of which 64 g. boiled at 152–160° (38 mm.) and melted at 96–97°. This was *t*-butylphenol. The remainder of the material boiled over a wide range and probably consisted of the polybutylphenols.

B. Small Quantities of Hydrogen Fluoride.—Equimolar quantities of the olefin and the phenol were mixed and added to 20 g. of 70% hydrogen fluoride. After sixty hours the usual procedure was followed and the product treated with Claisen solution.[4] The latter, when examined, did not give any compound that corresponded to a dodecylphenol. When 33 g. of anhydrous hydrogen fluoride was used with 105 g. of phenol and 174 g. of the olefin, for a reaction time of fourteen hours, 52 g. of *t*-butylphenol and considerable residual phenolic material were obtained.

(4) Claisen, Eisleb and Kremers, *Ann.*, **418,** 96 (1919).

DEPARTMENT OF CHEMISTRY
THE PENNSYLVANIA STATE COLLEGE
STATE COLLEGE, PENNSYLVANIA
RECEIVED DECEMBER 1, 1939

Activity Coefficients in Concentrated Aqueous Solutions of Strong Electrolytes Described by Means of a Formula Containing the Mean Ionic Diameter as Single Parameter. II. Corrected Formulation

BY PIERRE VAN RYSSELBERGHE AND SYLVAN EISENBERG

In a previous paper of the same title[1] a formula with a single parameter was set up which provided

(1) P. Van Rysselberghe and S. Eisenberg, THIS JOURNAL, **61,** 3030 (1939).

a good description of the behavior of activity coefficients of concentrated aqueous electrolytes. The formula was tested successfully in a large number of cases besides those reported in our previous paper and we consider it as valuable in itself as a purely empirical contribution It has, however, no theoretical basis and we are very much indebted to Dr. H. C. Eckstrom for calling our attention to the fact that in formula (15) of this previous paper the quantity $F_{iw} = -kT \log Y$, calculated from Ursell's theory of imperfect gases should have been set equal to $N_i \Delta\mu_{iw} + N_0 \Delta\mu_{ow}$, N_0 being the number of molecules of solvent in the volume V and $\Delta\mu_{ow}$ the van der Waals contribution to the chemical potential of the solvent (other notations as in our previous paper), and not to $N_i \Delta\mu_{iw}$ alone. A complete calculation should take the solvent into account explicitly, but in our treatment it appears as the volume term. If one accepts the various other assumptions previously made, one has for the total van der Waals free energy of the solution (considered as a Gibbs free energy)

$$G_w = N_i \Delta\mu_{iw} + N_0 \Delta\mu_{ow} = kT \left[\frac{1}{2}\frac{N_i^2}{V} v + \frac{5}{64}\frac{N_i^3}{V^2} v^2\right] \quad (1)$$

Differentiating at constant pressure, temperature and N_0, we get the following contribution to the logarithm of the average activity coefficient of the ions:

$$\begin{aligned} \log f_{\pm w} &= \frac{\Delta\mu_{iw}}{kT} = \frac{1}{kT}\frac{\partial G_w}{\partial N_i} \\ &= \frac{N_i}{V} v + \frac{15}{64}\left(\frac{N_i}{V}\right)^2 v^2 + \frac{1}{kT}\cdot\frac{\partial G_w}{\partial V}\cdot\frac{\partial V}{\partial N_i} \\ &= \frac{N_i}{V} v + \frac{15}{64}\left(\frac{N_i}{V}\right)^2 v^2 - \\ &\qquad \left[\frac{1}{2}\left(\frac{N_i}{V}\right)^2 v + \frac{10}{64}\left(\frac{N_i}{V}\right)^3 v^2\right]\frac{\partial V}{\partial N_i} \quad (2) \end{aligned}$$

in which $\partial V/\partial N_i$ is the average partial molecular volume of the positive and negative ions. For the activity coefficient of the solvent we deduce similarly the contribution

$$\log f_{\pm ow} = \frac{\partial G_w}{\partial V}\cdot\frac{\partial V}{\partial N_0} = - \left[\frac{1}{2}\left(\frac{N_i}{V}\right)^2 v + \frac{10}{64}\left(\frac{N_i}{V}\right)^3 v^2\right]\frac{\partial V}{\partial N_0} \quad (3)$$

The first effect of the correction (indicated to us by Dr. Eckstrom) is that the term in C of formula (19) of our previous paper is multiplied by 2 and the term in C^2 by 3. Our first additional term in $\partial V/\partial N_i$ may significantly affect the dependence of the activity coefficient on C^2, since v and $\partial V/\partial N_i$ are likely to be of the same order of magnitude.

In an entirely rigorous treatment one should, moreover, take into account a term containing the partial volume $\partial V/\partial N_i$ which arises from the electrostatic portion of the free energy and which is always neglected in the case of dilute solutions. The variation of dielectric constant with concentration might also be considered. We shall examine these points in the complete reinvestigation of the problem which we are planning to carry out.

Neglecting, as a provisional approximation, the terms in $\partial V/\partial N_i$ in (2), *i. e.*, using the formula

$$\log_{10} f_{\pm w} = -0.5059 \frac{\sqrt{C}}{1 + \frac{a}{3.042}\sqrt{C}} + 2.20626 \times 10^{-3} a^3 C + 2.62692 \times 10^{-6} a^6 C^2 \quad (4)$$

we have redetermined the ionic diameters for the fifteen alkali halides studied in our previous paper, in the range of concentrations 0.1 to 3 molar. We found the following average values (in parentheses we give the definite decrease observed in all cases from 0.2 to 3 molar):

LiCl:	3.82	(3.86–3.74)
LiBr:	3.93	(3.95–3.90)
LiI:	4.29	(4.43–4.20)
NaCl:	3.31	(3.43–3.15)
NaBr:	3.53	(3.58–3.41)
NaI:	3.69	(3.75–3.58)
KCl:	2.93	(3.10–2.75)
KBr:	3.02	(3.16–2.83)
KI:	3.22	(3.38–3.00)
RbCl:	2.72	(2.75–2.55)
RbBr:	2.71	(2.85–2.58)
RbI:	2.64	(2.78–2.53)
CsCl:	2.42	(2.50–2.37)
CsBr:	2.36	(2.48–2.30)
CsI:	2.17	(2.45–1.88)

CHEMISTRY DEPARTMENT
STANFORD UNIVERSITY
STANFORD UNIVERSITY, CAL. RECEIVED JANUARY 10, 1940

COMMUNICATIONS TO THE EDITOR

INHIBITION OF THE HYDROGENATION OF ETHYLENE BY NITRIC OXIDE

Sir:

Since the dissociation of ethane to yield ethylene and hydrogen is inhibited by nitric oxide,[1] one might expect the reverse reaction to be similarly affected. We find this to be the case. Times to 16% ethylene converted (by analysis) are given in the following table for mixtures of 180 mm. ethylene and 540 mm. hydrogen with and without 20 mm. nitric oxide.

Temp., °C.	t_{16} (min.) Pure	NO added	Ratio
500	38	48	0.79
550	6.2	13.5	0.46

The effect of the nitric oxide tends to fade out after about 20% reaction, just as in the case of the dissociation of *n*-butane.[2] The above ratios are therefore not a true measure of the maximum inhibition. There is little doubt, however, that the nitric oxide is more effective at the higher temperature.

Stavely[1] found that with 150 mm. of ethane at 620° the initial rates of pressure increase with and without addition of 20 mm. of nitric oxide were in the ratio 0.086. Although the dependability of pressure measurements is open to serious question, it is nevertheless evident that this result is in qualitative agreement with our data for the reverse reaction. A rough extrapolation of the latter gives 0.22 for the ratio at 620°. The maximum inhibition (at zero time) would be less than this.

We believe this is the first case in which forward and reverse reactions have been shown to be equally subject to inhibition.

(1) Stavely, *Proc. Roy. Soc.* (London), **162A**, 557 (1937).
(2) Echols and Pease, THIS JOURNAL, **61**, 1024 (1939).

FRICK CHEMICAL LABORATORY H. D. BURNHAM
PRINCETON, NEW JERSEY R. N. PEASE

RECEIVED JANUARY 22, 1940

INHIBITION OF ETHYLENE POLYMERIZATION BY NITRIC OXIDE

Sir:

A number of investigators have shown that the polymerization of ethylene is subject to acceleration by substances believed to give rise to radicals.[1] We find that the reaction is also subject to inhibition by nitric oxide. Thus, with 720 mm. of ethylene at 500° the time to 20% reaction is twenty-four minutes. Addition of 20 mm. of nitric oxide increases this to seventy-three minutes, the ratio of times being 0.33.

As in the hydrogenation of ethylene and the dissociation of *n*-butane,[2] the effect of nitric oxide fades out as reaction proceeds. The maximum effect is therefore greater than the data given above would indicate.

Since the polymerization of ethylene is subject to inhibition as well as acceleration, there can be little doubt that the reaction is of the radical chain type.

(1) Metal alkyls: H. S. Taylor and Jones, THIS JOURNAL, **52**, 1111 (1930); azomethane: O. K. Rice and Sickman, *ibid.*, **57**, 1384 (1935); oxygen: Lenher, *ibid.*, **53**, 3737, 3752 (1931).
(2) See previous communication, and Echols and Pease, THIS JOURNAL, **61**, 1024 (1939).

FRICK CHEMICAL LABORATORY H. D. BURNHAM
PRINCETON, NEW JERSEY R. N. PEASE

RECEIVED JANUARY 22, 1940

SODIUM SALT OF 2-METHYL-1,4-NAPHTHOHYDROQUINONE DIPHOSPHORIC ACID ESTER

Sir:

Fieser and Fry [THIS JOURNAL **62**, 228 (1940)] have described some sulfuric and phosphoric acid esters of substituted 1,4-naphthohydroquinones. In this Laboratory we have been occupied for some time with similar phosphoric acid esters and have also prepared such materials as were described by the above workers. In our syntheses we also isolated the intermediate phosphoryl chlorides and free phosphoric esters.

In particular we have investigated the pharmacology of the sodium salt of 2-methyl-1,4-naphthohydroquinone diphosphoric acid ester, and have found that by a slightly modified Ansbacher vitamin K eighteen-hour bioassay technique [*J. Nutrition*, **17**, 303 (1939)] the above material in doses of 0.6 to 0.8 gamma per chick administered subcutaneously reduces the clotting time to below ten minutes. Intravenously, the activity is similar, while the dose for oral effectiveness lies below 2 gamma, the minimum dose not yet having been determined. The lethal dose in mice by both

subcutaneous and intravenous administration is approximately 450 mg./kg. More complete pharmacological investigations will be reported elsewhere. All preliminary tests indicate an enormous margin of safety and absence of serious side reactions in any but the highest doses.

When it is considered that the anhydrous sodium salt has the molecular weight of 422 as compared with the molecular weight of 172 for 2-methyl-1,4-naphthoquinone, the most active material (0.5 gamma) hitherto reported, it appears that this sodium salt represents probably the most active antihemorrhagic substance known when compared on a molecular basis with methylnaphthoquinone. It also encourages speculation as to whether the antihemorrhagic effects of 2-methyl-1,4-naphthoquinone, of its reduced form, and of like substances, are not mediated through a phosphoric ester.

RESEARCH LABORATORIES R. H. K. FOSTER
HOFFMANN-LA ROCHE, INC., JOHN LEE
NUTLEY, N. J. ULRICH V. SOLMSSEN

RECEIVED JANUARY 20, 1940

THE PHOTOCHEMICAL REACTIONS OF OXALYL CHLORIDE AND PHOSGENE WITH CYCLOHEXANE

Sir:

The occurrence of the hypothetical —COCl free radical has been postulated as an intermediate in certain photochemical reactions: notably in the formation of phosgene [Bodenstein, *et al.*, *Z. physik. Chem.*, **B3,** 459 (1929)] and in the photochemical decompositions of both phosgene and oxalyl chloride [Rollefson, *et al.*, THIS JOURNAL, **56,** 1089 (1934); **58,** 443 (1936)]. In line with the program under way in this Laboratory on chain reactions in solution involving atoms and free radicals, we have studied the photolysis of both phosgene and oxalyl chloride dissolved in cyclohexane. In both cases we have been able to isolate the acid chloride of cyclohexane carboxylic acid. The yields appear to be quantitative. The over-all reactions are

$$C_6H_{12} + (COCl)_2 \longrightarrow C_6H_{11}COCl + HCl + CO$$
$$C_6H_{12} + COCl_2 \longrightarrow C_6H_{11}COCl + HCl$$

The following experiment with oxalyl chloride is typical of the procedure used. A 100-cc. flask (Pyrex glass) containing 25.2 g. of cyclohexane (0.3 m.) and 9.6 g. of oxalyl chloride (0.075 m.) was illuminated by a 300-watt tungsten lamp placed immediately below the flask. The heat from the lamp kept the reaction mixture refluxing gently. Gases were evolved. These were collected after passing through a trap at −80° and shown to consist of equal parts of carbon monoxide and hydrogen chloride. After twenty-four hours, the reaction mixture was fractionated and it was found that 4.2 g. of oxalyl chloride had reacted to form 4.1 g. of the acid chloride of cyclohexanecarboxylic acid (b. p. 99–101° at 52 mm.). The calculated yield is 4.8 g. The identification of the product was made by a determination of the neutralization equivalent and the preparation of the amide, m. p. 185–186°.

Phosgene reacts with cyclohexane in a similar manner. In this case quartz apparatus was used (a quartz reaction flask with a quartz mercury arc). In both cases the reaction takes place in the liquid phase as shown by identical results obtained in experiments in which care was taken to shield the vapor phase.

There can be little doubt that the reaction of phosgene and oxalyl chloride with cyclohexane in the light takes place through a free radical or atom mechanism in which the formation of the —COCl free radical plays a conspicuous rôle. In the gas phase the primary process in the photolysis of oxalyl chloride and phosgene has been postulated as follows

$$(1)\quad COCl_2 \xrightarrow{h\nu} {-}COCl + Cl^-$$
$$(2)\quad (COCl_2) \xrightarrow{h\nu} {-}COCOCl + Cl^-$$
$$(\text{or } 2)\quad (COCl)_2 \xrightarrow{h\nu} 2\,{-}COCl$$

In solution the absorption of light appears to be accompanied by the same primary step. This must be followed by reaction of the photolytic fragments with the hydrocarbon solvent. We hope to elaborate on the mechanism in our next publication.

The method of direct carboxylation appears to be fairly general and has been applied to a number of saturated hydrocarbons and their halogen derivatives. We are now engaged in studying the carboxylation of other types of organic compounds and the effect of various catalysts. It is of importance that means other than light of inducing the reaction have been found (*i. e.*, small quantities of organic peroxides are quite effective).

We are actively engaged in working out the details of this investigation and we hope to publish a full report shortly.

GEORGE HERBERT JONES LABORATORY
THE UNIVERSITY OF CHICAGO M. S. KHARASCH
CHICAGO, ILLINOIS HERBERT C. BROWN

RECEIVED JANUARY 18, 1940

NEW BOOKS

Molekülspektren und Molekülstruktur. I. Zweiatomige Moleküle. (Molecular Spectra and Molecular Structure. I. Diatomic Molecules.) By DR. GERHARD HERZBERG, Professor of Physics in the University of Saskatchewan. Verlag von Theodor Steinkopff, Residenzstrasse 32, Dresden-Blasewitz, Germany, 1939. xvi + 404 pp. 169 figs. 15.5 × 22.5 cm. Price, RM. 21; bound, RM. 22.50.

In the first chapter, the author gives a short survey of the principles of the theory of atoms and of atomic spectra, essentially a collection of the formulas and concepts necessary for the subsequent molecular theory. An empirical treatment of the molecular spectra is presented in the second chapter. In about twenty-five excellent figures, the different spectral types are reproduced; their interpretation in band head schemes for vibrational analysis or Fortrat diagrams for rotational analysis are represented in figures and tables. The theory for the rigid rotator and for the harmonic oscillator are developed by classical and wave-mechanical methods; the selection rules and the formation of the infrared and Raman spectra are derived from the theory in the next chapter. The expansion of the simple theory to the anharmonic oscillator and the connection between potential curves and dissociation are treated; besides that the non-rigid rotator and the symmetric top model are considered. The wave-mechanical derivations show the symmetry properties of the rotational functions; after the introduction of the nuclear spin, the author gives the explanation for the ortho and para modifications of hydrogen, heavy hydrogen and nitrogen. In an appendix, the isotope effect on rotation and vibration is derived.

Chapter IV includes a general empirical treatment of the visible and ultraviolet bands, based on an electronic transition and the superposition of the vibrational and rotational motions of molecules. The selection rules and the intensity relations of the Franck–Condon principle are derived. There is presented a very thorough and critical treatment of those methods, by which the molecular constants may be obtained from the measured spectrum lines. Chapter V contains the finer details of electronic bands: the multiplicity of the electronic states and the coupling of the molecular rotation with the motion of the electrons. In twenty-five pages, all the known types of electronic bands are explained with excellent figures and with typical examples. Quadrupole radiation, Zeeman effect in bands and perturbations are dealt with briefly. In Chapter VI, the Aufbauprinzip and the problems of the derivation of the term scheme of a molecule from those of the separated atoms on one hand and from the united atom on the other are given, as well as the symmetry properties of the single electrons and of the terms containing equivalent or different electrons. We find there the Heitler–London theory of valence and its extension to other molecules, and the concept of the ionic bond and of the van der Waals bond. In Chapter VII, continuous and diffuse molecular spectra are explained by potential energy curves. Here is presented the determination of the dissociation and predissociation limits, one of the methods of the band spectra research which finds valuable application to chemistry and astrophysics. It is no surprise to find this chapter is just perfect, for Herzberg is the leading physicist in this field, and we owe to him its major development. All the different methods for getting the heats of dissociation for molecules are excellently described. In the concluding chapter, we find some term schemes and potential energy curves and, in addition, a table of the constants for the normal electronic states of all the diatomic molecules and their isotopes, as far as they are known. Besides that, a brief summary is given of some applications of the results of band spectra analysis to other fields of physics, chemistry and astrophysics. The very extensive indices of books, papers, authors and subjects facilitate the use of the book.

The book appears at a time when the subject is well established and is written by one of the leaders in the field. Herzberg has carried through many analyses of bands, has explained diffuse spectra and determined final values for the heats of dissociation of nitrogen and oxygen. He has described all the methods he used so comprehensively and lucidly that no one faced with a problem in molecular analysis can find a better presentation. There are other books which treat the wave mechanical theory more thoroughly, but none which is more useful to the experimenter. In 1932, Max Born told in a lecture that band spectra theory is not difficult at all, only very complicated. I had my doubts. But Herzberg's book seems to prove that Born was right. Herzberg shows that there are no difficulties; but he could not possibly eliminate the complexities.

Every experimenter in band spectroscopy looks forward to the appearance of the second volume treating polyatomic molecules.

HANS G. BEUTLER

Qualitative Analysis by Spot Tests. Inorganic and Organic Applications. By Dr. Ing. FRITZ FEIGL, Director of the Research Laboratory, Soc. Belge de Recherches et d'Etudes, Gand.-Emerit. Professor of Analytical and Inorganic Chemistry of the University of Vienna. Second English Edition, translated from the Third German Edition by JANET W. MATTHEWS, Ph.D., F.I.C. Nordemann Publishing Company, Inc., 215 Fourth Avenue, New York, N. Y., 1939. xv + 462 pp. 27 figs. 36 tables. 16 × 24.5 cm. Price, $7.00.

The appearance of the second English edition of Feigl within less than two years of the first attests both the importance and recognition of an indispensable chemical tool. This second English edition is an authorized translation of the Third German edition, a review of which was published by THIS JOURNAL, **60**, 2831 (1938). It does not,

however, include the theoretical part, separate publication of which is announced in an insert.

This second English edition contains 62 more pages, 3 more figures and 5 more tables than the first. The general arrangement and sequence is precisely the same as that of the first, *cf. ibid.*, **60**, 734 (1938), the substantial increase of material being rather evenly distributed over the whole book. A very substantial increase in the number of references to the literature is particularly noticeable. The subject index has been greatly improved and occupies 37 pages as compared with 15 in its predecessor.

ERNEST H. HUNTRESS

Applied Mathematics in Chemical Engineering. By THOMAS K. SHERWOOD, Associate Professor of Chemical Engineering, and CHARLES E. REED, Assistant Professor of Chemical Engineering, Massachusetts Institute of Technology. McGraw-Hill Book Company, Inc., 330 West 42nd Street, New York, N. Y., 1939. xi + 403 pp. 113 figs. 16 × 23.5 cm. Price, $4.00.

Teachers of physical chemistry and of chemical engineering commonly find that the great majority of their students cannot use the calculus as an effective tool in dealing with chemical problems. Even those who have taken Freshman and Sophomore courses in college mathematics commonly have difficulty in thinking of a derivative as anything else than the slope of a curve or of an integral as anything except the area under a curve. Most of them have trouble when the independent variable is time or temperature, or pressure, or volume, or mole fraction. They may be able to differentiate or integrate complicated functions covering the whole range of Peirce's Tables of Integrals but many of them are unable to set up the proper differential equations applicable to chemical or chemical engineering problems, or evaluate integration constants from the boundary conditions. Many teachers of chemistry handle this situation either by avoiding the use of calculus or by devoting the time in the chemistry classes to teaching calculus; and in their spare time they cuss the Mathematics Department. Sherwood and Reed have attempted to meet this pedagogical difficulty by writing a book covering the calculus and some other branches of mathematics with the illustrative examples taken mainly from the field of chemical engineering and chemical thermodynamics. The authors are justified in the claim made in the preface, "It should be possible for anyone with a good grounding in the calculus to follow the text without great difficulty." But a student who really had a good grounding in the calculus would find a large fraction of this text already familiar to him from his previous study, since much of the text is devoted to definitions of terms and explanation of mathematical procedures with the customary illustrations taken from geometrical problems to be found in any standard text on the calculus, supplemented by illustrations taken from chemical engineering which are not found in the texts written by mathematicians. It therefore appears that the text is really aimed at the student or professional chemical engineer whose previous grounding in the calculus is not good or at least partly forgotten so that he needs to renew his study of old material before tackling the problems drawn from chemical engineering and thermodynamics.

On the other hand, the book would not be suitable for a student with no previous knowledge of the calculus because too much that is fundamental is taken for granted, including the rules for the differentiation and integration of sums, products, ratios, surds, trigonometrical and exponential functions. Considerable systematic drill on the simpler parts of Peirce's Tables is essential for the mastery of the calculus and is not provided in this text. However, this is not a criticism because the book is not intended to be used in this way.

Although most of the book is devoted to the calculus, the other branches of mathematics discussed include infinite series (including Taylor's Theorem, Fourier's series and Bessel's Functions); numerical analysis (formulation of empirical equations to fit a set of data, numerical differentiation and integration and interpolation); graphical analysis including a discussion of logarithmic, polar and triangular graph papers and alignment charts; theory of errors, probability distribution curves and method of least squares.

The applications of the mathematical principles to chemical engineering are numerous and varied and are worked out in considerable detail in the text. In some cases the solution is given in generalized form and in others by highly specific numerical examples.

There are no practice examples for solution by the student scattered through the text but an appendix gives 38 problems of varied character, including some that are purely mathematical.

The authors in their preface say "Chemical engineering gives many indications of rapid advancement along quantitative and mathematical lines." This book will undoubtedly aid and stimulate this advancement as well as help many a laggard to keep up with the procession.

GRINNELL JONES

Vapor Charts and Special Tables for Turbine Calculations. By FRANK O. ELLENWOOD and CHARLES O. MACKEY, Professors of Heat-Power Engineering, Cornell University. John Wiley and Sons, Inc., 440 Fourth Avenue, New York, N. Y., 1939. iv + 43 pp. 21.5 × 28.5 cm.

The original "steam charts" first published by Professor Frank O. Ellenwood in 1914 showed the convenience in making calculations of having a chart of thermodynamic properties divided into many parts for easy reading. The present book of charts shows the thermodynamic properties of water, ammonia, dichlorodifluoromethane (freon), and air–water–vapor mixtures.

The steam charts employ specific enthalpy and log volume, the latter coördinates extending from 0.05 to 3500 cu. ft. per pound. A new chart for liquid water is also included accompanied by tables of jet velocities, squares of numbers, and barometric corrections. The design and test of performance of modern high pressure turbines requires a series of tedious and time-consuming calculations which will be much facilitated by the new charts.

Paper quality, type character, sharpness of intersections are everything that could be desired. The exact data

available have enabled the authors to prepare a set of tables which should possess a high degree of permanency.

FREDERICK G. KEYES

The Nature of the Chemical Bond and the Structure of Molecules and Crystals. By LINUS PAULING. Cornell University Press, 124 Roberts Place, Ithaca, New York, 1939. 429 pp. Price, $4.50.

The need for a modern and comprehensive discussion of the electronic structure of molecules, in particular as it affects their stability and their spatial configuration, has been keenly felt for some time and no other book could be more welcome than this treatise of Pauling. An idea of its scope may be given by a brief summary of contents. In order the chapter headings are as follows: I. Resonance and the chemical bond; II. The partial ionic character of covalent bonds and the relative electronegativity of atoms; III. The directed covalent bond. Bond strengths and bond angles. The magnetic criterion for bond type; IV. The resonance of molecules among several valence-bond structures; V. Interatomic distances and their relation to the structure of molecules and crystals; VI. Types of resonance in molecules; VII. The structure of molecules and complex ions involving bonds with partial double-bond character; VIII. The one-electron bond and the three-electron bond; IX. The hydrogen bond; X. The sizes of ions and the structure of ionic crystals; XI. The metallic bond; XII. A summarizing discussion of resonance and its significance for chemistry.

The author makes full use of the results of quantum-mechanical treatment of molecules but the presentation is substantially non-mathematical; as he says "The ideas involved...require for their understanding no more, or little more, mathematical preparation than the familiar concepts of chemistry." In the application of these general ideas to specific molecules examples are drawn from all fields of chemistry, so that an organic chemist will find in the book as much of immediate interest as, for instance, a specialist in the chemistry of complex inorganic ions.

The presentation, by and large, is lucid and a student with little more preparation than the four basic courses in chemistry should be able to digest most of the contents; yet even for one familiar with the field the reading will prove interesting and stimulating. Only few unimportant misprints and dubious statements have been noted in the text. To mention some: it would be desirable either to omit the numbers on the coördinate axes of figures like those on pp. 18 and 19 or to explain their meaning by giving the units; the statement on page 118 that a molecule resonates "with a high frequency" between two valence structures is unfortunate, if only from the pedagogical point of view. The reviewer objects to the casual manner in which the resonance energy is set equal to the free energy change (p. 189) without any discussion of the entropy changes accompanying the formation of a resonating structure.

Dr. Pauling has been so successful in his attack upon many of the problems in the field that his advocacy of the doctrine of the infallibility of Pasadenean research and the somewhat pontifical style in which this book is written are understandable and should not be taken amiss. The book is highly recommended to all who are not satisfied with the bond-dashes of a chemical text and wish to get a deeper understanding of their meaning.

G. B. KISTIAKOWSKY

Gmelins Handbuch der anorganische Chemie. (Gmelin's Handbook of Inorganic Chemistry.) Edited by E. PIETSCH. **Aluminum, Part A. Aluminum Alloys,** Supplementary Volume, Collection of Patents, Part I. By G. Apel. Verlag Chemie G. m. b. H., Corneliusstrasse 3, Berlin W 35, Germany, 1939. 880 pp. Price, RM. 72.

It is stated in the Preface that this Supplementary Volume covers all the patents on aluminum alloys which have appeared in Germany, England, France, Switzerland and the United States in the interval since the completion of the original volume on the subject (beginning of 1935) and up to February, 1938. Some 10,000 different specific combinations of elements are listed, the arrangement being alphabetical, based on the first letter of the symbols of the constituent elements. In a second column are given the percentage amounts of the alloying constituents; in a third the characteristics and uses of these combinations; and in a fourth column the patentee and the patent literature references. There is an additional list of the trade names or brands of aluminum alloys, with their manufacturer or inventor and their composition.

The concluding Part II of this volume is announced to appear by the end of 1939.

ARTHUR B. LAMB

Colloid Chemistry. (A Textbook.) By HARRY BOYER WEISER, Professor of Chemistry at The Rice Institute. John Wiley and Sons, Inc., 440 Fourth Avenue, New York, N. Y., 1939. viii + 428 pp. 103 figs. 15.5 × 23.5 cm. Price, $4.00.

Professor Weiser has rendered a further service to colloid science by writing this authoritative textbook. Apart from his own experimental contributions, he has been in a key position to observe the development of the subject as Chairman of the annual National Colloid Symposia for many years, and through the detailed consideration of the existing information with regard to inorganic colloids compiled in his previous three-volume monograph. Added to this is his power of clear and precise presentation.

This textbook is addressed to advanced undergraduate and graduate students and the purpose of the author is three-fold, "to acquaint the student with the foundations of colloid chemistry and with the role that the classical experiments have played in the development of the modern theories and applications of the subject; to formulate systematically and to correlate critically the theories underlying colloid chemical behavior; and to illustrate the widely diversified applications of the principles of colloid chemistry in such fields as the industrial arts, agriculture, and biology." However, it is the more purely scientific aspects of the subject that are chiefly dealt with, rather than applications and practical information.

The book is organized into six parts. The first occupies

one quarter of the text and deals with surface phenomena and the various manifestations of adsorption. Part II is the main section of the book. It deals with sols, their formation, purification, properties, constitution, stability and interaction with electrolytes and each other. Part III discusses gelatinous precipitates, jellies and gels. Part IV describes emulsions and foams; Part V, aerosols and solid sols. Part VI gives more extended consideration to contact catalysis, to dyeing and to colloidal clay.

This textbook is indispensable to serious students of the subject. It is attractively published and interestingly written.

JAMES W. MCBAIN

Biological Oxidation. By CARL OPPENHEIMER and KURT G. STERN. Nordemann Publishing Company, Inc., 215 Fourth Avenue, New York, N. Y., 1939. 317 pp. Illustrated. Price, $8.25.

The authors have divided their treatment of biological oxidations into two sections. In the first of these, the "General Part," which occupies the smaller half of the book, the theoretical aspects of oxidative enzymes are considered. Wieland's hydrogen activation theory and Warburg's interpretations of his experimental work are developed historically. Then the authors attempt to fuse these conflicting ideas into a "unitary theory" to represent the present status of an admittedly complex field. But unfortunately this scheme is not enough to make the present treatment a reasonably intelligible one. The writer feels that a more condensed and straightforward account with less emphasis on scattered literature references (there are 1383 in the book) would have been more acceptable.

The "Special Part" or second half of the book is most successful in its presentation of the chemistry of the enzymes. The following topics are treated: the hemin systems, the vitamin enzymes, the nucleotide derivatives, the quinoid mesocatalysts and the fumaric and citric acid systems. The material is complete, but not confusing, and is arranged in a logical way. Its careful study is full of reward for the reader.

The publisher, Dr. Junk of The Hague, Holland, is to be congratulated for the large number of valuable books he is now making available in the English language. It is hoped that he may soon be able to overcome the fairly abundant typographical errors, which in this particular volume are ever present and often confusing.

WILLIAM F. ROSS

Vitamin E. A Symposium held under the auspices of the Food Group (Nutrition Panel) of the Society of Chemical Industry on Saturday, 22nd April, 1939, at the School of Hygiene and Tropical Medicine, Keppel Street, London, W. C. 1, England. Published by the Society of Chemical Industry, Clifton House, Euston Road, London, N. W. 1, England, 1939. 88 pp. 13.5 × 21 cm. Price, 5/- post free.

This small book contains the papers presented at the Symposium, and the remarks made from the floor during the ensuing discussions. The Symposium was organized into three sections. Section I dealt with the "Chemical Structure and Properties of Tocopherol," and papers were presented by A. R. Todd, P. Karrer, A. Emmerle and Chr. Engel, and E. L. Smith and R. Bailey. As the Symposium occupied only one day, and there were many papers, the individual contributions were of necessity brief. As a consequence the papers cannot be regarded as complete reviews, for instance, those of Todd and Karrer (Dr. Karrer's paper was read by Dr. Bergel) in no way compare in extent or in critical value with reviews of the chemistry of vitamin E published elsewhere.[1] Nevertheless the brief papers serve admirably to define the position of various phases of vitamin E research at the time of the meeting. The paper by Emmerle and Engel contains a good discussion of their ferric chloride–α,α'-dipyridyl analytical method, and the paper by Smith and Bailey contains a critical discussion of all of the analytical methods in common use for the determination of tocopherols.

Section II of the Symposium dealt with "Physiological Action of Vitamin E and the Consequences of Vitamin E Deficiency." Papers in this group were contributed by J. C. Drummond, K. E. Mason, S. W. F. Underhill, T. Moore, A. J. P. Martin and K. R. Rajagopal, A. M. Copping and V. Korenchevsky, and A. L. Bacharach. The topics included a general discussion of the physiological aspects of vitamin E (Drummond, Moore, *et al.*); the relationship between the vitamin and the reproductive functions (Mason); the connection between vitamin E deficiency and the endocrine glands (Underhill); the effect of vitamin E deficiency on the weights of organs of male and female rats (Copping and Korenchevsky); and a critical discussion of the methods of bioassay (Bacharach). The papers in this group are uniformly good, although, again, the manuscripts are too brief to be classed individually as comprehensive reviews.

Section III of the Symposium dealt with "Clinical and Veterinary Uses of Wheat Germ Oil and Vitamin E Preparations." Papers in this group were presented by P. Vogt-Moller, E. Shute, D. W. Currie, C. R. MacDonald, and F. J. Browne. The papers in this group show a lack of agreement as far as the uses of vitamin E in human and veterinary medicine are concerned: it is claimed (V-M.) that 75% of the cases of habitual abortion are treated successfully; the usefulness of vitamin E in the treatment of this condition is denied, but it is claimed that success is achieved in 68% of the cases of threatened abortion (S.), while again habitual abortion is amenable to treatment with vitamin E, while threatened abortion is not (MacD.). Such disagreements as to the results and value of the clinical experiments are to be expected at the present stage in the development of vitamin E therapy, and much good cannot fail to result from an open discussion among the active workers in the field. These papers are presented with candor and restraint, and with an admirable regard for the variables and uncertainties involved.

The reports of the discussions of the various papers, while very brief [some of the discussions are reported in greater detail in *Angew. Chem.*, **52**, 427–430 (1939)] constitute one of the most interesting features of the book,

(1) (a) Karrer, *Helv. Chim. Acta*, **22**, 334 (1939); (b) John, *Angew. Chem.*, **52**, 413 (1939); (c) John, *Ergeb. Physiol. biol. Chem. exptl. Pharmakol.*, **42**, 1 (1939).

for these discussions serve to emphasize, even more than the papers themselves, unsettled questions and so point the way to future researches.

This Symposium, including among its members a large number of the foremost authorities in the various phases of vitamin E research, is a tribute to its promotors and to the Society which they represent and the little volume issued as a report is a most welcome addition to the rapidly growing literature on vitamin E. While the papers are presented by and for specialists in the field, nevertheless the general reader may gain from the book an accurate picture of the general knowledge concerning vitamin E as it existed last April, when such a congress of authorities from many nations was still possible.

LEE IRVIN SMITH

Nomogramme zum Mineral Bestimmen mit Röntgenstrahlen. (Charts for the Analysis of Minerals by X-Rays.) By M. MEHMEL. University of Rostock. Verlag der Deutschen Mineralogischer Gesellschaft e.V. through the Verlagsbuchhandlung Gustav Fischer in Jena, 1939. 13 charts. 21 × 29 cm.

The identification of crystalline compounds by means of their X-ray powder diffraction patterns has potential possibilities which have not yet been fully utilized. The recent tables of Hanawalt, Rinn and Frevel (*Ind. and Eng. Chem., Anal. Edition*, **10**, 475 (1938)) giving the spacings and relative intensities for 1000 compounds, represent the first big step toward making X-ray identification a practical working method. The Mehmel charts are essentially supplementary to data such as given in the Hanawalt tables. The charts give the diffraction diagrams for 17 minerals of interest in sedimentary petrography (quartz, calcite, clays, feldspar, etc.). Each pattern is represented by a series of vertical lines, the height of a line giving the intensity, and the lines being plotted against log sin Θ as abscissa. For each mineral there are three charts corresponding to Cu, Fe and Cr radiation. Since the charts give a direct picture of the diffraction pattern, they are a useful supplement to tabulated spacing data.

The wisdom of plotting intensity against log sin Θ seems to be very questionable. Plotting against Θ gives directly the appearance of the diffraction pattern, plotting against sin Θ crowds together the lines at large angle, and plotting against log sin Θ crowds the large angle lines still more. The only advantage to be had from plotting against log sin Θ comes from the fact that one chart will suffice to give the line positions for any wave length. In this series, however, since charts are given for three different wave lengths, there is no advantage to plotting against log sin Θ. The three charts for each structure would have been better spaced, and better suited to direct comparison, if plotted against Θ or 2Θ.

In order to make the identification of unknowns by powder patterns a working method, it would be ideal to have the tabulated spacing and intensity data, charts giving the appearance of the diffraction patterns, and the type of index suggested by Hanawalt which gives the strongest lines of various substances catalogued in order of decreasing spacing. An enormous amount of work is involved in the preparation of such tables and charts. It appears to the reviewer that before going farther with the preparation of a series of charts, the question of plotting against Θ rather than log sin Θ should be seriously considered. The charts are clearly labelled, well drawn, and of generous size. They appear to be quite accurate and reliable and will certainly find use.

B. E. WARREN

The Raman Effect and its Chemical Applications. By JAMES H. HIBBEN, Research Physical Chemist, Geophysical Laboratory, Carnegie Institute of Washington, with a Theoretical Discussion by JAMES H. HIBBEN and EDWARD TELLER, Professor of Physics, The George Washington University. American Chemical Society Monograph Series. Reinhold Publishing Corporation, 330 West 42nd Street, New York, N. Y., 1939. 544 pp. 72 figs. 15.5 × 23.5 cm. Price, $11.00.

For some time there has existed the need for a comprehensive survey in English on the Raman effect, and, in some respects, the present one may supply this need. The book is divided into three main sections of which the first, 122 pages, is devoted mainly to theory, the second discusses experimental results, their interpretation, and their applications to chemical problems and the third is an extraordinarily complete and useful bibliography.

The theoretical part treats in a clear and simple manner the rotations and normal vibrations of molecules, the infrared and Raman effect, and the far reaching conclusions that may be drawn from a consideration of the electric polarizabilities of molecules. The discussion of normal vibrations, polarizability, and the selection rules, is from a purely physical or intuitive point of view; no use is made of complicated dynamics or the intricacies of the group theory, and only a knowledge of elementary physics is necessary to understand the treatment given. A description of the fundamental modes of vibration is given for some of the important symmetrical molecules. The beginner and experienced worker alike will find the theoretical part of interest, but he may regret that additional chapters dealing with the subject in a more fundamental and complete manner are not included. It is regrettable that a more complete table of degeneracies and polarizations of permitted Raman lines for a larger variety of molecular types is not included, that the use of molecular spectra in thermodynamics is so briefly treated, and that the more familiar q and Q rather than Greek letters are not used to represent generalized and normal coördinates.

The second section of the book is divided into two parts, and it presents a survey and discussion of the experimental results for a large number of organic and inorganic compounds, respectively, both in their normal state of aggregation and in solution. In the case of gases and comparatively simple molecules in the liquid state for which fairly complete analyses of the spectra have been made, the results are given in moderate but not always sufficient detail; but since the great majority of molecules and solutions studied are too complicated to permit of exact treatment, a more or less qualitative point of view is adopted. This method of treatment has some value, but it is not as satisfying or illuminating as the exact one, and its extensive use often makes the content of the book descriptive rather

than analytical. An attempt is made to present the large mass of available material critically and to clarify, augment, or correct statements found in the literature, but the imposed brevity decreases the value of the effort somewhat; not infrequently the content consists of a mere abstract of results. In some cases, for example that of the intensity relations in the pure rotation spectrum of nitrogen, the fundamental importance of the results is not even stated. In spite of these defects, those working in the field may find the survey of results very useful and timesaving. Many applications of Raman spectra to chemical problems are clearly described, and data are to be found that have been published only in inaccessible journals.

In the last section of the book the reader will find an excellent bibliography arranged alphabetically according to authors, and an index of compounds whose Raman spectra have been studied. References to nearly two thousand papers are given.

The book contains a good many errors of one sort or another: thus, none of the calculated interatomic distances in Table 60 are in accord with either the accepted values or the values calculated from frequencies by more precise methods; the force constants in Table I are not precisely defined; the use of the term "symmetrical vibration" is confusing (pages 79 and 80); Fig. 11 represents ClCN as bent, when in fact this molecule is linear; equation 27 is wrong by a factor of 2π; and on page 221 the structural formulas of cedrene are confusing and apparently incorrect. The typography in this book is of indifferent quality; for example, the type used for the symbols M, D, K and Roman subscripts and superscripts is too large, the signs of integration are much too long and a capital T in place of the more acceptable t is used to represent time. There are typographical errors in equation 39, and in the one leading to 20.

We consider that this book will prove useful to those interested in the field. We also believe that the price is too high. This country has now taken the lead in scientific research, and the publication of books of a research character becomes our responsibility; it would be a pity if excessively high prices prevented the free circulation of such books among the very people for whom they are intended.

DON M. YOST

BOOKS RECEIVED

December 10, 1939, to January 10, 1940

PAUL ARTHUR. "Lecture Demonstrations in General Chemistry." McGraw-Hill Book Co., Inc., New York, N. Y. 455 pp. $4.00.

EUGENE C. BINGHAM, Editor. "Rheological Memoirs." Volume 1, No. 1. Rheological Memoirs, Easton, Pa. 101 pp. $2.00 per volume.

G. W. SCOTT BLAIR. "Einführung in die technische Fleisskunde." Translated from the English by H. Kauffmann. Verlag von Theodor Steinkopff, Dresden-Blasewitz, Germany. 132 pp. RM. 6, bound, RM. 6.75.

W. BÖTTGER, Editor. "Physikalische Methoden der analytischen Chemie." Dritter Teil. Akademische Verlagsgesellschaft m. b. H., Leipzig, Germany. 863 pp. RM. 63, bound RM. 65.

WILLIAM C. BRAY AND WENDELL M. LATIMER. "A Course in General Chemistry." Third edition. The Macmillan Co., 60 Fifth Avenue, New York, N. Y. 206 pp. $1.60.

NEIL E. GORDON AND WILLIAM E. TROUT, JR. "Introductory College Chemistry." Second edition. John Wiley and Sons, Inc., 440 Fourth Avenue, New York, N. Y. 753 pp. $3.50.

W. H. HATCHER. "An Introduction to Chemical Science." John Wiley and Sons, Inc., 440 Fourth Avenue, New York, N. Y. 423 pp. $3.00.

JOEL H. HILDEBRAND. "Principles of Chemistry." Fourth edition. The Macmillan Co., 60 Fifth Avenue, New York, N. Y. 359 pp. $2.50.

N. A. MCKENNA. "Theoretical Electrochemistry." D. Van Nostrand Co., Inc., 250 Fourth Avenue, New York, N. Y. 469 pp. $5.50.

C. I. REED, H. C. STRUCK AND I. E. STECK. "Vitamin D." The University of Chicago Press, Chicago, Illinois. 389 pp. $4.50.

BRUCE H. SAGE AND WILLIAM N. LACEY. "Volumetric and Phase Behavior of Hydrocarbons." Stanford University Press, Stanford University, California. 299 pp. $5.00.

ALFRED T. SHOHL. "Mineral Metabolism." No. 82, American Chemical Society Monograph Series. Reinhold Publishing Corporation, 330 West 42d St., New York, N. Y. 384 pp. $5.00.

THE SVEDBERG AND K. O. PEDERSEN. "Die Ultrazentrifuge." Band VII of the "Handbuch der Kolloidwissenschaft." Verlag von Theodor Steinkopff, Dresden-Blasewitz, Germany. 433 pp. RM. 26.25; bound RM. 27.25.

"Gmelins Handbuch der anorganischen Chemie." System Nummer 68. "Platin. Vorkommen." Teil A, Lieferung 2. Verlag Chemie, G. m. b. H., Berlin W 35, Germany. 165 pp. RM. 19.50.

"Gmelins Handbuch der anorganischen Chemie." System Nummer 68. "Platin. Physikalische Eigenschaften des Metalls." Teil B, Lieferung 2. Verlag Chemie, G. m. b. H., Berlin W 35, Germany. 107 pp. RM. 12.75.

"Gmelins Handbuch der anorganischen Chemie." System Nummer 68. "Platin. Electrochemisches Verhalten des Metalls." Teil B, Lieferung 3. Verlag Chemie, G. m. b. H., Berlin W 35, Germany. 81 pp. RM. 10.50.

JOURNAL OF THE
AMERICAN CHEMICAL SOCIETY

VOLUME 62 MARCH 9, 1940 NUMBER 3

[CONTRIBUTION FROM EASTERN EXPERIMENT STATION, BUREAU OF MINES, U. S. DEPARTMENT OF THE INTERIOR]

The System Calcium Oxide–Silica–Water at 30°. The Association of Silicate* Ion in Dilute Alkaline Solution

BY PAUL S. ROLLER AND GUY ERVIN, JR.

Knowledge of the compounds of hydrated calcium silicate and their equilibria is important in cement technology and in regard to the use of siliceous minerals in cement.

Hydrated calcium silicate is gelatinous at room temperature, regardless of method of preparation or time. However, the units of physical structure may be well-organized and definite, since X-ray analysis has shown that most inorganic gelatinous or amorphous materials are in reality crystalline, while all are crystalline (to X-rays) whose atoms or radicals are di- or monovalent.[1] A diffraction pattern has in fact been reported by Chassevant[2] for hydrous calcium silicate and has been corroborated by Foret.[3]

A high adsorption will be expected of the gelatinous silicate because of the minute size of the particles. Kolthoff and Moskovitz[4] observed that hydrous $Fe(OH)_3$ adsorbed $Cu(OH)_2$ up to 0.42 mole per mole. Weiser[5] found that gelatinous cupric ferrocyanide adsorbed potassium ferrocyanide continuously up to 0.85 mole per mole. The constancy of the x-ray diffraction pattern of the gel with varying ratios of alkali to copper[6] furnished direct proof of the adsorption character of the combination, although the possibility of a small amount of solid solution was not excluded. Similar results were obtained with the ferrocyanides of cobalt, nickel and manganese. A low adsorption was exhibited by lead ferrocyanide, which conformed to its coarsely crystalline character.

In general, owing to fineness of the microcrystals, solubility values for hydrous calcium silicate may be high. However, they will be generally reproducible if a similar state of growth of the microcrystals persists, so that active, or conversely normal, peripheral atoms are consistently dominant. The exclusively gelatinous character of calcium silicate formed at room temperature and lack of evidence of aging indicate the possibility of a fairly definite physical configuration and corresponding fairly definite solubilities.

The time required to reach equilibrium depends on the mode of experiment, the character of the starting materials and the degree of agitation. Fused calcium silicate may be decomposed with water, or, conversely, silica may be combined with dissolved calcium hydroxide. In both cases, observers have found that weeks or months may be required for complete reaction, particularly if agitation is poor; in side experiments with continuously rotated mixtures of silica gel and lime water of limited concentration we noticed that the concentration was decreasing appreciably after seven days. To expedite reaction, steel balls have been recommended for breaking up the

(*) U. S. Bureau of Mines, College Park, Md. Published by permission of the Director of the Bureau of Mines, U. S. Department of the Interior. (Not copyrighted.)

(1) J. Böhm and H. Niclassen, *Z. anorg. Chem.*, **132**, 1–9 (1923).

(2) L. Chassevant, *Compt. rend.*, **199**, 673–675 (1934).

(3) J. Foret, *ibid.*, **203**, 80–83 (1936).

(4) I. M. Kolthoff and B. Moskovitz, *J. Phys. Chem.*, **41**, 629–644 (1937).

(5) H. B. Weiser, *J. Phys. Chem.*, **34**, 335–351 (1930).

(6) H. B. Weiser, W. O. Milligan and J. B. Bates, *J. Phys. Chem.*, **42**, 945–954 (1938).

coagula.[7,8] A third method of experiment consists in precipitating hydrous calcium silicate and treating this with lime water. Because in this method the initial solid phase is a hydrous compound more or less closely related to the final products of equilibrium, a comparatively rapid approach to equilibrium would be expected. This in fact has been realized in the present work.

Chemical analysis has in the past frequently neglected the correction due to dissolved silica. The solubility of silica is relatively high at the lower lime concentrations and so will affect acid titration, conductivity measurement, and the apparent composition of the solid phase if the latter is estimated by difference. In the present work, separate analysis has been made for CaO and SiO_2 in the liquid and solid phases.

Experimental

The preparation of the calcium silicate and the equilibrium experiments were carried out in a three-necked flask which was contained in a water-bath controlled at 30.2° and was protected at all times from air by tested soda-lime tubes appropriately placed. The solid was prepared by the slow addition from a buret of 15–40 cc. of sodium metasilicate solution, preheated to 30.2°, to 2 liters of 15–50% saturated lime water, the mixture being stirred vigorously by means of a mercury-seal stirrer during the addition. About 300 mg. of flocculent precipitate was thus formed in the presence of excess calcium hydroxide in solution. After the precipitate had settled, the supernatant liquid was decanted, and the precipitate was washed by decantation and settling seven times with 500-cc. portions of lime water. The solid was then stirred with 2 liters of lime water of known concentration for twelve hours to five days until equilibrium had been well established. The supernatant liquid was then drawn off, filtered through a Jena G3 filter, and its analysis begun immediately. The wet solid was next drawn off for analysis into a stoppered centrifuge tube. In this tube it was washed with 10 times its volume of aqueous acetone of such concentration (50% or stronger) that a precipitate of calcium hydroxide just was avoided. Activity of calcium hydroxide in the wash solution was secured in this way sufficient for avoiding decomposition of the solid. The second wash was made with a stronger solution of acetone, or with pure acetone; this was followed by three washings with acetone and three with ether, after which the solid was filtered and allowed to dry. For solid phases in equilibrium with very dilute lime water (3 mmole of $Ca(OH)_2$/l. or less) the washing with acetone was omitted and a slight correction made for the calcium oxide in the centrifuged wet residue. The dry solid contained only about 0.05% Na_2O by spectrographic test.[8a]

All reagents were C. P. and were examined under the microscope for noticeable impurity. The lime water was made up by dilution, in the absence of carbon dioxide, of a filtered solution. The sodium metasilicate crystals were kept in a tightly stoppered bottle in a desiccator; 200 cc. of solution was made up as required. The solution always contained a small amount of carbonate that was determined by a sensitive turbidimetric method described elsewhere.[9] The carbonate was assumed to have reacted with the calcium hydroxide in solution, so that the equivalent amount of calcium oxide was subtracted in determining the composition of the solid phase. The correction amounted rather uniformly to 0.07%.

Hydroxyl was estimated by titrating 50 to 200 cc. with 0.1 *N* hydrochloric acid in the presence of phenolphthalein. Calcium was determined in the usual manner by precipitating as calcium oxalate, and titrating hot with 0.1 *N* potassium permanganate solution. Silica in solution was determined by the colorimetric method of King and Dolan[10] in which silicomolybdate is reduced with 1:2:4 aminonaphtholsulfonic acid containing sulfite. The solution of the reagent was kept in a refrigerator as directed. The standard silica solution was made up by dilution of a gravimetrically analyzed solution of sodium metasilicate. For constancy of standard it was found absolutely necessary to paraffin the bottles containing the metasilicate solutions. A calibration curve was used, and the precision of estimating silica was ±0.8%.

The solid phase was analyzed by dissolving in hydrochloric acid, evaporating to dryness in a platinum dish, and determining the silica by repeated dehydration in the usual way. The ignited silica was treated with hydrogen fluoride and the insoluble residue corrected for. The silica filtrate was analyzed for calcium as described.

Equilibrium and Reversibility.—The ratio CaO/SiO_2 in the solid phase (written for short C/S) is shown in Table I and Fig. 1 as a function of the concentration of Ca^{++} at equilibrium. There are four phase ranges, I, II, III and IV, of which II and IV are invariant with respect to concentration. All experimental points are included, except one in range IV where the initial washing out of the alkali had been neglected. In range I, which differs from IV in its much higher *p*H, omission of the same wash in two instances did not affect the consistency of the values obtained, and they were included in the total.

In these experiments, three factors were involved in the attainment of equilibrium: the time of contact (column 6), the direction of approach to equilibrium (column 7), and the nature of the solid phase. The direction is labeled S (synthesis) when the final solid phase was formed by combination of the initial solid with lime from

(7) W. M. Shaw and W. H. MacIntire, *Soil Sci.*, **29**, 429–456 (1930).

(8) T. Thorvaldson and V. A. Vigfusson, *Trans. Roy. Soc. Canada*, Ser. 3, **22**, 423–431 (1928).

(8a) Made by M. Slavin, of this Station.

(9) P. S. Roller and G. Ervin, Jr., *Ind. Eng. Chem., Anal. Ed.*, **11**, 150–153 (1939).

(10) E. J. King and M. Dolan, *Can. Med. Assoc. J.*, **31**, 21–26 (1934).

TABLE I

EQUILIBRIUM CONCENTRATIONS OF CALCIUM ION AT DIFFERENT RATIOS OF CaO TO SiO_2 IN THE SOLID PHASE

Phase range	Expt.	Millimoles/liter Ca^{++}	Activity Ca^{++}	CaO/SiO_2	Time of contact, days	Approach
I	1	20.67	6.87	1.401	5	S
	2	19.96	6.75	1.447	1	S
	3	19.90	6.74	1.417	5	S
	4	19.60	6.70	1.427	8	S
	5	17.51	6.32	1.387	1	S
	6	14.98	5.81	1.326	5	S
	7	13.53	5.51	1.309	5	S
	8	12.08	5.14	1.267	0.5	S
	9	9.81	4.54	1.235	1	D
	10	7.49	3.80	1.187	5	S
	11	6.99	3.62	1.168	1	D
	12	6.60	3.49	1.164	5	S
	13	4.89	2.82	1.116	5	S
	14	4.02	2.45	1.100	1	D
II	15	3.11	1.99	1.053	1	D
	16	3.10	1.99	1.048	5	S
	17	3.05	1.97	1.008	4	D
	18	3.11	1.99	1.014	1	S
	19	3.07	1.98	1.000	2	S
III	20	2.84	1.87	0.955	2	D
	21	2.69	1.79	.957	2	D
	22	2.57	1.72	.955	4	D
	23	2.24	1.54	.964	1	D
	24	2.09	1.46	.936	1	D
	25	2.07	1.44	.933	2	D
	26	1.64	1.19	.910	2	S
	27	1.60	1.17	.918	1	D
	28	1.60	1.17	.919	1	D
	29	1.37	1.03	.921	1	D
	30	1.18	0.902	.901	1	D
	31	0.990	.768	.895	2	D
IV	32	.897	.705	.869	4	D
	33	.923	.724	.854	4	D
	34	.900	.707	.852	2	D
	35	.900	.707	.819	2	D

a more concentrated solution than that in which the solid was formed. Conversely, the direction is labeled D (decomposition) when calcium oxide was released to a more dilute solution.

In range I, the same results were obtained after three hours as after five days, as may be seen from the following data (S direction):

	3 hr.	5 d.	3 hr.	5 d.	3 hr.	5 d.
Concn. Ca^{++} (mml./l.)	4.85	4.93	7.49	7.48	15.18	14.78
C/S in solid	1.110	1.116	1.188	1.186	1.326	1.326

To test reversibility in range I, a D approach was effected by diluting the mixture of expt. 5 (Table I). After one day of contact the results of expt. 11 were obtained, which agree very closely with those obtained by the reverse approach.

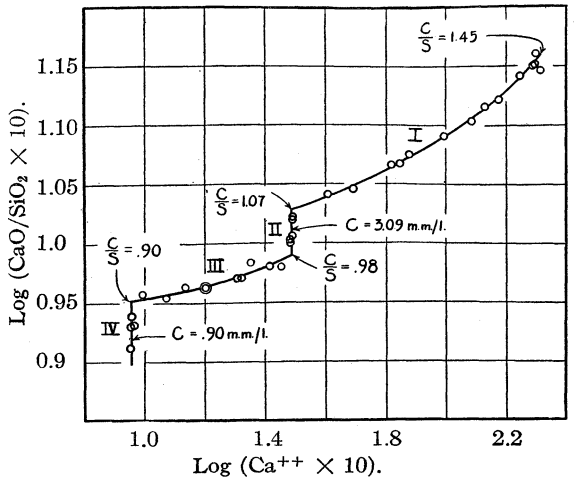


Fig. 1.—Mole ratio of CaO to SiO_2 in solid against concentration of calcium ion in solution (millimoles/liter).

The rapid and reversible equilibrium observed for range I also has been observed by Baylis.[11]

In range II no special tests were made, but the two directions of approach, and widely varying times, were used (Table I).

In range III, after one day of contact (D approach) a concentration of 2.57 mml./l. and a C/S ratio of 0.957 were obtained; the result after four days was 2.43 and 0.954, so that one day appeared adequate for attainment of equilibrium. However, in the reverse approach in the same region, it seemed that two days were required, since the results of expt. 26, which are comparable with those of expt. 27, were arrived at in not less than this time.

In range IV at least two days were required in a D approach to reach the invariant concentration, the greater time being due no doubt to comparative slowness of the compound transformation. It did not seem feasible to test reversibility in this range because of complete solution of the solid when it was treated with water in attempting to obtain a sufficiently low C/S ratio in preparation for an S approach.

The above tests indicate that the stirring times listed in Table I were sufficient; the consistency of the results for widely varying times and different directions of approach attests further to the establishment of equilibrium.

Nature of the Solid Phases

Because of their gelatinous adsorptive character, the composition of compounds in the solid phases may not be determined in the usual way.

(11) J. R. Baylis, *J. Phys. Chem.*, **32**, 1236–1262 (1928).

However, they may be identified by the application of physical chemical considerations. Two of these are: adsorption isotherm and ion product constant.

Evidence of Adsorption Isotherm.—The continuously changing composition and the rapid approach to equilibrium in ranges I and III are characteristic of adsorption. However, only part of the calcium oxide in the solid phase is adsorbed; the rest is combined in an adsorbing compound. Since in range I the C/S ratio was 1.07 to 1.45, the absorbent may be a 1/1, 4/5, 2/3 or 1/2 compound, etc. For a given ratio, the moles of calcium oxide adsorbed may be calculated with reference to any one of these possible combinations. In Fig. 2, the adsorption per mole of 2/3, 4/5 and 1/1 compound has been plotted against log concentration of Ca^{++} and against log activity of Ca^{++}, as for a Freundlich isotherm. Activity coefficient of Ca^{++} was calculated by the usual Debye–Hückel formula, $-\log \gamma_2 = 2.02 \sqrt{\mu} - 0.40 \mu$, the coefficient 0.40 being deduced from the data of Fosbinder[12] for calcium hydroxide.

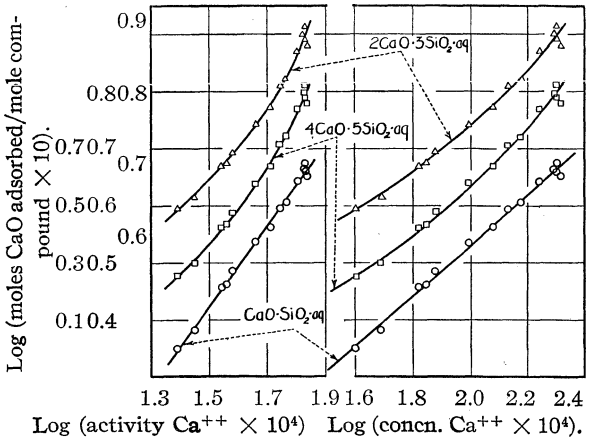


Fig. 2.—Freundlich adsorption isotherm plots for different assumed compounds (range I). (Ordinates reading from left to right are for 1:1, 4:5 and 2:3 compounds, respectively.)

It is observed that a straight line is obtained for a 1/1 compound, thus satisfying a Freundlich isotherm, but a curved line is obtained for a 4/5 compound, and a still more curved line for a 2/3 compound. Due to a fortuitous rate of increase in the activity coefficient for Ca^{++}, the same relations are obtained for concentration or activity but the distinctions are more pronounced for activity. It is inferred, therefore, that the adsorbing compound in range I is, empirically, $CaO \cdot SiO_2 \cdot aq$. The value of n in the Freundlich equation ($x/m = ac^{1/n}$) is 0.70 for activity and 1.13 for concentration.

According to Lefol[13] and to Cirilli,[14] calcium silicate retains one mole of water at high temperatures, and so this molecule is constitutional. The empirical monosilicate is probably, therefore, structurally the acid salt of orthosilicic acid, or $CaH_2SiO_4 \cdot aq$. The existence of orthosilicic acid is known from vapor tension measurements.[15,16] Its existence is demonstrated further by the wet preparation of thallous orthosilicate by Vesterberg and Willers.[17] For these and other reasons, we shall consistently adhere to the orthosilicate, rather than the metasilicate, terminology. However, the terminology is essentially immaterial as far as our conclusions are concerned.

The adsorption isotherm holds right up to lime saturation, so there is no indication of a silicate higher than the 1/1 compound. Furthermore, the mean maximum C/S ratio, corresponding to 20.7 mml. CaO/l. (somewhat in excess of true lime saturation, or 19.4 mml./l.),[18] was only 1.45, whereas even for a 3/2 compound a ratio more nearly equal to 2 would be expected due to adsorption. The apparent non-existence at 30° of $3CaO \cdot 2SiO_2 \cdot aq$., or of $2CaO \cdot SiO_2 \cdot aq$., may be explained by the difficulty of displacing the first two hydrogens of orthosilicic acid. Britton[19] found no break in the titration curve that would correspond to dissociation of these. Sodium orthosilicate has never been crystallized, even in the presence of a great excess of sodium hydroxide. Although Vesterberg and Willers obtained insoluble thallous orthosilicate, this occurred only under unusually favorable conditions, as by digestion of the insoluble 1:1 compound with concentrated thallous hydroxide.

Nacken and Mosebach[20] believed that they had prepared hydrated calcium orthosilicate on treating tricalcium silicate with water; however, on prolonging the experiment (which involved intermittent shaking) from 30 to 278 days, the C/S ratio dropped to 1.55 and 1.68 in two experi-

(12) R. J. Fosbinder, THIS JOURNAL, **51**, 1345–1356 (1929).

(13) J. Lefol, *Compt. rend.*, **201**, 669–672 (1935); *Compt. rend. 17 Congr. Chim. Ind., Paris*, Sept.-Oct. 1937, 562–571.

(14) V. Cirilli, *Ann. chim. applicata*, **28**, 239–244 (1938).

(15) R. Spychalski, *Z. anorg. allgem. Chem.*, **239**, 317–320 (1938).

(16) P. A. Thiessen and O. Koerner, *Z. anorg. Chem.*, **189**, 168–182 (1930).

(17) K. A. Vesterberg and C. U. Willers, *Arkiv. Kemi Mineral. Geol.*, **9**, 1–8 (1926); *Chem. Abs.*, **20**, 1963 (1926).

(18) H. Bassett, *J. Chem. Soc.*, 1270–1275 (1934).

(19) H. T. S. Britton, *J. Chem. Soc.*, 425–436 (1927).

(20) R. Nacken and R. Mosebach, *Z. anorg. allgem. Chem.*, **223**, 161–173 (1935).

ments.[21] Beitlich[22] obtained a ratio of 1.95, from which he inferred the existence of an orthosilicate; however, he added solid lime to his mixture, and this may have become entangled in the gel or for some other reason did not dissolve completely. Moreover, a 2/1 compound would again require an appreciably higher ratio than 1.95 owing to adsorption.

In addition to the above, the following maximum ratios, corresponding to approximate lime saturation, have been reported: 1.4–1.5,[7,8,11,23,24] 1.5–1.6,[25,26] 1.6–1.7.[27,28,29] The adsorption character of the continuously increasing C/S ratio has generally been recognized, and usually a 1/1 compound has been assumed to be the adsorbent.

Range III was insufficiently large and the data insufficiently accurate to permit discrimination of the nature of the adsorbing compound by means of a Freundlich isotherm. The C/S ratio in this range was 0.98 to 0.90, so that the solid might be a 5/6, 4/5, 3/4, 2/3 or 1/2 compound.

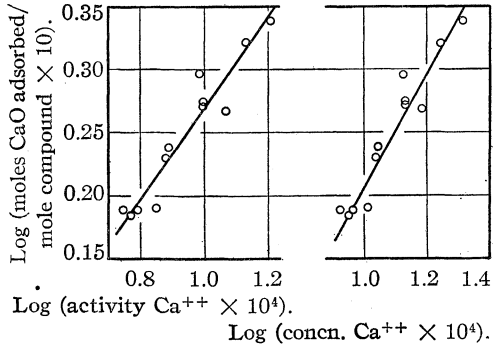


Fig. 3.—Freundlich adsorption isotherm plot for $3CaO \cdot 4SiO_2 \cdot aq.$ (range III).

It is observed from Fig. 3 that the assumption of an adsorbing compound having the formula $3CaO \cdot 4SiO_2 \cdot aq.$ satisfies the requirements of the isotherm. The value of the exponent n is for activity as variable, 2.2, and for concentration as variable, 2.7. The apparent agreement for a 3/4 compound does not exclude the possibility of any of the others. Its existence was independently inferred from an ion product study that will now be considered.

Evidence of Solubility Product Constant.—During the course of an adsorption isotherm, the concentrations of the ions are continuously changing, but if the adsorbent is one and the same compound, AB_n, then the product of the ion activities, $A \times B^n$, should be constant, and a plot of log A against log B should give a straight line of slope, n. The fulfillment of this condition may be used to ascertain the composition of the adsorbing compound. The activities A and B must of course be accurately determined as a prerequisite to the application of the method.

For the purpose of calculating the activities of the silicate ions, accurate values for dissolved silica were obtained in a special series of experiments in which the reaction flask was paraffined. After ample time, based on previous experience, had been allowed for equilibrium, the solution phase was analyzed. The paired values of silica and Ca^{++} are shown in Table II and plotted in Fig. 4. (The two lowest values for silica are in parentheses, as the color during analysis was unstable and the result therefore unreliable.) It is observed that silica increases continuously with decrease in Ca^{++}. The absence of a sharp change in passing from range I to range III may be due to the fact that the dissolved silica consists of several ions and molecules, so that a discontinuity for one of these is dulled by the presence of the others.

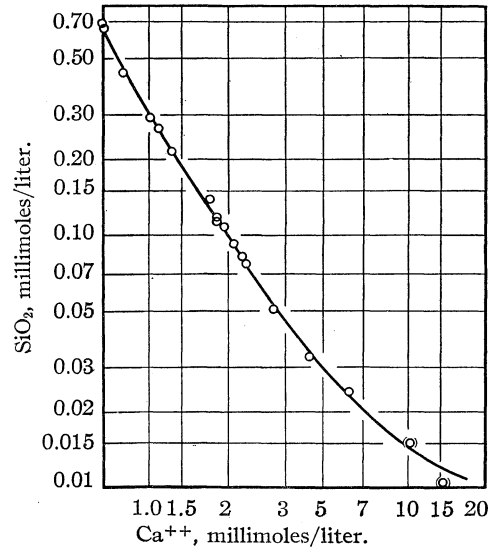


Fig. 4.—Variation of concentration of silica with concentration of calcium ion.

(21) *Z. anorg. allgem. Chem.*, **225**, 285–288 (1935).
(22) A. E. Beitlich, THIS JOURNAL, **60**, 1832–1836 (1938).
(23) H. Kühl and A. Mann, *Tonind. Ztg.*, **58**, 862, 896, 918, 930, 944, 955, 990, 1003, 1014 (1934).
(24) A. J. P. van der Burgh, *Chem. Weekblad*, **29**, 616–618 (1932).
(25) B. Tavasci, *Ann. chim. applicata*, **23**, 413–427 (1933).
(26) P. Jolibois and L. Chassevant, *Compt. rend.*, **188**, 452–454 (1929).
(27) H. Le Chatelier, "Constitution of Hydraulic Mortars," trans. by J. L. Mack, McGraw-Hill Book Co., Inc., New York, N. Y., 1905.
(28) E. P. Flint and L. S. Wells, *Bur. Standards J. Research*, **12**, 751–783 (1934).
(29) F. Klasse, *Zement*, **17**, 2–9, 49–56 (1928).

TABLE II

EQUILIBRIUM CONCENTRATIONS OF CALCIUM ION, HYDROXYL ION, AND SILICA, AND CALCULATED CONCENTRATIONS OF SILICIC ACID COMPONENTS

Millimoles/liter			Activity coefficients		Millimoles/liter — Non-association		Millimoles/liter — Association							
Ca^{++}	SiO_2	OH^- (exptl.)	OH^- (by diff.)	γ_1	γ_2	γ_3	$H_3SiO_4^-$	$H_3SiO_4^-$	H_4SiO_4	$H_3SiO_4^-$	$H_2SiO_4^=$	$H_3Si_2O_6^-$	$H_2Si_2O_6^=$	$HSi_2O_6^{\equiv}$	SiO_2 (Sum)	% Devn. in SiO_2
Range I																
20.47	(0.0105)	40.81	40.93	0.876	0.334	0.21	0.02313	0.02737	0.05660	0.02270	0.0110	0.07392	0.04369	0.04210	(0.0138)	(−23.9)
15.36	(.0151)	30.70	30.70	.876	.384	.24	.02596	.02920	.04135	.02417	.0111	.06124	.04765	.04316	(.0156)	(− 3.2)
8.76	.0238	17.50	17.50	.885	.482	.33	.0139	.02990	.04572	.0100	.0124	.05126	.03360	.04809	.0234	+ 1.6
6.24	.0337	12.45	12.45	.894	.538	.40	.0229	.0106	.03139	.0174	.0139	.05532	.03983	.03148	.0337	± 0
4.54	.0510	8.94	9.03	.904	.592	.46	.0386	.0121	.03317	.0292	.0159	.04210	.02262	.03275	.0512	− 0.4
3.52	.0777	6.85	6.96	.910	.629	.51	.0624	.0145	.03651	.0454	.0181	.04654	.02599	.03469	.0772	+ 0.6
3.41	.0821	6.66	6.74	.912	.632	.51	.0664	.0148	.03714	.0480	.0186	.04755	.02669	.03511	.0819	+ 0.2
3.16	.0924	6.18	6.23	.914	.642	.52	.0757	.0154	.03880	.0548	.0194	.03107	.02861	.03605	.0937	− 1.4
Range III																
2.92	0.108	5.72	5.73	0.915	0.653	0.54	0.0895	0.0165	0.02118	0.0677	0.0216	0.03176	0.0129	0.03820	0.118	− 8.5
2.84	.112	5.38	5.57	.916	.657	.55	.0933	.0168	.02125	.0698	.0216	.03192	.0137	.03835	.122	− 8.2
2.81	.107	5.50	5.51	.917	.660	.55	.0895	.0159	.02128	.0704	.0215	.03199	.0139	.03842	.123	−13.0
2.70	.114	5.27	5.29	.918	.660	.55	.0959	.0162	.02140	.0740	.0218	.03228	.0154	.03896	.130	−12.3
2.69	.119	5.25	5.26	.918	.660	.55	.100	.0170	.02141	.0741	.0218	.03230	.0155	.03898	.131	− 9.2
2.55	.140	4.90	4.96	.920	.672	.57	.119	.0186	.02158	.0783	.0214	.03273	.0170	.03916	.138	+ 1.4
1.83	.215	3.46	3.44	.930	.714	.63	.190	.0199	.02329	.113	.0206	.03820	.0342	.02124	.209	+ 2.9
1.64	.267	3.12	3.01	.932	.729	.65	.237	.0214	.02430	.129	.0202	.02122	.0438	.02137	.246	+ 8.5
1.52	.293	2.63	2.75	.934	.738	.66	.262	.0214	.02516	.142	.0202	.02161	.0525	.02150	.279	+ 5.0
1.18	.442	2.08	1.92	.940	.764	.70	.398	.0223	.0103	.197	.0191	.02447	.0992	.02195	.438	+ 0.9
1.01	.660	1.69	1.36	.944	.777	.73	.595	.0233	.0190	.259	.0177	.0108	.169	.02231	.659	+ 0.2
.99	.690	1.82	1.29	.945	.779	.73	.620	.0233	.0208	.268	.0173	.0123	.182	.02236	.698	− 1.1

It is usually assumed that the silica in dilute alkaline solution is made up simply of $SiO_3^=$, $HSiO_3^-$, and H_2SiO_3. Following the orthosilicate terminology, we shall write these components $H_2SiO_4^=$, $H_3SiO_4^-$ and H_4SiO_4, respectively. The presence of the ions $SiO_4^{\equiv}$ and $HSiO_4^{\equiv}$ will be neglected on the basis of a trifling dissociation of the hydrogens from $H_2SiO_4^=$. If CaH_2SiO_4 is the adsorbing compound in range I, as the adsorption isotherm shows, then the product of the activities of Ca^{++} and $H_2SiO_4^=$ should be constant over the whole range of adsorption. To calculate the concentration of $H_2SiO_4^=$, it is necessary to know the ionization constants of the acid anions. These have been determined only approximately. For the ionization of $H_3SiO_4^-$ ($HSiO_3$), K_2 has been given as 10^{-12}[30,31] and 10^{-13}[32] and for the ionization of H_4SiO_4 (H_2SiO_3), K_1 has been given, respectively, as 10^{-10}, $10^{-9.7}$ and 10^{-9}. We have chosen for the calculation $K_1 = 10^{-9.8}$ and $K_2 = 10^{-12.4}$; these values are slightly less than the mean of the reported values, but the difference was partly premeditated since the thermodynamic constants, with which we are concerned, are smaller than the constants calculated, as in these citations, from *p*H measurement without correction for activity coefficients of the ions. K_W was taken equal to $10^{-13.8}$ from "International Critical Tables." OH^- was estimated by difference, assuming one charge per SiO_2. This assumption could be corrected on the basis of the calculated proportions of the silicate ions and a second approximation made, but the original assumption proved sufficiently accurate both in the present and in

(30) H. F. Joseph and H. B. Oakley, *J. Chem. Soc.*, **127**, 2813–2818 (1925).

(31) W. D. Treadwell and W. Wieland, *Helv. Chim. Acta*, **13**, 842–864 (1930).

(32) G. Hägg, *Z. anorg. allgem. Chem.*, **155**, 21–41 (1926).

subsequent calculations. In view of the dilute character of the solutions and lacking better information, the same activity coefficient was used for all ions of the same charge. γ_1, or that for singly charged anions and for OH^-, was taken from the equation of Flint and Wells[33] for OH^- in a solution of $Ca(OH)_2$. γ_2 was the same as that for Ca^{++}, and γ_3 (for use in subsequent calculations) was assumed by comparison with the values for a trivalent ion.[34]

From the above known values, the concentrations of $H_2SiO_4^=$, $H_3SiO_4^-$ and H_4SiO_4 have been calculated, as shown in Table II (case of non-association). For range I, a plot of log activity $H_2SiO_4^=$ against log activity Ca^{++} gives a straight line of slope equal to $-1/1$ (plot I′ of Fig. 5). This shows that the product of the activities of Ca^{++} and $H_2SiO_4^=$ is constant, and that the adsorbing compound is CaH_2SiO_4, or calcium monosilicate, in agreement with the adsorption data.

$H_3SiO_4^-$ being the only remaining silicate ion, one would expect that the compound of range III would be $Ca(H_3SiO_4)_2$, so that a plot of log activity $H_3SiO_4^-$ against log activity Ca^{++} should give a straight line of slope $-1/2$. Plot III′ of Fig. 5 shows that a straight line is obtained, but the slope instead of being $-1/2$ is much too high at about $-2/1$. The impossible compound $Ca_2H_3SiO_4$ is therefore indicated, and the apparent linearity of the plot is fortuitous.

The reason for the high slope is that the silica in solution is increasing much more rapidly with decreasing Ca^{++} than it should in order for an acid silicate to be satisfied. The consequent high rate of increase in calculated $H_5SiO_4^-$ could be reduced by choice of a smaller constant than $10^{-9.8}$ for K_1, which would transfer the silica to H_4SiO_4 from $H_3SiO_4^-$. Calculation shows, however, that to approach the theoretical slope of $-1/2$, K_1 would have to be reduced to a very low value, 10^{-12} or less. This is about equal to or less than K_2, which is not only untenable, but would lead to predictions of very high hydrolysis for sodium disilicate ($Na_2O\cdot 2SiO_2$ or $NaHSiO_3$), instead of only 5% or so obtained by Bogue[35] and by Harmon.[36]

An alternative to the compound $Ca(H_3SiO_4)_2$ is an addition compound of the type $nCaH_2SiO_4\cdot Ca(H_3SiO_4)_2$. For this the ion product $(Ca^{++} \times H_2SiO_4^=)^n \times (Ca^{++} \times [H_3SiO_4^-]^2)$ would have to be constant. However, in order to approach a steady value of the product, n, it is found, would have to be unreasonably large. Substituting the activities of $H_2SiO_4^=$, $H_3SiO_4^-$ and Ca^{++} of Table II, n would have to be about 8 for a reasonably steady value of the product. This corresponds to the hypothetical compound $9CaO\cdot 10SiO_2\cdot aq.$, which is not only unexpected and irregular, but is so close to the molar ratio of calcium oxide to silica in the solid phase as to allow for practically none of the undoubted adsorption by the gelatinous solid.

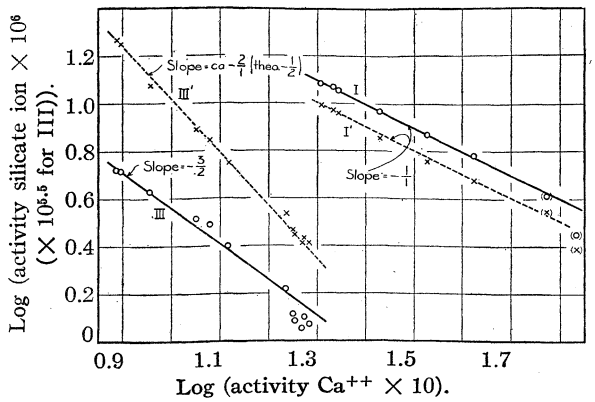


Fig. 5.—Test of compound by solubility product constant.

We were thus led to the presumption that association of silicate ion takes place, even at the high dilution of silicon dioxide and high pH of the solutions. However, association could not be considered as having advanced to the colloid stage. The proof of this is as follows. A solution of $Na_2O\cdot 2SiO_2$ has a pH that is about the same as for the present solutions, about 10.7 and up, depending on the concentration;[35,36] comparison may therefore be made with $Na_2O\cdot 2SiO_2$ solution as respects the properties of dissolved silica. Harmon[37] and Ganguly[38] found for such a solution practically complete molecular diffusion at concentrations up to 0.3 N. Ganguly[39] and Burgess and Krishnamurti[40] observed no colloidal scattering at concentrations of the order of 2 N. Finally, Main[41] saw in the results of viscosity measurement no evidence of colloidality for concentrations up to 3 N.

(33) E. P. Flint and L. S. Wells, *Bur. Standards J. Research*, **11**, 163–171 (1933).
(34) G. N. Lewis and M. Randall, "Thermodynamics," McGraw-Hill Book Co., Inc., New York, N. Y., 1923.
(35) R. H. Bogue, THIS JOURNAL, **42**, 2575–2582 (1920).
(36) R. W. Harmon, *J. Phys. Chem.*, **30**, 1100–1111 (1926).
(37) R. W. Harmon, *ibid.*, **31**, 616–625 (1927).
(38) P. B. Ganguly, *ibid.*, **31**, 407–416 (1927).
(39) P. B. Ganguly, *ibid.*, **30**, 706–712 (1926).
(40) L. L. Burgess and K. Krishnamurti, *Trans. Faraday Soc.*, **26**, 574–577 (1930).
(41) V. R. Main, *J. Phys. Chem.*, **30**, 535–561 (1926).

It seemed reasonable therefore to assume that association was confined to a molecular-type of compound, and in the first instance to a dimer, so that corresponding to $SiO_4^{==}$, $HSiO_4^{=}$, $H_2SiO_4^{=}$, $H_3SiO_4^{-}$ and H_4SiO_4, a new series of ions was to be considered, which in the order of decreasing alkalinity is $Si_2O_6^{==}$, $HSi_2O_6^{=}$, $H_2Si_2O_6^{=}$, $H_3Si_2O_6^{-}$, and $H_4Si_2O_6$. As far as the possibility of combination of Ca^{++} with any of the latter ions to form a compound in range III is concerned, we may rule out $Si_2O_6^{==}$, the most alkaline anion, because the ratio CaO/SiO_2 would be 1/1 which is greater than any of the experimental ratios in range III. Compound formation with the next most alkaline ion, $HSi_2O_6^{=}$, is feasible, as will be shown. For the sake of completeness we have also considered in great detail the independent possibility of combination with the still more acid anion, $H_2Si_2O_6^{=}$, and also the possibility of combination with $H_3SiO_4^{-}$ in the new situation of association. The former compound would require a slope of $-1/1$ in plotting log activity $H_2Si_2O_6^{=}$ against log activity Ca^{++}. However, here again, as for the case of nonassociation, the rate of increase of silica in solution is so great that a very small ionization constant would be required for $H_3Si_2O_6^{-}$ and for H_4SiO_4. The expected hydrolysis of $Na_2O{\cdot}2SiO_2$ would again then be very much greater than is actually found. The postulate of a tetra polymer did not avoid the calculated high degree of hydrolysis. With respect to the possible compound $Ca(H_3SiO_4)_2$, the same impasse of high hydrolysis existed as before.

The combination of $HSi_2O_6^{=}$ with Ca^{++} to give $Ca_3(HSi_2O_6)_2{\cdot}aq.$ (or empirically $3CaO{\cdot}4SiO_2$) would require a slope of $-3/2$. This slope was readily realized in preliminary test. The problem that remained was to determine accurately the magnitude of the various equilibrium constants. For this purpose we have the four ionization constant equations for H_4SiO_4 (K_1), $H_3SiO_4^{-}$ (K_2), $H_3Si_2O_6^{-}$ (K_{II}) and $H_2Si_2O_6^{=}$ (K_{III}), the equations of association (1), of solubility product constant (2) and (3), and of conservation of mass (4).

$$\frac{\gamma_2 H_2Si_2O_6^{=}}{\gamma_1^2(H_3SiO_4^{-})^2} = K_S \quad (1)$$

$$\gamma_2^3\gamma_3^2(Ca^{++})^3 \times (HSi_2O_6^{=})^2 = K_{S.P.}(C_3S_2) \quad (2)$$

$$\gamma_2^2\, Ca^{++} \times H_2SiO_4^{=} = K_{S.P.}(CS) \quad (3)$$

$$H_4SiO_4 + H_3SiO_4^{-} + H_2SiO_4^{=} + 2H_3Si_2O_6^{-} + 2H_2Si_2O_6^{=} + 2HSi_2O_6^{=} = SiO_2 \quad (4)$$

By substituting into (4), equation (5) is obtained for range III in which each of the silicic acid unknowns is replaced one by one by a function of the different constants as unknown, whose coefficient is a function of Ca^{++}, OH^{-} and the activity coefficients.

$$\frac{MK_W/K_1}{o^{3/2}c^{3/4}} + \frac{M}{\gamma_1 o^{1/2}c^{3/4}} + \frac{o^{1/2}MK_2/K_W}{\gamma_2 c^{3/4}} + \frac{NK_W/K_{II}}{\gamma_1 o^2 c^{3/2}} + \frac{N}{\gamma_2 o c^{3/2}} + \frac{K_{S.P.}(C_3S_2)}{\gamma_3 c^{3/2}} = SiO_2 \quad (5)$$

in which, $M = (K_W/K_{III})^{1/2}K_{S.P.}^{1/4}(C_3S_2)K_S^{-1/2}$, $N = 2K_W/K_{III}K_{S.P.}^{1/2}(C_3S_2)$, o = activity OH^{-}, c = activity Ca^{++}.

By making use of (3) instead of (2), a similar equation is obtained for range I

$$\frac{AK_W/K_1}{o^2 c} + \frac{A}{\gamma_1 o c} + \frac{K_{S.P.}(CS)}{\gamma_2 c} + \frac{BK_W/K_{II}}{\gamma_1 o^3 c^2} \frac{B}{\gamma_2 o^2 c^2} + \frac{BK_{III}/K_W}{\gamma_3 o c^2} = SiO_2 \quad (6)$$

in which $A = K_W/K_2K_{S.P.}(CS)$, $B = 2K_S{\cdot}(K_W/K_2\,K_{S.P.}(CS))^2$.

Since the same ultimate unknowns enter in both equations (5) and (6), their solution is not independent, but is conditional and based on successive approximations. In equation (6), the unknown terms of greatest weight are the second and third, so this equation is solved for $K_{S.P.}(CS)$ and K_2 (from A) after substituting for the other unknowns their values obtained from a previous sufficiently close solution of (5). By combining in the latter the second and the less important third term containing the substituted value of K_2, the number of unknowns is reduced to five. The general solution of the resultant equation led however to absurd negative values. This is due to the fact that in the range of pH under consideration, H_4SiO_4, $H_3Si_2O_6^{-}$ and $HSi_2O_6^{=}$ are very small (compare Table II under association), so that treating the corresponding terms as independent unknowns was virtually the same as introducing arbitrary unknowns whose effect on the solution of an inexact (observational) equation is arbitrary. Therefore these terms were converted into knowns by substituting for K_1, K_{II} and K_{III} values based on the electrometric titration results previously referred to. Naturally the solution depends upon the substituted values, but since the combined magnitude of these averaged only 4% of the total, small errors of quantitation would be immaterial. The solution of the reduced equation (5) gave values for $K_{S.P.}(C_3S_2)$ and for $K_W/K_{III}K_{S.P.}^{1/2}(C_3S_2)$(from N).

In every case the actual solution was carried out by applying the method of least squares to the

observational equations and solving the resultant normal equations simultaneously. The precision was estimated from the residuals,[42] or the differences in silica found and calculated.

The results of the solution may be summarized as follows: $K_S = 2200 \pm 150$; $K_2 = 10^{-12.16 \pm .02}$; $K_{S.P.}(CS) = 2.53 \pm 0.10 \times 10^{-8}$; $(K_W/K_{III})^2 \cdot K_{S.P.}(C_3S_2) = 1.37 \pm 0.10 \times 10^{-23}$; $K_{S.P.} \cdot (C_3S_2) = 1.37 \times 10^{-21}$ (based on $K_{III} = 10^{-12.8}$); $K_1 = K_{II} = 10^{-9.8}$, and $K_{III} = 10^{-12.8}$ (all assumed from electrometric results).

K_{III} in the above tabulation was taken as different from the determined value of K_2 because of anomalies[19,31] observed in the titration of sodium silicate in the range of pH dominated by the second ionization constant, and it was taken as less because of the somewhat high value of K_2 compared to the mean of the electrometric values.

K_2 it may be noted is very much smaller than K_{II} even though the valence of the respective acids $H_3SiO_4^-$ and $H_3Si_2O_6^-$ is the same. The greater ionization of $H_3Si_2O_6^-$ may be explained by the electrical screening effect of the additional SiO_2 in the dimer ion.

From the above values of the equilibrium constants, the concentrations of the different silicic acids have been calculated in Table II under association; also given is their sum and the percentage deviation of the experimental silica from the latter. From the table, log activity $H_2SiO_4^=$ and log activity $HSi_2O_6^=$, corrected to zero deviation, have been plotted in Fig. 5 against log activity Ca^{++}. The resultant graphs, I and III, respectively, are within the limit of error straight lines of theoretically correct slope $-1/1$ and $-3/2$. That the correct slope was previously gotten in range I for the case of non-association is explained by the small degree of association in this range due to the relatively low concentration of SiO_2.

In view of its non-existence (non-precipitation) in range III, the product of the ion activities for CaH_2SiO_4 should be less than $K_{S.P.}(CS)$ in this range. Making use of the values of Table II, this is confirmed for each of the determinations of range III, except that the low group of first five determinations (*cf.* Fig. 5) deviates in the wrong direction by an average of 3%. Likewise the product of the ion activities for $Ca_3(HSi_2O_6)_2$ should be less than $K_{S.P.}(C_3S_2)$ in range I. Surmounting the obstacle raised by the approximate character of K_{III} and hence of $HSi_2O_6^=$ (and this alone), the equivalent condition is $(\gamma_2 Ca^{++})^3(\gamma_2 H_2Si_2O_6^=)^2 \cdot (\gamma_1 OH^-)^2 < N^2/4 < 1.37 \times 10^{-23}$. This is found to be satisfied by each of the determinations of range I.

By comparison of the respective $K_{S.P.}$, it is noted that the (intrinsic) solubility of CaH_2SiO_4 is 1.7 times that of $CaCO_3$. If the monosilicate were crystalline instead of gelatinous, its solubility product would presumably be less. The solubility of $Ca_3(HSi_2O_6)_2$ (based on K_{III} equal to $10^{-12.8}$) is slightly less than that of $CaCO_3$.

The association of silicate ion explains the peculiar result of a decided increase in pH with increase in concentration, even for solutions of buffer character.[35,36] By equation (1) an increase in concentration results in the loss of two acid anions and gain of only one acid anion of nearly equal ionization constant, so the pH must also increase with concentration.

Because of the high value of 2200 for the association constant, comparatively much $H_2Si_2O_6^=$ and little $H_3SiO_4^-$ should be present in a solution of $Na_2O \cdot 2SiO_2$. This condition is indicated by the comparatively low depression of the freezing point of a solution of this substance. Harmon[43] found, for example, that in a solution that is 0.102 molar with respect to Na_2O the depression is 0.548° for sodium metasilicate but only 0.415° for the disilicate. However, (in the orthosilicate terminology) since $Na(H_3SiO_4)$ dissociates into four ions per mole of Na_2O (or more depending on hydrolysis and dissociation), while $Na_2(H_2SiO_4)$ dissociates into three ions (or more), a greater depression would be expected for the disilicate. Thus, for the comparable salt Na_2CO_3, at a concentration that is 0.10 molar with respect to Na_2O the depression is 0.444°, whereas for $NaHCO_3$ the depression is 0.702° and therefore considerably higher ("International Critical Tables"). The difference in behavior between HCO_3^- and a supposedly exclusive $H_3SiO_4^-$ is too great to be explained by differences in ionization constant or activity coefficient, but is accounted for by molecular association of $H_3SiO_4^-$. An abnormally low depression of the freezing point by sodium disilicate is also seen in the measurements of Kahlenberg and Lincoln.[44] The vapor pressure lowering[43] and the dew-point depression[45] are also comparatively low.

(42) T. W. Wright and J. F. Hayford, "Adjustment of Observations," D. Van Nostrand Co., New York, N. Y., 1906.

(43) R. W. Harmon, *J. Phys. Chem.*, **31**, 355–373 (1927).

(44) L. Kahlenberg and A. T. Lincoln, *J. Phys. Chem.*, **2**, 77–90 (1898).

(45) A. N. C. Bennett, *J. Phys. Chem.*, **31**, 890–896 (1927).

TABLE III

INVARIANT CONCENTRATIONS AND SOLID PHASES IN EQUILIBRIUM

Millimoles/liter CaO	Millimoles/liter SiO_2	Ratios	Compounds (Hydrated) Formulas
3.09	0.090	$CaO \cdot SiO_2 + 3CaO \cdot 4SiO_2$	$CaH_2SiO_4 + Ca_3(HSi_2O_6)_2$
.900	.931	$3CaO \cdot 4SiO_2 + CaO \cdot 2SiO_2$	$Ca_3(HSi_2O_6)_2 + CaH_2Si_2O_6$ or $Ca(HSiO_3)_2$

Invariant Ranges.—The invariant concentrations and the compounds in equilibrium therewith are given in Table III. The silica concentration for the upper invariant point was interpolated from the curve of Fig. 4. The value for the lower invariant point was the average of two accurate analyses carried out in the paraffined flask. A solution containing 0.924 millimole of CaO/l. was diluted one-third with water; after four days of stirring the concentration of Ca^{++} was 0.900 millimoles/l. and of SiO_2, 0.936 millimole/l. On a one-fold dilution of the latter solution, the concentrations after three days were, respectively, 0.900 and 0.926. The *p*H of the solutions, measured colorimetrically with acyl red, was 10.3–10.5. The values for Ca^{++} agree with those independently obtained when analyzing for the solid phase (Table I).

The existence of an invariant concentration corresponding to our value of 3.09 millimoles CaO/l. is indicated by the work of Thorvaldson and Vigfusson,[8] who decomposed tri- and dicalcium silicate with water till a steady state was reached. When their results are replotted as C/S ratio in the solid against concentration, a large break is observed at about 4 millimoles/l. for the trisilicate and at 2 millimoles/l. for the disilicate, both at a C/S ratio as in the present work close to 1/1. Shaw and MacIntire[7] found that uniform adsorption of calcium hydroxide by silica gel held to approximately 2.5 millimoles/l. when an arrest occurred; an arrest at about 3.5 millimoles/l. is shown by the results of Maffei[46] and at about 2 millimoles/l. by the results of van der Burgh,[24] who used twenty-four hour shaking periods. In treating silicate melts with lime water, Kühl and Mann[23] observed an arrest at 2.3 millimoles/l. and C/S ratio of 1/1.

The lower invariant concentration was early recognized by Le Chatelier,[27] who repeatedly extracted precipitated calcium silicate and obtained an arrest at 0.93 millimole CaO/l. The results of Baylis[11] in the same type of experiment show invariance at about the same concentration. Tavasci,[25] in decomposing tricalcium silicate with water, corroborated Le Chatelier's value; he believed, however, that an arrest occurred also at 0.55 millimole/l. In treating silica gel with lime water over a long period of time, Jolibois and Chassevant[26] obtained an invariant concentration of 0.95 millimole/l. The value obtained by Beitlich[22] in the same reaction was 0.75 millimole/l.; this, however, is low because the author did not take into account, in the conductivity measurements, the presence of silica in solution.

If the new solid that makes its appearance in range IV were silica, the concentration of silica would be expected to be equal to or greater than the solubility of gelatinous silica in water, which according to Lenher and Merrill[47] is 2.7 millimoles/l., and according to Hitchen[48] is 3.3 millimoles/l. However, the actual value of 0.931 millimoles/l. (Table III) is much lower, so the solid phase is not silica. The next less alkaline anion after $HSi_2O_6^{\equiv}$ is $H_2Si_2O_6^{=}$, and, in the monomer series, $H_3SiO_4^{-}$. Combination of either of these anions with Ca^{++} would result in the compound $CaO \cdot 2SiO_2 \cdot aq$. Having eliminated silica, calcium disilicate is therefore strongly indicated to be the compound that makes its appearance in the second invariant range. It may be noted that hydrated calcium disilicate occurs naturally as the mineral okenite.

It is easily shown that the ion activity product for $CaH_2Si_2O_6$ is equal to

$$\frac{N}{2}\frac{1}{\gamma_1 OH^-}\frac{1}{\gamma_2^{1/2}Ca^{++1/2}}$$

and that the product for the other possible form of the disilicate, namely, $Ca(H_3SiO_4)_2$, is $1/K_S$ times this. Substituting for Ca^{++} and OH^- (assuming one charge per SiO_2) from Table III, $K_{S.P.}$ for $CaH_2Si_2O_6$ is calculated to be $1.69 \pm 0.06 \times 10^{-7}$, and $K_{S.P.}$ for $Ca(H_3SiO_4)_2$ $7.68 \pm 0.60 \times 10^{-11}$. The mean activity of the solute at saturation is given by the square and cube roots of the respective $K_{S.P.}$, and is, respectively, 4.11×10^{-4} and 4.25×10^{-4}. The practical identity

(46) A. Maffei, *Gazz. chim. ital.*, **66**, 197–204 (1936).

(47) V. Lenher and H. B. Merrill, THIS JOURNAL, **39**, 2630–2638 (1917).

(48) C. S. Hitchen, *Bull. Inst. Mining and Met.* No. **364**, 26 pp. (1935).

of the values shows that the free energy of formation of calcium disilicate is the same whether the solid arises from the monomer or dimer forms; it would appear, therefore, that there is only one disilicate which may be formed indifferently from one or the other of the anions. The disilicate is intrinsically 2.6 times as soluble as the monosilicate. The ion product in range III is less than $K_{S.P.}$ for either $Ca_2H_2Si_2O_6$ or $Ca(H_3SiO_4)_2$, as is proper.

In view of the consistent rapid approach to equality of the CaO/SiO_2 ratio in solid and in solution, and the closeness of the ratios in invariant range IV, it is likely that calcium disilicate dissolves congruently in the next less-alkaline univariant range and is the last remaining compound. No hydrated silicate richer in silica than the disilicate is known in nature.

Summary

Hydrated calcium silicates are gelatinous. The effects to be expected from this in a phase rule study are discussed briefly.

Measurements were made of the ratio of CaO to SiO_2 in the solid phase, and of the concentrations of CaO and SiO_2 in solution at 30.2°. Equilibrium and reversibility were tested for.

Four phase ranges were distinguished; in two of these the concentrations were invariant. Adsorption of CaO by the solid phases occurred throughout. The compositions of the hydrated compounds, deduced from considerations of adsorption isotherm and solubility product constant, were: (1) $CaO \cdot SiO_2$ (CaH_2SiO_4), (2) $3CaO \cdot 4SiO_2$ ($Ca_3(HSi_2O_6)_2$), (3) $CaO \cdot 2SiO_2$ (indifferently either $CaH_2Si_2O_6$ or $Ca(HSiO_3)_2$). The invariant concentrations for the mixture of (1) and (2) were: 3.09 millimoles CaO/l. and 0.090 millimole SiO_2/l. and for the mixture of (2) and (3), 0.900 millimole CaO/l. and 0.931 millimole SiO_2/l.

The assumed exclusive presence of the simple ions $SiO_3^=$ and $HSiO_3^-$, or in the more rational and preferred orthosilicate terminology, $H_2SiO_4^=$ and $H_3SiO_4^-$, was inconsistent with the existence of the only alternatives of $Ca(H_3SiO_4)_2$ or any reasonable double compounds of the latter with CaH_2SiO_4. It was necessary to assume therefore that association took place in the dilute alkaline solutions. The postulate of two sets of silicate ions, based on an association equilibrium between $H_3SiO_4^-$ and $H_2Si_2O_6^=$, led to reasonable and concordant results. The association constant, solubility product constants, and one of the ionization constants, were calculated to a known precision. A high tendency toward association is evidenced.

COLLEGE PARK, MD. RECEIVED AUGUST 18, 1939

[CONTRIBUTION FROM THE PHYSICAL CHEMICAL RESEARCH LABORATORY OF NORTHWESTERN UNIVERSITY]

Isotopic Composition of Oxygen in Carbonate Rocks and Iron Oxide Ores

BY MALCOLM DOLE AND ROBERT L. SLOBOD[1]

Introduction

In recent years the isotopic composition of oxygen in various natural substances has been the subject of a number of investigations beginning with the research of Manian, Urey and Bleakney,[2] who studied stony meteorites and terrestrial silicate rocks. Unfortunately, after these workers had performed the difficult task of recovering the oxygen from these rocks by reaction with graphite and carbon tetrachloride vapors at 1000°, their methods of isotopic analysis were too inaccurate to demonstrate any significant differences between the various samples of oxygen; thus their specific gravity determinations of 0.47 cc. of water were accurate only to ± 63 γ[3] or 29% in the O^{18} abundance ratio while their more accurate mass spectrographic abundance measurements had for their average error 2.5%, which is equivalent to 6 γ. They found no significant variations in the isotopic composition of the oxygen between the stony meteorites and terrestrial silicate rocks, and they concluded that the absolute value of the abundance ratio O^{18}/O^{16} is 0.973/500. In a slightly more accurate mass spectrographic investigation of this abundance ratio in the oxygen from the thermal decomposition of

(1) University Fellow, 1937–1938.

(2) S. H. Manian, H. C. Urey and W. Bleakney, THIS JOURNAL, 56, 2601 (1934). This paper contains many references to earlier investigations concerning possible variations in the abundance of isotopic elements in meteors.

(3) The symbol refers to excess density of sample over that of normal water in parts per million; a negative value of γ means that the sample of water is lighter than normal. In this paper we shall take purified Lake Michigan water as being our standard of normal water.

lead dioxide, Smythe[4] obtained 0.994/500. Since both of these values are within the experimental error equal to the rounded-off ratio 1/500, we shall adopt the latter for the calculations of this paper.

Urey and Greiff[5] estimated the statistical mechanical partition functions for the molecular species CO_2^{16}, CO_2^{18}, H_2O^{16}, H_2O^{18}, from which they calculated that if carbon dioxide gas is brought into equilibrium with liquid water at 0°, the O^{18} isotope will concentrate in the gas phase until its abundance ratio becomes 1.046/500 or +10.3 γ. Weber, Wahl and Urey[6] checked this prediction experimentally. Urey and Greiff calculated also the isotopic exchange equilibrium constants for many other reactions, but the carbon dioxide–water equilibrium is the one of interest to us here. A relatively large variation in the oxygen isotope ratio in natural substances was first demonstrated by one of us,[7] who found that if the oxygen isotope ratio O^{18}/O^{16} in Lake Michigan water is taken as 1/500, then that of atmospheric air is 1.029/500 or 6.6 γ. This abnormality in the distribution of the heaviest oxygen isotope may be caused by the equilibrium

$$O_2^{16} + 2H_2O^{18}\,(g) \rightleftharpoons O_2^{18} + 2H_2O^{16}\,(g) \quad (1)$$

being set up in the stratosphere at −50° under the action of the ultraviolet light from the sun, or it may be due to the isotopic exchange equilibrium existing on the surface of the earth

$$2H_2O^{18}\,(l) + CO_2^{16}\,(g) \rightleftharpoons 2H_2O^{16}\,(l) + CO_2^{18}\,(g) \quad (2)$$

followed by the irreversible reaction

$$CO_2^{10}\,(g) + H_2O^{0}\,(l) \xrightarrow{\text{chlorophyll}} (HCHO^{6.6})_x + O_2^{6.6} \quad (3)$$

as suggested by Greene and Voskuyl.[7] In Eq. (3) the superscripts on the oxygen symbols represent the value of γ for each sample of the element.

Since the exact or average temperature at which reaction (2) takes place is unknown at the present time and since the extent of irreversibility of reaction (3) is also unknown, we cannot state definitely the mechanism giving rise to the greater abundance of O^{18} in the atmosphere. We are inclined, however, to the theory postulated by Greene and Voskuyl, because it is believed by geologists that all our atmospheric oxygen arose through the agency of the photosynthesis reaction. The theory of Greene and Voskuyl is also substantiated in part by the work of Morita, Goto and Titani,[8] who decomposed cane sugar in the presence of deuterium-free hydrogen, obtaining thereby 73% of the oxygen of the sugar in the form of water whose density could be measured. They found that the average γ-value of the water obtained in this way was 4.6 γ (6.6 γ was predicted by Greene and Voskuyl assuming no exchange of the sugar oxygen with the oxygen of water); if the oxygen of the sugar had been obtained entirely from water, its γ-value would naturally have been zero.

Continuing the study of oxygen isotope abundance ratios, we decided to investigate carbonate rocks and iron oxide ores, not only because of the interest in these important rocks and because of the ease in recovery of the oxygen in the form of water, but also because ores precipitated during widely different geologic eras could be obtained, thus making it possible to study the isotopic composition of the oxygen as a function of age. There was the additional possibility that some inferences might be drawn from the data concerning the origin of the oxygen in the rocks; *i. e.*, whether the oxygen came from water or from the air.

Part I. Carbonate Ores

Experimental

Density Measurements.—The most sensitive method of detecting slight variations in oxygen isotope ratios is the well-known totally submerged float method. The chief improvement adopted by us in this research was the use of a platinum resistance thermometer to measure the temperature of floating equilibrium of the float. In the first measurements a fairly large cylindrical quartz float, volume 10 cc., which balanced at 29.9° was used, but although this float was more sensitive than the smaller, 1 cc. Pyrex float used later, see Fig. 1, and did not have to be corrected for expansion with rise of temperature, we abandoned it in favor of the Pyrex "swimmer" which reached floating equilibrium at 25.0°; because the latter was not "pressure sensitive" and because the smaller size of the float enabled us to reduce from 60 to 15 cc. the volume of water actually used in the density measurement. In Fig. 2 we illustrate the velocity of the quartz swimmer as a function of depth of immersion; naturally a pressure correction had to be applied for each measurement, not only for

(4) W. R. Smythe, *Phys. Rev.*, **45**, 299 (1934).

(5) H. C. Urey and Lotti J. Greiff, THIS JOURNAL, **57**, 321 (1935).

(6) L. A. Weber, M. H. Wahl and H. C. Urey, *J. Chem. Phys.*, **3**, 129 (1935).

(7) M. Dole, THIS JOURNAL, **57**, 2731 (1935); *J. Phys. Chem.*, **4**, 268, 778 (1936). For a recent accurate measurement of this effect see J. A. Swartout and M. Dole, THIS JOURNAL, **61**, 2025 (1939). Morita and Titani, *Bull. Chem. Soc. Japan*, **11**, 403 (1936), independently discovered the same effect and it has been confirmed by C. H. Greene and R. J. Voskuyl, THIS JOURNAL, **58**, 693 (1936); W. H. Hall and H. L. Johnston, *ibid.*, **58**, 1920 (1936); T. O. Jones and N. F. Hall, *ibid.*, **59**, 259 (1937); E. R. Smith and H. Matheson, *J. Research Natl. Bur. Standards*, **17**, 625 (1936).

(8) N. Morita, K. Goto and T. Titani, *Bull. Chem. Soc. Japan*, **11**, 695 (1936); *ibid.*, **13**, 99 (1938).

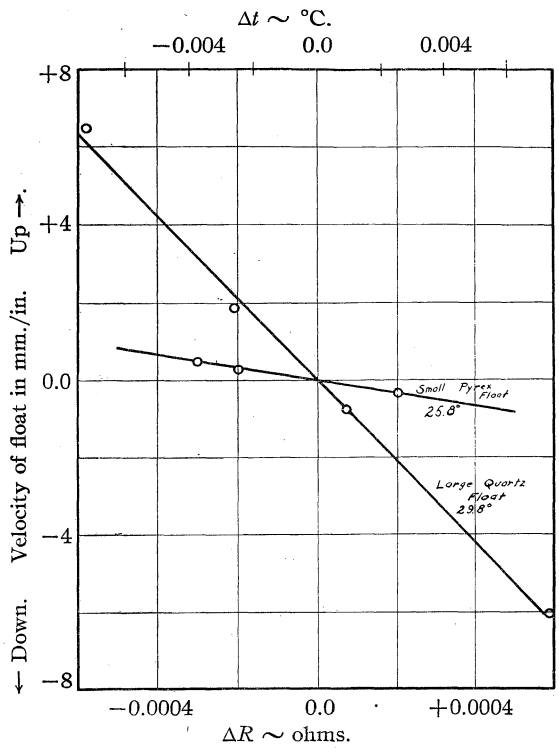


Fig. 1.

the weight of water above the float, but also because of variations in barometric pressure from day to day. In all the calculations of density obtained from the velocity readings on the Pyrex swimmer, the expansion of the latter with rise of temperature was corrected for by taking 9.6×10^{-6} as the volume coefficient of expansion of Pyrex. The density of a large sample (300 cc.) of standard water

TABLE I

TEMPERATURE OF FLOATING EQUILIBRIUM OF PYREX FLOAT

Date	Temp., °C. (variation from mean)	Δγ	Barometric pressure, mm.
11/15/38	+0.0001	+0.03	752.2
11/16/38	− .0008	− .19	736.2
11/17/38	− .0005	− .13	739.4
11/21/38	+ .0006	+ .16	745.7
11/22/38	+ .0003	+ .06	756.9
11/23/38	+ .0008	+ .19	757.2
11/29/38	− .0003	− .06	745.0
12/ 1/38	+ .0006	+ .16	...
12/ 2/38	0	0	745.9
12/ 3/38	− .0006	− .16	740.0
12/ 6/38	− .0014	− .35	740.0
12/ 9/38	− .0003	− .06	739.0
1/16/39	+ .0011	+ .28	752.3
1/17/39	− .0009	− .22	746.5
1/18/39	− .0019	− .47	741.8
1/19/39	+ .0001	+ .03	745.5
1/23/39	− .0009	− .22	745.9
2/ 6/39	+ .0009	+ .22	737.7
2/ 7/39	+ .0011	+ .28	748.8

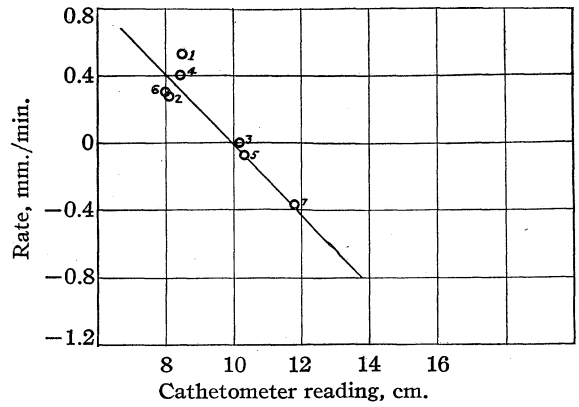


Fig. 2.—Velocity of float as function of position in water.

was compared with that of a 300-cc. sample of a light water, using both the Pyrex and quartz floats. All samples of water, both the standard and the light water, were purified and distilled in exactly the same way. With the Pyrex float the light water gave a γ-value of -12.9 while -12.8 γ was obtained with the quartz float; thus, despite the different floats, temperatures and correction factors employed in the two comparisons, the results were identical within the experimental error of 0.1 γ.

Most of the density measurements using the Pyrex float were made during a three-month interval; the data of Table I indicate that no significant change in the temperature of floating equilibrium of the Pyrex swimmer in the standard water occurred during this period (the samples of standard water were taken from the same large stock of laboratory distilled water). Furthermore, no pressure dependence of the floating temperature is indicated and in the nineteen measurements recorded, only four give results deviating from the mean by more than 0.22 γ. The average fluctuation is 0.17 γ. Apparently the small 1 cc. cylindrical Pyrex swimmer is a satisfactory float.

Occasionally it was found necessary to clean the Pyrex float with a warm solution of mixed concentrated nitric and sulfuric acids.

The wooden box containing the Mueller bridge of the platinum resistance thermometer was housed in a larger wooden air constant temperature bath, lined with two layers of $^3/_4$-inch (2-cm.) celotex, whose temperature was maintained constant at 30° to a few hundredths of a degree. The platinum thermometer of 20 ohms resistance (at 0°) could not be immersed directly into the water under investigation because the electric current flowing through the thermometer during a measurement caused too great a heating effect in the small sample of test water, although a two-volt rather than a six-volt battery was used as the source of bridge current. The platinum thermometer was therefore placed in the inner bath of the constant temperature water-bath whose outer bath temperature was controlled by the usual mercury–toluene thermostat, relay, heating and cooling coils arrangement. The temperature of the outer water-bath which fluctuated about ±0.002° was varied at will by a screw mechanism on the contact wire of the thermostat; the temperature of the inner bath through which water slowly circulated from the outer bath varied about ±0.0002° while the tempera-

ture of the test water remained even more constant. The constancy of the temperature of the inner bath can be judged from the data plotted in Fig. 2 (the number by each circle indicates the order in which the observations were made) where the maximum variation from the straight line corresponds to a fluctuation in temperature of 0.0001° (except for the first measurement, which was probably taken before temperature equilibrium was reached).

The velocity of the float was observed and measured with a travelling telescope, millimeter scale and stop watch. By taking measurements both on the slightly hotter and slightly colder sides of the temperature of floating equilibrium, the latter could be interpolated quite accurately from a plot of the observed velocities and temperatures such as illustrated in Fig. 1. We believe that the actual density measurements were obtained with an error less than $\pm 0.1\ \gamma$, and that our chief sources of error were contained in the chemical reactions used in liberating the oxygen from the rocks and in the process of purifying and distilling the impure condensates from the reduction experiments.

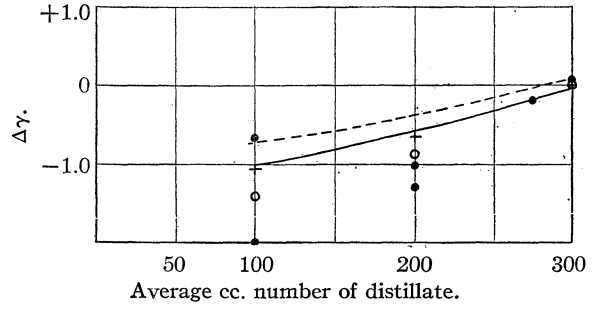


Fig. 3.—Change in water density on distillation: ○, standard water; +, sample (C) of D-free water; ●, sample (B) of D-free water.

Purification and Distillation of Water Samples.—The more accurate density measuring apparatus required much more careful preliminary treatment of the water than that used in our previous investigations. As Greene and Voskuyl[9] have recently stated, "It should be remembered that a number of successive distillations are usually made in the purification of samples of water so that although the change in density caused by a single distillation is small, the total change occasioned by the purification may be significant. The fact that this change in the case of deuterium-free water is different from and less than the change with ordinary water must also be taken account of in determinations of the deuterium–protium ratio by the method of densities." We adopted the following procedure in the treatment of the 300-cc. samples in the first case (when using the large quartz swimmer) and the 40 cc. samples in the second case. The 300-cc. samples of water were placed in a 500-cc. Pyrex distilling flask, and completely distilled from alkaline permanganate through a two foot (61-cm.) 30 mm. Pyrex tube packed with copper oxide and heated to 550°. All the water was distilled in this purification step to avoid any isotopic fractionation; the copper oxide column effectively prevented any permanganate solution spray from contaminating the condensate. The sample was then distilled from acid permanganate in a flask fitted with a bulb spray trap through a block tin condenser. The middle 100-cc. fraction was used in the density determination. To check the density measurements, the entire sample, including the 100 cc. rejected initial and end fractions, was redistilled as before. By recombining the various distillation fractions, the accumulation of errors due to repeated isotopic fractionation was prevented. The treatment of the 49-cc. sample was similar except that the bulb spray trap was steam-jacketed to prevent additional fractionation in the column, and the various glass connections and the glass to block-tin joints were made tighter since it was found that no water could be lost during the distillations without isotopic fractionation errors entering in. The sample taken for analysis consisted of the eleventh to the twenty-fifth cc. of the forty cc. sample, and the distillation rate was adjusted to a speed of one cc. per minute. The 15 cc. middle fraction was out-gassed with a water pump for one minute at 35° with continuous shaking, and allowed to stand in the constant temperature bath for half an hour before making the float velocity observations.

The standard Lake Michigan water taken from the large stock of laboratory distilled water was purified and distilled in exactly the same way as the test samples. We discuss below the question of the density differences between our standard water and the water used by other investigators.

Several experiments were performed to test the isotopic fractionation of the water in our distilling apparatus. For this purpose large (450-cc.) samples were used, the first 50 cc. of water to be distilled was rejected, the next three 100-cc. portions were separately collected and their densities measured. The 500-cc. distilling flask was equipped with a steam-jacketed spray trap and the water condensed in a block-tin condenser. Sample A (represented by the open circles in Fig. 3) was the standard water, Sample B (closed circles of Fig. 3) was nearly deuterium-free water whose oxygen was air oxygen, and Sample C was water that resulted from two electrolytic fractionations to remove the deuterium, γ-value equal to -16 (represented by crosses in Fig. 3). Changes in density only are plotted in Fig. 3, the curves being adjusted vertically to coincide at the density of the third 100-cc. portion whose density, theoretically, should be nearly identical with that of the water before distillation. The dotted line in Fig. 3 represents the changes in density to be expected on the basis of one theoretical plate in the case of D-free water and the solid line, the density changes for normal water. These calculations were made using the Rayleigh distillation formula and the fractionation factors adopted by Greene and Voskuyl.[9] The observed changes are within a few tenths of a part per million of the theoretical; in one case the distillation of D-free water produced smaller changes in density than the normal water, as expected, but in the case of Sample B the density changes were larger and fluctuated more. Evidently this last distillation was not carried out in the same manner as the other two; perhaps the water was actually impure so that the γ-values of Fig. 3 represent a change in the purity of the water. In the dis-

(9) C. H. Greene and R. J. Voskuyl, THIS JOURNAL, **61**, 1342 (1939).

tillations of the 40-cc. samples we calculate that the 15-cc. distillate was 0.58 γ lighter than normal in the case of the standard water and 0.41 γ lighter than the original sample in the case of D-free water. The difference between the changes in the two distillations, 0.17 γ, is negligible in view of the experiments to be described. We conclude that an uncertainty of about ± 0.2 γ results from isotopic fractionations on distillation in our experiments.

Reduction of the Carbonate Ores.—Most of the carbonate ore experiments were performed on Grenville marble from the Gouverneur Marble Quarry, Gouverneur, N. Y. The Grenville formation is one of the oldest geologic deposits, with a reputed age of 1.2 billion years. Niagara dolomite and Pennsylvania limestone of the La Salle formation, about 0.5 billion year old, and clam shells of recent origin also were investigated. All of these carbonate samples were supposed to be laid down from large bodies of water (oceans); we did not investigate any carbonate rocks precipitated from fresh water. Some synthetic barium carbonate made in the following way was also studied. Five liters of water whose oxygen came from the air were prepared and in this water anhydrous barium chloride was dissolved. Carbon dioxide also containing atmospheric oxygen was obtained by burning charcoal in dry, carbon dioxide-free air. After passing the gases from the charcoal combustion over hot copper oxide and calcium chloride, they were then mixed with ammonia and passed into the barium chloride solution contained in several absorption vessels connected together in series. Barium carbonate was precipitated, the nitrogen and some of the ammonia sweeping out through the absorption system. When the last absorption bottle showed traces of the carbonate, the process was stopped, the barium carbonate filtered off, and the filtrate returned to the absorption bottles. The barium carbonate was dried at 160°, the water vapor being condensed and added to the filtrate. In this way barium carbonate was prepared containing oxygen of known isotopic composition provided no fractionation of the oxygen isotopes occurred in the precipitation. We discuss this point below.

The natural carbonate rocks were broken up in a rock crusher to pebble size and treated in two different ways to eliminate the oxygen. The easiest method to accomplish this consists in the treatment of the rock with hydrochloric acid, followed by reduction of the carbon dioxide evolved with hydrogen over a nickel catalyst to methane and water. A large quantity of the rock was placed in a tall Pyrex tube and 6 *N* hydrochloric acid dropped on the rock at a constant rate using a constant head device. The apparatus was so arranged that the spent acid and calcium chloride solution could automatically siphon off. After the evolved carbon dioxide had been passed through a glass wool spray and dust trap and through a drying chamber, it entered the electrically heated catalyst chamber along with practically D-free hydrogen with the hydrogen–carbon dioxide volume ratio slightly in excess of four to one. The catalyst was pumice supported nickel heated to 280–300°. The water resulting from the reduction was condensed in a water condenser and the last traces frozen out in a dry ice–acetone trap. The yield was about 90% of the theoretical, assuming the rock to be pure calcium carbonate.

Since the exact isotopic composition of the hydrogen was not known, although it was nearly D-free, the methane resulting from the reduction was burned with air over hot copper and the density of the resulting water determined.

From isotopic fractionation considerations this method of winning the oxygen is not entirely satisfactory since the acid treatment leaves one third of the carbonate oxygen in the calcium chloride solution, thereby giving rise to the possibility of isotopic fractionation. To measure the extent of this uncertainty several samples of Grenville marble were pyrolyzed in iron tubes at high temperatures (from 800–1000°), the thermally evolved carbon dioxide stored over glycerol in 50-liter acid bottles, and later reduced to water and methane as in the acid treatment. The efficiency of the thermal decomposition method was about 80%.

All the data collected in the carbonate rock research are presented in Tables II and III.

TABLE II

DENSITY DATA OBTAINED IN PRELIMINARY EXPERIMENTS

No. of sample	Description of water	γ
1	Lake Michigan water	+0.35
2	Lake Michigan water	+ .32
3	Lake Michigan water	+ .44
4	Tank No. 1 CO_2 in large excess reduced with tank H_2	−4.92 −4.73
5	Tank no. 1 CO_2 reduced with tank H_2 in stoichiometric proportion	−3.77 −3.61
6	Water from combustion in air of CH_4 from expt. 5	−4.98 −5.30
7	Tank H_2 combined with air O_2	−6.39 −6.26
8	Tank no. 2 CO_2 reduced with excess D-free H_2	−8.59 −8.69
9	Water from combustion in air of CH_4 from expt. 8	−8.56 −8.69
10	Water from combustion in air of D-free H_2 similar to that used in expt. 8	−8.69 −8.65

Discussion

We must first consider the density of the standard water we have chosen as a reference in relation to purified Lake Michigan water, and in relation to standard waters selected by other investigators. In this research we made one density measurement on three samples of purified Lake Michigan water with the results given in Table II, 1, 2, and 3. The average of these data, 0.37 γ, indicates that the laboratory distilled water is slightly lighter than the purified lake water, but in another research more recently performed,[10] Mr. J. A. Swartout could detect no difference between the two waters greater than ± 0.1 γ. In Mr. Swartout's research more than one density measurement was made on each sample, so that

(10) J. A. Swartout and M. Dole, THIS JOURNAL, **61**, 2025 (1939).

TABLE III

DENSITY DATA OBTAINED IN CARBONATE EXPERIMENTS

Expt.	Description of water	γ	Av. γ	γ from CH_4 combustion	Correction to bring H_2 to normal	γ due to O_2 alone
11	Acid treatment of Niagara dolomite	−5.65 −6.11	−5.9	.....	+15.0	9.1
12	Acid treatment of Pennsylvania limestone	−5.2	−5.2	− 9.3	+15.0	9.8
13	Acid treatment of clam shells	−5.08 −4.92	−5.0	− 8.81 − 9.01	+15.2	10.2
14	Acid treatment of clam shells cleaned in boiling NaOH solution	−5.14	−5.1	− 7.9	+15.0	9.9
15	Acid treatment of Grenville marble	−5.65 −6.11	−5.9	− 9.92 − 9.62	+15.0	9.1
16	Acid treatment of Grenville marble	−5.91 −5.75	−5.8	− 8.46 − 8.60	+15.1	9.3
17	Special acid treatment of Grenville marble	−5.38 −5.12	−5.3	−10.11 −10.05	+15.2	9.9
18	Grenville marble pyrolyzed at 1000°	−7.34 −7.25	−7.3	− 8.90 − 7.98	+15.0	7.7
19	Grenville marble pyrolyzed at 1000°	−6.55 −6.67	−6.6	− 7.76	+14.6	8.0
20	Grenville marble pyrolyzed at 1000°	−5.59 −5.84	−5.7		+15.0	9.3
21	Grenville marble pyrolyzed at 1000° (diluted)	−3.61 −3.29	−3.45 (−6.9)	− 8.11 − 8.11	+15.1	7.8
22	Grenville marble pyrolyzed at 800° (diluted)	−4.06 −4.22	−4.1 (−5.6)		+15.0	9.4
23	Grenville marble pyrolyzed at 800°	−6.61 −6.64	−6.6		+14.6	8.0
24	Acid treatment of synthetic barium carbonate	−6.39 −6.83	−6.6	− 7.95 − 8.49	+14.9	8.3
25	Acid treatment of synthetic barium carbonate	−6.04 −5.75	−5.9	− 8.14 − 7.82	+14.6	8.7
26	Acid treatment of special barium carbonate	−9.6	−9.6	− 8.59 − 8.53	+15.2	5.6

we consider his results more reliable. In any case the difference is so slight that we shall consider it negligible.

It is more difficult to demonstrate the relation between our standard and standards used in other researches. Greene and Voskuyl[9] found that Cambridge, Massachusetts, tap water is 0.61 γ lighter than Lake Michigan water, Hall and Jones[11] found that Lake Mendota (Madison, Wisconsin) water is 0.3 γ lighter than Lake Michigan water, but Greene and Voskuyl found Lake Mendota water to be +0.16 γ heavier than Lake Michigan water. Greene and Voskuyl found the density of purified ocean water taken one mile off shore at Gloucester, Mass., to be 1.8 γ greater than their standard while we found[10] water taken 45 miles off shore at Gloucester to be 1.7 γ heavier than our standard. If we correct this measurement to the Greene and Voskuyl standard, we obtain +2.3 γ for the density of ocean water which agrees with the value found by Greene and Voskuyl for ocean water taken about 200 miles East of Cape Race, Newfoundland (Lat. 45° 13′ N.; Long. 49° W.). Incidentally this last water could hardly be considered as coming from the "Mid-Atlantic" and must consist very largely of arctic current water. From this point of view there seems little reason to believe that water from 45 miles off Gloucester should be different from Greene and Voskuyl's "Mid-Atlantic" water; hence we conclude that we should apply the correction of −0.6 γ to bring our standard water into coincidence with Greene and Voskuyl's standard. However, in an earlier publication Greene and Voskuyl[7] give +6.0 γ as the density of water containing normal hydrogen and atmospheric oxygen whereas our new result recently published[10] would be +7.0 γ instead of 6.6 γ if to the latter we applied a correction of 0.4 (two-thirds of 0.6 γ, which would be the contribution due to oxygen isotopic fractionation). Because

(11) N. F. Hall and T. O. Jones, THIS JOURNAL, **58**, 1915 (1936).

of these conflicting lines of evidence we shall leave unsettled for the time being the exact difference between Cambridge, Mass., tap water and Lake Michigan water.

The difference in γ-values for water samples 4 and 5 of Table II indicates that the carbon dioxide should be reduced with hydrogen in excess while the data for samples 6 and 7 indicate that D-free hydrogen should be used in the catalytic reduction. Experiments 8, 9, and 10 prove clearly that the use of D-free hydrogen is justified and that the method of hydrogen analysis by combustion of the unused hydrogen and methane produced in the catalytic reduction is sound.

In Table III are collected all the density data obtained in the carbonate experiments. For some inexplicable reason the first density measurements of the water from the methane combustions gave too low results since water made from air and containing no deuterium has for its minimum density, $-8.9\ \gamma$; yet in some of the experiments listed in Table III we found $-9.9\ \gamma$ and $-10.1\ \gamma$. Toward the end of this research, the reduction of the carbon dioxide from the acid treatment of the Grenville marble was repeated and the density of the water formed in the reduction and in the methane combustion carefully redetermined with the results given under experiment no. 16 of Table III. The density of the water obtained from the reduction of the carbon dioxide agreed well with that obtained in the first experiment, no. 15 of Table III, thus indicating that the early results on the water from the carbon dioxide reduction were correct, but the density of the water from the methane combustion was different from the earlier figure, yet entirely reasonable and close to the expected value. For this reason we have disregarded the early data on the densities of the water from the methane combustion and estimated the correction to be applied to bring the hydrogen of the water to normal from the later more accurate results. If the hydrogen were completely D-free, the correction would be $-15.5\ \gamma$[10]; all the corrections used in Table III are within one part per million of this figure.

The last column of Table III contains the values of the excess density over normal water of the water containing the oxygen under consideration and normal hydrogen. First of all it is interesting to note from experiments 11 through 16 that no significant difference (*i. e.*, any difference greater than 1 part per million) exists between the isotopic composition of the oxygen in the oldest rocks (Grenville marble) and the youngest (clam shells). We can make the tentative conclusion, therefore, that there has been no change in the isotopic composition of the oxygen in the oceans (from which these rocks were precipitated) over a period greater than a billion years. We must assume in making this last statement that the oxygen at present in the rocks is identically the same oxygen that was originally in the rocks when they were first laid down. Nier and Gulbransen[12] have recently similarly demonstrated in a mass-spectrographic study of the carbon isotopes in Grenville carbonates and clam shells that no apparent change in this ratio has occurred during a period of 1.2 billion years.

From Table III it is evident that a slight difference exists between the data obtained in the acid treatment of the rocks and in the thermal decomposition. The average value of γ for the acid treatment on the Grenville marble (omitting no. 17) is $9.2\ \gamma$ whereas the thermal decomposition of the Grenville marble gave $7.9\ \gamma$ as the average difference in density omitting the data obtained in experiments 20 and 22 in which some of the carbon dioxide liberated was lost. In experiment 17 the Grenville marble was decomposed with hydrochloric acid made by dissolving anhydrous hydrogen chloride in water made from the oxygen of the air. This experiment was performed to see whether the isotopic composition of the oxygen in the water of the acid solution influenced in any way the isotopic ratio of the oxygen in the liberated carbon dioxide, but as the results indicated very little effect was noted; increase in the density of the water due to the oxygen by $6.6\ \gamma$, changed the final results for experiment 17 by only $0.7\ \gamma$. The reason for the absence of any pronounced effect here is the rapidity with which the carbon dioxide is evolved, insufficient time being allowed for equilibrium with water to be attained. Since no measurable fractionation of the oxygen isotopes at the high temperatures of the thermal decomposition is to be expected, we can accept the thermal decomposition result, $7.9\ \gamma$, as giving the true oxygen isotope ratio, 1.034/500, in the carbonate rocks.

The difference between 9.2 and 7.9, or $1.3\ \gamma$, must be explained by the isotopic fractionation which takes place when the carbonate is decomposed by the acid. Whether fractionation also

(12) A. O. Nier and E. A. Gulbransen, THIS JOURNAL, **61**, 697 (1939).

occurs at the time of the precipitation of the carbonate was tested by studying the synthetic barium carbonate made in two ways. In experiments 24 and 25, the carbonate was precipitated by adding carbon dioxide made from oxygen of the air to water made from oxygen of the air. If, on liberation of the carbon dioxide, no isotopic fractionation had taken place at any step in the process, the γ-value of the water obtained by the carbon dioxide reduction should be equal to 6.6, but the value 8.5 was found, Table III. This difference, 1.9 γ, is slightly greater than the value 1.3 γ mentioned above, but it is sufficiently close to it to conclude that a greater fractionation of the oxygen isotopes occurs when the carbonate ion decomposes than when it forms. Some barium carbonate was also prepared by adding carbon dioxide containing oxygen of the air to normal water. In this case one would expect the density of the water resulting in experiment 26 to be $\frac{1}{3}$ (6.6 + 6.6 + 0), or 4.4 γ. Actually 5.6 γ was found, or 1.2 γ greater than expected. This also agrees well with the difference, 1.3 γ, found between the results of the acid and thermal treatments of the carbonate.

Having reached the conclusion that the oxygen isotope fractionation probably occurs mainly when the carbonate is decomposed rather than when it is precipitated, it is possible and of interest to suggest a mechanism to explain the excess value of the atomic weight of oxygen in the rocks. When carbon dioxide is brought into equilibrium with water, the heavier isotopes of oxygen concentrate in the carbon dioxide phase, the fractionation factor for the O^{18} isotope being 1.047 at 0° and 1.039 at 25° as Urey and Greiff have calculated.[5] When this carbon dioxide dissolves in ocean water whose oxygen is 1.2 γ heavier than Lake Michigan water, the calcium carbonate precipitated should contain oxygen whose γ-value (when converted to water) is the average of the oxygen in the water and in the carbon dioxide. Thus at 0° we have for the carbon dioxide a γ-value equal to 11.5 and for the water, 1.2 γ, the average being $\frac{1}{3}$ {2(11.5) + 1.2} or 8.2 γ. At 25° a similar calculation yields 7.0 γ as the theoretical value for the oxygen in the carbonate rocks. Unfortunately no measurements have been made of the γ-value of the oxygen in atmospheric carbon dioxide and we do not know the average temperature to use in calculating the fractionation factor; however, our experimental result, 7.9 γ, is slightly less than that calculated for 0°, and thus agrees with the theory reasonably well.

Part II. Iron Oxide Ores

Experimental

Composition of the Ores.—The iron ores studied were classified geologically as follows: first, a sample from the Soudan mines in the Vermillion range representing an ore of the Keewatin period, 1.5 billion years old; second, a Middle Huronian iron ore from the Mesabe range (Biwabik iron formation), 1.0 billion years old; third, a Silurian iron ore of the oölitic type from Clinton, N. Y., 375 million years old; and fourth, another Silurian ore of the same age, also from Clinton, containing small fossils. Since the data obtained in the case of the last two ores made us suspect that they might contain carbonates whose oxygen would probably be quite different in isotopic composition from the oxygen of the iron oxide, the ores were analyzed with the results given in Table IV.

TABLE IV

COMPOSITION OF SILURIAN IRON OXIDE ORES IN PER CENT.

	H_2O	Fe	Ca	CO_2	Residue unreactive to acid
Oölitic	1.4	34.2	7.29	8.1	16.2
Fossil	1.2	23.9	13.25	28.7	7.0

The Keewatin ore contained no detectable water, but 450 g. of the Middle Huronian ore evolved 20 cc. of water (4.4%) on being heated to red heat in a slow stream of nitrogen. No detectable carbonate was present in either the Keewatin or Middle Huronian ore.

Reduction of the Ores.—All the ores were reduced in Pyrex tubes heated to 600° in an electric furnace; the hydrogen used was practically deuterium-free, and the water formed was first condensed in a water condenser and then the last traces frozen out in a dry-ice–acetone trap. The reduction usually lasted from thirty to sixty hours.

Purification of Samples and Density Measurements.—In all of the iron ore experiments the water distillation and density measurement technique was exactly the same as that described in Part I of this paper. The data are collected in Table V where the last column gives the final corrected γ-value for the oxygen in the ores.

Discussion

From experiments 1, 2, and 3 it is evident that the oxygen in the iron oxide of the Keewatin and Middle Huronian ores has the same isotopic composition as the oxygen in water, within the experimental uncertainties, but the data are not accurate or conclusive enough for us to state whether the oxygen corresponds to the oxygen of ocean water or to that of fresh (rain) water. Probably the former is the case since the average of the three reductions is +0.9 γ, fairly close to +1.2 γ, which is the value for the oxygen in ocean water. In expt. 3, 83.5% of the ore was reduced,

TABLE V

DATA OBTAINED IN THE ISOTOPIC ANALYSIS OF IRON ORES

Expt.	Type of ore	Ore, g.	Water obtained, cc.	Density of water		Correction for hydrogen	Density of water due to oxygen
1	Keewatin	400	51	−13.80	−13.67	+14.9	+1.2
2	Middle Huronian	450	61	−13.57	−13.57	+15.2	+1.6
3	Middle Huronian	310	87.5	−14.7	−14.7	+14.6	−0.1
4	Silurian (oölitic)	350	46	−11.62	−11.43	+15.0	+3.5
5	Silurian (fossil)	345	41	−10.06	−10.06	+14.6	+4.5

assuming it to be pure hematite, so that one might be inclined to give greater weight to the result for this experiment, yet we can think of no reason why a partial reduction of the ore at red heat should favor one or the other of the isotopes. We can conclude definitely, however, that the Keewatin and Middle Huronian ores contain very little, if any, oxygen which was in the atmosphere before being bound to the iron. The conclusion of the geologists that these ores were formed by precipitation from water seems to be completely substantiated.

The presence of the carbonates in the Silurian ore may have been responsible for the greater density of the water obtained on reduction of these ores by virtue of either of the following sets of reactions

$$CaCO_2 \xrightarrow[\text{heat}]{} CaO + CO_2$$
$$CO_2 + 2H_2 \longrightarrow 2H_2O + CH_4 \quad (4)$$

$$FeCO_3 \xrightarrow[\text{heat}]{} FeO + CO_2$$
$$FeO + H_2 \longrightarrow Fe + H_2O \quad (5)$$

since the oxygen in the carbonate ores is heavier than normal. Of reactions (4) and (5) the latter seems the more probable as ferrous oxide would be reduced more readily than carbon dioxide, yet we estimate that some carbon dioxide must have been reduced to give a total of 41 cc. of water which is more than complete reduction of all the iron oxides present would yield. We conclude that enough water was formed from the oxygen of carbonates in both the fossil type and oölitic type experiments to account for the small excess in observed density.

Acknowledgments

We are greatly indebted to the Alexander Dallas Bache Fund of the National Academy of Sciences for a grant with which the platinum resistance thermometer and accessory equipment was purchased, as well as to Northwestern University for a grant from its research fund. We wish to thank Mr. J. S. Brown of the St. Joseph Lead Company for going to the trouble and expense in providing us with several large sections of Grenville marble, and particularly do we wish to thank Professor C. H. Behre, Jr., and other members of the Department of Geology and Geography at Northwestern for aid in procuring geologic samples and for many helpful suggestions.

Summary

1. Improvements in density measuring apparatus have been developed and applied to the isotopic analysis of oxygen in carbonate rocks and iron oxide ores.

2. A study of Grenville marble, Niagara dolomite and Pennsylvania limestone and clam shells, all carbonates of widely different geologic age, reveals no significant difference in the isotopic composition of the oxygen in the rocks as a function of age.

3. The oxygen of the Grenville marble when liberated as carbon dioxide with acid and reduced with hydrogen gives water 9.2 p. p. m. heavier than normal, but when the carbon dioxide is driven out of the rock thermally, the resulting water is only 7.9 p. p. m. heavier. The difference in these two data is attributed to the isotopic fractionation which takes place when the carbonate ion is decomposed by acid.

4. The observed value of 7.9 p. p. m. can be explained quantitatively with the aid of the isotopic exchange equilibrium theory of Urey and Greiff.

5. The oxygen in iron ores of the Keewatin and Middle Huronian ages does not differ significantly in its isotopic composition from that of oxygen in normal water, the slight excess density observed in the experiments on the oölitic and fossil type Silurian ores is probably due to the presence of carbonates in the ores.

EVANSTON, ILL. RECEIVED OCTOBER 30, 1939

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

The Bromine–Bromine Distance in the Dibromides of *cis*- and *trans*-Stilbene[1]

BY JAMES D. McCULLOUGH

The configuration of the products resulting from the addition of halogens to the double bonds of *cis* and *trans* isomers has been of considerable interest in connection with the problem of restricted rotation about the resulting single bond.

Weissberger has measured the electric dipole moments of the stilbene dichlorides[2] and dibromides[3] in benzene solution. His results are shown in Table I. The difference in moment for a given pair of isomers indicates a lack of free rotation in at least one member of the pair, since completely free rotation in both members would lead to identical moments. The low moment of the *meso* dibromide is an indication that the bromine atoms are restricted to the *trans* position or nearly so, the slight deviation from zero moment being possibly due to thermal vibration.

TABLE I

ELECTRIC DIPOLE MOMENTS

	meso	*dl*
Stilbene dichlorides	1.27 *D*	2.75 *D*
Stilbene dibromides	0.4–0.9 *D*	2.8 *D*

Rate studies have been made in this Laboratory by Young, Pressman and Coryell[4] for the reaction between potassium iodide and the dibromides of various pairs of *cis–trans* isomers. It was found for each pair investigated that the rate of reaction of the *trans* derivative is faster and the heat of activation smaller than for the corresponding *cis* derivative. Young and Pressman[5] have attributed these differences to restriction of the rotation about the single bond between the two carbon atoms carrying the bromine and have correlated the specific reaction rate constants with the configurations postulated on the basis of preferred orientation due to this restriction. It was in connection with this work that the present problem presented itself and the author is indebted to Dr. Young and Mr. Pressman for the pure crystalline materials used in this investigation.

Although free rotation about the carbon to carbon single bond in question in the stilbene dibromides would seem highly improbable in the crystalline solids, there is, it seems, a high degree of probability that if there is a preferred orientation in the liquid or dissolved state the same or very nearly the same orientation will also be assumed by the molecules on entering the crystal.

Taking 1.54 Å. as the carbon to carbon single bond distance, 1.91 Å. for the carbon to bromine distance, and tetrahedral bond angles, one may calculate the expected bromine–bromine separation for the absolute *cis* position to be 2.82 Å. and for the absolute *trans* position 4.57 Å. Thermal vibration at room temperature would make the average separation for *cis*-restricted molecules greater and for *trans*-restricted molecules less than these calculated values.

For purposes of describing the configuration about the bond, use is made of the azimuthal angle, ϕ, such that ϕ is 0 for the *cis* position and 180° for the *trans*. Using the above angles and distances, the bromine separation, l, then becomes

$$l = [7.95 + 6.48\ (1 - \cos\phi)]^{1/2}$$

The method employed in measuring this distance was the radial distribution treatment essentially as described by W. V. Medlin.[6]

In this treatment the radial distribution function, $4\pi r^2 \rho(r)$, is given by the following summation over all lines observed on the photograph

$$4\pi r^2 \rho(r) = 4\pi r^2 \rho_0 + \frac{2r}{\pi} \sum_{i=1}^{i=\infty} s_i I_i \sin s_i r$$

where $s = 4\pi \sin \Theta_i/\lambda$, Θ_i being the Bragg angle or one-half the scattering angle for the ith line on the film, λ the wave length of the X-rays and I_i the intensity of the ith line.

The above function represents the product of scattering powers in volume elements which are separated by the distance r as a function of this distance. The magnitude of these maxima will be proportional to the products of the atomic numbers of the atoms involved. When one particular

(1) Presented at the Stanford University meeting of the Pacific Division of the American Association for the Advancement of Science, June, 1939.

(2) Arnold Weissberger, *J. Org. Chem.*, **2**, 245 (1937).

(3) Private communication to the author.

(4) William G. Young, David Pressman and Charles D. Coryell, THIS JOURNAL, **61**, 1640 (1939).

(5) William G. Young and David Pressman, results not as yet published; see abstract of paper presented by William G. Young at the Eighth National Organic Chemistry Symposium of the American Chemical Society, St. Louis, Missouri, December, 1939.

(6) W. V. Medlin, THIS JOURNAL, **57**, 1026 (1935), and **58**, 1590 (1936).

kind of atom is much heavier than any of the others present, as is the case in the present study, maxima due to the interaction of these heavy atoms with each other may be so strong as to blank out all other effects. Thus bromine–bromine interaction will be $(35)^2$ as compared to 35×6 for bromine–carbon and $(6)^2$ for carbon–carbon or in the approximate ratio of 35:6:1.

The crystalline samples of the *meso*- and *dl*-stilbene dibromides were finely ground and passed through a 200-mesh sieve. The resulting powder was packed with only slight pressure into capillary tubes with a bore of about 0.3 mm. The cylinders thus formed were then pushed out of the capillary by means of a stiff wire and mounted in the X-ray camera. No collodion or other binder was used in holding the samples together.

Filtered radiation from a copper target was employed in a cylindrical camera of 5 cm. radius. Both of the photographs used showed 35 measurable lines, covering a range of $\sin \theta/\lambda$ out to 0.375 for *trans*-stilbene dibromide and to 0.318 for *cis*-stilbene dibromide. The intensities were estimated both visually and with the aid of microphotometer tracings made on the Smith–Leighton–Hensen microphotometer at Stanford University, the two methods giving values in fairly good agreement. The weaker lines did not show on the tracings so it was necessary to rely entirely on the visual estimates for their intensities.

The relative intensities so obtained were corrected by means of the Lorentz and polarization factors and multiplied by a factor $e^{-B \sin^2 \theta}$ following the procedure of Medlin, so as to reduce the importance of the lines at large scattering angles. In both cases a value of $B = 7.5$ was used. Medlin has shown, and it was tested in this case as well, that the positions of the maxima are quite independent of the value of B.

The results of the summations are shown in Fig. 1, the constant term $4\pi r^2 \rho_0$ being omitted. In the case of *trans*-stilbene dibromide (the *meso* compound), only one maximum is observed and that at 4.50 Å. The small shelf just under 3 Å. may be due to carbon–bromine interaction caused by a carbon atom and a bromine atom not directly bonded to each other, but each bonded to a common third atom. The calculated distance for such a case is 2.8 Å. The large maximum is without doubt due to bromine–bromine interaction and the distance 4.50 Å. corresponds to nearly the complete *trans* position which, as pointed out before, would require a separation of 4.57 Å. The distance 4.50 Å. corresponds to an azimuthal angle of 154° or a displacement of 26° from the full *trans* position assuming a static model.

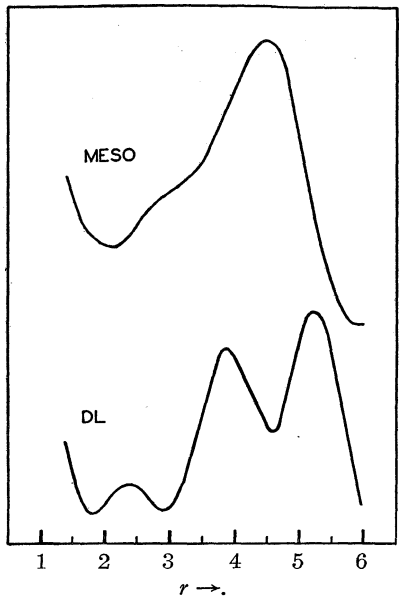
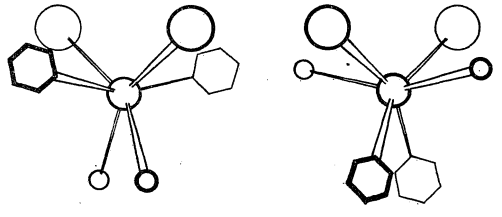


Fig. 1.—Radial distribution functions for the stilbene dibromides.

There is also the possibility that the single large maximum in this case is the resultant of two different pairs of bromine–bromine distances of nearly the same magnitude, one of them being within the molecule and the other due to bromines in different molecules. For example, the bromine separation within the molecule might be that for the full *trans*, 4.57 Å., and that for the pair on adjacent molecules about 4.4 Å., giving the observed peak at 4.50 Å. as an unresolved doublet. Only a more complete structure determination could answer this question. In spite of this difficulty, it still may be said safely that the bromine atoms are close to *trans* in configuration.

The function for *cis*-stilbene dibromide (the *dl* mixture), shows three maxima in the range covered, one small one at 2.40 Å. and larger ones at 3.85 and 5.25 Å. The value 2.40 is too small to be attributed to a bromine–bromine separation where the two atoms are not directly bonded to each other since the minimum distance between non-bonded bromine atoms in crystalline bromine at liquid air temperature is 3.30 Å. and twice the van der Waals radius is 3.80 Å. the normally

expected closest distance of approach of non-bonded atoms. The smallness of the peak, too, would eliminate it as being due to bromine–bromine interaction and it is therefore attributed to unresolved carbon–bromine interaction, from the bonded distance for these atoms of 1.91 Å. and the non-bonded separation of 2.82 Å. The maximum at 5.25 is to be attributed to a bromine separation in different molecules because the distance is greater than that for full *trans*. The remaining peak at 3.85 appears, therefore, to be the one due to the bromine atoms within the molecule. This distance corresponds to an azimuthal angle 90°. It is interesting to note that the bromine separation is only slightly different from twice the van der Waals radius for bromine which is 3.80 Å. If the phenyl groups were fully *trans* to each other, the bromine azimuthal angle would be 60°, requiring a separation of only 3.35 Å., which is less than twice the van der Waals radius. The tendency of the phenyl groups to be *trans* to each other would be opposed by the repulsion of the bromine atoms and the observed structure may be the resultant of these two forces. A second configuration with the phenyl groups 30° from *cis* to each other is also permitted by the observed bromine separation. In this case the bromine atoms would again be brought as close as possible to each other by the tendency of the phenyl groups to get apart. These two possibilities are shown in Fig. 2.



A B

Fig. 2.—Configurations permitted for the dibromide of *cis*-stilbene, looking down the axis of the bond between the two carbon atoms to which bromine is bonded. The circles represent in order of decreasing size, bromine, carbon and hydrogen atoms. The phenyl groups are indicated by means of hexagons. No significance is to be attached to the absolute sizes or scale used.

These findings lend support to the postulate of Young and Pressman and are in fairly good agreement with the electric dipole moments found by Weissberger[2] and shown in Table I.

In order to estimate the dipole moments expected for the observed bromine separation, the molecules were considered as being made up of two C_6H_5CHBr groups joined together by a carbon–carbon bond and rotated with respect to each other through the angle ϕ. If the component of the electric moment of the C_6H_5CHBr group perpendicular to the axis of the bond by means of which the two are joined is represented by m, and if polarization is neglected, the molecular dipole moment, μ, is given by the function, $\mu = 2m \cos(\phi/2)$.

The value of m was estimated by making use of the electric moment for benzyl bromide which was found by Mohler[7] to be 1.88 D. The moment of a C–H bond taken as 0.4 D[8] was subtracted vectorially and the component of the remainder perpendicular to the C–H bond was taken assuming tetrahedral angles. This procedure gives a value of 1.7 D for m. Making use of the values of ϕ calculated from the bromine–bromine distances, this leads to a moment of 0.8 D for the *meso* dibromide, which falls in Weissberger's range, and 2.4 D for the *dl* dibromide as compared to the observed value of 2.8 D. In this simplified treatment the phenyl groups have received no special attention and the same function is assumed for both the *meso* and the *dl* dibromides.

The author is indebted to Dr. William G. Young and David Pressman for their kindness in making available the crystalline dibromides from which the X-ray powder photographs were prepared.

Summary

The bromine–bromine separations in the molecules of the crystalline stilbene dibromides have been measured by means of the radial distribution treatment of X-ray powder photographs. The separation was found to be 4.50 Å. in the *meso* dibromide and 3.85 Å. in the *dl* dibromide. In the former, all like groups are *trans* to each other, while in the latter the bromine atoms are as close to each other as the van der Waals radius for bromine will permit. The results support the postulate of Young and Pressman and are in agreement with the electric dipole moments found by Weissberger.

LOS ANGELES, CALIF. RECEIVED DECEMBER 19, 1939

(7) H. Mohler, *Helv. Chim. Acta*, **21**, 67 (1938).

(8) Linus Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1939, pp. 67, 68.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CITY OF CARDIFF TECHNICAL COLLEGE]

The Anomalous Strength of *n*-Butyric Acid

BY H. O. JENKINS AND J. F. J. DIPPY

Thermodynamic dissociation constants[1] are now available for the saturated aliphatic *n*-acids extending from formic to nonoic acid and the following features have become apparent. In the first place there is a very pronounced fall in dissociation constant in going from formic to acetic acid. Second, although the general trend is for the acid strength to diminish as the alkyl chain lengthens and to approach a limiting value in the higher members of the series, there is a distinct increase in K in proceeding from propionic to *n*-butyric acid, and it has been suggested[1a] that this enhancing influence still persists in the succeeding *n*-acids (elevation of the dissociation constant being attributed to some interaction between the hydrogens of the γ-carbon and the carboxyl group). Further consideration is now given to this anomaly.

Undoubtedly some correlation exists between the length of the alkyl chain and the corresponding acid strength. For a working hypothesis we shall be concerned with the distance separating the carbon of the carboxyl group and the terminal carbon atom, or the terminal hydrogen in the case of formic acid. Table I gives these distances r (the carbon–carbon valency angle being taken as 109° in propionic acid) and the dissociation constants for the first three members of the series.

TABLE I

Acid	r (A)	$1/r^6$	$10^5 K$	$5 + \log K$
Formic	1.06	0.705	17.72	1.248
Acetic	1.54	0.075	1.75_5	0.244
Propionic	2.54	.004	1.33_5	.125

The distances are unambiguous, that is, they are not affected by the presence or absence of free rotation, and a plot of log K against $1/r^6$ reveals linearity (see Fig. 1). Moreover, a relation of this type predicts a limiting value for the dissociation constant of a *n*-aliphatic acid as the alkyl chain lengthens. The equation to the line using Napierian logarithms is $\ln K = a + b/r^6$ where b has the value 3.7×10^{-48} in absolute units; this approximates to $N\alpha_0\mu^2/RT = 10^{-46}$ where N is the Avogadro number, R the gas constant, T the absolute temperature if α_0, the polarizability of the carbon–carbon bond, is taken as 0.5×10^{-24} and μ, the inducing dipole, as $2D$.

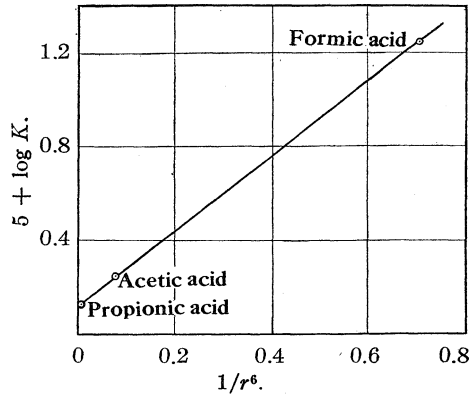


Fig 1.

Now proceeding to *n*-butyric acid and higher members of the series, we are confronted with the possibility that free rotation moves the γ-carbon atom from one extreme of a *cis* position, where it is in close proximity to carboxyl, to the other extreme of a *trans* position. An average distance is evidently needed and we shall use $(\bar{r}^2)^{1/2}$ the root mean square distance between the ends of the structure; this has been calculated for *n*-butyric acid to be 3.36 Å. by the method of Eyring,[2] assuming complete free rotation about the valence bonds and no distortion of valency angles. The formula is

$$\bar{r}^2 = c_1^2\{n + 2(n-1)\cos\theta + 2(n-2)\cos^2\theta \ldots + 2\cos^{n-1}\theta\}$$

where c_1 is the distance between consecutive carbon atoms and is the supplement of the carbon–carbon valency angle, taken as 109°. However, since this distance in the *n*-butyric acid molecule is larger than the corresponding distance in the propionic acid molecule, while K for butyric acid (1.50×10^{-5}) is also larger than that for propionic acid ($1.33_5 \times 10^{-5}$), clearly *n*-butyric acid is anomalous, using the linear relation as criterion. To bring butyric acid into conformity with the linear relationship, the distance r (as determined by graphical interpolation) should be 1.8 Å. and not 3.36 Å. as calculated from Eyring's formula. Two suggestions can be made as

(1) (a) Dippy, *J. Chem. Soc.*, 1222 (1938); (b) Harned, *et al.*, THIS JOURNAL, **55**, 652, 2379 (1933); (c) **56**, 1042, 2039 (1934).

(2) Eyring, *Phys. Rev.*, (2) **39**, 746 (1932).

to how the effective distance is decreased. First, the hypothesis of completely unhindered rotation in the *n*-butyric acid molecule may be abandoned. A consideration of the geometry of the system reveals that the minimum distance of approach of the terminal carbon atom to the carbon atom of the carboxyl group is considerably less than the root mean square value and equal to 2.5 Å.; thus it seems very likely that the rotation is practically frozen in the *n*-butyric acid molecule which thus exists in a "*cis*" configuration. In this connection it should be noted that the strengths of simple monobasic olefinic acids of the *cis* configuration are always greater than their *trans* isomers; this is well illustrated by the crotonic acids (10^5 *K; trans* 2.03, *cis* 3.6) which have a carbon system comparable to *n*-butyric acid. Furthermore, there is now considerable evidence of restricted rotation about a single bond, derived from dipole moment, infrared absorption spectra, Raman spectra and heat capacity studies; for instance, in the case of formic acid Bauer and Badger[3] have reason to believe that the hydroxyl group is firmly established in the *cis* position. A *cis* configuration for butyric acid is favored by the facts that the C–CH_3 and C–O dipoles are of opposite sign and that their mutual potential energy is greater than kT, the energy of thermal agitation. It is likely nevertheless that in order to account adequately for the complete restriction of rotation, other influences beside dipole attraction will have to be taken into consideration, such as the London attraction which has been used by Weissberger to explain the dipole moments of disubstituted diphenyl derivatives, and the fact that *cis*-dichlorethylene is the more stable[4] of the two isomerides at 300°. The dipole attraction, however, must play a part, and be less potent the higher the temperature. As the temperature is raised, therefore, we would expect the dissociation constant of butyric acid to fall; Harned and Sutherland[5] record the temperature of maximum K for butyric acid as 8°, whereas for acetic, propionic, and other acids[6] differing in strength by more than an order of 10, the corresponding values lie between 20 and 25°. Thus we have in *n*-butyric acid some factor entering which influences the "normal" temperature change of K exemplified by acetic acid and propionic acid, and at the same time the butyric system is the first in the homologous series in which the extent of freedom of rotation determines the effective distance r. Since this complicating factor of the existence of a restricting potential must occur in all the higher fatty acids extending from *n*-butyric acid, their strengths must be abnormally high. As a further consequence of this valeric and isovaleric acids should show a temperature dependence of K similar to that of *n*-butyric acid and not to propionic acid. Work on this problem is now proceeding.

Again, another factor which helps to reduce the effective distance in the *n*-butyric molecule is the extreme flexibility of the four carbon system compared with that obtaining in the three carbon system of propionic acid. An electron diffraction investigation of the valency angles in the *n*-butyric molecule would contribute materially to the solution of the anomaly of this acid.

Summary

A linear relationship has been discovered between the logarithms of the dissociation constants of formic, acetic and propionic acids, and the inverse of the sixth power of r, the distance separating the carbon of the carboxyl and the terminal group of the acid. This relationship predicts a limiting value for the higher acids. The slope of the line shows good agreement with a theoretical expression. As a deduction from this relationship the abnormality already recognized to exist in *n*-butyric acid has been interpreted in terms of the existence of a restricting potential in the molecule; this is in harmony with conclusions reached in infrared absorption, Raman spectra, heat capacity, and dipole moment studies.

CARDIFF, GREAT BRITAIN RECEIVED AUGUST 26, 1939

(3) Bauer and Badger, *J. Chem. Phys.*, **5**, 852 (1937).

(4) Ebert and Bull, *Z. physik. Chem.*, **152A**, 451 (1931); Stuart, *Physik. Z.*, **32**, 793 (1931).

(5) Harned and Sutherland, THIS JOURNAL, **56**, 2039 (1934).

(6) Nims, *ibid.*, **58**, 987 (1936); Martin and Tartar, *ibid.*, **59**, 2672 (1937).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE PENNSYLVANIA STATE COLLEGE]

Hydrogen Fluoride as a Condensing Agent. X.[1] Rearrangements

BY J. H. SIMONS, S. ARCHER AND D. I. RANDALL

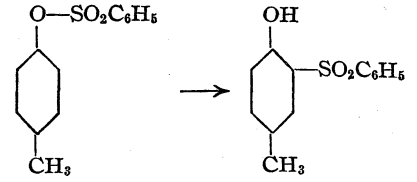
It has been found that a number of rearrangements commonly catalyzed by other condensing agents are also promoted by hydrogen fluoride. A few examples are reported here.

The exchange of alkyl groups by two aromatic compounds has been demonstrated repeatedly when aluminum chloride is employed.[2] Thus, polyamylbenzenes react with benzene to give monoamylbenzene.[3] We have found that *t*-butylbenzene reacts with phenol in the presence of hydrogen fluoride at 0° to give benzene and *t*-butylphenol, the latter in yields of about 10%. No attempt was made to carry out this conversion at higher temperatures, although it has been reported that disproportionation increases with temperature, when cymene is treated with aluminum chloride.[4]

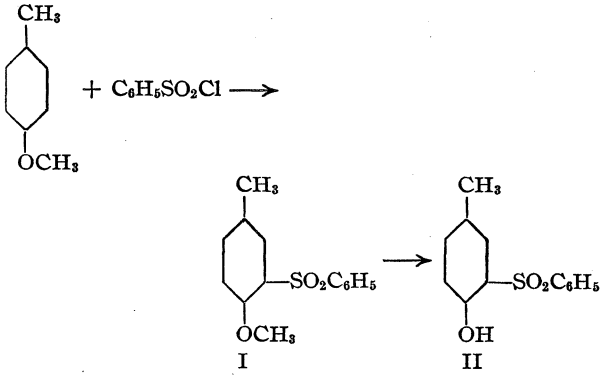
The conversion of a ketoxime to an anilide has been carried out in the cold using an acetic acid–hydrogen fluoride mixture, and also an ether–hydrogen fluoride mixture. Benzophenone oxime undergoes the Beckmann rearrangement with phosphorus pentachloride almost quantitatively, whereas with hydrogen fluoride under the conditions we employed only a 72% yield of benzanilide was obtained.

It has been reported previously that hydrogen fluoride would not effect a Fries rearrangement at room temperature.[5] This statement was amply confirmed by our observations of the behavior of phenyl acetate. A mixture of the ester and hydrogen fluoride gave no appreciable amounts of rearranged product. However, when warmed to 100° it was found that rearrangement to the *p*-acylphenol did take place, although there was much to be desired with respect to smoothness and yield.

A reaction similar to the Fries is the conversion of a phenol sulfonate to an hydroxy sulfone. Thus, in the presence of hydrogen fluoride at 100° *p*-cresyl benzenesulfonate was converted to 2-hydroxy-4-methyl-diphenyl sulfone in yields of 10%.



The hydroxy sulfone was synthesized by allowing *p*-cresyl methyl ether to react with benzenesulfonyl chloride in the presence of aluminum chloride to give I. The methoxy sulfone was then treated with aluminum chloride at an elevated temperature to produce the hydroxy sulfone II.



Due to the strong ortho directing tendency of the methoxy group it is reasonably certain that the sulfonyl radical entered the position ortho rather than meta to the methoxyl. At any rate, the synthesized sulfone was identical with the one obtained from the rearrangement.

We wish to thank Prof. E. H. Cox of Swarthmore College for a sample of *p*-cresyl sulfonate.

Experimental

Reaction of Phenol with *t*-Butylbenzene.—One-half molar quantities of phenol and the alkylbenzene were mixed and added to 70 g. of hydrogen fluoride at 0°. The reaction was allowed to proceed with stirring for a period of thirteen hours, after which time it was poured onto ice, neutralized, taken up in ether, and dried. There was isolated from the reaction mixture, 2.6 g. of benzene, identified by conversion to a dinitro derivative, and 7.5 g. of *p*-*t*-butylphenol, m. p. and mixed m. p. 98–99°.

Beckmann Rearrangement of Benzophenone Oxime.—Five grams of the ketoxime was dissolved in 75 cc. of acetic acid and the solution then was added slowly to 86 g. of hydrogen fluoride at 0°. After standing overnight the mixture was warmed on the steam-bath to remove the more volatile acid. Upon cooling the solution was diluted with water, the precipitate filtered and washed, and then

(1) For the previous paper of this series see THIS JOURNAL, **62**, 45 (1940).

(2) Calloway, *Chem. Rev.*, **17**, 336 (1935).

(3) Boedtker and Halse, *Bull. soc. chim.*, **19**, 444 (1916).

(4) Schorger, THIS JOURNAL, **39**, 2671 (1917).

(5) Fieser and Hershberg, *ibid.*, **61**, 1272 (1939).

recrystallized from dilute ethanol. The melting point and mixed melting point was 161–162°. The yield was 3.6 g. (72%). A mixture of 145 g. of hydrogen fluoride, 7 g. of the oxime, and 150 cc. of dry ether was made at 0° and then kept at room temperature for twenty-four hours. After removal of hydrogen fluoride and subsequent recrystallization from a methanol–water solvent, 5 g. of benzanilide representing a 72% yield was obtained. When the reaction was carried out using phosphorus pentachloride as the agent for the isomerization, 8 g. of the oxime gave 7.2 g. of the anilide.

Fries Rearrangement of Phenyl Acetate.—A solution of 33 g. of the ester in 75 cc. of pentane was placed in a copper bomb; 20 g. of hydrogen fluoride was added, the vessel sealed and heated for twenty-four hours at 100°. The mixture was then poured onto ice and neutralized. The dark red organic layer was ether extracted, dried, and distilled; 11 g. of an impure solid fraction was obtained which after recrystallization from ligroin melted at 108–110°. It was converted to the semicarbazone in the usual way. The derivative melted at 195–198°. When admixed with a sample of the semicarbazone of *p*-hydroxyacetophenone, m. p. 198–199°, there was no depression in melting point.

Rearrangement of *p*-Cresyl Benzenesulfonate.—Ten grams of the ester was dissolved in 400 cc. of ligroin and placed in a copper bomb; 140 g. of hydrogen fluoride was added, the bomb closed and heated at 100° for fourteen hours. The mixture was processed in the previously described manner, the ether solution finally being extracted with a 10% sodium hydroxide solution. Acidification of the latter precipitated 1 g. of the hydroxy sulfone, m. p. 135–136°.

Preparation of 2-Methoxy-4-methyl-diphenyl Sulfone (I).—One-tenth of a mole of *p*-cresol methyl ether and one-tenth mole of benzenesulfonyl chloride were dissolved in 50 cc. of carbon disulfide. To this solution, 15 g. of aluminum chloride was added gradually. When the catalyst had all been added, the mixture was refluxed on the steam-bath for five hours, and the solvent was removed. The residue was cooled and dilute hydrochloric acid was added cautiously. The organic solid which remained was washed with water by decantation, filtered, washed again, and then recrystallized from dilute ethanol to give 18.5 g. of the sulfone, m. p. 137–138°. The yield was 71% of the theoretical.

Anal. Calcd. for $C_{14}H_{14}O_3S$: S, 12.21. Found: S, 11.84.

Preparation of 2-Hydroxy-4-methyl-diphenyl Sulfone (II).—Six grams of aluminum chloride was intimately mixed with 3 g. of the methoxy sulfone (I), placed in a 50-cc. round-bottomed flask, and heated in an oil-bath to 140°. The temperature was maintained at 140–150° for two hours. Upon cooling, the mixture was treated with dilute hydrochloric acid and thoroughly freed from attendant salts. The mass was then dissolved in 10% sodium hydroxide, the solution filtered, and then acidified. The precipitated hydroxy sulfone was recrystallized from diluted ethyl alcohol to give 2.6 g. of pure sulfone, m. p. 137–138°. From the mother liquor there was obtained another 0.1 g. of pure sulfone, making the total yield 95% of the theoretical.

A mixed m. p. determination with the sulfone obtained from the rearrangement was 136–137°. A mixture of the hydroxy and methoxy sulfones (I and II) melted at 105–112°.

Summary

Hydrogen fluoride has been used to effect a number of exchange reactions or rearrangements of organic compounds. The following are examples: *t*-butylbenzene reacted with phenol to form *t*-butylphenol and benzene. Benzophenone oxime rearranged to benzanilide. Phenyl acetate rearranged to *p*-hydroxyacetophenone. *p*-Cresyl benzenesulfonate rearranged to 2-hydroxy-4-methyl-diphenyl sulfone.

STATE COLLEGE, PA. RECEIVED DECEMBER 6, 1939

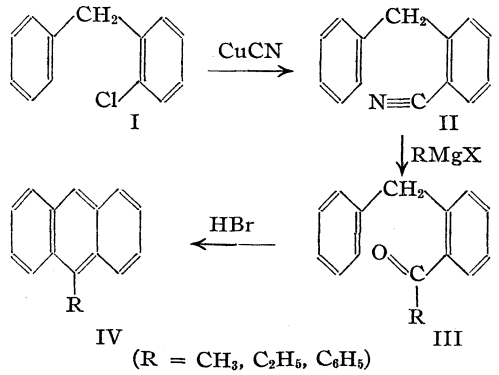
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF DUKE UNIVERSITY]

A New Route to 9-Alkyl- and 9-Arylanthracenes

BY CHARLES K. BRADSHER

Recently Bergmann[1] observed that hydrolysis of the acetal of *o*-benzylbenzaldehyde in boiling hydrochloric acid gave not only the expected aldehyde (III, R=H), but also a small amount of anthracene. From this observation and from considerations which we shall discuss later, we concluded that *o*-benzyl phenyl ketones (III) should cyclize to form 9-alkyl- and 9-arylanthracenes (IV).

The required ketones were obtained from



I II III IV

(R = CH_3, C_2H_5, C_6H_5)

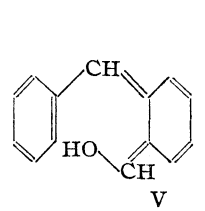
(1) E. Bergmann, *J. Org. Chem.*, **4**, 1 (1939).

o-benzylbenzonitrile (II) by the Grignard reaction. The nitrile (II) was prepared by two methods, the first of which, the action of lead thiocyanate on *o*-benzylbenzoic acid, did not seem capable of wide application and was discarded in favor of the action of cuprous cyanide on *o*-chlorodiphenylmethane (I). The latter compound was prepared by reduction of the benzohydrol obtained when phenylmagnesium bromide was allowed to react with *o*-chlorobenzaldehyde.[2] One would expect that Grignard reagents from a wide variety of aryl halides might be substituted for phenylmagnesium bromide, providing a means for the synthesis of a number of *o*-chlorodiphenylmethanes.

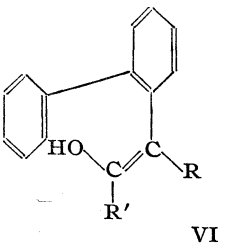
Three *o*-benzylphenyl ketones (III) were prepared, the phenyl, the methyl and the ethyl, of which only the first has been prepared previously.[1] Cyclization was effected by refluxing the ketones for four days in a mixture of hydrobromic and acetic acids. The expected hydrocarbons (IV) were obtained in yields ranging from 69% in the case of the ethyl ketone (III, R = C_2H_5) to 80% in the case of the methyl (III, R = CH_3). It is interesting to note that the phenyl ketone (IV, R = C_6H_5), despite the greater size of the phenyl group, cyclizes in a yield (75%) comparable with that of the alkyl ketones.

Bergmann[1] regarded the cyclization of *o*-benzylbenzaldehyde as a "modification of the Elbs synthesis of anthracene derivatives" and proposed a mechanism based on that advanced by Cook[3] for the latter reaction.

In our opinion, the cyclization of the aldehyde may be better understood if comparison is made instead with two other reactions which take place under similar conditions, *i. e.*, in boiling mineral acids. The first is the ring closure used by us in the synthesis of phenanthrene derivatives and for which we have recently proposed as an intermediate, a carbonyl compound of type VI[4] (here written in the enol form). The other comparable reaction is the formation of β-phenylnaphthalene from two molecules of phenylacetaldehyde. Carter and Van Loon[5] have suggested that the intermediate in this reaction is the enol VII. If *o*-benzylbenzaldehyde is represented in the enol form and this structure compared with those of



V



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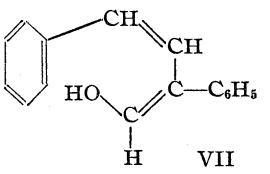
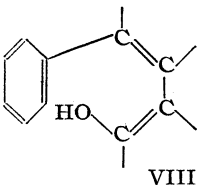


VII



VIII

the proposed intermediates, it will be seen that the feature common to all three is the β-(β-styryl)-vinyl alcohol system (VIII). It seems reasonable that the terminal hydroxyl on such a completely conjugated system would activate the *ortho* position of the aromatic ring so that cyclization could take place with the loss of water.

Although perfectly aware that the sum of these speculations does not constitute a proof, we do consider that the assumption of such an intermediate forms a satisfactory working hypothesis. Further, by assuming that cyclization is preceded by enolization[6] we may explain the slow rate at which the anthracene hydrocarbons are formed since it would not be expected that *o*-benzylphenyl ketones would exist in the enolic form to any great extent.

A further study is being made of compounds containing the β-(β-styryl)-vinyl alcohol system, and work is in progress on the extension of the synthesis reported in this paper to the preparation of 1,2-benzanthracene derivatives.

Experimental

***o*-Chlorobenzohydrol** was prepared by the action of phenylmagnesium bromide on *o*-chlorobenzaldehyde by a procedure essentially that of Tschitschibabin and Sheshler.[2] It was obtained as a colorless oil of b. p. 170–176° (5 mm.) and in a yield of 76%. The material crystallized on standing, m. p. 62–65°.

***o*-Chlorodiphenylmethane (I).**—A mixture of 49.7 g. of *o*-chlorobenzohydrol, 10 g. of iodine, 10 g. of red phosphorus, 500 cc. of acetic acid and 50 cc. of water was refluxed for twenty-nine hours. The excess red phosphorus was then filtered off and the filtrate poured on ice and extracted with ether. The ethereal extract was washed with ice-cold 10% sodium hydroxide solution to remove the acids and the free iodine. The solution was dried, concentrated and the residue distilled under re-

(2) This synthesis of *o*-chlorodiphenylmethane is essentially that used previously by Tschitschibabin and Sheshler, *J. Russ. Phys.-Chem. Soc.*, **56**, 149 (1925).

(3) Cook, *J. Chem. Soc.*, 487 (1931).

(4) Bradsher, THIS JOURNAL, **61**, 3131 (1939).

(5) Carter and Van Loon, *ibid.*, **60**, 1077 (1938).

(6) It should be pointed out that the Bergmann mechanism likewise involves enolization as its first step.

duced pressure. The fraction boiling at 144° (5 mm.) weighed 37.4 g. (81%) and was water-white.

o-**Benzoylbenzonitrile (II).** (a) **From *o*-Benzoylbenzoic Acid.**—The nitrile was prepared by the method of Bergmann[1] in yields of 35–50%.

(b) **From *o*-Chlorodiphenylmethane.**—By heating *o*-chlorodiphenylmethane with 10.8 g. of cuprous cyanide for twenty-three hours at 250°, and working up the product in the usual manner, the nitrile was obtained as a colorless oil, b. p. 160–164° (4 mm.); yield 10.3 g. (54%). A forerun of *o*-chlorodiphenylmethane (4.6 g.) was recovered.

o-**Benzylacetophenone (III, R = CH_3).**—A Grignard reagent was prepared in ether from 28.4 g. of methyl iodide and 5.4 g. of magnesium. Most of the ether was distilled off, 14.6 g. of *o*-benzylbenzonitrile added in 100 cc. of dry benzene, and the solution refluxed overnight. The mixture was decomposed by the addition of 20% ammonium chloride solution and the benzene layer separated. This layer was extracted with ice-cold 2 *N* hydrochloric acid, the acid layer separated, refluxed for one hour to hydrolyze the imine hydrochloride, cooled and extracted with ether. The ethereal extract was evaporated and the residue distilled under reduced pressure. The ketone, a yellow oil, b. p. 167° (5 mm.), crystallized on standing; yield 11.5 g. (72%). A sample recrystallized from petroleum ether was obtained as white needles, m. p. 49–50°.

Anal. Calcd. for $C_{15}H_{14}O$: C, 85.7; H, 6.7. Found: C, 85.5.; H, 6.8.

9-Methylanthracene (IV, R = CH_3).—A mixture of 2 g. of *o*-benzylacetophenone, 20 cc. of acetic acid and 20 cc. of 34% hydrobromic acid was refluxed for four days. Upon cooling, the product solidified and was collected and recrystallized from methanol. It was obtained as flat yellow needles, m. p. 80–81°; yield 1.45 g. (80%). The melting point was not raised by repeated recrystallization.

Anal. Calcd. for $C_{15}H_{12}$: C, 93.7; H, 6.3. Found: C, 93.4; H, 6.4.

o-**Benzylpropiophenone (III, R = C_2H_5).**—This ketone was prepared by the action of an excess of ethylmagnesium bromide on *o*-benzylbenzonitrile in a manner analogous to that employed in the synthesis of *o*-benzylacetophenone. The product was a yellow oil, b. p. 156° (3 mm.), and was obtained in a yield of 73%.

Anal. Calcd. for $C_{16}H_{16}O$: C, 85.7; H, 7.2. Found: C, 85.6; H, 7.3.

The phenylhydrazone was prepared by refluxing the ketone for three hours with phenylhydrazine in alcohol. Recrystallized from alcohol, it was obtained as white needles, m. p. 97–98°. These were unstable and decomposed on standing for two days.

9-Ethylanthracene.—This hydrocarbon was obtained by refluxing 2.05 g. of the above ketone with acetic and hydrobromic acids in a manner analogous to that employed in the synthesis of 9-methylanthracene. The product, recrystallized from methanol, was obtained as yellowish irregular plates, m. p. 58–59°; yield 1.3 g. (69%).

Anal. Calcd. for $C_{16}H_{14}$: C, 93.2; H, 6.8. Found: C, 93.0; H, 7.1.

o-**Benzylbenzophenone** was prepared by the method used in the preparation of the other two ketones, except that hydrolysis of the imine hydrochloride required two hours of refluxing. The product was obtained as a yellow, very slightly fluorescent oil,[7] b. p. 199–200° (3 mm.) and in a yield of 82%. On seeding, the ketone crystallized to a yellowish solid, m. p. 50–52°.

9-Phenylanthracene was prepared by refluxing 2.06 g. of the above ketone with acetic and hydrobromic acids as in the preparation of the other hydrocarbons. The product formed fluorescent plates on crystallization from ethanol, m. p. 154–155°; yield 1.44 g. (75%). Upon concentration of the mother liquor, an additional 0.1 g. was obtained, m. p. 153–155°.

Anal. Calcd. for $C_{20}H_{14}$: C, 94.5; H, 5.5. Found: C, 94.4; H, 5.8.

Summary

A new and general method has been found for the synthesis of 9-substituted anthracene hydrocarbons.

The theory has been presented that the cyclization involved is one characteristic of the β-(β-styryl)-vinyl alcohol system.

DURHAM, NORTH CAROLINA
RECEIVED DECEMBER 11, 1939

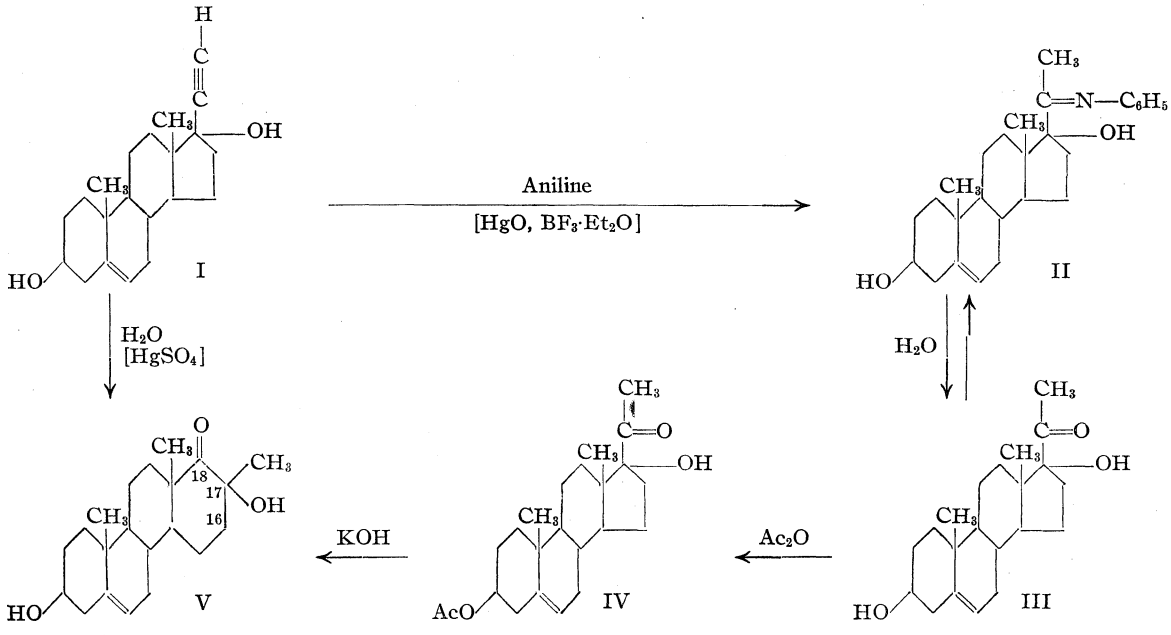
(7) Bergmann, ref. 1, who prepared this ketone by refluxing the imine hydrochloride for *six* hours with dilute hydrochloric acid, reported that the oil had an intense green fluorescence. This difference undoubtedly is due to the formation of more 9-phenylanthracene during the longer period of refluxing.

[CONTRIBUTION FROM THE SQUIBB INSTITUTE FOR MEDICAL RESEARCH, DIVISION OF ORGANIC CHEMISTRY]

The Preparation of Δ^5-Pregnenediol-3,17-one-20 from Δ^5-17-Ethynyl-androstenediol-3,17

BY HOMER E. STAVELY

The transformation of Δ^5-17-ethynyl-androstenediol-3,17 (I) into the hydroxy ketone III has been studied by Ruzicka and Meldahl,[1] who added acetic acid to the acetylene bond and then saponified the resulting acetate. An identical compound was obtained by Stavely[2] by the direct hydration of the acetylene compound in the presence of mercuric sulfate.



Degradation studies by Ruzicka, *et al.*,[3] have revealed the very noteworthy fact that this product cannot have the expected structure III. Oxidation of the corresponding acetylated and hydrogenated hydroxy ketone (presumed to have the side chain structure of III) led to a keto acid without the loss of any carbon atoms, instead of giving the expected acetate of *trans*-androsterone. To explain this unlooked for result Ruzicka proposed that in the preparation of substance III from the corresponding 17-ethynyl compound a rearrangement into a structure V had occurred, which readily explains the oxidation into the keto acid. Although the formulation of the compound V may be hypothetical in its details, there is not much doubt that a transformation of a five-membered into a six-membered ring must have occurred. The name chrysopregnane is now proposed for the parent hydrocarbon of the series to express the relationship to chrysene as well as to pregnane. Compound V should then be named Δ^5-3,17-dihydroxy-18-keto-chrysopregnene.

Since the appearance of an article by Loritsch and Vogt,[4] who condensed 1-heptyne and 3-octyne with aniline in the presence of ether–boron fluoride and mercuric oxide catalysts, and split the anils into the corresponding ketones, the reaction has been applied by me to ethynylandrostenediol (I). While this work was in progress Goldberg and Aeschbacher[5] described in a preliminary form an anil obtained by the condensation of the same compounds, using mercuric chloride as a catalyst. It seems certain that their anil is identical with the one described in this paper.

The anil (II) seems to be hydrolyzed on standing in aqueous methanol, although the reaction is not complete even on prolonged heating. Apparently an equilibrium between ketone and anil

(1) Ruzicka and Meldahl, *Helv. Chim. Acta*, **21**, 1760 (1938).
(2) Stavely, THIS JOURNAL, **61**, 79 (1939).
(3) Ruzicka, Gätzi and Reichstein, *Helv. Chim. Acta*, **22**, 626 (1939).
(4) Loritsch and Vogt, THIS JOURNAL, **61**, 1462 (1939).
(5) Goldberg and Aeschbacher, *Helv. Chim. Acta*, **22**, 1188 (1939).

is established. Separation of the ketone III from the mixture was difficult, but after acetylation it was possible to remove the sparingly soluble anil acetate and obtain both products in pure form. Since ketone IV is not identical with the acetate of the chrysopregnane ketone V, it was probable that the acetate of Δ^5-pregnenediol-3,17-one-20 (III) had been obtained. In order to prove this assumption the acetate IV was oxidized with chromic acid and from the neutral fraction was isolated the acetate of dehydroandrosterone as the semicarbazone. When saponification of the acetoxy group of IV was attempted by heating with methyl alcoholic potassium hydroxide, the alcohol obtained was identical with Δ^5-3,17-dihydroxy-18-keto-chrysopregnene (V). In view of the rearrangement of IV to V, it seems remarkable that Reichstein[6] can subject the 3-acetates of his natural adrenal steroids with 17-hydroxyl and 17-acetyl groups, such as his substance L, to alkali saponification without a similar rearrangement. However, he points out[7] that all pregnane derivatives obtained by the interaction of ethylmagnesium bromide or acetylene with 17-ketoandrostane compounds belong to the same series (precipitated by digitonin), designated as the 17(α)-series; whereas natural adrenal steroids belong to the 17(β)-series (not precipitated by digitonin). Therefore, it would seem that only members of the 17(α)-series are susceptible to rearrangement into chrysopregnane compounds. The anil II and the ketone IV appear to be sensitive to dilute acid also. By splitting the anil with dilute acid and acetylating, a product was isolated which is not identical with IV or with the acetate of V. The influence of both acid and alkali on these compounds is being more extensively investigated.

Experimental

Δ^5-Pregnenediol-3,17-one-20-anil (II).—A mixture of 1 g. of Δ^5-17-ethynyl-androstenediol-3,17, 500 mg. of mercuric oxide, 0.3 cc. of ether–boron fluoride catalyst,[8] and 5.0 cc. of dry aniline was allowed to stand at room temperature for a week. The excess aniline was then removed by steam distillation, and the flask was cooled and saturated with hydrogen sulfide. The next morning the mixture was thoroughly extracted with ether, the ether washed with water, dried over sodium sulfate, evaporated to dryness and the residue crystallized from aqueous methanol; yield, 500 mg., m. p. 148°, $[\alpha]^{23}D$ −196 ± 2.0° (12.3 mg. in 2.0 cc. chloroform, 1 dm. tube, α^{23} −1.20).

Anal.[9] Calcd. for $C_{27}H_{37}O_2N$: C, 79.56; H, 9.15. Found: C, 79.61; H, 9.60.

Using mercuric chloride as a catalyst,[5] a better yield was obtained by working up the reaction mixture as above, instead of by the method used by Goldberg and Aeschbacher.

Δ^5-Pregnenediol-3,17-one-20 (III).—From the aqueous methanol mother liquor of the anil crystallization, after standing for about ten days, another crop of crystals was isolated. After purification the substance analyzed for Δ^5-pregnenediol-3,17-one-20, sinters at 158°, m. p. 161–163°.

Anal. Calcd. for $C_{21}H_{32}O_3$: C, 75.85; H, 9.71. Found: C, 75.60; H, 9.61.

Δ^5-3-Acetoxypregnenol-17-one-20 Oxime from (III).—Fifty milligrams of Δ^5-pregnenediol-3,17-one-20 was acetylated in pyridine and acetic anhydride overnight. The solvents were removed in a vacuum and the residue heated with 50 mg. of hydroxylamine hydrochloride, 50 mg. of potassium acetate and 10 cc. of ethanol for two hours. Water was then added, the precipitate filtered, washed with water, dried, and recrystallized from benzene–petroleum ether; m. p. 254–256°.

Anal. Calcd. for $C_{23}H_{35}O_4N$: C, 70.92; H, 9.08. Found: C, 71.15; H, 9.29.

Separation of Δ^5-3-Acetoxypregnenol-17-one-20 (IV) from Δ^5-3-Acetoxypregnenol-17-one-20-anil.—Two grams of the crude anil II was refluxed with aqueous methanol for twenty-eight hours. The products crystallized on cooling, but melted over a 30° range and were a mixture. The crystals were dried and acetylated by standing at room temperature overnight in pyridine and acetic anhydride. The solvents were removed in a vacuum and the residue dissolved in a large volume of methanol. On cooling 700 mg. of beautiful crystals separated, m. p. 232–234° after recrystallizing twice from methanol–ether. The mother liquors yielded 200 mg. more; $[\alpha]^{24}D$ −176 ± 2.0° (13.0 mg. in 2.0 cc. of chloroform, 1 dm. tube, α^{24} −1.14).

Anal. Calcd. for $C_{29}H_{39}O_3N$: C, 77.46; H, 8.75; N, 3.13. Found: C, 77.60; H, 8.68; N, 3.39.

The mother liquors were concentrated to a small volume and the Δ^5-3-acetoxypregnenol-17-one-20 precipitated by addition of water. After drying, the precipitate was crystallized as beautiful needles from benzene–petroleum ether; yield, 520 mg.; m. p. 196–198°; $[\alpha]^{23}D$ −61 ± 1.5° (9.2 mg. in 2.0 cc. chloroform, 1 dm. tube, α^{23} −0.28).

Anal. Calcd. for $C_{23}H_{34}O_4$: C, 73.76; H, 9.16. Found: C, 74.06; H, 9.24.

Oxidation of Δ^5-3-Acetoxypregnenol-17-one-20 (IV) to 3-Acetoxydehydroandrosterone.—To 100 mg. of Δ^5-3-acetoxypregnenol-17-one-20 in 4.0 cc. of glacial acetic acid, 43 mg. of bromine in acetic acid (1 mole) was added dropwise with cooling. Chromic oxide, 170 mg. dissolved in acetic acid, was added and the mixture allowed to stand for twenty hours at room temperature. Since no oxida-

(6) Reichstein and Gätzi, *Helv. Chim. Acta*, **21**, 1497 (1938), etc.

(7) Reichstein and Gätzi, *ibid.*, **21**, 1185 (1938).

(8) Hennion, Hinton and Nieuwland, THIS JOURNAL, **55**, 2858 (1933).

(9) Analyses herein reported are by Mr. J. F. Alicino, Fordham University.

tion was apparent, the flask was heated to 45° for four hours. Methanol was added to destroy excess chromic acid, then 200 mg. of zinc dust, and the mixture heated on the steam-bath for one hour. The solution was concentrated in a vacuum. After addition of water, it was extracted with ether. The ether extract was washed with 1 *N* potassium hydroxide and with water, dried over sodium sulfate, and evaporated to dryness. The residue weighed 45 mg. It was refluxed with semicarbazide hydrochloride and potassium acetate in ethanol for an hour, water was added, the precipitate filtered, washed with water and ether, and recrystallized several times from chloroform–ethanol. Seventeen milligrams of pure 3-acetoxydehydroandrosterone semicarbazone was obtained, m. p. 275–278°. A mixed m. p. with an authentic specimen showed no depression.

Anal. Calcd. for $C_{22}H_{33}O_3N_3$: C, 68.18; H, 8.59. Found: C, 67.90; H, 8.88.

Δ^5-3-Acetoxypregnenol-17-one-20 Oxime from (IV).—The oxime was prepared from the ketone in the usual manner. It was crystallized from benzene–petroleum ether, m. p. 253–256°; mixed m. p. with the 3-acetoxy oxime prepared from the Δ^5-pregnenediol-3,17-one-20 isolated directly from the products of the anil hydrolysis showed no depression.

Anal. Calcd. for $C_{23}H_{35}O_4N$: C, 70.92; H, 9.08; N, 3.60. Found: C, 70.71; H, 9.21; N, 3.79.

Rearrangement of Δ^5-3-Acetoxypregnenol-17-one-20 (IV) to Δ^5-3,17-Dihydroxy-18-keto-chrysopregnene (V).—Fifty milligrams of Δ^5-3-acetoxypregnenol-17-one-20 was refluxed with 3% methanolic potassium hydroxide for two hours. The alkali was neutralized with carbon dioxide, the solution concentrated, and water added. The precipitate was filtered, washed with water, and crystallized in beautiful hexagonal prisms from acetone, m. p. 278–280°; $[\alpha]^{22}D$ −104° (9.8 mg. in 2.0 cc. dioxane, 1 dm. tube, α^{22} −0.51). A mixed m. p. with Δ^5-3,17-dihydroxy-18-keto-chrysopregnene prepared by the direct hydration of Δ^5-17-ethynyl-androstenediol-3,17[2] showed no depression. The specific rotations of the two substances were the the same.

Summary

Δ^5-17-Ethynyl-androstenediol-3,17 and aniline have been condensed in the presence of ether–boron fluoride and mercuric oxide catalysts to form Δ^5-pregnenediol-3,17-one-20-anil.

The anil is partially hydrolyzed by contact with water to form Δ^5-pregnenediol-3,17-one-20. The acetate of this substance has been oxidized to 3-acetoxydehydroandrosterone, thus proving its pregnane structure.

By saponification of Δ^5-3-acetoxypregnenol-17-one-20 with methyl alcoholic potassium hydroxide a rearranged product is obtained for which the name Δ^5-3,17-dihydroxy-18-keto-chrysopregnene is proposed. The substance is identical with the ketone obtained by the direct hydration of Δ^5-17-ethynylandrostenediol-3,17.

NEW BRUNSWICK, N. J. RECEIVED DECEMBER 13, 1939

[CONTRIBUTION FROM THE BIOCHEMISTRY DEPARTMENT OF THE UNIVERSITY OF OKLAHOMA MEDICAL SCHOOL]

The Isolation of Keturonic Acids. II[1,2]

BY L. T. CREWS, J. P. HART AND M. R. EVERETT

The authors are reporting the isolation of crystalline brucine salts of keturonic acids prepared by oxidation of *l*-xylose, *l*-arabinose and *d*-glucosamine, together with a new type of oxidation product, an anhydride of a dicarbonyl sugar, from oxidized levoglucosan. Brucine keturonates also have been prepared from oxidized *α*-*d*-glucoheptose and *l*-fucose but to date these salts have not been separated completely from accompanying non-reducing substances. Ultimate analysis and melting point determinations of the reported preparations are given in Table I and other properties of these substances in Table II.

Experimental

Oxidation of the 1% carbohydrate solutions, preparation of the mixed barium salts, and isolation of the crystalline brucine salts were conducted according to the general methods of Hart and Everett.[2] Yields of mixed barium salts from 4-g. quantities of the carbohydrates were as follows: *l*-xylose, 4.1 g.; *l*-arabinose, 3.0 g.; and *d*-glucosamine hydrochloride, 1.7 g. Reducing barium salts could not be obtained from oxidized levoglucosan solutions but during concentration of the barium salt solution *in vacuo* the substance designated as ketolevoglucosan crystallized directly. Non-reducing barium salts could be precipitated from the mother liquor by the addition of acetone.

Brucine-*l*-xyloketuronate.—A solution of this salt was prepared from 3.75 g. of the mixed barium salts obtained from oxidized *l*-xylose. The reducing brucine salt began to crystallize during concentration of the solution *in vacuo*. After two hours in the refrigerator it was filtered off, washed with alcohol and ether and dried in a desiccator. The yield was 2.5 g. The salt was recrystallized from water.

Brucine-*l*-araboketuronate.—A solution of this salt was prepared from 2.9 g. of the mixed barium salts obtained

(1) Aided by a grant from the Research Appropriation of the University of Oklahoma Medical School.

(2) For previous paper in this series see THIS JOURNAL, **61**, 1822 (1939).

TABLE I

Brucine-	Source	M. p., °C.[a]	Formula	Ultimate analysis, % Found C	Found H	Calcd. C	Calcd. H
l-Xyloketuronate	*l*-Xylose	147–148 (dec.)	$C_{23}H_{26}N_2O_4 \cdot C_5H_8O_6 \cdot H_2O$	58.11	6.12	58.32	6.30
l-Araboketuronate	*l*-Arabinose	160–161[b]	$C_{23}H_{26}N_2O_4 \cdot C_5H_8O_6 \cdot 2H_2O$	56.79	6.61	56.54	6.44
d-Chitoketuronate[c]	*d*-Glucosamine·HCl	177–178	$C_{23}H_{26}N_2O_4 \cdot C_6H_8O_6 \cdot 1^1/_2H_2O$	58.53	6.08	58.26	5.91
Ketolevoglucosan	Levoglucosan	181–182 (dec.)	$C_6H_8O_5 \cdot {}^1/_2H_2O$	42.62	5.37	42.77	5.36

[a] All melting points uncorrected with short stem thermometers. [b] Mixed m. p. with brucine *d*-xyloketuronate was 162°. [c] % N: found by ultimate analysis, 4.73; calcd., 4.69.

TABLE II

OPTICAL ROTATIONS, REDUCING EQUIVALENTS AND COLOR REACTIONS[e]

Brucine-	Color reactions: Naphtho-resorcinol	Bial	Molisch	$[\alpha]^{25}D$[a]	*d*-Glucose equivalent by Sumner's method[b]: Salt	Calcd. for free acid
l-Xyloketuronate	Pink	Negative	Brown	−29.5°	0.23	0.81
l-Araboketuronate	Pink	Negative	Brown	−13°	.20	.71
d-Chitoketuronate	Orange	Negative	Red purple	−50.5°	.34	1.15
Ketolevoglucosan	Red purple	Green[d]	Negative	−62°	[c]	

[a] For 1% aqueous solutions. [b] For 2 mg. per ml. concentrations of the salts. [c] For crystalline ketolevoglucosan, 0.52; calcd. for the anhydrous substance, 0.55; Folin–Wu equivalent for crystalline ketolevoglucosan, 0.26. [d] Color developed slowly. [e] M. R. Everett and Fay Sheppard, *Proc. Soc. Exp. Biol. Med.*, **34**, 7 (1936).

from oxidized *l*-arabinose. Crystals appeared during concentration *in vacuo*. The mixture was then placed in the refrigerator for twenty-four hours and filtered. A second crystalline fraction obtained by concentrating the mother liquor *in vacuo* proved to be non-reducing. The first fraction was recrystallized several times by dissolving in hot water and adding five volumes of alcohol. The yield of recrystallized salt was 0.78 g. This keturonate was difficult to free from a small contamination of non-reducing salt. With repeated recrystallization, properties of this substance approached those of the brucine *d*-xyloketuronate isolated by Hart and Everett.[2] Ultimate analysis indicated the presence of an extra mole of water of crystallization in the *l*-arabinose derivative and the melting point of this brucine salt was 8° lower than that of brucine-*d*-xyloketuronate. The mixed melting point was intermediate (Table I). If future experimentation confirms these indications of similarity, *d*-xyloketuronic acid will be shown to have the structure postulated by Everett and Sheppard,[3] namely, *l*-xyloketo-5-uronic acid according to the classification of Hart and Everett.[4]

Brucine-*d*-chitoketuronate.—A solution of this salt was prepared from 1.95 g. of the mixed barium salts obtained from oxidized *d*-glucosamine hydrochloride. Concentration *in vacuo* gave a crystalline fraction of reducing salt that was filtered off after twenty-four hours in the refrigerator. The salt was recrystallized by dissolving in hot water, adding four volumes of alcohol and placing in the refrigerator for two hours. After filtering, washing with alcohol and ether and drying in the desiccator the yield was 0.52 g. This salt lost no weight upon heating to 175° for several hours *in vacuo* over phosphorus pentoxide. Ultimate analysis indicated a brucine salt of a nitrogen-free anhydroketuronic acid. The authors have therefore provisionally designated the acid as *d*-chitoketuronic acid, with the position of the reducing carbonyl group undetermined.

Ketolevoglucosan.—A well-crystallized barium-free substance separated during concentration of the barium salt solution prepared from oxidized levoglucosan. After placing in the refrigerator for several hours it was filtered off, washed twice with cold water and recrystallized from water. The yield was 0.65 g. of recrystallized substance from 4.0 g. of levoglucosan. The substance reduced Sumner's reagent at room temperature, contained no titratable acid group and was very sparingly soluble in water at room temperature (1% aqueous solution could be obtained by warming). It lost no weight upon heating to 156° *in vacuo* over phosphorus pentoxide. Hydrolysis with 0.6 *N* sulfuric acid for 2.5 hours on a boiling water-bath caused a gradual diminution in specific rotation from −62 to −34° together with a 33% decrease in reducing power (Sumner's method). The Sumner/Folin–Wu ratio of reducing equivalents also changed from 1.99 to 1.45, indicating hydrolysis of the anhydride linkage.[3,5] Subsequent oxidation of the hydrolyzate with bromine for forty-eight hours at 25° caused a 50% loss of reduction, which indicated the appearance of an aldose radical during hydrolysis. The original reducing substance was not affected by similar bromine oxidation. The derivation and properties of this product of levoglucosan oxidation indicate that it is the anhydride of a dicarbonyl sugar.[6]

(3) M. R. Everett and Fay Sheppard, University of Oklahoma Medical School Monograph, "Oxidation of Carbohydrates in Acid Solution," 1936.

(4) J. P. Hart and M. R. Everett, "A Suggested Nomenclature for Keturonic Acids," Abst. of Papers, 96th Meeting of Am. Chem. Soc.

(5) M. R. Everett and Fay Sheppard, THIS JOURNAL, **60**, 1792 (1938).

(6) In view of the present ambiguity in dicarbonyl sugar nomenclature and the possible need for naming several new dicarbonyl sugars whose preparation we are attempting, the following suggestions are made:

1. That the group name for sugars with two potential aldehyde radicals be *alduroses* and that their configurations be referred to the parent polyhydric alcohols. Example: *d-sorbitoaldurose* for the identical structures, 6-aldehydo-*d*-glucose and 6-aldehydo-*d*-gulose.

2. That the group name for sugars with one potential aldehyde

Determination of the position of the reducing carbonyl radical necessitates the preparation of larger quantities of ketolevoglucosan.

Molecular Weights of the Anhydro Derivatives.—The ordinary cryoscopic method for determination of molecular weight could not be employed due to the slight solubility of ketolevoglucosan in ordinary solvents and the limited quantities of *d*-chitoketuronic acid available. Barger's method as modified by Rast[7] gave satisfactory results in control determinations of the molecular weight of glucose but it proved entirely inapplicable to the anhydro derivatives under investigation. A series of dilutions lost water to an intermediate glucose standard, probably because of gradual association or polymerization of the anhydro derivatives. Rast's camphor method[8] gave the following molecular weight values: 330 for ketolevoglucosan, 1100 for brucine *d*-chitoketuronate and 350 for pure levoglucosan. These values are approximately dimolecular but levoglucosan has been shown by the ordinary cryoscopic method to be monomolecular. A common interpretation would imply that the anhydro derivatives reported here are also monomolecular.

and one potential ketone radical be *keturoses* and that their configurations be referred to the parent ketoses, as in the suggested nomenclature for keturonic acids.[4] Examples: *l-sorbo-6-urose* for the identical structures, *d*-gluconose and *l*-idonose; and *d-fructo-1-urose* for *d*-glucosone.

This terminology avoids multiple naming, is generally applicable and suggests functional relations of these sugars to their uronic acid oxidation products. Present indications are that the dicarbonyl sugar anhydride isolated by the authors is 1,6-anhydro-*l*-sorbo-6-urose (1,6-anhydro-gluconose) but the temporary designation as ketolevoglucosan is preferred until the position of the second carbonyl radical is proven.

(7) Abderhalden, "Handbuch der biologischen Arbeitsmethoden," 1928, Abt. III, Teil AI, p. 751.

(8) Kamm, "Qualitative Analysis," John Wiley and Sons, New York, N. Y., 1932, p. 131.

Summary

1. *l*-Xyloketuronic acid and *d*-chitoketuronic acid have been isolated as crystalline brucine salts.

2. The keturonic acid similarly isolated from oxidized *l*-arabinose solutions resembles *d*-xyloketuronic acid closely but complete identity of these acids has not been proven.

3. An anhydride of a dicarbonyl sugar has been isolated from oxidized levoglucosan solutions.

OKLAHOMA CITY, OKLA. RECEIVED NOVEMBER 23, 1939

[CONTRIBUTION FROM THE PEARSON MEMORIAL LABORATORY OF TUFTS COLLEGE]

The Action of Aromatic Amines on 3-Nitro-6-iodonitrostyrene

BY DAVID E. WORRALL AND FREDERICK BENINGTON

Whereas nitration of 2-chloro- and 2-bromonitrostyrene does not entirely inhibit its addition capacity for certain aromatic amines,[1] the halogenated derivatives are not as reactive as nitrostyrene itself. We now find that the analogous iodo derivative closely parallels nitrostyrene in all its reactions with nitrogen bases.

Experimental

α-Nitro-β-(2-iodophenyl)-ethylene.—Iodobenzaldehyde prepared through the diazo reaction[2] from *o*-aminobenzaldehyde[3] was condensed with nitromethane in the presence of triethylamine; yield, after steam distillation, 65–70%. It separated from alcohol as pale yellow needles, m. p. 113–114°. On oxidation with potassium permanganate it gave 6-iodo-3-nitrobenzoic acid[4] which recrystallized from alcohol in long yellow needles, m. p. approx. 190°.

Anal. Calcd. for $C_8H_6INO_2$: C, 34.8; H, 2.2. Found: C, 35.2; H, 2.5.

α-Nitro-β-(6-iodo-3-nitrophenyl)-ethylene.—Prepared by nitration of the above compound using fuming acid, it was obtained from alcohol as tiny pale yellow needles, m. p. 145–146°.

Anal. Calcd. for $C_8H_5IN_2O_4$: C, 30.0; H, 1.5. Found: C, 30.2; H, 1.3.

The product from bromination of the iodo compound separated as an oil on treatment with a warm alcoholic solution of potassium acetate. On mixing with fuming nitric acid, it solidified and was recrystallized from alcohol in yellow prismatic needles, m. p. 136–137°.

Anal. Calcd. for $C_8H_4BrIN_2O_4$: C, 24.0; H, 1.0. Found: C, 24.4; H, 1.2.

It was observed to form an addition compound with *p*-toluidine, but was not further investigated.

The same procedure previously developed[1] was used for the preparation of the addition compounds. The products, yellow or orange-yellow and deeper in color than the parent nitrostyrene, were recrystallized from alcohol, separating as narrow plates or prismatic needles. The melting points frequently were not sharp and were always accompanied by decomposition so that they varied with the rate of heating. Difficulty was experienced in preparing the *o*-toluidino compound as it did not always separate even on long standing. The anilino derivative formed only after several days. The *o*- and *m*-anisidine derivatives formed more readily than the corresponding toluidine. The hydroxylamino and semicarbazido products were colorless.

(1) Worrall, THIS JOURNAL, **60**, 2845 (1938).
(2) Patterson, *J. Chem. Soc.*, **69**, 1006 (1896).
(3) Bamberger, *Ber.*, **60**, 319 (1927).
(4) Goldstein and Grampoloff, *Helv. Chim. Acta*, **13**, 310 (1930).

TABLE I

β-DERIVATIVES OF α-NITRO-β-(6-IODO-3-NITROPHENYL)-ETHANE

Substance	M. p., °C.	Formula	Analyses, % Calcd. C	Calcd. H	Found C	Found H
Anilino	115–116	$C_{14}H_{12}IN_3O_4$	40.7	2.9	41.3	2.8
o-Toluidino	168–170	$C_{15}H_{14}IN_3O_4$	42.2	3.3	42.5	3.5
m-Toluidino	113–114	$C_{15}H_{14}IN_3O_4$	42.2	3.3	42.7	3.4
p-Toluidino	130–132	$C_{15}H_{14}IN_3O_4$	42.2	3.3	42.7	3.5
o-Anisidino[a]	146–148	$C_{15}H_{14}IN_3O_5$	40.6	3.2	40.9	3.2
m-Anisidino	140–142	$C_{15}H_{14}IN_3O_5$	40.6	3.2	41.1	3.2
p-Anisidino	123–124	$C_{15}H_{14}IN_3O_5$	40.6	3.2	40.9	3.4
Phenylhydrazine	142–144	$C_{14}H_{13}IN_4O_4$	39.3	3.0	40.2	3.0
β-Naphthylhydrazine	143–144	$C_{18}H_{15}IN_4O_4$	45.2	3.1	..	3.3
Hydroxylamine	103–105	$C_8H_8IN_3O_5$	27.2	2.3	27.6	2.5
Semicarbazide	187–188	$C_9H_{10}IN_5O_5$	27.3	2.5	27.8	2.5

[a] Both *o*- and *m*-anisidine also react readily with nitrochloronitrostyrene.

α,α'-Di-(6-iodo-3-nitrophenyl)-β,β'-dinitro-diethylamine.—A dry benzene solution of the iodostyrene saturated with ammonia was allowed to evaporate spontaneously to a small bulk. The product, recrystallized from benzene, separated in clusters of nearly colorless needles, m. p. 113–114° with foaming.

Anal. Calcd. for $C_{16}H_{13}I_2N_5O_8$: C, 29.2; H, 2.0. Found: C, 29.7; H, 2.1.

Summary

3-Nitro-6-iodonitrostyrene has been prepared and its additive capacity examined with certain organic bases. It is in this respect the most active nitrostyrene so far studied.

MEDFORD, MASS. RECEIVED OCTOBER 9, 1939

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY, THE UNIVERSITY OF CHICAGO]

The Condensation of Butyraldehyde and Aniline

BY M. S. KHARASCH, ISADORE RICHLIN AND FRANK R. MAYO

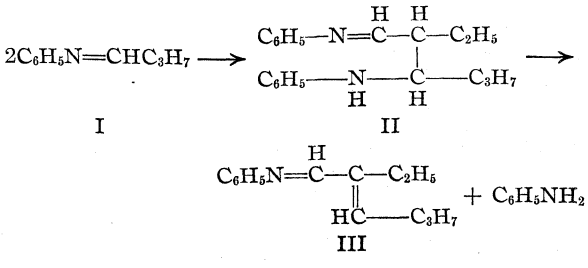
Introduction

Two general types of structure have been suggested for the dimeric Schiff bases, the cyclic structure by Ingold and Piggott,[1] and the aldol-type structure by Miller and Plöchl.[2] The weight of chemical evidence is in favor of the latter. The work of Eibner is particularly convincing.[3] Our research has been concerned with the determination of the structure of the compounds formed by the condensation of *n*-butyraldehyde and aniline in neutral and in acid media.

Discussion of Results

Two products have thus far been isolated from the reaction of aniline and *n*-butyraldehyde in neutral media: one, a monomeric Schiff base (as the hydrogen cyanide addition product), by Rampini, and the other, its dimer, by Williams.[4]

We have found that in the presence of even small amounts of acid, a yellow oil is formed during the condensation. The same oil is formed by treating the crystalline dimer with small amounts of organic acids or by allowing the dimer preparation to stand for several days. In the latter case, the catalyst is the butyric acid formed by atmospheric oxidation, since a similar preparation, carried out in an evacuated bomb-tube, will not produce the oil unless acid had been previously added. Rampini noted this oil but did not investigate it; his failure to obtain the dimer was due to his using aldehyde containing acid. It has been shown by us that this oil is the anil of α-ethyl-β-propylacrolein, formed as follows



(1) Ingold and Piggott, *J. Chem. Soc.*, **121**, 2793 (1922); **123**, 2745 (1923).

(2) Miller and Plöchl, *Ber.*, **25**, 2020 (1892).

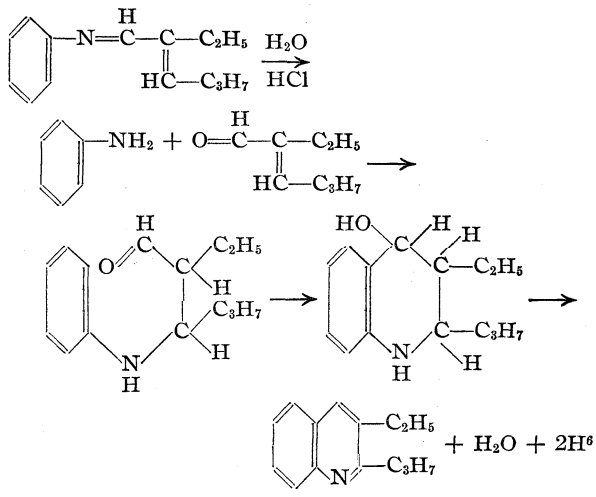
(3) Eibner, *Ann.*, **318**, 58 (1901); **328**, 121 (1903); **329**, 210 (1903).

(4) Rampini, *Ber.*, **25**, 2038 (1892); Williams, U. S. Patent 1,908,093. May 9, 1933; *C. A.*, **27**, 3854 (1933).

The structure, III, for the oil has been confirmed in several ways. Synthetically, we have prepared the same compound from aniline and α-ethyl-β-propylacrolein. Analytically, we have recovered benzanilide and acetanilide in good yields by treating the oil with benzoyl chloride and acetyl chloride, respectively; and we have prepared the 2,4-dinitrophenylhydrazone and semicarbazone of α-ethyl-β-propylacrolein by the use of the hydrazine and semicarbazide. Molecular weight determinations and elementary analyses are consistent with the molecular formula proposed.

The production of the oil of above structure seems to require that II be the structure of the dimer. This is in accord with the work of Miller, Plöchl and Eibner.[2,3] Catalytic reduction of the dimer indicates that one mole of hydrogen is taken up per mole of dimer to form a diamine. The diamine character of the reduction product is shown by its forming a dihydrochloride and a diacetyl derivative. Furthermore, the dimer exhibits properties which one would expect from a compound so closely related, in structure and in formation, to aldol. Both the elimination of aniline to form the oil (analogous to the formation of crotonaldehyde from aldol), the low boiling point (below that of the oil) and the range of the boiling point (about 50°) are indications of dissociation. Cryoscopic molecular weight determinations in triphenylmethane agree with those calculated for the dimer, while in camphor, at a temperature higher by 80°, they indicate 40–50% depolymerization.

The Condensation in the Presence of Acid.—The most general syntheses of the quinoline compounds are those in which a primary aromatic amine is condensed with an aldehyde or ketone in the presence of a mineral acid.[5] We have considered the action of concentrated hydrochloric acid on: (a) mixtures of *n*-butyraldehyde and aniline, (b) the dimer, (c) a mixture of α-ethyl-β-propylacrolein and aniline and (d) the anil of α-ethyl-β-propylacrolein. We have obtained in each instance 2-propyl-3-ethylquinoline. We believe that the formation of the quinoline from α-ethyl-β-propylacrolein anil, which at first glance seems remarkable, may best be explained as follows



Thus, the anil must be hydrolyzed so that aniline can add to the carbon-to-carbon double bond. The subsequent reaction[5] and the hydroxytetrahydroquinoline intermediate[7] in the crotonaldehyde-aniline reaction have been described previously.

Experimental Part

The Preparation of Butylidene Aniline Dimer.—Aniline, freshly distilled from zinc dust *in vacuo*, and freshly distilled *n*-butyraldehyde are mixed in equimolar proportions. The immediate separation of water and the evolution of heat require constant stirring and cooling under the water-tap. The flask is stoppered and allowed to stand for eighteen to twenty-four hours, by which time the reaction mixture is an almost solid mass of the crystalline dimer. This is crystallized from alcohol. The purest material in the best yields is obtained by taking the utmost precautions to avoid the presence of acid; this is accomplished by adding to the reaction mixture a small amount of aqueous sodium carbonate, and by adding the same to the crystallization media. Yields up to 78% of the product melting at 92.5° are obtained.

Anal. Calcd. for $C_{20}H_{26}N_2$: C, 81.61; H, 8.88; N, 9.51. Found: C, 81.49, 81.75; H, 8.88, 8.89; N, 9.41, 9.64.

Molecular Weight Determinations.—The average of ten molecular weight determinations in triphenylmethane by Rast's method[8] at two different concentrations is 281.4 (±12), compared with the value of 294.4 calculated for the dimer. The same determinations carried out in camphor, m. p. 176.7–176.9°, give values from 176 (5% solution) to 251 (10% solution) for the dimer, indicating dissociation. The low boiling point, 130–180° at 25 mm., and its range indicate dissociation. If water and acid be excluded, up to 75% of pure crystallized material may be recovered from a vacuum distillation of the crystals.

(5) For references to the Skraup and Doebner-Miller syntheses, see Sidgwick, "The Organic Chemistry of Nitrogen," Oxford, 1937, pp. 544 ff.

(6) The hydrogen here indicated is found to reduce the monomeric Schiff base present to N-*n*-butylaniline (see experimental part).

(7) Edwards, Garrod and Jones, *J. Chem. Soc.*, **101**, 1376 (1912).

(8) Rast, *Ber.*, **55B**, 1051 (1922).

Hydrogenation of the Dimer.—By the use of a nickel catalyst[9] and hydrogen at 100 atmospheres pressure, the dimer is hydrogenated quantitatively. In the hydrogenation, one mole of dimer takes up one mole of hydrogen. The hydrogenated material is a heavy, viscous oil of boiling point 240–245° at 20 mm. A diacetyl compound is formed which has a melting point of 131°.

Anal. Calcd. for 1,3-diacetanilido-2-ethylhexane, $C_{24}H_{31}N_2O_2$: N, 7.24. Found: N, 7.47.

Anil of α-Ethyl-β-propylacrolein.—In the presence of small amounts of acid, as when old butyraldehyde is used, or as when as little as 0.03 mole % of acetic or butyric acid is added to the reaction mixture, the product from the condensation of butyraldehyde and aniline is a yellow oil of boiling point 146–148° at 15 mm. The crystalline dimer may or may not precipitate during the course of the reaction. Similarly, if an acid-free preparation is allowed to stand in air for several days, the oil is formed. The crystals are stable for much longer periods of time when the reaction is carried out in tubes from which the air is carefully evacuated. That acid and not air is responsible for the instability of the crystals is shown by their rapid decomposition in the presence of acid and absence of air. Analyses show that the oil differs from the crystalline dimer by one molecule of aniline per mole.

Anal. Calcd. for $C_{14}H_{19}N$: C, 83.47; H, 9.57; N, 6.96. Found: C, 83.64; H, 9.40; N, 6.95, 6.97.

A series of ten concordant determinations, some in triphenylmethane by Rast's method and some in freezing benzene by Beckmann's cryoscopic method gave an average value of 208.4 (±15) compared with the calculated value of 201.3 for $C_{14}H_{19}N$.

Treatment of the oil in benzene with excess benzoyl chloride at room temperature gives a 93% yield of benzanilide. Treatment of the oil with excess acetyl chloride in hot pyridine gives a 60% yield of acetanilide. The identities of these compounds were confirmed by melting points and mixed melting points with known samples.

The use of 2,4-dinitrophenylhydrazine–sulfuric acid reagent according to the directions of Ferrante and Bloom results in the production, either from the oil or from α-ethyl-β-propylacrolein, of the 2,4-dinitrophenylhydrazone of the latter.[10] In either case, the yield is 83%. The melting point of both substances is 119–120°, and mixed melting points demonstrate their identity. Similarly, a hot aqueous solution of semicarbazide hydrochloride reacts with either the oil or with α-ethyl-β-propylacrolein to give the known[11] semicarbazone of melting point 132°. The yield from the oil is 60% and the identity of the semicarbazone with that from the known aldehyde is shown by mixed melting point.

Synthesis of the Anil of α-Ethyl-β-propylacrolein from Aniline and α-Ethyl-β-propylacrolein.—α-Ethyl-β-propylacrolein is prepared from butyraldehyde in 58% yield by the method of Raupenstrauch.[12] It boils at 171–172° at 747 mm. When equimolar quantities of aniline and the acrolein are mixed, reaction takes place within five minutes as shown by the separation of water. After standing for two days, distillation of the mixture gives 70% yield of a product of boiling point 146–148° at 15 mm. Reactions of this compound with benzoyl chloride, acetyl chloride, semicarbazide hydrochloride and 2,4-dinitrophenylhydrazine give the same derivatives as those obtained from similar reactions with the oil from aniline and butyraldehyde.

Preparation of 3-Ethyl-2-propylquinoline.—We have used as a reference material the 3-ethyl-2-propylquinoline formed by the method of Kahn and purified through the picrate by the method of Spady.[13] Our product boils at 182–184° at 23 mm. The boiling point recorded by Kahn was 290–292° at atmospheric pressure. We have also obtained the material by the action of concentrated hydrochloric acid on butylidene aniline dimer and the anil of α-ethyl-β-propylacrolein. In each case the reaction proceeded for twenty to twenty-four hours at room temperature and 0.05 mole of aldehyde or its equivalent was used. The experiments are summarized in Table I.

TABLE I

PREPARATION OF 3-ETHYL-2-PROPYLQUINOLINE

Form of reactants	Moles of HCl per mole aniline[a]	Yield of 3-ethyl-2-propyl-quinoline, %[d]
Aldehyde and amine[b,c]	0.1	20
Aldehyde and amine	.5	58
Aldehyde and amine	1.0	79
Aldehyde and amine	1.5	60
Aldehyde and amine	2.0	56
Aldehyde and amine	5.0	54
Butylidene aniline dimer	1.0	50
α-Ethyl-β-propylacrolein	2.0	10
Anil of α-ethyl-β-propylacrolein	2.0	15
Aniline and the anil of α-ethyl-β-propylacrolein	1.0	20

[a] The hydrochloric acid used was concentrated aqueous reagent, approximately 12 *N*. The use of both anhydrous hydrogen chloride and of the concentrated acid diluted 20:1 gave poorer yields. [b] The aldehyde and amine were present in proportions of 2:1, in accordance with the directions of Kahn, although the reaction requires only 3:2 proportions. It was found, however, that the use of 3:2 proportions did not vary the yield significantly. [c] The best yields are obtained when the aldehyde and amine are first mixed and the hydrochloric acid then added. Adding the hydrochloric acid over a period of either five minutes or thirty minutes gave the same results. [d] Calculated on the basis: $3C_3H_7CHO + 2C_6H_5NH_2 \rightarrow C_{14}H_{17}N + C_6H_5NHC_4H_9 + 3H_2O$.

Identification and Determination of 3-Ethyl-2-propylquinoline.—The quinoline, either pure or in a mixture, was diluted with about one-third its volume of 95% alcohol. It was then treated with an excess of saturated alcoholic picric acid. The picrate precipitated immediately. After crystallization from alcohol the picrate melts at 161–163°. Since 3-ethyl-2-propylquinoline is the only quinoline formed, we have been able to use this as a quantitative method.[14] Analyses of mixtures containing 0 to 4 parts by weight of aniline to 3-ethyl-2-propylquinoline have yielded 98–100% of the theoretical picrate. In general, better

(9) Covert, Connor and Adkins, THIS JOURNAL, **54**, 1651 (1932).
(10) Ferrante and Bloom, *Am. J. Pharm.*, **105**, 381 (1933).
(11) Weizmann and Garrard, *J. Chem. Soc.*, **117**, 324 (1920).
(12) Raupenstrauch, *Monatsh.*, **8**, 112 (1887).
(13) Kahn, *Ber.*, **18**, 3361 (1885); Spady, *ibid.*, **18**, 3373 (1885).
(14) *Cf.* Schöpf and Lehmann, *Ann.*, **497**, 16 (1932).

results are obtained if the quinoline fraction is separated from the tars by distillation before the determination.

By-products of the 3-Ethyl-2-propylquinoline Preparation.—The reaction mixture of the Doebner–Miller synthesis, when distilled, gives, besides the water and unchanged reagents (all of which distill below 120° at 15 mm.), two rather well-defined fractions. The first, b. p. 120–200°, consists of N-*n*-butylaniline and 3-ethyl-2-propylquinoline; the second, b. p. over 200° at 15 mm., is made up of tarry materials which may contain tetra- and di-hydro-quinolines (whose homologs have been previously reported as being present in other Doebner–Miller syntheses) and complicated polymerization products. We have confirmed the presence of N-butylaniline (67% of the yield predicted on basis of ethylpropylquinoline formed) as a by-product by the formation of its hydrochloride, m. p. 112–114° (recorded, 114°),[15] and N-butyl-N-phenyl-N′-α-naphthylurea, m. p. 277°. The hydrochloride gave neutral equivalents of 181, 182 and 185, compared with a calculated value of 185. The naphthylurea, a new compound, was prepared by the method of French and Wirtel,[16] and it has the same m. p. as that formed from known N-butylaniline. A mixed melting point showed no depression.

Anal. Calcd. for the N-butyl-N-phenyl-N′-α-naphthylurea, $C_{21}H_{22}N_2O$: N, 8.80. Found: N, 9.03.

In attempting to form the methiodide of 3-ethyl-2-propylquinoline of melting point 172°, described by Kahn,[13] we were able to isolate a material of this melting point. This compound, however, was unstable and gave neutral equivalents on titration with alkali varying from 320 to 381 (theoretical for the hydriodide is 341), showing that it was not a quaternary salt. When we attempted to form the methiodide from highly purified quinoline (through the picrate as above described), the material formed had a m. p. 160–165° and was not titratable with alkali. This is probably the true quaternary methiodide.

Anal. Calcd. for 3-ethyl-2-propylquinoline methiodide, $C_{15}H_{20}NI$: I, 37.28. Calcd. for 3-ethyl-2-propylquinoline hydriodide, $C_{14}H_{18}NI$: I, 38.63. Found (by Fajans' method): I, 37.11.

That the compound described by Kahn was probably the quinoline hydriodide was shown by its formation on passing anhydrous hydrogen iodide through a low-boiling ligroin solution of the pure quinoline. The melting point of this hydriodide was 171–172° and the material was titratable with base. A mixed melting point with the material originally isolated from treatment with methyl iodide was 169–171°.

(15) Braun and Murjahn, *Ber.*, **59**, 1202 (1926).

(16) French and Wirtel, THIS JOURNAL, **48**, 1736 (1926).

Summary

1. The condensation of butyraldehyde and aniline in acid and neutral media has been studied.

2. The structure of the dimer of butylidene aniline has been established as well as that of the compound formed from it by the loss of aniline.

3. 3-Ethyl-2-propylquinoline has been prepared in several ways. A mechanism has been suggested for the Doebner–Miller synthesis.

4. The following new compounds have been prepared: the anil of α-ethyl-β-propylacrolein, 1,3-diphenylamino-2-ethylhexane, its diacetyl derivative, α-ethyl-β-propylacrolein-2,4-dinitrophenylhydrazone, N-butyl-N-phenyl-N′-α-naphthylurea, and 3-ethyl-2-propylquinoline hydriodide and methiodide.

CHICAGO, ILLINOIS RECEIVED OCTOBER 16, 1939

[CONTRIBUTION FROM THE MENDENHALL LABORATORY OF PHYSICS, OHIO STATE UNIVERSITY]

Spectroscopic Evidence for Hydrogen Bonds: SH, NH and NH_2 Compounds

BY WALTER GORDY[1] AND SPENCER C. STANFORD[2]

Introduction

The hydrogen bond theory,[3] which asserts that under certain conditions a proton may form a bond, or bridge, between two electronegative atoms such as N or O, was proposed by Latimer and Rodebush[4] in 1920. Earlier isolated cases of this type of bonding had been recognized.[5] The wide occurrence of hydrogen bonds, however, has just begun to be realized, largely through measurements of infra-red absorption spectra. The importance of these bridges is evidenced by the fact that chelation, and association between like and unlike molecules, resulting from hydrogen bonds, in turn cause appreciable variations in boiling points, freezing points, viscosities, dielectric constants, heats of mixing and of vaporization, vapor pressures, etc., of many compounds in the liquid and solid states as well as in solution. These bonds also play an important role in the determination of protein structure.[6]

Infrared spectroscopy is particularly well suited

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(3) For a very able discussion of the nature of the hydrogen bond, see L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1939, Chap. IX.

(4) W. M. Latimer and W. H. Rodebush, THIS JOURNAL, **42**, 1419 (1920).

(5) T. S. Moore and T. F. Winmill, *J. Chem. Soc.*, **101**, 1635 (1912); P. Pfeiffer, *Ann.*, **398**, 137 (1913).

(6) Mirsky and Pauling, *Proc. Nat. Acad. Sci.*, **22**, 439 (1936).

to the study of hydrogen bonds because it gives direct information about the particular groups of the molecule which participate in the formation of the bonds. For this reason it is generally recognized as superior to methods based on measurements of other physical properties. The usual approach in the spectroscopic method is to observe the effects of the bonding on the group which donates the proton. The bonding weakens the binding force of this group and hence shifts its vibrational band to lower frequencies. The strength of the bond can be estimated from the magnitude of the shift.[7] Also, for hydrogen bonds between unlike molecules it is possible in the same way to compare the intrinsic strengths of organic bases by the effects which these different bases, when used as solvents, will produce on the spectrum of the proton donor group of a suitable solute.[8] In undertaking the present investigation we sought to extend the hydrogen bond theory by discovering other molecules which would donate their proton in hydrogen bond formation. Compounds containing SH, NH or NH_2 were selected because of their importance, especially in biological phenomena, and because they have not been studied extensively by the infrared method.

Instrument.—Although a prism spectrometer was used as a resolving instrument, much better resolution was obtained than is possible with the usual prism instrument. The current was amplified by a Moll thermal relay. Large reflecting mirrors made possible effective use of a 60° rock salt prism, of 7 × 6 cm. face, through which the light was passed twice to increase the dispersion. It was found that with this prism better results could be obtained in the regions studied than with a 60°, 4 × 6 cm., fluorite prism, which was available. The design of the Wadsworth–Littrow type of instrument which was used has been described fully by Strong.[9]

Discussion

SH Compounds.[10]—Numerous instances of hydrogen bonding with the first period elements carbon, nitrogen, oxygen and fluorine have been verified by infrared absorption spectroscopy and other physical methods.[3,11] It was thought for a long time that hydrogen bonding between elements of the second period or between first and second period elements did not exist. For example, Sidgwick[12] has emphasized the improbability of hydrogen bonding with an atom in the second period of elements, saying that as we pass from OH to SH and from hydrogen fluoride to hydrogen chloride the electron acceptor power of the hydrogen practically vanishes. Recently, however, evidence for the association of hydrogen chloride and for the formation of complexes, through hydrogen bonding, between chlorine and an element of the first period has been obtained.[13]

It is known that hydrogen sulfide and the mercaptans are not associated. The molecular weights of some of the mercaptans in benzene solution have been shown to be normal, and in the lower mercaptans the boiling points are less than the corresponding alcohols, in spite of their higher molecular weight. In the present investigation it is shown that spectroscopic methods confirm these conclusions. With regard to the formation of hydrogen bonds between sulfur and elements of the first period, Huggins[11a] states that he knows of no examples of hydrogen bridges joining a sulfur atom with another electronegative atom. He suggests, nevertheless, the possibility of such bridges, saying that they would undoubtedly be very weak. Lassettre[11b] says that molecular weight data show that SH groups do not form hydrogen bonds to any appreciable extent.

The alcohols, with low acidity constants, act as proton donors in complex formation with amines and oxygenated solvents.[14] Although there is a dearth of information on the acidity of the mercaptans, it is usually assumed that they are much more acid than the alcohols.[15] Lucas[16] gives $K_a = 3 \times 10^{-11}$ for ethyl mercaptan as compared with $K_a = 7.3 \times 10^{-20}$ for ethyl alcohol. It

(7) J. J. Fox and A. E. Martin, *Proc. Roy. Soc.* (*London*), **A162**, 419 (1937); R. M. Badger and S. H. Bauer, *J. Chem. Phys.*, **5**, 839 (1937).

(8) (a) W. Gordy and Spencer C. Stanford, *J. Chem. Phys.*, in press; (b) W. Gordy, *ibid.*, **7**, 93 (1939).

(9) J. Strong, *Rev. Sci. Inst.*, **2**, 585 (1931).

(10) The part of this paper concerned with the mercaptans was given before the American Chemical Society at the Boston Meeting, September, 1939.

(11) (a) M. L. Huggins, *J. Org. Chem.*, **1**, 407 (1936); (b) E. N. Lassettre, *Chem. Rev.*, **20**, 259 (1937); (c) R. Freymann, *J. Phys. Rad.*, **9**, 517 (1938); *ibid.*, **10**, 1 (1939); (d) G. F. Zellhoefer, M. J. Copley and C. S. Marvel, THIS JOURNAL, **60**, 1337, 2666, 2714 (1938); (e) A. M. Buswell, W. H. Rodebush and M. F. Roy, *ibid.*, **60**, 2528 (1938); (f) W. Gordy, *J. Chem. Phys.*, **7**, 163 (1939); THIS JOURNAL, **60**, 605 (1938).

(12) N. V. Sidgwick, "The Covalent Link in Chemistry," Cornell University Press, Ithaca, N. Y., 1933.

(13) (a) W. Gordy and P. C. Martin, *Phys. Rev.*, **52**, 1075 (1937); *J. Chem. Phys.*, **7**, 99 (1939); (b) B. Vodar, R. Freymann and Y. Ta, *J. Phys. Rad.*, **9**, 282 (1938).

(14) W. Gordy, *J. Chem. Phys.*, **7**, 93 (1939).

(15) W. M. Malisoff, E. M. Marks and F. G. Hess, *Chem. Rev.*, **7**, 493 (1930).

(16) H. J. Lucas, "Organic Chemistry," American Book Company, 1935, p. 267.

seemed possible, therefore, that the mercaptans with their larger acidity constants might donate their proton to form complexes such as those formed with the alcohols.

Williams[17] has shown recently that the fundamental vibrational band of the SH group for benzyl, *n*-butyl and *n*-propyl mercaptans lies in the region 3.8–3.9 μ. For comparison we have repeated his results on benzyl and *n*-butyl mercaptans. Curves for these compounds, for thiophenol and for thioacetic acid are given in Fig. 1. The SH band is much more intense for the latter two compounds than for the former.

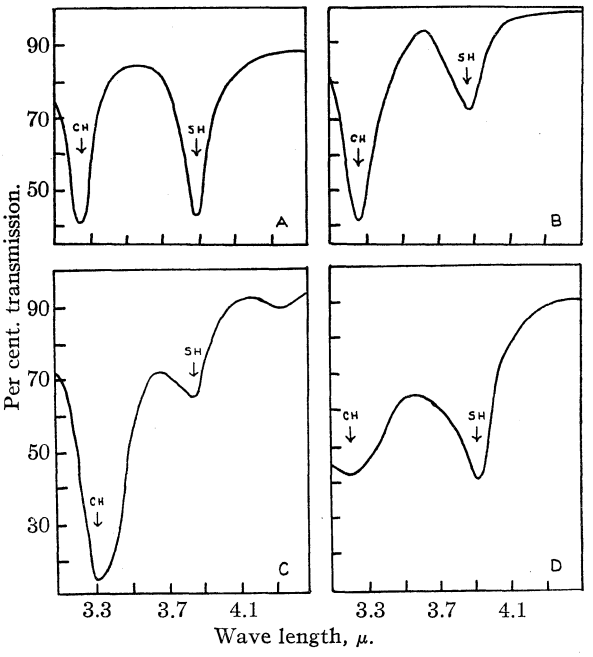


Fig. 1.—Transmission of: A, thiophenol, t = 0.005 cm.; B, benzyl mercaptan, t = 0.005 cm.; C, *n*-butyl mercaptan, t = 0.005 cm.; D, thioacetic acid, t = 0.002 cm.

A comparison of the intensities of the SH bonds of the compounds in Fig. 1 together with a comparison of their acidities leads to the conclusion that if any of these compounds are associated thiophenol would be. To ascertain whether polymerization occurs we measured the absorption of thiophenol in dilute solution in benzene. Figure 2 shows that the SH band does not shift to the shorter wave lengths upon dilution in an inert solvent as does the OH alcohol band,[18] thus confirming the evidence of molecular weights and other physical properties that the mercaptans are not associated in the liquid state.

(17) D. Williams, *Phys. Rev.*, **54**, 504 (1938).

(18) J. Errera and P. Mollet, *Nature*, **138**, 882 (1936); *Compt. rend.*, **204**, 259 (1937).

To test for complex formation we studied, in the region of the SH band, mixtures of some mercaptans with several liquids which previously had been found to form complexes with heavy methyl alcohol through interaction with the OD group.[8b] Transmission curves for the different mixtures were observed and these were compared with theoretical transmission curves computed from Beer's law using the absorption coefficients obtained from the transmission curves of the pure liquids. The results for the thiophenol mixtures are shown in Fig. 3. The broken curves represent the transmission which would be expected of the mixtures if no interaction whatever occurred between the components; the solid

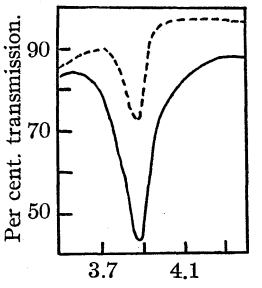


Fig. 2.—Broken line, 0.1 *M* thiophenol in benzene *versus* pure benzene, t = 0.361 cm.; solid line, pure thiophenol, t = 0.005 cm.

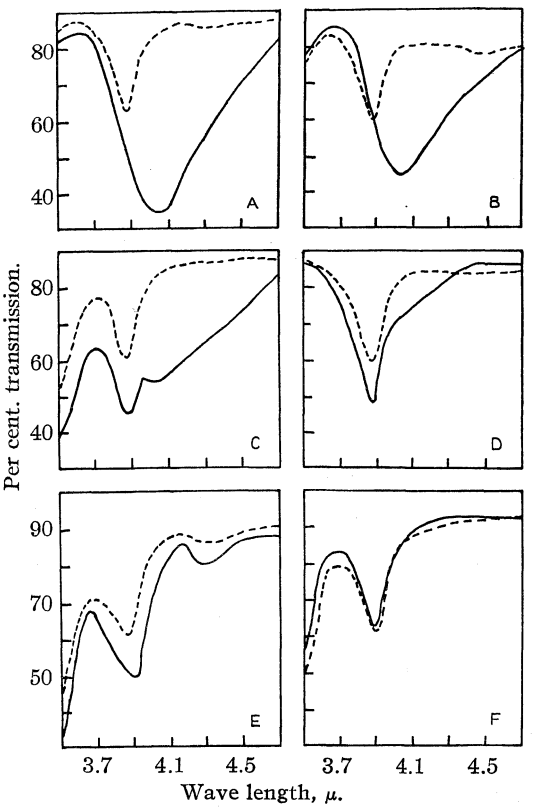


Fig. 3.—Theoretical (broken lines) and observed (solid lines) transmission of mixtures (1:1 vol., t = 0.005 cm.) of thiophenol with: A, pyridine; B, α-picoline; C, dibenzylamine; D, aniline; E, isopropyl ether; F, ethyl-*o*-toluidine.

curves represent the transmission which was actually observed.

The most pronounced variations observed were for thiophenol with pyridine and with α-picoline. For these mixtures the SH band is shifted to the longer wave lengths by about 0.18 μ or 114 wave numbers, and its intensity is increased several fold. We believe that these results give proof of the formation of SH → N bonds between the thiophenol and the amines.

The results indicate that thiophenol also forms a complex with dibenzylamine, but that the tendency to do so is slightly less than with pyridine or α-picoline. The position of the associational band is 4.04 μ for thiophenol–dibenzylamine as compared with 4.06 μ for thiophenol–pyridine. The rather strong band at 3.88 μ, the position of the SH band of pure thiophenol, indicates that a large percentage of the thiophenol is not linked to the dibenzylamine.

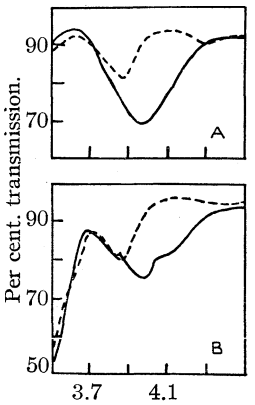


Fig. 4.—Theoretical (broken lines) and observed (solid lines) transmission of mixtures (1:1 vol., t = 0.005 cm.) of benzyl mercaptan with: A, pyridine; B, benzylamine.

Thiophenol tends to form a complex with aniline even less than it does with dibenzylamine. There is no minimum beyond 3.88 μ in the thiophenol–aniline curve although the departure of the experimental from the theoretical curve on the long wave length side of the band probably indicates some interaction. It may be that aniline (K_b = 4.6 × 10^{-10}) is too weakly basic to attract the proton from thiophenol sufficiently to form a hydrogen bridge. The existence of weak hydrogen bonds between the aniline molecules in the liquid state, for which there is evidence,[19] may also be a contributing factor in the non-formation of a complex. Hydrogen bonding between the aniline molecules could of course prevent the aniline nitrogen from accepting a proton from the mercaptan SH. In this connection Zellhoefer, Copley and Marvel[11d] have shown that aniline is a poor solvent for certain haloforms, and they attribute this to the association of the aniline.

Only one oxygenated solvent, isopropyl ether, was investigated for the formation of a complex with thiophenol. In the comparison of the proton-attracting power of liquids previously made,[8b] the ethers were found to form stronger hydrogen bonds with alcohols than did any of the other oxygenated solvents studied. Therefore, it was concluded that if isopropyl ether did not form bonds with the mercaptans, none of the oxygenated solvents would form them. As may be seen from a comparison of the experimental and theoretical curves for thiophenol–isopropyl ether, there is very little interaction. Thus it was not considered worth while to study mixtures of the mercaptans with other oxygenated solvents as there would probably be little complex formation between them.

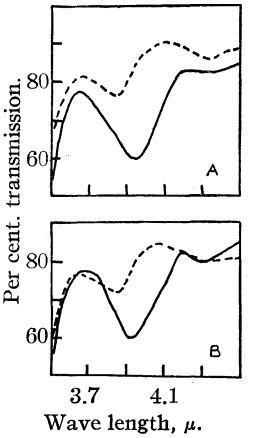


Fig. 5.—Theoretical (broken lines) and observed (solid lines) transmission of mixtures (1:1 vol., t = 0.005 cm.) of n-butyl mercaptan with: A, pyridine; B, α-picoline.

The experimental curve for the ethyl-o-toluidine–thiophenol mixture is almost identical with the theoretical curve computed from Beer's law. This result could be anticipated, for even if the nitrogen of the ethyl-o-toluidine strongly attracted the proton of the SH, steric hindrance would probably prevent association with the thiophenol.

Piperidine (K_b = 1.6 × 10^{-3}) formed a white crystalline solid immediately upon being mixed with thiophenol. Similar results were obtained with cyclohexylamine and with triamylamine. Apparently thiophenol forms hydrogen bonds with substances of a rather narrow range of basicities. For substances with basicity constants much lower than that of pyridine, no appreciable interaction occurs. For substances with basicities much higher than that of pyridine, the thiophenol

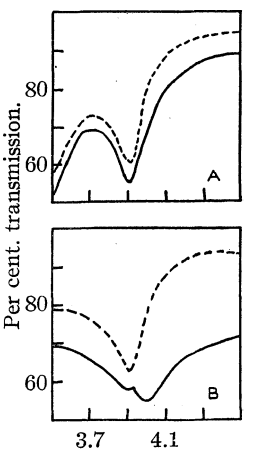


Fig. 6.—Theoretical (broken lines) and observed (solid lines) transmission of mixtures (1:1 vol., t = 0.002 cm.) of thioacetic acid with: A, isopropyl ether; B, pyridine.

(19) W. Gordy, *J. Chem. Phys.*, **7**, 167 (1939).

appears to be completely ionized by the base to form a salt.

Because the aliphatic mercaptans and benzyl mercaptan probably have lower acidity constants than thiophenol, they would be expected to show less tendency to share their proton in hydrogen bond formation. This was found to be true for the cases studied. Figure 4 gives the results obtained for benzyl mercaptan with pyridine and with benzylamine. Both of these liquids form hydrogen bonds with the benzyl mercaptan. The shift in the SH band of benzylamine caused by the pyridine is less than that caused by the pyridine on the SH band of thiophenol. Figure 5 shows the evidence secured for the interaction of *n*-butyl mercaptan with pyridine and α-picoline. A curve was obtained for piperidine which gave a minimum at 4.04 μ, but because of the intense CH absorption of piperidine and the weakness of the mercaptan band, the position of the associational band is probably not very accurate. Evidence was also found for weak hydrogen bonds between pyridine and thioacetic acid, Fig. 6. Isopropyl ether produced no shift in the thioacetic acid band.

TABLE I

THIOPHENOL MIXTURES

Solvent	Position of SH band, μ	Shift, μ	K_b
Pure thiophenol	3.88		
Aniline	3.88	None	4.6×10^{-10}
Pyridine	4.06	0.18	1.2×10^{-9}
α-Picoline	4.06	.16	4.0×10^{-8}
Dibenzylamine[a]	4.04	.16	
Piperidine	White cryst. solid		1.6×10^{-3}
Cyclohexylamine	White cryst. solid		
Triamylamine	White cryst. solid		
Ethyl-*o*-toluidine	3.88	None	
Isopropyl ether	3.91	0.03	
Benzyl Mercaptan Mixtures			
Pure benzyl mercaptan	3.87		
Benzylamine[a]	3.97	0.10	2.4×10^{-5}
Pyridine	3.96	.09	1.2×10^{-9}
Cyclohexylamine	White cryst. solid		
***n*-Butyl Mercaptan Mixtures**			
Pure *n*-butyl mercaptan	3.86		
Pyridine	3.95	0.09	1.2×10^{-9}
Piperidine	4.00	.14	1.6×10^{-3}
α-Picoline	3.94	.08	4.0×10^{-8}
Cyclohexylamine	White cryst. solid		
Thioacetic Acid Mixtures			
Pure thioacetic acid	3.91		
Isopropyl ether	3.91	None	
Pyridine[a]	3.99	0.08	1.2×10^{-9}

[a] In each of these cases a weak band due to unmodified SH appeared.

The results for all the SH compounds are summarized in Table I.

NH and NH_2 Compounds.—Hydrogen bridges formed through an amine hydrogen probably play a significant role in the determination of protein structure.[6,11a,20] Attempts have been made to study directly hydrogen bonds in protein molecules.[21] Nevertheless the complexity of the protein molecules with their overlapping OH and NH_2 absorption makes the method difficult and the interpretation of the data somewhat uncertain. Thus it seems well to obtain all the data possible on the simpler NH and NH_2 compounds. This should be valuable in predicting behavior in the more complex cases.

Buswell, Rodebush and Roy[22] have made a significant contribution in their work on the acid amides. Although they succeeded in showing that association is present they could not tell whether it was due to NH → N or NH → O bonds, as both are possible. Even though there is some evidence for the very weak association of liquid ammonia,[3] physical data indicate that the aliphatic amines are not generally associated.[23] That the lack of association is not due to the weaker proton acceptor power of the amine nitrogen is evidenced by the marked perturbation produced by the amine nitrogen on the OD band of heavy alcohol[8] and is also evidenced by the basicity constants of these compounds.

Certain aromatic amines, nevertheless, are sufficiently acidic to share their proton to form hydrogen bridges. One of us has already shown that aniline is associated through NH → N bonds and that it will form complexes through NH → O bonds to certain oxygenated solvents.[19] The bonds are very weak, the shifts obtained being about one-fourth that found for methyl alcohol. Although Buswell, Rodebush and Roy[24] failed to find spectroscopic evidence for the association of aniline, their failure to observe the small shift may have been due to the low resolving power of their instrument, as other physical data[11d] agree

(20) L. Pauling and C. Niemann, THIS JOURNAL, **61**, 1860 (1939).

(21) J. W. Ellis and J. Bath, *J. Chem. Phys.*, **6**, 723 (1938).

(22) A. M. Buswell, W. H. Rodebush and M. F. Roy, THIS JOURNAL, **60**, 2444 (1938).

(23) W. D. Kumler, *ibid.*, **60**, 2239 (1938).

(24) (a) A. M. Buswell, W. H. Rodebush and M. F. Roy, THIS JOURNAL, **60**, 2239 (1938). (b) As this paper goes to press A. M. Buswell, J. R. Downing and W. H. Rodebush (THIS JOURNAL **61**, 3252 (1939)) publish two curves for aniline in CCl_4: one 0.64 *M* and the other 0.01 *M*, showing the NH_2 absorption at the same position in both of these solutions. They offer these curves as evidence that aniline does not associate in the liquid state. That they did not detect the weak association of aniline was obviously due to their failure to study a sufficiently concentrated solution or the pure liquid.

with the interpretation that it is weakly associated. The work which has just appeared by Yeou Ta[25] on the third harmonic of the xylidines shows that they are associated except in the cases where steric hindrance prevents.

Wulf and Liddel[28] studied a number of amines by the infrared method. Their measurements were made in the region of the second harmonic of the NH band. As they made observations of only very dilute solutions in carbon tetrachloride, they could not study intermolecular association. They found that whenever a C=O group is adjacent to the NH_2 group, as in benzamide or methyl anthranilate, the NH band is appreciably perturbed. Hendricks, Wulf, Hilbert and Liddel[29] made similar studies of numerous compounds in which chelation was found to occur through OH → N bridges.

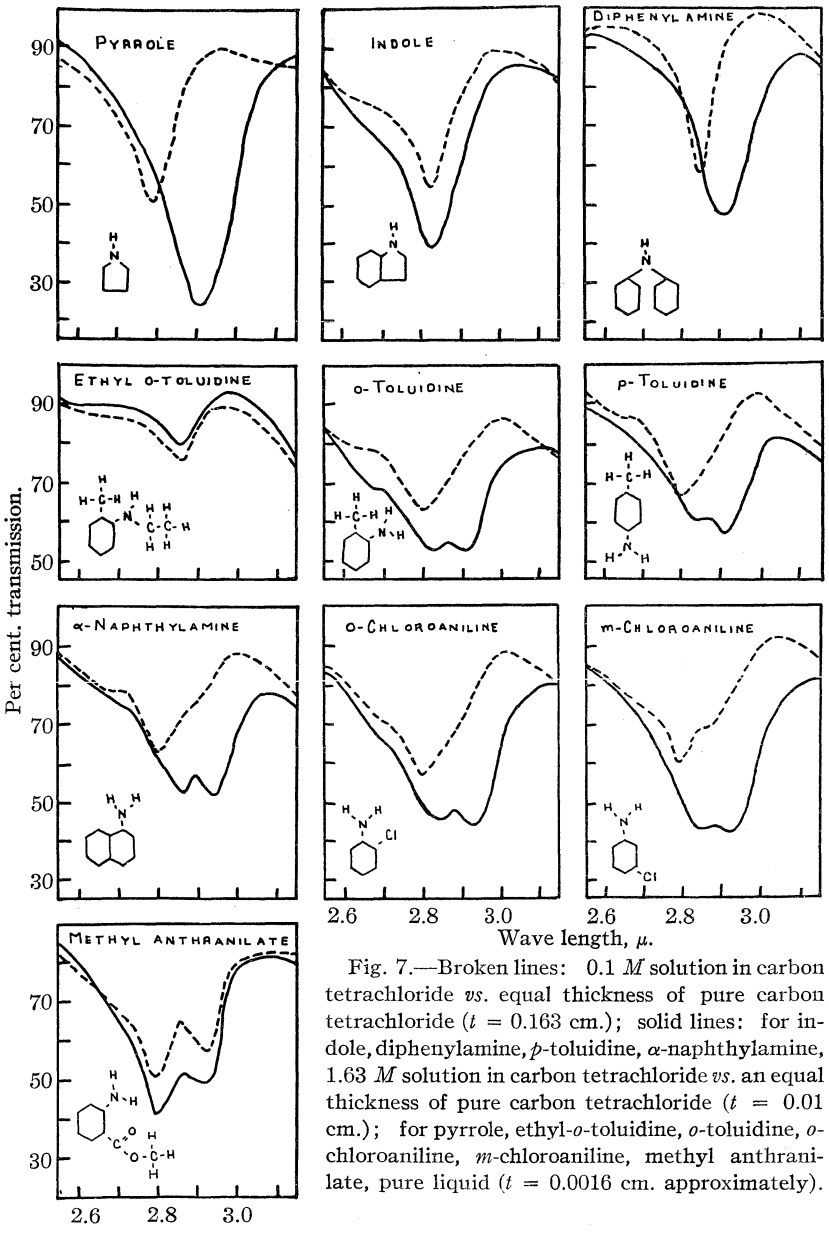


Fig. 7.—Broken lines: 0.1 *M* solution in carbon tetrachloride *vs.* equal thickness of pure carbon tetrachloride (t = 0.163 cm.); solid lines: for indole, diphenylamine, *p*-toluidine, α-naphthylamine, 1.63 *M* solution in carbon tetrachloride *vs.* an equal thickness of pure carbon tetrachloride (t = 0.01 cm.); for pyrrole, ethyl-*o*-toluidine, *o*-toluidine, *o*-chloroaniline, *m*-chloroaniline, methyl anthranilate, pure liquid (t = 0.0016 cm. approximately).

The present investigation included a number of amines having lower basicity constants than that of aniline, previously found to be weakly associated through hydrogen bonds. We obtained the absorption spectrum characteristic of the NH or NH_2 group of the unassociated amine in dilute solution of carbon tetrachloride and compared this with the absorption of the same group in the pure liquid or in concentrated solution when the compound was a solid. We also ran each of these compounds in an oxygenated solvent, *n*-butyl ether, in order to detect complex formation through NH → O bonds with the ether. In each case the cell thickness and concentration were arranged so that the different curves for the same substance represent approximately the same number of absorbers. Thus it is possible to observe the effects of association upon the intensity of the band as well as upon its position.

Figure 7 shows the study of the association of the pure substance. The dotted lines represent

Pyrrole is more acidic than the aliphatic amines, and there are reasons to believe that it is associated.[26] Freymann[27] has shown that the third harmonic shifts to the longer wave lengths and is broadened appreciably as the pyrrole is changed from the vapor to the liquid state.

(25) Y. Ta, *Compt. rend.*, **208**, 1993 (1939).
(26) J. M. Robertson, *J. Chem. Soc.*, 615 (1935); 1195 (1936).
(27) M. Freymann, *Compt. rend.*, **205**, 852 (1937).
(28) O. R. Wulf and U. Liddel, THIS JOURNAL, **57**, 1464 (1935).
(29) S. B. Hendricks, O. R. Wulf, G. E. Hilbert and U. Liddel, *ibid.*, **58**, 1991 (1936).

the absorption of the dilute solution, 0.1 molar, and the solid lines represent that of the pure liquid or concentrated solution. The solution curves represent the ratio of the transmission of the solution to that of an equal thickness of the pure solvent. For the pure liquid the curves represent the ratio of the transmission of the cell containing the liquid to that of the empty cell. Because, for the reason discussed above, the associational bonds here are likely weaker than those for alcohol, we think that we are safe in assuming that the band which appears in the 0.1 molar solution is that of the monomeric form. The departure of the curve for the concentrated solution from that for the dilute solution may therefore be taken as a measure of the interaction which occurs.

For pyrrole, diphenylamine, *o*- and *p*-toluidine, α-naphthylamine, *o*- and *m*-chloroaniline, the shifts to the longer wave lengths and the increase of intensity in the band are evidence that hydrogen bonding occurs in the pure liquid or the concentrated solution. It is interesting to note that for indole, ethyl-*o*-toluidine and methyl anthranilate no shift nor marked intensity change occurs, an indication that these substances do not polymerize. From a consideration of the structural formula for ethyl-*o*-toluidine, which is given in the figure, it is rather obvious that steric hindrance may prevent polymerization of this compound. Intermolecular hydrogen bonds between the methyl anthranilate molecules are no doubt prevented by the formation of intramolecular bonds to the C=O group. That intramolecular bonds exist here is clear from a comparison of the curve for the dilute solution with those for the other NH_2 compounds given in the figure. This chelation is also evident from the experiments of Wulf and Liddel.[28] In view of the association of the similar compound, pyrrole, the failure of indole to polymerize is not so obvious. That it is not due to the fact that indole holds its proton too firmly to share it is shown by its donating it to form a complex with *n*-butyl ether. We are inclined toward the interpretation that steric hin-

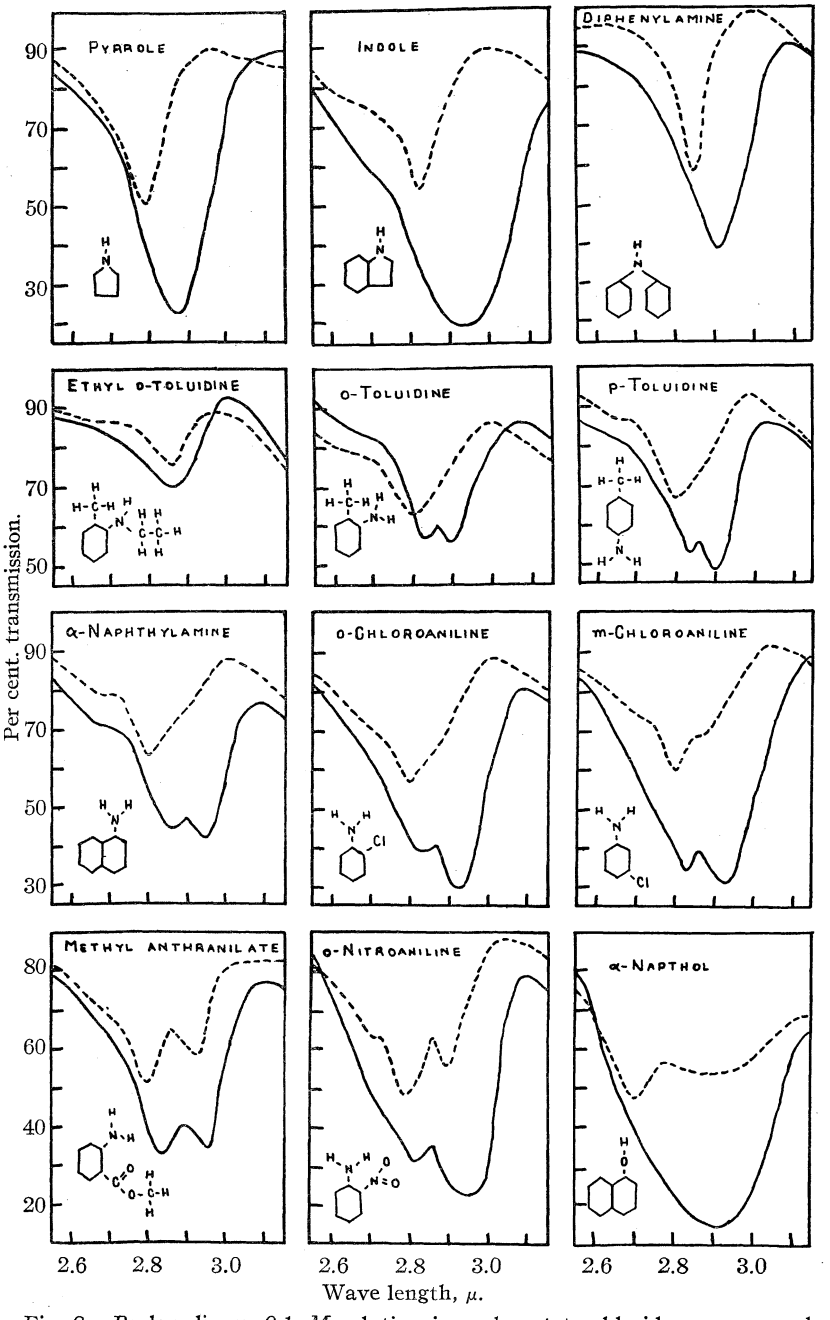


Fig. 8.—Broken lines: 0.1 *M* solution in carbon tetrachloride *vs.* an equal thickness of pure carbon tetrachloride (t = 0.16 cm.); solid lines: 0.1 *M* solution in *n*-butyl ether *vs.* an equal thickness of *n*-butyl ether (t = 0.163 cm.).

TABLE II

Substance	Minima in transmission curves, μ: 0.1 mol. sol. in CCl_4	1.63 mol. sol. in CCl_4	Pure liquid	0.1 mol. sol. in *n*-butyl ether	K_b
Pyrrole	2.79		2.90	2.87	
Indole	2.82	2.83		2.93	
Diphenylamine	2.85	1.91		1.91	
Ethyl-*o*-toluidine	2.86		2.86	2.86	
o-Toluidine	2.80		2.83 2.91	2.83 2.90	3.5×10^{-10}
p-Toluidine	2.80	2.84 2.91		2.83 2.90	2.1×10^{-10}
α-Naphthylamine	2.80	2.86 2.94		2.86 2.94	1.0×10^{-13}
o-Chloroaniline	2.80		2.84 2.93	2.83 2.93	9.2×10^{-12}
m-Chloroaniline	2.80		2.84 2.93	2.83 2.93	3.4×10^{-11}
Methyl anthranilate	2.80 2.93		2.80 2.93	2.83 2.96	
o-Nitroaniline	2.79 2.89			2.82 2.95	1.5×10^{-14}
α-Naphthol	2.70 2.91			2.91	1.0×10^{-8}

drance prevents this polymerization. On the other hand, it may seem a little strange, though not impossible, that steric hindrance would prevent association between indole molecules and yet not prevent association between indole and ether.

The bands for the NH compounds are rather symmetrical and sharp. For the NH_2 compounds the association splits the band into a doublet with one component only slightly shifted from the position of maximum absorption of the monomeric band. This splitting may arise from the possibility that only one of the protons of the NH_2 group is involved in hydrogen bond formation. Even for the monomeric form of these compounds the bands are broader and more complex than those for the NH compounds. Wulf and Liddel[28] pointed out that in the region of the second harmonic the NH_2 absorption is complex as compared with that of NH and OH. Our curves, however, do not resemble closely those of these researchers. It is not to be expected that bands in the fundamental region should be similar to those of the second harmonic, as no simple relation exists between them.

Figure 8 shows a study of complex formation between *n*-butyl ether and the above-mentioned compounds. In addition, one other NH_2 compound, *o*-nitroaniline, is included, also an OH compound, α-naphthol. The curves for 0.1 molar solution in carbon tetrachloride are repeated here for comparison. All the curves given in this figure are for 0.1 molar solutions of the same thickness, 0.163 cm. Therefore any appreciable departure of the curves for the *n*-butyl ether solutions from those of the same substances in carbon tetrachloride is evidence for the interaction of the solute with *n*-butyl ether.

The same substances which were found to be polymerized through hydrogen bonds were also found to form complexes with the *n*-butyl ether. Yet indole, which, as was mentioned above, apparently does not polymerize, interacts strongly with the ether. The results indicate that ethyl-*o*-toluidine does not form a complex with the *n*-butyl ether. The curve for the methyl anthranilate in the *n*-butyl ether solution is somewhat more intense than the curve for the carbon tetrachloride solution of the same concentration, but the minima are only slightly shifted from the position of those for the carbon tetrachloride solution. Since the intermolecular bonds with the ether, if they are formed, would probably be of the same order of strength as the intramolecular bonds, which are already formed and which would probably be broken if a complex is formed, it is not possible to predict whether there is much interaction between the *n*-butyl ether and the methyl anthranilate. For *o*-nitroaniline the departure of the curve for the *n*-butyl ether solution from that for the solution in carbon tetrachloride is much more pronounced, an indication that the intramolecular hydrogen bonds to the NO_2 group do not prevent interaction with the ether. From previous measurements it is known that an ether oxygen attracts the proton of an hydroxyl group more strongly than does an oxygen of the nitro group of nitrobenzene or nitrotoluene.

The curves which are included for α-naphthol make possible a comparison of the strength of the bonds formed through an NH_2 group with those through an OH group. It is obvious that the effects of *n*-butyl ether on the OH band of the α-naphthol are much more pronounced than the effects of this solvent upon the absorption of the NH_2 group of the α-naphthylamine. The curve for the 0.1 molar solution of α-naphthol in carbon tetrachloride shows that the polymerization of the α-naphthol is not completely broken down at this

concentration, as there is still absorption in the region of 2.9 μ. The band appearing at 2.7 μ is the monomolecular band.

The positions of minima in the transmission curves for the pure liquids and different solutions are given in Table II.

In other reports[8] there is a comparison of the proton-attracting power of many different solvents, including *n*-butyl ether. By use of the data given there with the shifts in the NH or NH_2 bands caused by the *n*-butyl ether, it is possible to predict the interaction of these other solvents with the amines studied here.

The authors wish to thank Dr. Alpheus W. Smith and Dr. H. H. Nielsen for their constant interest and support, and Vida Miller Gordy for her assistance in the preparation of the manuscript. They also wish to acknowledge a very helpful discussion with Dr. G. B. B. M. Sutherland.

Summary

The association of the mercaptans with certain electron donor solvents has been investigated by means of infrared spectroscopy. The study included 1:1 volume mixtures of thiophenol with isopropyl ether, ethyl-*o*-toluidine, aniline, pyridine, α-picoline and dibenzylamine. For the ethyl-*o*-toluidine mixture the SH band of the thiophenol was virtually unaffected. For the mixtures with isopropyl ether, and with aniline, only a slight perturbation of the band occurred. For the mixtures with pyridine, α-picoline and dibenzylamine there was a shift of approximately 0.18 μ to the longer wave lengths, together with a broadening and a marked increase in intensity. These effects, we believe, indicate hydrogen bonding between the latter solvents and the thiophenol, with the SH group donating the proton. Similar but less pronounced effects were observed for *n*-butyl mercaptan, benzyl mercaptan and thioacetic acid with some of these solvents. A 0.1 *M* solution of thiophenol in benzene was studied, and the SH band was found to appear at the same position for the solution as for the pure liquid. This failure of the SH band to shift to shorter wave lengths upon dilution in an inert solvent is evidence that thiophenol is not polymerized in the liquid state.

The study included a number of amines having basicity constants about the same as or lower than that of aniline. All were found to be associated through hydrogen bonds except those for which steric hindrance would be expected to prevent the association. The absorption spectrum of the NH or NH_2 group of the unassociated amine in dilute solution in carbon tetrachloride was obtained and compared with the absorption of the same group of the pure liquid or of a concentrated solution when the compound was a solid. Each of the compounds was studied in an oxygenated solvent, *n*-butyl ether, in order to detect complex formation through NH $\rightarrow$ O bonds with the ether. The following compounds were found to be polymerized in the pure state, also to form complexes with the ether: pyrrole, diphenylamine, *o*- and *p*-toluidine, α-naphthylamine, *o*- and *m*-chloroaniline. Although the results indicate that indole does not polymerize, it appears to form a complex with *n*-butyl ether. Ethyl-*o*-toluidine apparently neither polymerizes nor forms complexes. Its lack of association can be ascribed to steric hindrance. Evidence was found for chelation in methyl anthranilate and *o*-nitroaniline. This chelation likely prevents appreciable polymerization or complex formation with these compounds. α-Naphthol, the one OH compound included, was found to be more strongly associated than the NH or NH_2 compounds of similar structure.

COLUMBUS, OHIO RECEIVED OCTOBER 23, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF THE GENERAL ELECTRIC CO.]

The Conductance of Some Salts in Chlorobenzene at 25°

BY ROBERT L. MCINTOSH AND DARWIN J. MEAD WITH RAYMOND M. FUOSS

I. Introduction

Specific interaction between solute and solvent is expected when an acid solute such as tributylammonium picrate is dissolved in a basic solvent. For example, in tricresyl phosphate[1] ($D = 6.92$ at 40°) this salt has a dissociation constant of 1.18×10^{-6}, which gives an ion size of 4.66×10^{-8} cm. But in ethylene chloride[2] ($D = 10.23$ at 25°), the dissociation constant is only 2.10×10^{-8}, which leads to an ion size of 2.4×10^{-8} cm. The ion sizes are calculated on the assumption that the interaction between ions can be represented as that between uniformly charged spheres in a homogeneous medium,[3] and if this model were correct, the ion size calculated from the dissociation constant of the solute and the dielectric constant of the solvent would be independent of solvent. Clearly tributylammonium picrate in tricresyl phosphate is electrolytically quite different from tributylammonium picrate in ethylene chloride, even after allowing for the difference in dielectric constant. A possible explanation can be found in an interaction between solute and solvent, which gives an effectively stronger electrolyte in the former solvent, which is equivalent to saying that the non-electrolytic dissociation[1] is suppressed in the basic solvent. Ethylene chloride is aprotonic and does not enter the equilibria.

But for completely substituted quaternary salts, independence of ion size on solvent has in general been found, so that it was possible to predict approximate values of dissociation constant from the dielectric constant of the solvent. In this paper, we shall present data showing that specific interaction between solute and solvent, as indicated by variation of ion size with solvent, is also possible for quaternary salts. The dissociation constants of tetrabutylammonium bromide and picrate in chlorobenzene ($D = 5.63$ at 25° and 60 cycles) are only about one-tenth as large as the values calculated from the ion sizes found for these salts in a number of other solvents.

II. Materials, Apparatus and Procedure

C. p. chlorobenzene was redistilled, and initial and final portions were discarded. It was then dried by two successive treatments with activated aluminum oxide. The solvent conductance was very sensitive to traces of moisture, as was the conductance of dilute solutions of the electrolytes. The best value obtained for the pure solvent was 2×10^{-12} mho. The solvent was stored over aluminum oxide, and filtered just before use directly into the dilutions flasks through a glass cotton plug by dry air pressure.

Tributyl and **tetrabutylammonium picrates** were those used by Elliott and Fuoss.[1] **Tetrabutylammonium bromide** was prepared by neutralizing a solution of tetrabutylammonium hydroxide (from tetrabutylammonium iodide and moist silver oxide in alcohol) with hydrogen bromide. It was recrystallized from ethyl acetate; m. p.[4] 103.1–103.3°. *Anal.* Subs., 0.3034, 0.2965: AgBr, 0.1760, 0.1722. Calcd. for Bu_4NBr: Br, 24.80. Found: Br, 24.69, 24.72.

Electrical Equipment and Cells.—Measurements were made at low voltage and 60 cycles, using the Schering or resistance bridge.[5] Solutions were made up by weight, and pumped by dry air pressure from the dilution flask into a platinum conductance cell,[6] which was then placed in an oil-filled thermostat at 25.00°. Several cell fillings were made with each solution in order to eliminate sorption errors.[4]

III. Results

The conductance data are summarized in Table I, and are shown as log Λ–log c plots in Fig. 1. Several dilution runs were made for each salt. In the case of the tributyl salt, three solu-

TABLE I

CONDUCTANCE OF SALTS IN CHLOROBENZENE AT 25° AND 60 CYCLES

Tributylammonium picrate		Tetrabutylammonium bromide		Tetrabutylammonium picrate	
$c \times 10^3$	$\Lambda \times 10^3$	$c \times 10^4$	Λ	$c \times 10^4$	Λ
19.84	1.093	12.38	0.1570	19.62	0.266
18.19	1.015	7.67	.1585	14.24	.284
14.26	0.917	6.01	.1593	11.87	.305
10.08	.834	4.84	.1701	6.94	.370
7.62	.800	2.550	.1966	6.50	.380
5.17	.790	2.436	.1909	2.827	.542
3.165	.824	2.408	.1888	1.310	.770
2.998*	.847	1.284	.2352	0.610	1.103
2.000*	.847	0.534	.333	.407	1.340
1.076	1.043	.512	.328	.172	2.02
1.000*	1.001	.512	.338	.091	2.72
		.1998	.504		
		.1501	.574		
		.0710	.830		

(1) Elliott and Fuoss, THIS JOURNAL, **61**, 294 (1939).
(2) Mead, Kraus and Fuoss, *ibid.*, **61**, 3257 (1939).
(3) Fuoss, *Chem. Rev.*, **17**, 27 (1935).
(4) Cox, Kraus and Fuoss, *Trans. Faraday Soc.*, **31**, 749 (1935), report 113° for the m. p. of the bromide; in view of our analytical results, we conclude that the earlier figure is a misprint.
(5) Fuoss, THIS JOURNAL, **60**, 451 (1938).
(6) Mead and Fuoss, *ibid.*, **61**, 2047 (1939).

tions in the dilute range, marked with an asterisk in Table I, were also prepared directly, in order to be certain that solvent of low conductance was used. The point at 1.076×10^{-3} N looks high, as would be expected if the solutions absorbed a little moisture during preceding dilutions.

IV. Discussion

As is seen in Fig. 1, the conductance curves approach a straight line of slope $(-1/2)$ in the dilute region, indicating a simple binary equilibrium in this range. The curve for the bromide shows a broad minimum, similar to that shown by this salt in other solvents. As expected, the quaternary bromide is a weaker electrolyte than the quaternary picrate, while the tertiary picrate is much weaker than either. Quantitative comparison can be made by determining the constants of the curves.

From the viscosity[7] of chlorobenzene, $\eta_{25} = 0.00752$, and the limiting conductance of salts of this type in ethylene chloride[4,8] we estimate $\Lambda_0 = 60$. The $\Lambda\sqrt{cg}(c)$–c plots[9] are linear, and give the values found in Table II for the dissociation constants K and k corresponding to the ion pair and triple ion equilibria. In the last line are the a values calculated from K by the relationship[3]

TABLE II

CONSTANTS IN CHLOROBENZENE AT 25°

	Bu_4NPi	Bu_4NBr	Bu_3HNPi
K	1.88×10^{-8}	1.13×10^{-9}	2.10×10^{-13}
k	6.75×10^{-3}	0.42×10^{-3}	4.22×10^{-3}
a	4.75×10^{-8}	3.86×10^{-8}	2.98×10^{-8}

$$K^{-1} = \frac{4\pi N}{1000}\left(\frac{\epsilon^2}{DkT}\right)^3 Q\left(\frac{\epsilon^2}{aDkT}\right) \qquad (1)$$

where $Q(x)$ is the function

$$Q(x) = \int_2^x e^y y^{-4} dy \qquad (2)$$

The ratio of the dissociation constants of the quaternary picrate and bromide is 16.6, with an ion size *difference* of 0.89×10^{-8} cm. This is about the same as was found in anisole[4] (5.60 − 4.61 = 0.99) and in diphenyl ether[10] (5.33 − 4.60 = 0.73). In other words, the two salts have about the same *relative* strengths in these three solvents. But both have equivalent ion sizes nearly an ångström unit smaller in chlorobenzene than in the ethers; that is, they are much weaker electrolytes in chlorobenzene than their behavior in the other solvents would lead one to expect.

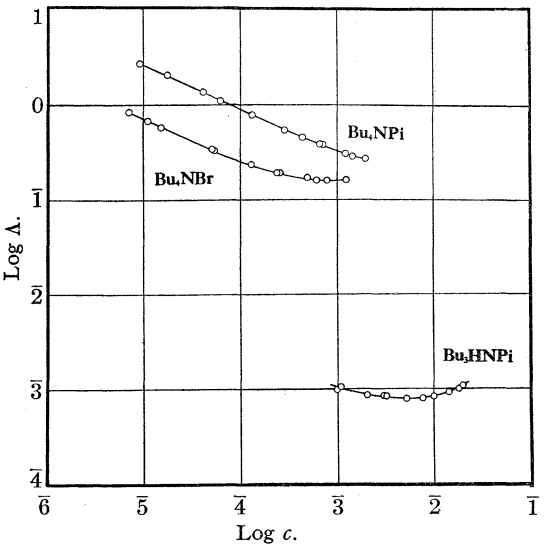


Fig. 1.—Conductance curves in chlorobenzene at 25°.

The following values for the parameter a for tetrabutylammonium picrate have been found: 5.83 in ethylene chloride[8] ($D_{25} = 10.23$), 5.80 in tricresyl phosphate[1] ($D_{40} = 6.92$), 5.60 in anisole[4] ($D_{25} = 4.27$), 5.33 in diphenyl ether[6] ($D_{50} = 3.53$) and 5.7 in benzene[11] ($D_{25} = 2.28$). A salt in chlorobenzene, for which $a = 5.6 \times 10^{-8}$, would have at 25° $K = 21.3 \times 10^{-8}$, which is 11.3 times as large as the dissociation constant found here for tetrabutylammonium picrate.

The tributyl salt is very weak in chlorobenzene, although relatively stronger than in ethylene chloride; the corresponding ion sizes are 2.98 and 2.40×10^{-8} cm.

The only conclusion to be reached at present is that other forces than coulomb interaction between ions must be considered in a general quantitative description of electrolytic behavior. Equation (1) gives the dependence of the ionic equilibrium on dielectric constant of solvent, but the variation of the parameter a from solvent to solvent for a given electrolyte shows that the present model is an over-simplification, and that even for strong electrolytes, specific interactions with solvent may be expected in some cases.

Summary

1. The conductances of tributylammonium picrate, tetrabutylammonium picrate and tetrabutylammonium bromide in chlorobenzene at 25° have been determined.

(7) Meyer and Mylius, *Z. phys. Chem.*, **95**, 349 (1920).
(8) Mead, Kraus and Fuoss, *Trans. Faraday Soc.*, **32**, 594 (1936).
(9) Fuoss and Kraus, THIS JOURNAL, **55**, 2387 (1933).
(10) D. J. Mead, unpublished observation.
(11) Fuoss and Kraus, THIS JOURNAL, **55**, 3614 (1933).

2. The effective ion sizes of the quaternary bromide and picrate in chlorobenzene are about one ångström unit smaller than in a number of other solvents; this result indicates that specific interaction between solvent and solute can appear even in the case of strong electrolytes.

SCHENECTADY, N. Y. RECEIVED DECEMBER 8, 1939

[CONTRIBUTION NO. 164 FROM THE BIOLOGICAL RESEARCH LABORATORIES, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, CAMBRIDGE, MASSACHUSETTS]

Relative Efficiency of Active Wave Lengths of Ultraviolet in Activation of 7-Dehydrocholesterol

BY JOHN W. M. BUNKER, ROBERT S. HARRIS AND L. MALCOLM MOSHER

The sterols which have received major attention in respect to their photochemical conversion into antirachitics are ergosterol and cholesterol, associated respectively with lower plants and with animal materials. Crystalline ergosterol may be regarded as the precursor of vitamin D_2 (Calciferol), the principal form of antirachitic vitamin now available from commercial activation; crystalline cholesterol, on the other hand, does not itself constitute a significant provitamin, but its derivative, 7-dehydrocholesterol, when irradiated with appropriate ultraviolet energy, is converted into vitamin D_3,[1,2] a form which has been found only in animal tissues.

In the present study the quantum efficiencies of certain wave lengths of ultraviolet in the activation of 7-dehydrocholesterol in ether have been measured and compared.

Irradiation Procedure.—Details of the irradiation procedure already have been published.[3] A cylindrical quartz vessel of 80 cc. capacity was filled with a 0.1% solution of 7-dehydrocholesterol[4] in anhydrous ether, C. P., and placed in the optical axis of the beam emerging from a quartz monochromator.[5] Exposure times were calculated from data on preliminary tests so that an approximation of 33 U. S. P. XI units (10 Steenbock units) would be produced with each batch. Since one batch would give sufficient active material for assay on only ten rats and since the protocol for this series called for groups of forty or fifty rats each, the irradiation procedure was repeated four or five times for each wave length. This was done over a period of five days during which time repetitive irradiations were scattered at random through the whole series, thereby distributing any undetected variations in the conditions of the irradiation. At each wave length each unit batch was subjected to 2475×10^{12} quanta of monochromatic ultraviolet energy.

(1) Boer, Reerink, van Wijk and van Niekerk, *Proc. Acad. Sci., Amsterdam*, **39**, 622 (1936).

(2) Windaus and Bock, *Z. physiol. Chem.*, **245**, 168 (1936).

(3) Harris, Bunker and Mosher, THIS JOURNAL, **60**, 2579 (1938).

(4) Acknowedgment is made for the contribution of the 7-dehydrocholesterol by Winthrop Chemical Company.

(5) Bunker and Harris, *New Engl. J. Med.*, **216**, 165 (1937).

Feeding of Activated Materials.—All batches of 7-dehydrocholesterol solution irradiated at a given wave length were pooled with three ether washings of the quartz vessel and with olive oil in the proportion of one gram of oil for each rat to be fed. The ether was removed under carbon dioxide in a moderate vacuum and the oil residue thoroughly incorporated into Steenbock #2965 ration in the proportion of 29 g. of diet to each gram of oil solution. The eight milligrams of treated 7-dehydrocholesterol which this oil contained had an expected potency of about 3.3 U. S. P. units of vitamin D.

These mixtures were then fed to groups of rats previously rendered rachitic in twenty-one days on the Steenbock #2965 ration. Group size was selected as follows (based on probability predictions from previous similar experiments involving a total of approximately three hundred rachitic rats): 40 rats each for the testing of materials irradiated with 2483 Å., 2537 Å., 2652 Å., and 3025 Å.; 50 rats each for testing 2804 Å., 2894 Å., and 2967 Å.; and 18 rats for testing 3130 Å., which previous tests had shown to be probably inactive.

During the six-day feeding period each animal consumed its quota of 30 g. of ration. Empty feeding jars were replenished with additional amounts of the #2965 diet, unfortified, until the end of the seventh day.

Observations.—A total of 328 rats entered the test period and all but two survived. At the end of this period these animals were killed, the left leg of each was X-rayed, then line tested, and the right legs were taken for ashing.

A summary of essential data including line test observations is presented in Table I. The whole bone ash values (on a fat-free dry basis) were between 31.7 and 33.6% for all active wave lengths; 28.8% for the inactive 3130 Å. line; and 27.3% for the rachitic controls.

In a previous communication we expressed the opinion that recorded differences between group responses must be greater than the quantities which by purely statistical computation are barely significant, if they are to be accepted as real. This restriction of the use of statistical methods applies to the evaluation of data derived from the usual sized bioassay groups but the restriction is lifted when the number of animals tested concurrently is sufficiently large.

Interpretation of Observations.—In respect to bone ash determinations, the group values for the active wave lengths varied within a small range

inconsistently with respect to X-ray and line test evaluations which are mutually confirmatory. This strengthens the opinion that bone ash determinations, because of variations inherent in the method or for some other undetected reason, fail to afford criteria sufficiently precise for detection of small differences in degrees of antirachitic response in rats. The line test or the roentgenogram procedures are more delicate.

TABLE I

SUMMARY OF EXPERIMENTAL DATA

Wave length, Å.	Number of rats	Weights, g. First	Weights, g. Last	Healing response	Arithmetic mean response
2483	2	55.0	72.0	0.5	
	10	52.0	72.9	1.0	
	11	54.5	73.1	1.5	
	12	53.4	72.3	2.0	
	5	55.2	77.2	2.5	1.6000[a]
Total	40				
2537	1	50.0	64.0	0.0	
	2	55.5	76.0	0.5	
	6	52.2	69.5	1.0	
	14	53.5	72.7	1.5	
	10	52.5	68.0	2.0	
	7	52.4	78.7	2.5	1.6375
Total	40				
2652	2	56.5	74.5	0.5	
	7	53.1	76.4	1.0	
	11	53.1	72.5	1.5	
	17	53.1	73.9	2.0	
	3	52.0	70.7	2.5	1.6500
Total	40				
2804	4	53.5	72.3	0.5	
	7	51.9	73.9	1.0	
	15	52.4	71.5	1.5	
	18	52.7	71.3	2.0	
	5	43.2	68.4	2.5	
	1	52.0	66.0	3.0	1.6600
Total	50				
2894	2	54.0	76.0	0.0	
	2	53.0	75.7	0.5	
	5	53.2	74.8	1.0	
	14	52.1	70.5	1.5	
	13	53.2	74.5	2.0	
	12	52.4	73.7	2.5	
	1	56.0	67.0	3.0	
	1	58.0	..	Died	1.7551
Total	50				
2967	1	50.0	62.0	0.5	
	4	54.8	79.0	1.0	
	11	52.7	72.5	1.5	
	21	53.1	74.3	2.0	
	6	50.8	70.3	2.5	
	5	51.8	68.8	3.0	
	0	..	..	3.5	
	1	51.0	60.0	4.0	
	1	56.0	..	Died	1.9796
Total	50				
3025	4	52.5	78.8	0.0	
	1	50.0	72.0	.5	
	6	54.5	77.0	1.0	
	9	54.3	75.3	1.5	
	17	53.7	73.8	2.0	
	2	51.0	68.5	2.5	
	1	50.0	59.0	3.0	1.5500
Total	40				
3130	18	53.4	74.4	0.0	0.00

[a] The computation of means to the fourth decimal is for subsequent mathematical treatment of these values.

In respect to line test observations, inspection of the arithmetic mean responses indicates a peak of response for 2967 Å. over all other wave lengths, and a suggestion that 2894 Å. may be slightly more active while 3025 Å. is slightly less active than the remaining four wave lengths.

This interpretation by inspection was tested by statistical analysis in which the significance of the differences among arithmetic mean responses was determined. That a real difference of means existed was shown when the variance within groups was proven significantly less than the variance among groups.

In order to determine which differences among means are real, the "*t*" test was applied, as an appropriate method in view of the numbers of observations available.

Let "*t*" represent the ratio of the difference between two means to the best estimate of a standard error of that difference. Then

$$t = \frac{\overline{X}_1 - \overline{X}_2}{s\sqrt{\frac{1}{N_1} + \frac{1}{N_2}}}$$

where $\overline{X}_1$, $\overline{X}_2$ = any two arithmetic mean response values, N_1, N_2 = the number of observations in the two groups, respectively, s = the best estimate of a standard deviation of a single group based on the data of the two groups considered, the value "*s*" being derived from the expression

$$s^2 = \frac{\Sigma(X_1 - \overline{X}_1)^2 + \Sigma(X_2 - \overline{X}_2)^2}{(N_1 - 1) + (N_2 - 1)}$$

where X_1, X_2 = each observation in the first or second group, respectively.

A "significant" value of "*t*" was taken to be 2.5, which gives approximately nineteen out of twenty chances that the differences found are real.

By the above test it appears that the response to 7-dehydrocholesterol activated by 2967 Å. is

TABLE II

SHOWING ESSENTIAL DATA USED IN THE "t" TEST

Wave lengths compared, Å.	Difference of arithmetic means	$s\sqrt{\frac{1}{N_1}+\frac{1}{N_2}}$	"t"	Interpretation
2483–2537	0.0375	0.13055	0.287	
2483–2652	.0500	.11930	.419	
2483–2804	.0600	.12035	.498	
2483–2894	.1551	.13355	1.161	
2483–**2967**	.3796	.12840	2.956	Significant
2483–3025	.0500	.14320	0.349	
2537–2652	.0125	.12555	.100	
2537–2804	.0225	.12530	.180	
2537–2894	.1176	.13810	.852	
2537–**2967**	.3421	.13315	2.569	Significant
2537–3025	.0875	.14850	0.589	
2652–2804	.0100	.11600	.086	
2652–2894	.1051	.12955	.811	
2652–**2967**	.3296	.12425	2.653	Significant
2652–3025	.1000	.13870	0.721	
2804–2894	.0951	.12630	.753	
2804–**2967**	.3196	.12195	2.621	Significant
2804–3025	.1100	.13590	0.809	
2894–**2967**	.2051	.14800	1.386	
2894–3025	.2245	.13290	1.689	
2967–3025	.4296	.14335	2.997	Significant

significantly greater than for any other wave length examined except for 2894 Å., which seems to have an effect intermediary between the effects of adjacent lines. There appears to be no significant difference between the activities of any other wave lengths tested.

The statistical analysis of results confirms the interpretation derived by inspection, and indicates that the lower efficiency of 3025 Å. may be regarded as not significant.

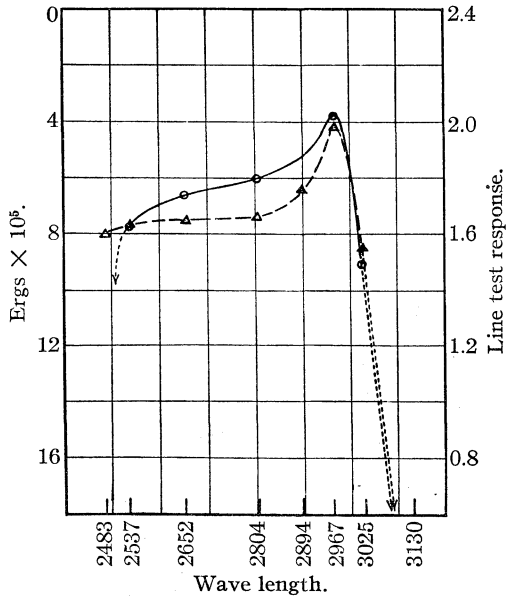


Fig. 1.—Relative antirachitic efficiencies of certain wave lengths of ultraviolet as determined by animal response: ○ = from direct irradiation of skin; △ = from feeding of activated 7-dehydrocholesterol.

Discussion.—When mammals are exposed to sources of ultraviolet of suitable wave length and energy, rickets can thereby be cured or prevented. It is assumed that there is produced in living tissues, by such activation of the skin, vitamin D of one of the major types. Although vitamin D_2 is absorbable from the intestinal tract of mammals and exerts in them an antirachitic therapeutic effect, its precursor, ergosterol, is not absorbed nor has it been identified in mammalian tissues. On the other hand, 7-dehydrocholesterol has been identified as the provitamin of animal tissues[1,2] and may be presumed to be the precursor of the vitamin D produced by irradiation of mammalian skin.

It has been shown[5,6] that rats whose skins have been irradiated with dominant mercury lines in the region bounded by 2537 and 3025 Å. exhibit an antirachitic response. The degrees of response to the various wave lengths tested are not equal per unit of applied energy, the potency of line 2967 Å., as determined by us,[5] being significantly greater than that of the other wave lengths. It also has been reported[3] that the photochemical activation of ergosterol (in ether) results in substantially equal production of antirachitic per quantum of ultraviolet energy applied over a similar range of wave lengths. This may be taken as an indication of a difference between ergosterol and the provitamin of the skin.

The results of this research are displayed in Fig. 1, together with those of a previous investigation of the activation of the skin of living rats. It is to be noted that there is a qualitative similarity between the activation curve of 7-dehydrocholesterol and of rat skin, whereas the activation of ergosterol[3] is dissimilar. This further strengthens the hypothesis that 7-dehydrocholesterol is the predominant provitamin D of the skin.

Summary

1. The photochemical activation of crystalline 7-dehydrocholesterol in ether by monochromatic ultraviolet of 2483, 2537, 2652, 2804 and 3025 Å. is substantially uniform per quantum of energy applied.

2. On a quantum basis, the activation by 2967 Å. is significantly greater than for any other

(6) Knudson and Benford, *J. Biol. Chem.*, **124**, 287 (1938).

wave length examined, with the possible exception of 2894 Å.

3. The activation by 2894 Å. appears to be intermediate between that of 2967 Å. and the other wave lengths tested.

4. No demonstrable antirachitic properties were produced by irradiation of 7-dehydrocholesterol in ether by ultraviolet of 3130 Å.

5. The superior effectiveness of 2967 Å. in antirachitic activation of 7-dehydrocholesterol parallels the significant superiority of this wave length in inducing healing upon direct irradiation of depilated rachitic rats, which supports the hypothesis that 7-dehydrocholesterol is a significant precursor of vitamin D in the skin.

CAMBRIDGE, MASS. RECEIVED NOVEMBER 16, 1939

[CONTRIBUTION NO. 211 FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Identification of Organic Compounds. I. Chlorosulfonic Acid as a Reagent for the Identification of Aryl Halides

BY ERNEST H. HUNTRESS AND FREDERICK H. CARTEN[1,2]

Although the action of chlorosulfonic acid has been studied upon many compounds, either as a means of introducing the sulfonic acid group or the chlorosulfonyl group, no systematic attempt to employ it as a reagent for the identification of organic compounds has been reported. The present paper reports the study of chlorosulfonic acid as applied to the identification of a considerable number of halogenated aromatic hydrocarbons.

The object of this work was to find a set of standard conditions such that treatment of the sample with chlorosulfonic acid would yield readily the corresponding arylsulfonyl chloride which in turn could be converted to the corresponding sulfonamide. The process of introducing the $-SO_2Cl$ group is hereafter designated as "chlorosulfonylation."

Two standard procedures (I and II) for effecting chlorosulfonylation have been devised and tested upon a large number of compounds. The first carries out the chlorosulfonylation in chloroform solution; the second uses no solvent. Both procedures employ a relatively large excess of chlorosulfonic acid in order to convert the intermediate sulfonic acid (to be expected from one mole of chlorosulfonic acid) as completely as possible to the corresponding sulfonyl chloride. The yields of arylsulfonyl chloride thus obtained are generally high (60–90%) and the process is extremely simple to execute.

(1) This paper is constructed from part of a dissertation submitted by Frederick H. Carten to the Faculty of the Massachusetts Institute of Technology in partial fulfillment of the requirements for the degree of Doctor of Philosophy in June, 1939.

(2) This work was assisted by a grant from the Warren Fund of the American Academy of Arts and Sciences for which grateful acknowledgment is hereby made.

Conversion of the arylsulfonyl chloride thus obtained to the corresponding arylsulfonamide was effected either by treatment with concentrated aqueous ammonium hydroxide, or by reaction with solid ammonium carbonate. The yields on this step were invariably nearly quantitative.

In a few cases the reaction with chlorosulfonic acid yielded abnormal products. Thus fluorobenzene, iodobenzene, *o*-dichlorobenzene and *o*-dibromobenzene at 50° with chlorosulfonic acid in the absence of any solvent, chloroform, yielded the corresponding sulfones. In a few other instances a small amount of the corresponding sulfones accompanied the usual sulfonyl chloride. From the point of view of identification, however, these sulfones serve just as well as the sulfonyl chlorides. Furthermore, in those cases where they accompany the sulfonyl chloride, they are readily separable from the final sulfonamide by their insolubility in alkali, the sulfonamides readily dissolving and being reprecipitable on acidification.

Another abnormal type of reaction occasionally observed was nuclear chlorination. This occurred notably with *p*-diiodobenzene and 1,2,4,5-tetrachlorobenzene but does not interfere with the identification of these compounds since the substitution products are readily obtained and have characteristic melting points.

Unsatisfactory results were obtained with the following compounds: *o*-chloroiodobenzene, *p*-chloroiodobenzene, *m*-chloroiodobenzene, *o*-bromoiodobenzene, *p*-bromoiodobenzene, *o*-iodotoluene, *m*-iodotoluene and *p*-iodotoluene. Treatment

of *o*- and of *p*-chlorobiphenyl by either procedure I or II gave only water soluble products.

Of the 28 sulfonamides reported in Table I six are new. The structures assigned in these six cases are, therefore, tentative and are based on analogies with other compounds actually studied. Of the four sulfones described two are previously unreported. The tentative structures assigned to these are, therefore, based only on analogies, and their complete establishment was not attempted in this research.

Since the three isomeric trichlorobenzenes yield sulfonamides which are not well adapted for their positive identification, we have studied the utility of nitration for this purpose. All of the mono- and dinitro derivatives of these three compounds have been reported but by such diversified procedures that we have devised a set of standard conditions for nitration. The dinitration products serve conveniently for characterization of the trichlorobenzenes, confirmatory evidence being supplied by their reaction with aniline.

Experimental Work

The melting points reported in this paper are uncorrected. They were determined on a standard rod form 360° melting point thermometer in a copper melting point block of the Berl and Kullmann type. Observation of the sample was assisted by means of a small 25 power microscope permanently attached to the apparatus.

The chlorosulfonic acid used in this work was obtained by distilling Eastman Kodak Co. practical grade in a stream of hydrogen chloride, retaining only the portion distilling between 153–157° (92% of the original material).

The organic compounds were carefully purified until their melting or boiling points checked closely with the values accepted in the literature.

Chlorosulfonylation with Chlorosulfonic Acid

Procedure I.—The compound (1.0 g.) was dissolved in chloroform (5 cc.), the solution placed in a six-inch (15 cm.) test-tube resting in an ice-bath at 0°, and treated dropwise with chlorosulfonic acid (5.0 g.). After the initial evolution of hydrogen chloride had subsided, the reaction mixture was brought to room temperature. After about twenty minutes the contents of the tube were poured into a 50-cc. beaker filled with crushed ice, the chloroform layer separated and washed with cold water, and the solvent evaporated. The residual crude arylsulfonyl chloride was then recrystallized from dry low boiling petroleum ether or from chloroform and dried in vacuum over concentrated sulfuric acid.

Procedure II.—This was exactly like Procedure I except that no solvent was employed. After pouring the sirupy reaction mixture onto crushed ice, the resultant arylsulfonyl chloride or sulfone was filtered with suction if a solid, or separated by means of a small separatory funnel if a liquid, washed with water and recrystallized from low boiling petroleum ether or benzene.

Some of the aryl halides used in this work react but slowly with chlorosulfonic acid at room temperature. Deviations from the above standard procedures found to result in improved yields are noted under the individual descriptions.

Every arylsulfonyl chloride described in this report when dissolved in alcohol and boiled with solid ammonium thiocyanate gives (on cooling) a yellow amorphous precipitate. The precise nature of the reaction is unknown but it serves as a qualitative means of detection of the sulfonyl chloride group. Our use of it represents an extension of the observations of Remsen and Turner,[3] on the reaction of benzenesulfonyl chloride.

Conversion of Arylsulfonyl Chlorides to Sulfonamides

Procedure A.—The arylsulfonyl chloride (0.5 g.) prepared according to Procedures I or II was boiled for ten minutes with concentrated (sp. gr. 0.90) ammonium hydroxide (5 cc.). After cooling to room temperature, and adding cold water (10 cc.), the resultant solid sulfonamide was filtered with suction and thoroughly washed. It was then recrystallized to constant melting point from dilute ethanol and dried at 105°.

Procedure B.—The product from either of the chlorosulfonylation procedures I or II (0.5 g.) was mixed with dry powdered ammonium carbonate (2.0 g.) and heated at 100° for thirty minutes. After washing with several 10-cc. portions of cold water, the residual solid was filtered off and recrystallized from dilute ethanol.

Remarks.—Any sulfone which may have been formed by the action of chlorosulfonic acid in Procedures I or II is of course entirely unaffected by either ammonium hydroxide or ammonium carbonate in Procedure A or B. It may be separated from the corresponding aryl sulfonamide by virtue of its insolubility in cold 6 *N* sodium hydroxide. The sulfonamides dissolve in the alkali and after filtration of the inert sulfone may be reprecipitated by addition of 6 *N* hydrochloric acid.

Sulfones Obtained with Chlorosulfonic Acid.—In four cases application of Procedure II to the original aryl halide gave only sulfones in 71–74% yield. Thus, fluorobenzene gave 4,4′-difluorodiphenylsulfone, white needles from benzene, m. p. 97–98 uncor. This product was obtained in 100% yield by heating the reaction mixture at 40° for one hour.

Anal. Calcd. for $C_{12}H_8F_2O_2S$: C, 56.70; H, 3.15. Found: C, 56.43, 56.82; H, 3.38, 3.54.

Iodobenzene by either Procedure I or II gave 4,4′-diiododiphenylsulfone, needles from benzene or glacial acetic acid, m. p. 201–202°.

Anal. Calcd. for $C_{12}H_8I_2O_2S$: S, 6.81; I, 53.99. Found: S, 6.92, 6.86; I, 53.93, 53.71.

The compound is undoubtedly identical with the so-called x,x-diiododiphenylsulfone of Beilstein VI-336.[4] From *o*-dichlorobenzene, Procedure II yielded 3,4,3′,4′-tetrachlorodiphenylsulfone, accompanied by a small pro-

(3) Remsen and Turner, *Am. Chem. J.*, **25**, 198 (1901).

(4) Willgerodt and Waldmeyer, *J. prakt. Chem.*, (2) **59**, 195 (1899).

TABLE I

SULFONYL CHLORIDES AND SULFONAMIDES

Original	Resultant sulfonyl chloride[a,d] Isomer obtd.	M. p., °C. uncor.	Corresponding sulfonamide[b,c,d] M. p., °C. uncor.
A. Benzene series (—SO_2Cl or —SO_2NH_2-1)			
F	4-F	35–36	124–125
Cl	4-Cl	53.5	142–143
Br	4-Br	75.4	161.5
1,2-diCl	3,4-diCl	18–19[e]	134–135
1,3-diCl	2,4-diCl	52–53	179–180[g]
1,4-diCl[f]	2,5-diCl	38	179.5–180[g]
1,2-diBr	3,4-diBr[h]	31–34	175–176
1,3-diBr	2,4-diBr	78–79	188–189
1,4-diBr[f]	2,5-diBr	71	194–195
1-CH_3, 2-F	3-CH_3, 4-F	oil	104–105
1-CH_3, 3-F[i]	2-CH_3, 4-F	oil	172–173
1-CH_3, 4-F[i]	2-CH_3, 5-F	oil	140–141
1-CH_3, 2-Cl	3-CH_3, 4-Cl	63	126
1-CH_3, 3-Cl[i]	2-CH_3, 4-Cl	52–53	184–185
1-CH_3, 4-Cl[i]	2-CH_3, 5-Cl	21	142–143
1-CH_3, 2-Br	3-CH_3, 4-Br	59–60	145–146
1-CH_3, 3-Br[i]	2-CH_3, 4-Br	49–50	167–168
1-CH_3, 4-Br[i]	2-CH_3, 5-Br	33–35	164–165
1-CH_3, 2,4-diCl[i]	2,4-di-Cl, 5-CH_3	71–72	175–176
1-CH_3, 2,6-diCl[i]	2,4-di-Cl, 3-CH_3	54–56	199–201
1,2,3-triCl[j]	2,3,4-triCl	64–65	226–230 dec.
1,2,4-triCl[k]	2,4,5-triCl	31–34	>200
1,3,5-triCl[l]	2,4,6-triCl	35–40	210–212 dec.
1,3,5-triBr	2,4,6-triBr	58–60	220–222 dec.
B. Naphthalene series (—SO_2Cl or —SO_2NH_2-1)			
1-Cl	4-Cl	92–93	185–186
2-Cl	7-Cl	124–126	231–232
1-Br	4-Br	81–83	191–193
2-Br	7-Br	142–143	207–208

[a] Except for those from fluorobenzene and chlorobenzene which were recrystallized from benzene and ether, respectively, all other sulfonyl chlorides were recrystallized from petroleum ether. [b] All sulfonamides were recrystallized from dilute alcohol. [c] All sulfonamides were analyzed for nitrogen (or halogen in two cases) and gave results in excellent accord with the theoretical values. [d] In order to save space references to m. p.'s previously reported are not included. [e] Accompanied by 8% of the corresponding sulfone. [f] Does not react at room temperature but gives 80% yield on refluxing for one hour. [g] The m. p. of a mixture of these two compounds was depressed to 168–171°. [h] Accompanied by 3% of the corresponding sulfone. [i] Followed by heating at 50° for ten minutes. [j] Followed by heating at 80° for one hour. [k] Followed by heating at 150° for one hour. [l] Followed by heating at 150° for thirty minutes.

portion (3–4%) of 3,4-dichlorobenzenesulfonamide. The sulfone crystallizes in plates from absolute alcohol or glacial acetic acid, m. p. 175–176° uncor.

Anal. Calcd. for $C_{12}H_6Cl_4O_2S$: S, 9.00; Cl, 39.85. Found: S, 8.76, 9.00; Cl, 39.65, 39.57.

It is undoubtedly identical with the so-called bis-[x,x'-dichlorophenyl]-sulfone (Beilstein VI-330).[5] From *o*-dibromobenzene Procedure II yielded 3,4,3',4'-tetrabromodiphenylsulfone, plates from hot alcohol, m. p. 176–177°.

Anal. Calcd. for $C_{12}H_6Br_4O_2S$: Br, 59.87. Found: Br, 60.66, 60.96.

(5) Friedel and Crafts, *Ann. chim.* (6) **10**, 415 (1887).

Chlorosulfonic acid gave "abnormal" results in three cases.

2,3,5,6-Tetrachloro-1,4-diiodobenzene: from *p*-diiodobenzene heated to 50° for five minutes with five parts of chlorosulfonic acid. Vigorous evolution of sulfur dioxide occurred and a pale brown solid precipitated. After pouring onto ice the crude product recrystallized from absolute alcohol or from glacial acetic acid in long white needles, m. p. 210–211° uncor.

Anal. Calcd. for $C_6Cl_4I_2$: Cl, 30.32; I, 54.27. Found: Cl, 30.42, 29.69; I, 52.12, 52.12.

Hexachlorobenzene: from 1,2,4,5-tetrachlorobenzene (5.0 g.) refluxed with chlorosulfonic acid (20.0 g.) for one hour. During this period, the reaction mixture turned dark green and a white solid appeared on its surface. As this solid gradually sublimed into the condenser its solution in the condensing chlorosulfonic acid was deep red, changing to green upon striking the mixture in the flask. After cooling, and pouring onto ice, the separating white solid (5.2 g., 78%) recrystallized from petroleum ether as needles, m. p. 218–219° uncor., and failed to depress the melting point of an authentic sample of hexachlorobenzene.

Anal. Calcd. for C_6Cl_6: Cl, 74.70. Found: Cl, 74.35, 74.29.

2-Bromo-5-chlorobenzenesulfonamide: from *p*-chlorobromobenzene by refluxing for one hour with five times its weight of chlorosulfonic acid, pouring onto ice and converting the resultant sulfonyl chloride (86% yield, m. p. 40–42°) to amide via Procedures A or B. The product showed m. p. 189–190° uncor.

Anal. Calcd. for $C_6H_5BrClNO_2S$: N, 5.18. Found: N, 5.23, 5.27.

The chlorosulfonylation of *p*-bromochlorobenzene could yield either 2-bromo-5-chlorobenzenesulfonyl chloride or 2-chloro-5-bromobenzenesulfonyl chloride or both. Armstrong and Briggs[6] report melting points of 46 and 66°, respectively, for these two isomers and melting points of 191 and 178° for the respective corresponding sulfonamides. Moreover, they report that the two sulfonamides are isomorphous and that their mixture showed no depression of melting point. This indicates that in our experiments both isomers may be formed but that our final product is mainly 2-bromo-5-chlorobenzenesulfonamide.

Nitration of the Trichlorobenzenes.—One gram of the compound was dissolved in five grams of fuming nitric acid (d = 1.49). 1,2,3-Trichloro- and 1,2,4-trichlorobenzene dissolved promptly with evolution of heat; 1,3,5-trichlorobenzene required warming for fifteen minutes on the water-bath. After complete solution had occurred, the mixture was poured onto crushed ice, the solid filtered and recrystallized from alcohol; yield quantitative. By this procedure 1,2,3-trichlorobenzene yielded 2,3,4-trichloro-1-nitrobenzene, m. p. 55–56°; 1,2,4-trichlorobenzene yielded 2,4,5-trichloro-1-nitrobenzene, m. p. 56°; and 1,3,5-trichlorobenzene gave 2,4,6-trichloro-1-nitrobenzene, m. p. 67–68°.

Dinitration.—To the nitric acid solution of mononitro compound obtained above was added 5 g. of concentrated sulfuric acid and the mixture refluxed for one hour. After cooling the mixture was poured into 100 cc. of water

(6) Armstrong and Briggs, *Chem. News*, **65**, 138–139 (1892).

and the precipitated dinitrotrichlorobenzene filtered, washed and recrystallized from alcohol; yields quantitative. By this procedure 1,2,3-trichlorobenzene yielded 4,5,6-trichloro-1,3-dinitrobenzene, m. p. 92–93°; 1,2,4-trichlorobenzene yielded 2,4,5-trichloro-1,3-dinitrobenzene, m. p. 102.5–103.5°; and 1,3,5-trichlorobenzene gave 2,4,6-trichloro-1,3-dinitrobenzene, m. p. 128.5°.

Reaction of the Dinitrotrichlorobenzenes with Aniline.—One gram of the dinitrotrichlorobenzene and five grams of pure aniline were heated on a water-bath for one hour. The mixture was then cooled and extracted with successive portions of 6 *N* hydrochloric acid to remove excess aniline. After filtering off the residual solid and washing with water, it was recrystallized from benzene or ethyl alcohol.

Application of this procedure to the dinitration product from 1,2,3-trichlorobenzene gave 4,6-dianilino-5-chloro-1,3-dinitrobenzene, m. p. 136–138°.

Anal. Calcd. for $C_{18}H_{13}ClN_4O_4$: N, 14.56. Found: N, 14.88, 14.91.

From the dinitration product of 1,2,4-trichlorobenzene there resulted 2,6-dianilino-5-chloro-1,3-dinitrobenzene, m. p. 182°.

Anal. Calcd. N, 14.56; Cl, 9.21. Found: N, 14.79, 14.86; Cl, 9.20, 9.28.

From the dinitration product of 1,3,5-trichlorobenzene there was obtained the previously reported 2,4,6-trianilino-1,3-dinitrobenzene, m. p. 179–180°.

Summary

1. A method for the identification of aryl halides by means of chlorosulfonylation with chlorosulfonic acid has been shown to yield excellent results.

2. Of thirty-two aryl halides studied, thirty yield characteristic arylsulfonyl chlorides readily converted to the corresponding arylsulfonamides and the other two yield reaction products characteristic of the original compound.

3. Three trichlorobenzenes have been characterized by mono-, di- and tri-nitration and the reaction products of the dinitrotrichlorobenzenes with aniline have been found useful derivatives.

CAMBRIDGE, MASS. RECEIVED AUGUST 17, 1939

[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS, AND THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

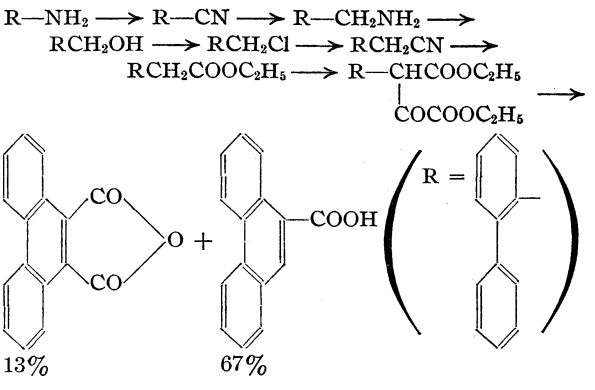
A New Synthesis of Phenanthrene Derivatives. I. Phenanthrene-9,10-dicarboxylic Anhydride and Phenanthrene-9-carboxylic Acid

BY T. A. GEISSMAN AND ROY W. TESS

In an attempt to develop a convenient method for the synthesis of phenanthrene-9,10-dicarboxylic anhydride, a modification of the Bougault method of ring closure[1] applied to the biphenyl ring system has been studied. While the results obtained are encouraging, those described in this paper are of a preliminary nature, and are published at this time because of the necessity for temporarily suspending work on the problem.

A new approach to the synthesis was sought for two reasons: the method used appeared to offer (1) a cheaper procedure and one more readily adapted to the preparation of large amounts than those of Jeanes and Adams[2] or of Weizmann, Bergmann and Berlin,[3] and (2) a synthesis which could be generalized more readily than either of those mentioned[4] to the preparation of analogous compounds containing other substituents in the rings.

The steps in the synthesis are



The synthesis proceeds smoothly in the manner shown, and although suspension of the study has made it impossible to work out conditions for a quantitative ring-closure without decarboxylation, the total yield of phenanthrene derivatives is good.

The synthesis of 2-biphenylacetic acid by von Braun and Manz[5] has been accomplished by the

(1) Bougault, *Comp. rend.*, **159**, 745 (1915); v. Auwers and Möller, *J. prakt. Chem.*, **109**, 124 (1925); Bardhan, *Nature*, **134**, 217 (1934); Fieser and Hershberg, THIS JOURNAL, **57**, 1508 (1935).

(2) Jeanes and Adams, THIS JOURNAL, **59**, 2608 (1937).

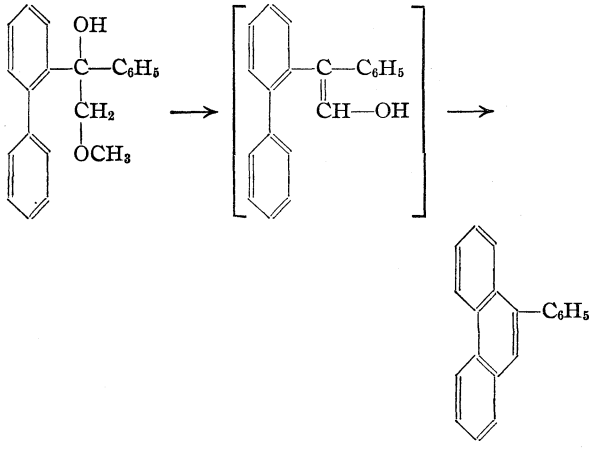
(3) Weizmann, Bergmann and Berlin, THIS JOURNAL, **60**, 1331 (1938).

(4) The synthesis of Weizmann, *et al.*[3] is based upon the preparation by Gruber and Adams [THIS JOURNAL, **57**, 2555 (1935)] of the adduct of dicyclohexenyl and maleic anhydride.

(5) Von Braun and Manz, *Ann.*, **468**, 273 (1929).

same series of reactions up to the formation of 2-biphenylacetonitrile. The step involving the reduction of the nitrile to the methylamine has been improved in the present work with the elimination of the side-reaction leading to unwanted secondary amine.

The suggestion of Bradsher[6] that ring closure of compounds such as 1-phenyl-1-(2-biphenyl)-2-methoxyethanol-1 proceeds through an intermediate carbonyl compound (or its enol form)



finds support in the present work. The alkali-solubility and violet color with ferric chloride shown by ethyl 2-biphenyloxalylacetate indicate that it exists completely as the enol and lead to the belief that 2-biphenylacetaldehydes or acetones are cyclized through their respective enols.

Experimental

The synthesis of 2-biphenylacetonitrile is described by von Braun and Manz[5] but since numerous details are lacking in this article, a more detailed description of several of the steps involved seems desirable.

o-Phenylbenzylamine.—A mixture of 122.5 g. of *o*-cyanobiphenyl (distilled from Raney nickel), one teaspoonful of Raney nickel, 150 cc. of liquid ammonia and 50 cc. of ether was placed in a bomb under a pressure of 3350 lb. (223 atm.) of hydrogen. Upon heating to 120° the pressure rose to 4500 lb. (300 atm.), then gradually fell to 1670 lb. (111 atm.) in about four hours. After the bomb was cooled and the pressure released, the ammonia was allowed to evaporate and the residue dissolved in ether and filtered. The filtrate was extracted with dilute hydrochloric acid and the product recovered by ether extraction of the neutralized solution and distilled. The product boiled almost entirely at 163–168° (15 mm.) and practically no higher-boiling residue remained in the distillation flask (von Braun and Manz[5] give b. p. 163° (12 mm.)).

o-Phenylbenzyl Alcohol.—A solution of 17.9 g. of sodium nitrite in 25 cc. of water was added over ten minutes to a cooled solution of 12.0 g. of *o*-phenylbenzylamine in 50 cc. of acetic acid. When all the nitrite had been added the solution was stirred for ten minutes at room temperature and poured into water. The solution was neutralized with solid sodium carbonate and extracted with ether. Unchanged amine was removed by washing the ether solution with dilute acid and after removal of the ether the product was distilled. The fraction boiling at 177–184° (15 mm.) weighed 11.5 g. (v. Braun and Manz[5] give b. p. 174° (13 mm.)).

o-Phenylbenzyl Chloride and o-Phenylbenzyl Cyanide.—These were prepared by methods too well known to require detailed description. The chloride boiled at 161–168° (16 mm.) (v. Braun and Manz[5] give 154° (12 mm.)). The cyanide boiled at 181–190° (15–16 mm.) (v. Braun and Manz[5] give 182° (12 mm.)).

Ethyl 2-Biphenylacetate.—To a solution of 55 g. of 95% alcohol and 45 g. of concentrated sulfuric acid was added 43.3 g. of 2-biphenylacetonitrile. The solution was gently refluxed for thirteen hours and poured into water. The ester was extracted with ether and distilled. There was obtained 55.2 g. of ester, b. p. 180–185° (15 mm.). The identity of the ester was established by saponifying a sample of it to the known[5] 2-biphenylacetic acid.

Phenanthrene-9,10-dicarboxylic Anhydride and Phenanthrene-9-carboxylic Acid.—The oxalylation of ethyl 2-biphenylacetate by means of dry potassium ethoxide was found to be superior to the method in which metallic sodium is used; the latter method was found to give good results when applied to the oxalylation of ethyl phenylacetate by Rising and Stieglitz.[7]

Potassium ethoxide was prepared by allowing 2.0 g. of powdered potassium covered with 50 cc. of dry ether to react with 2.5 g. of absolute ethanol. To the ice-cooled suspension of the resulting potassium salt was added a mixture of 7.5 g. of ethyl oxalate and 12.0 g. of ethyl 2-biphenylacetate. The potassium ethoxide dissolved and a greenish-brown solution resulted, which in the course of two days turned a yellow-red in color. The solution was decomposed with cracked ice and the aqueous layer separated. The ether layer was washed well with small portions of ice water and the combined aqueous extracts acidified with ice-cold, dilute sulfuric acid. The product was extracted with ether, the ether solution dried and evaporated. The oxalyl derivative was obtained as a pale yellow oil which gave a deep violet coloration with alcoholic ferric chloride. Attempts to crystallize it were fruitless; it showed a tendency to decompose upon prolonged exposure to air.

To the oily oxalyl ester was added a mixture of 50 cc. of glacial acetic acid and 30 cc. of 48% hydrobromic acid and the mixture refluxed for three hours. After fifteen to twenty minutes of refluxing, yellow needles began to form and a heavy precipitate soon filled the solution. The mixture was cooled and the product collected. It was pale yellow, crystalline and weighed 7.95 g.

The ether layer containing the non-acidic material from the oxalylation reaction yielded 2.7 g. of unchanged ethyl 2-biphenylacetate.

(6) Bradsher, THIS JOURNAL, **61**, 3131 (1939).

(7) Rising and Stieglitz, THIS JOURNAL, **40**, 723 (1918).

The crude material melted poorly and proved to be a mixture. Recrystallized from acetic anhydride, it yielded 1.25 g. of yellow needles of the anhydride melting at 310–315° (literature, 312°[3] and 322°[2]), and 6.0 g. of colorless needles of the acid, melting at 249–250° (literature[8] 250°). The acid was converted to methyl phenanthrene-9-carboxylate, white needles from methanol, m. p. 115–116° (literature[9] 116°).

(8) Werner and Kunz, *Ann.*, **321**, 327 (1902).
(9) Mosettig and van de Kamp, THIS JOURNAL, **52**, 3704 (1930).

Summary

1. The synthesis of phenanthrene-9,10-dicarboxylic anhydride and phenanthrene-9-carboxylic acid by ring closure of ethyl 2-biphenyloxalylacetate is described.

2. The method described constitutes a new synthesis of phenanthrene derivatives.

URBANA, ILLINOIS RECEIVED DECEMBER 26, 1939
LOS ANGELES, CALIFORNIA

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. LXXXVII. Cholesterol and Sitosterol Derivatives

BY RUSSELL E. MARKER AND EWALD ROHRMANN

Inasmuch as most of the oxidation studies on the sterols have been made with chromic anhydride in acetic acid, it seemed of interest to study the action of potassium permanganate in acetic acid on some of these substances. It is well known that potassium permanganate in alkaline medium oxidizes cholesterol to a cholestanetriol-3,5,6,[1,2,3] the reagent under these conditions apparently having no tendency to oxidize the secondary alcohols to ketones. The resulting triol differs from that obtained by the hydroxylation of cholesterol with hydrogen peroxide. That this difference is due to the configuration of the tertiary hydroxyl group at C-5 is indicated by the fact that the two triols on oxidation with chromic anhydride yield different cholestanol-5-diones-3,6.

In acetic acid solution cholesterol with potassium permanganate yields a cholestanol-5-dione-3,6 which is very probably identical with that obtained by oxidizing with chromic anhydride the alkaline permanganate oxidation product of cholesterol. With cholesteryl acetate a 3-acetoxy-5-hydroxy-6-ketocholestane was obtained. Similar results were obtained with sitosterol and sitosteryl acetate. The same products were obtained when the oxidations were conducted at room temperature or at 55°, there apparently being little tendency for ring B to open between C-5 and C-6.

The oxidation of cholestanol-3(β) with potassium permanganate in acetic acid solution at room temperature gave a good yield of cholestanone. At a temperature of 55° both cholestanone and 2,3-cholestane dicarboxylic acid were obtained. The oxidation of neocholestene at room temperature gave largely 2,3-cholestane dicarboxylic acid.

The preparation of 7-ketositosteryl chloride has been carried out by the chromic anhydride oxidation of sitosteryl chloride.[4] The substance undergoes reactions analogous to those of 7-ketocholesteryl chlorides.[4,5]

We wish to thank Parke, Davis and Company for their generous help and assistance during the various phases of this work.

Experimental Part

Oxidation of Cholesterol and Sitosterol Derivatives with Potassium Permanganate.—(a) **Cholesterol.**—To a solution of 2 g. of cholesterol in 150 cc. of acetic acid was added 75 cc. of 1 *N* aqueous potassium permanganate and 75 cc. of acetic acid. After standing for six hours at room temperature the mixture was diluted with water and the solid taken up with ether. The ethereal extract was washed with water and dilute sodium carbonate solution and the ether evaporated to yield approximately 1.6 g. of crystalline residue. This was crystallized from acetone to give compact white crystals, m. p. 248–251°.

Anal. Calcd. for $C_{27}H_{44}O_3$: C, 77.8; H, 10.65. Found: C, 78.0; H, 10.7.

(b) **Cholesteryl Acetate.**—To a solution of 2 g. of cholesteryl acetate in 210 cc. of acetic acid heated at 45–50° was added 50 cc. of 1 *N* aqueous potassium permanganate over a period of thirty minutes and the mixture was heated at 50° for an additional thirty minutes. The product was worked up and crystallized from acetone as described above to give white plates, m. p. 231–233°.

Anal. Calcd. for $C_{29}H_{48}O_4$: C, 75.6; H, 10.5. Found: C, 75.8; H, 10.7.

Similar results were obtained when the oxidation was conducted at room temperature.

(1) Windaus, *Ber.*, **40**, 257 (1907).
(2) Pickard and Yates, *J. Chem. Soc.*, **93**, 1678 (1908).
(3) Pimone, *Gazz. chim. ital.*, **62**, 1101 (1932).
(4) Marker, *et al.*, THIS JOURNAL, **59**, 619 (1937).
(5) Marker and Rohrmann, *ibid.*, **61**, 3022 (1939).

With hydroxylamine acetate the product yielded an *oxime* which was crystallized from aqueous methanol, m. p. 204–206°.

Anal. Calcd. for $C_{29}H_{49}O_4N$: C, 73.2; H, 10.4. Found: C, 73.5; H, 10.4.

(c) **Neocholestene.**—A suspension of 2 g. of neocholestene in 250 cc. of acetic acid was mixed with a solution of 1.5 g. of potassium permanganate in 200 cc. of 90% acetic acid. After standing at room temperature for seven hours the mixture was worked up as described previously. There was very little neutral material. The acidic fraction from the sodium carbonate washing was crystallized from aqueous acetic acid to yield white crystals, m. p. 193–195°. This gave no depression with an authentic sample of the 2,3-cholestane dicarboxylic acid, m. p. 193.5–195°.

(d) **Cholestanol.**—Oxidation of β-cholestanol at room temperature under the above conditions gave a product which crystallized from aqueous acetone as white needles, m. p. 126–128°. This gave no depression with a sample of cholestanone, m. p. 126.5–128°. There was no appreciable acid fraction.

When the oxidation was carried out at 55° for three hours using twice as much permanganate as in the room temperature oxidation approximately equal amounts of cholestanone and of the 2,3-diacid of cholestane were obtained.

(e) **Sitosterol.**—Sitosterol was oxidized as described for cholesterol. The neutral fraction was crystallized from acetone as compact white crystals, m. p. 240°.

Anal. Calcd. for $C_{29}H_{48}O_3$: C, 78.3; H, 10.9. Found: C, 78.3; H, 11.2.

(f) **Sitosteryl Acetate.**—This was oxidized as described for cholesterol. The product was crystallized from acetone as white needles, m. p. 251°.

Anal. Calcd. for $C_{31}H_{52}O_4$: C, 76.15; H, 10.75. Found: C, 76.1; H, 10.8.

$\Delta^{4,5}$-Cholestenedione-3,6 from Cholestanol-5-dione-3,6.—A mixture of 600 mg. of cholestanol-5-dione-3,6 and 12 g. of powdered potassium bisulfate was heated in high vacuum at 150–180°. The sublimate was crystallized from aqueous acetone as white plates, m. p. 121–123°.

Anal. Calcd. for $C_{27}H_{42}O_2$: C, 81.3; H, 10.6. Found: C, 81.3; H, 10.6.

7-Ketositosteryl Chloride.—To a well-stirred solution of 25 g. of sitosteryl chloride in 500 cc. of glacial acetic acid heated at 55° on a water-bath was added a solution of 20 g. of chromic anhydride in 30 cc. of 50% acetic acid during one hour. A small amount of ethanol was then added, the mixture evaporated *in vacuo* to a volume of 250 cc. and 20 cc. of water added to the residual solution. The solution was cooled at 0° for twenty hours. The product was washed with 75% acetic acid and 95% ethanol, and crystallized from acetone to give white plates, m. p. 155–156°.

Anal. Calcd. for $C_{29}H_{47}OCl$: C, 77.85; H, 10.6. Found: C, 77.7; H, 10.5.

7-Hydroxysitosteryl Chloride.—A solution of 1 g. of 7-ketositosteryl chloride and 1 g. of aluminum isopropylate in 45 cc. of dry isopropyl alcohol was refluxed for twelve hours. The residual material was diluted with water and extracted with ether. Evaporation of the ether gave a crystalline residue which was recrystallized from methanol–acetone to give white plates, m. p. 138–139°.

Anal. Calcd. for $C_{29}H_{49}OCl$: C, 77.5; H, 11.0. Found: C, 77.7; H, 10.8.

7-Ketositosterylene.—A mixture of 200 mg. of 7-ketositosteryl chloride, 9 cc. of 95% ethanol, 0.5 cc. of water and 300 mg. of potassium hydroxide was refluxed for ninety minutes. The solution was diluted with water and the precipitated solid extracted with ether. Evaporation of the ether gave a residue which was crystallized from acetone–ethanol as pale yellow plates, m. p. 106–107°.

Anal. Calcd. for $C_{29}H_{46}O$: C, 84.8; H, 11.3. Found: C, 84.7; H, 11.2.

7-Ketositostyl Chloride.—A mixture of 2 g. of 7-ketositosteryl chloride, 700 mg. of Adams catalyst and 100 cc. of ether was shaken with hydrogen at 3 atm. pressure at room temperature for six hours. The mixture was filtered and the filtrate evaporated. The residue was crystallized from acetone–ethanol as white plates, m. p. 128–129°.

Anal. Calcd. for $C_{29}H_{49}OCl$: C, 77.5; H, 11.0. Found: C, 77.7, 77.4; H, 10.9, 11.0.

This product was recovered unchanged after heating for two hours at 60° with chromic anhydride.

A mixture of 150 mg. of 7-ketositostyl chloride, 300 mg. of Adams catalyst and 100 cc. of glacial acetic acid was shaken with hydrogen at 3 atmospheres pressure for five hours at room temperature. The product was crystallized from acetone–methanol to give white needles, m. p. 107–109°. This gave no depression with a sample of sitostyl chloride, m. p. 107–109°.

Anal. Calcd. for $C_{29}H_{51}Cl$: C, 80.0; H, 11.8. Found: C, 79.7; H, 11.8.

Summary

A short study has been made of the action of potassium permanganate in acetic acid on cholesterol and sitosterol compounds.

The preparation and some reactions of 7-ketositosteryl chloride are reported.

STATE COLLEGE, PENNA. RECEIVED NOVEMBER 13, 1939

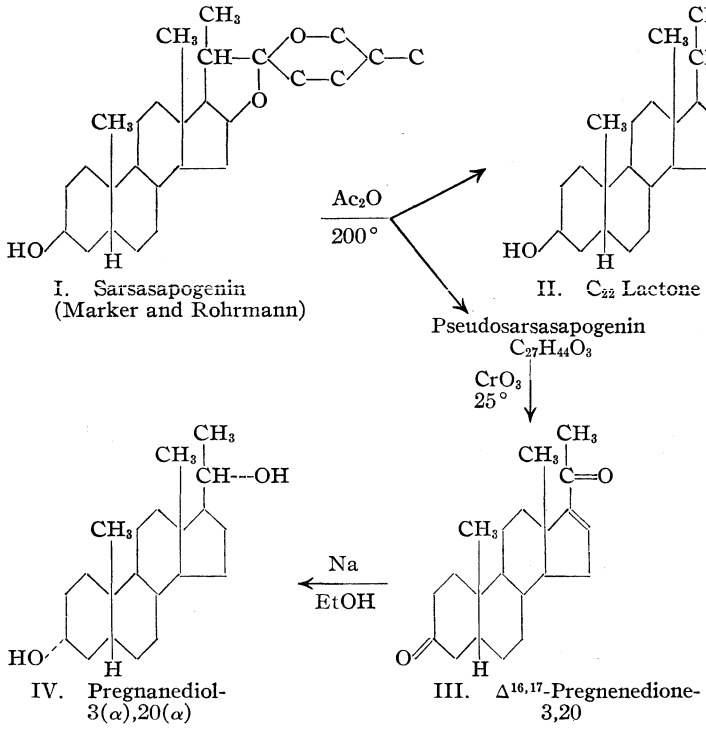
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. LXXXVIII. Pregnanediols from Sarsasapogenin

BY RUSSELL E. MARKER AND EWALD ROHRMANN

In a recent communication[1] we reported the successful conversion of sarsasapogenin to pregnanediol-3(α),20(α). The fact that this transformation can be accomplished by simple reactions in good yields makes sarsasapogenin one of the cheapest and most practical sources of pregnane derivatives from which it is possible to prepare progesterone, testosterone and desoxycorticosterone.

Sarsasapogenin (I) reacts with acetic anhydride at 200° to yield an isomeric substance, which because of its superficial resemblance to the sapogenins has been designated as pseudosarsasapogenin. While this substance undergoes many interesting reactions, the work herein reported is concerned with the preparation of the product, its oxidation to $\Delta^{16,17}$-pregnenedione-3,20 and a study of the reduction products of this latter substance.



I. Sarsasapogenin (Marker and Rohrmann)

II. C_{22} Lactone

IV. Pregnanediol-3(α),20(α)

III. $\Delta^{16,17}$-Pregnenedione-3,20

The isomerization of sarsasapogenin to pseudosarsasapogenin is also effected by acid anhydrides other than acetic anhydride. Propionic anhydride is quite effective while succinic anhydride is less effective and with phthalic anhydride no crystalline products were isolated. In the case of *n*-butyric anhydride (b. p. 198°) the isomerization was effected by simple refluxing. It is of interest that acidic products were encountered in all of these isomerization reactions. These were investigated in the acetic anhydride reaction and found to consist largely of the C_{22} hydroxy lactone (II) of sarsasapogenin.[2,3] Pseudosarsasapogenin forms a di-*p*-nitrobenzoate, indicating the presence of two hydroxyl groups.

In attempting to convert pseudosarsasapogenin to pseudosarsasapogenone by mild oxidation with chromic anhydride, an unsaturated diketone of the composition $C_{21}H_{30}O_2$, m. p. 202°, was obtained in good yields. This substance is unquestionably $\Delta^{16,17}$-pregnenedione-3,20 (III), a substance first reported by Masch[4] and referred to briefly by Butenandt, *et al.*,[5] in a recent publication concerning $\Delta^{16,17}$-*allo*-pregnenedione-3,20. The product was reported to melt at 196° and was obtained in a study of 17-bromopregnanol-3-one-20.

That our product is $\Delta^{16,17}$-pregnenedione-3,20 is shown by the fact that on reduction with sodium and ethanol it yields pregnanediol-3(α),20-(α) (IV) identical with that isolated from various urines. This reduction indicates that the ethylenic bond is conjugated with a carbonyl group. Reduction of $\Delta^{16,17}$-pregnenedione-3,20 with palladium catalyst gave pregnanedione-3,20 as would be anticipated. Catalytic hydrogenation of the unsaturated diketone with Adams catalyst in neutral medium gave pregnanediol-3(β),20(β),[6]

(1) Marker and Rohrmann, THIS JOURNAL, **61**, 3592 (1939).

(2) Askew, Farmer and Kon, *J. Chem. Soc.*, 1399 (1936).

(3) Marker and Rohrmann, THIS JOURNAL, **62**, 76 (1940).

(4) Masch, Dissertation, Danzig, 1938.

(5) Butenandt, Mamoli and Heusner, *Ber.*, **72**, 1614 (1939).

(6) Marker, Kamm and Jones, THIS JOURNAL, **59**, 1595 (1937).

pregnanediol-3(β),20(α)[7] and pregnanediol-3(α), 20(β). There appear to be appreciable amounts of other products formed in these reductions but we have not yet succeeded in isolating any product other than those of the regular pregnane series. One might expect to obtain some isopregnane compounds (*i. e.*, isomerized at C-17)[8] in these reactions.

The transformation of sarsasapogenin to $\Delta^{16,17}$-pregnenedione-3,20 definitely clears up several important points regarding the nuclear structure of sarsasapogenin, namely, the presence of a C-21 methyl group and the presence of an hydroxyl group at C-3. Inasmuch as the sarsasapogenin lactone (II) has been converted into tigogenin lactone,[9] it follows that the nuclear structure of tigogenin differs only in the configuration at C-5.

We wish to thank Parke, Davis and Company for their generous help and assistance in the various phases of this work.

Experimental Part[10]

Reaction of Sarsasapogenin Acetate with Acid Anhydrides. (a) **Acetic and Propionic Anhydrides.**—A mixture of 8 g. of sarsasapogenin acetate and 30 cc. of acetic anhydride was heated in a bomb tube at 195–200° for ten hours. The acetic anhydride was evaporated *in vacuo* and the residual sirup hydrolyzed with ethanolic potassium hydroxide. The alkaline solution was diluted with water and the precipitated solid taken up in ether. The ether was evaporated to a small volume and the white crystals collected, washed with ether and recrystallized from ethyl acetate to give white needles, m. p. 171–173°; yield 70%.

Anal. Calcd. for $C_{27}H_{44}O_3$: C, 77.8; H, 10.6; mol. wt., 416. Found: C, 77.8, 77.9; H, 10.6, 10.5; mol. wt. (Rast), 440.

The product gave a **di-*p*-nitrobenzoate** which crystallized rather poorly from acetone as pale yellow crystals, m. p. 156.5–159°.

Anal. Calcd. for $C_{41}H_{50}O_9N_2$: C, 68.9; H, 7.1. Found: C, 68.7, 68.9; H, 6.9, 7.0.

Attempts to prepare a crystalline acetate with boiling acetic anhydride were unsuccessful.

The aqueous alkaline layer from the above hydrolysis was acidified with hydrochloric acid and the mixture extracted with ether. The ethereal extract was washed with water, the ether evaporated and the residual material sublimed in high vacuum at 150–200°. The sublimate was crystallized from ether–pentane to give white needles, m. p. 199–201°. This gave no depression in melting point with an authentic sample of sarsasapogenin lactone, m. p. 199–200°.

Anal. Calcd. for $C_{22}H_{34}O_3$: C, 76.25; H, 9.9. Found: C, 76.4; H, 9.9.

With boiling acetic anhydride this yielded an **acetate** which was crystallized from ether–pentane as white needles, m. p. 184–185°. This gave no depression in melting point with an authentic sample of sarsasapogenin lactone acetate, m. p. 184.5–185.5°.

Anal. Calcd. for $C_{24}H_{36}O_4$: C, 74.15; H, 9.3. Found: C, 74.3; H, 9.4.

When sarsasapogenin acetate was treated with propionic anhydride as described for acetic anhydride, a good yield of pseudosarsasapogenin, m. p. 169–171°, was obtained.

When sarsasapogenin acetate (2 g.) was heated in a bomb tube with glacial acetic acid (20 cc.) at 210° for seven hours the only product which could be isolated crystalline was a small amount of sarsasapogenin (after hydrolysis).

(b) **Succinic Anhydride.**—A mixture of 2 g. of sarsasapogenin acetate and 12 g. of succinic anhydride was heated in a bomb tube at 195–200° for ten hours. The brown colored solid reaction mixture was refluxed for thirty minutes with an excess of ethanolic potassium hydroxide. The mixture was diluted with water and the precipitated solid taken up in ether. The ether was evaporated and the residual crystalline solid was treated with Norite and crystallized from ethyl acetate–acetone to give white needles, m. p. 169–172°. This gave no depression with the product obtained above, m. p. 171–173° obtained with acetic anhydride. A similar reaction using phthalic anhydride gave only non-crystalline products.

(c) **With *n*-Butyric Anhydride.**—A solution of 4 g. of sarsasapogenin acetate and 30 cc. of *n*-butyric anhydride was refluxed for eight hours. The *n*-butyric anhydride was evaporated *in vacuo* and the residual sirup hydrolyzed with ethanolic potassium hydroxide. The product was crystallized from ether–acetone as white needles, m. p. 170–173°. This gave no depression with a sample of pseudosarsasapogenin prepared above, m. p. 171–173°.

$\Delta^{16,17}$-Pregnenedione-3,20 from Pseudosarsasapogenin.—To a solution of 1 g. of pseudosarsasapogenin in 30 cc. of acetic acid was added a solution of 1.0 g. of chromic anhydride in 10 cc. of 80% acetic acid. After standing at room temperature for one hour the solution was diluted with water and the precipitate taken up in ether. The ethereal solution was washed with water and 3% sodium hydroxide solution. Evaporation of the ether gave a solid which was crystallized from acetone as large white plates, m. p. 200–202°. This substance is $\Delta^{16,17}$-pregnenedione-3,20. The yield varied from 50 to 70% in different preparations.

Anal. Calcd. for $C_{21}H_{30}O_2$: C, 80.2; H, 9.6. Found: C, 80.0, 80.1; H, 9.4, 9.6.

With semicarbazide acetate this gave a **semicarbazone** which crystallized from ethanol as white crystals, m. p. 310° dec.

Anal. Calcd. for $C_{23}H_{36}O_2N_6$: C, 64.4; H, 8.5. Found: C, 64.2; H, 8.6.

The acidic fraction from the oxidation gave a product which crystallized from ether–pentane as small white crystals, m. p. 234–237°. This gave no depression with a sample of 3-keto-*etio*-bilianic acid, m. p. 235–238°.

(7) Marker, Kamm, Wittle, Oakwood, Lawson and Laucius, THIS JOURNAL, **59**, 2291 (1937).

(8) Butenandt and Mamoli, *Ber.*, **68**, 1847 (1935).

(9) Marker and Rohrmann, THIS JOURNAL, **61**, 1291 (1939).

(10) Microanalyses by Dr. John R. Adams, Jr., of this Laboratory.

Anal. Calcd. for $C_{19}H_{28}O_5$: C, 67.8; H, 8.4. Found: C, 67.5; H, 8.5.

Reduction of $\Delta^{16,17}$-Pregnenedione-3,20. (a) With Sodium and Ethanol.—To a boiling solution of 300 mg. of $\Delta^{16,17}$-pregnenedione-3,20 in 100 cc. of absolute ethanol was added 7 g. of sodium over a period of seventy-five minutes. The solution was diluted with water and the precipitated solid taken up with ether. The ethereal extract was washed well with water and the ether evaporated until crystals began to separate. These were collected, washed with ether and crystallized from acetone as small white crystals, m. p. 236–239°. This gave no depression with an authentic sample of pregnanediol-3(α),20(α), m. p. 237–239°. The yield was 250 mg.

Anal. Calcd. for $C_{21}H_{36}O_2$: C, 78.8; H, 11.3. Found: C, 78.7; H, 11.3.

With boiling acetic anhydride this gave a **diacetate** which crystallized from methanol as small white plates, m. p. 177–179°. This gave no depression with a sample of the diacetate of pregnanediol-3(α),20(α), m. p. 177–179°.

Anal. Calcd. for $C_{25}H_{40}O_4$: C, 74.2; H, 10.0. Found: C, 74.2; H, 10.0.

(b) With Adams Catalyst.—A mixture of 700 mg. of $\Delta^{16,17}$-pregnenedione-3,20, 120 cc. of absolute ethanol and 400 mg. of Adams catalyst was shaken with hydrogen at 3 atm. pressure at room temperature for fifteen hours. The catalyst was removed and the filtrate evaporated to a volume of about 20 cc. To this hot solution was added a hot solution of 1 g. of digitonin in 50 cc. of 90% ethanol. After standing for two hours at room temperature the digitonide was filtered, washed and dried.

The filtrate containing the *epi*-fraction was evaporated *in vacuo* to a volume of about 10 cc. After the addition of 150 cc. of ether the mixture was filtered and the filtrate evaporated. The residue was crystallized from ethanol to give small, compact, white crystals, m. p. 232–234°. The mixture with a sample of pregnanediol-3(α),20(β), m. p. 231°, melted at 231–234°.

Anal. Calcd. for $C_{21}H_{36}O_2$: C, 78.8; H, 11.3. Found: C, 78.7; H, 11.3.

With hot acetic anhydride the product yielded a diacetate which crystallized from aqueous ethanol as white needles, m. p. 108–109.5°. This gave no depression with a sample of the diacetate of pregnanediol-3(α),20(β), m. p. 109–110°.

Anal. Calcd. for $C_{25}H_{40}O_4$: C, 74.2; H, 10.0. Found: C, 75.4; H, 9.9.

The digitonide (750 mg.) was dissolved in 10 cc. of pyridine and heated at 90° for one hour. The solution was diluted with ether and the turbid mixture filtered. The pyridine was removed from the filtrate with dilute hydrochloric acid and the ether evaporated. After treatment with Norite the product was crystallized from aqueous ethanol as compact white crystals, m. p. 173–175°. This gave no depression with an authentic sample of pregnanediol-3(β),20(β), m. p. 174–176°.

Anal. Calcd. for $C_{21}H_{36}O_2$: C, 78.8; H, 11.3. Found: C, 78.5; H, 11.2.

The first mother liquor from the beta-sterol fraction was freed from solvent and acetylated with boiling acetic anhydride. After repeated crystallization from aqueous ethanol a product was obtained as white needles, m. p 138–140°. This gave no depression with a sample of the diacetate of pregnanediol-3(β),20(α), m. p. 141°.

Anal. Calcd. for $C_{25}H_{40}O_4$: C, 74.2; H, 10.0. Found: C, 74.4; H, 9.9.

(c) With Palladium.—A mixture of 250 mg. of $\Delta^{16,17}$-pregnenedione-3,20, 120 cc. of absolute ethanol and 1 g. of palladium–barium sulfate catalyst was shaken with hydrogen at 1 atm. pressure at room temperature for ninety minutes. The catalyst was removed and the solvent distilled *in vacuo*. The residue was crystallized from aqueous ethanol to give compact white crystals, m. p. 117–119°. This gave no depression with an authentic sample of pregnanedione-3,20, m. p. 117.5–119°.

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.7; H, 10.2. Found: C, 79.5; H, 10.1.

With semicarbazide acetate in the usual manner the substance gave a **di-semicarbazone** which crystallized from aqueous ethanol as white crystals, m. p. 244° dec.

Anal. Calcd. for $C_{23}H_{40}O_2N_6$: C, 63.8; H, 9.3. Found: C, 63.6; H, 9.2.

Summary

The isomerization of sarsasapogenin to pseudosarsasapogenin with acid anhydrides is described.

Pseudosarsasapogenin on mild oxidation with chromic anhydride is converted into $\Delta^{16,17}$-pregnenedione-3,20.

The reduction products of $\Delta^{16,17}$-pregnenedione-3,20 have been studied.

STATE COLLEGE, PENNA. RECEIVED DECEMBER 6, 1939

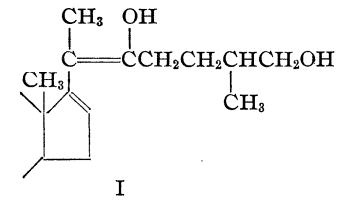
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. LXXXIX. Reactions of Pseudosarsasapogenin

BY RUSSELL E. MARKER AND EWALD ROHRMANN

Of the many reactions which are peculiar to sarsasapogenin,[1] probably the most interesting and certainly the most significant from the standpoint of elucidating the relationship existing between this sapogenin and the sterols is the isomerization by acid anhydrides[2] to yield pseudosarsasapogenin. This isomeric substance is of great significance because of the ease with which it is converted into $\Delta^{16,17}$-pregnenedione-3,20 by mild oxidation with chromic anhydride.

All of our evidence, which is derived largely from oxidation and reduction studies seems to indicate that pseudosarsasapogenin is best represented by structure I or possibly by one of its equivalents, II or III.



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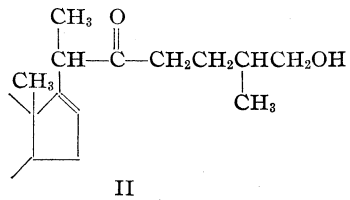
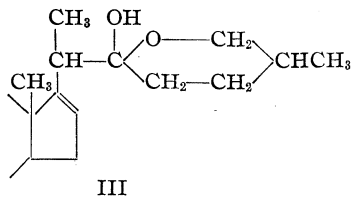


II



III

Pseudosarsasapogenin (suggested formulations)

As discussed in previous work,[2] pseudosarsasapogenin upon mild oxidation with chromic anhydride yields $\Delta^{16,17}$-pregnenedione-3,20 (VII) and 3-keto-*etio*-bilianic acid. Pseudosarsasapogenin upon acetylation with hot acetic anhydride gives a non-crystalline product which upon mild oxidation with chromic anhydride yields $\Delta^{16,17}$-pregnenol-3(β)-one-20 acetate (VI) and 3(β)-hydroxy-*etio*-bilianic acid (V).[3] Further oxidation of $\Delta^{16,17}$-pregnenol-3(β)-one-20 acetate yielded 3(β)-hydroxy-*etio*-bilianic acid. The oxidation of acetylated pseudosarsasapogenin at elevated temperatures gives largely the bilianic acid. Neither pseudosarsasapogenin nor the acetylated product reacts with semicarbazide acetate under the usual conditions.

Pseudosarsasapogenin upon hydrogenation with Adams catalyst in acetic acid, ethanol or acidic ethanol yields dihydropseudosarsasapogenin. This substance yields a diacetate and a di-*p*-nitrobenzoate. It is of interest that acetylated pseudosarsasapogenin upon hydrogenation with Adams catalyst yields a substance identical with the diacetate of dihydropseudosarsasapogenin. This fact does not appear to be in accordance with structure III for pseudosarsasapogenin.

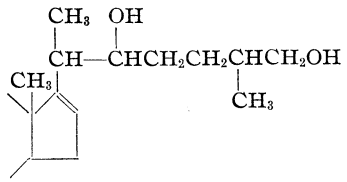
Dihydropseudosarsasapogenin upon oxidation at 15° with chromic anhydride readily yields $\Delta^{16,17}$-pregnenedione-3,20 and a diketo acid (VIII) of the composition $C_{27}H_{42}O_4$. This acid forms a disemicarbazone and a methyl ester and on further oxidation with chromic anhydride yields $\Delta^{16,17}$-pregnenedione-3,20. The fact that this acid readily forms a disemicarbazone while pseudosarsasapogenin does not react with semicarbazide acetate does not seem to be in accordance with structure II for pseudosarsasapogenin.

Dihydropseudosarsasapogenin diacetate upon oxidation with chromic anhydride at 90° gives a good yield of 3-(β)-hydroxy-*etio*-bilianic acid. No neutral product was obtained. Oxidation of the diacetate at 25–30° yields 3-(β)-hydroxy-*etio*-bilianic acid and a neutral fraction consisting of $\Delta^{16,17}$-pregnenol-3(β)-one-20 acetate and a mixture of neutral products which were not separated. When the diacetate was oxidized at 15° it was recovered largely unchanged which is in contrast to the analogous oxidation of the free dihydro compound. Evidently the presence of an acetoxy group at C-27 hinders the oxidation of a reactive group at C-22.

The ease of formation of $\Delta^{16,17}$-pregnenedione-3,20 from both pseudosarsasapogenin and dihydropseudosarsasapogenin suggests that both of these substances contain a non-reducible ethylenic linkage at C-16, C-17 and a reactive group at C-22.

(1) Marker and Rohrmann, THIS JOURNAL, **61**, 846 (1939).
(2) Marker and Rohrmann, *ibid.*, **62**, 518 (1940).
(3) Marker and Rohrmann, *ibid.*, **61**, 2722 (1939).

The occurrence of non-reducible ethylenic linkages in sterol compounds is of course not unusual, apocholic acid[4] being a notable example. Inspection of the three suggested formulations (I, II, and III) for pseudosarsasapogenin indicates that all of these should yield the same dihydro compound on reduction and that dihydropseudosarsasapogenin is probably best represented by structure IV.

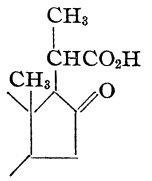


IV. Dihydropseudosarsasapogenin (suggested)

It seems peculiar that pseudosarsasapogenin and dihydropseudosarsasapogenin form *bis* rather than the expected *tris* derivatives. This is possibly due to hindrance at the C-22 position.

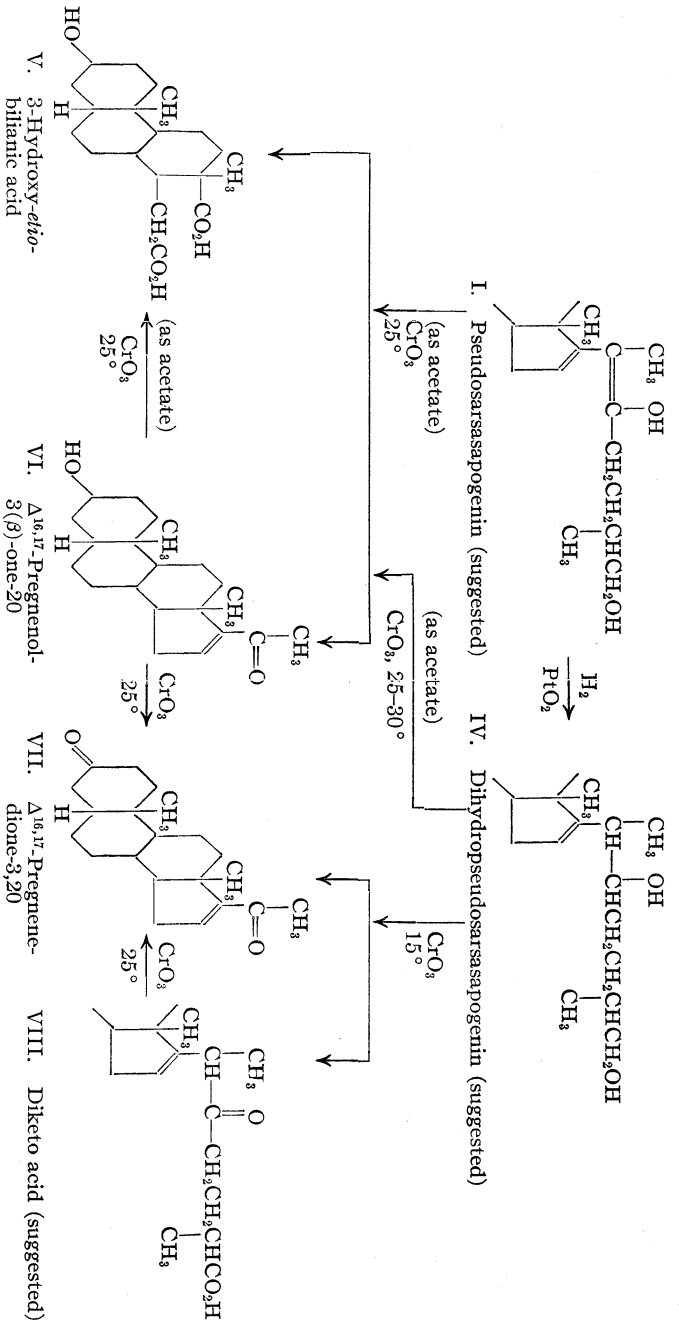
It is of interest that in the oxidation of the diacetates of pseudosarsasapogenin and dihydropseudosarsasapogenin an appreciable amount of the 3-(β)-hydroxy-*etio*-bilianic acid apparently is formed as the anhydride and occurs as such in the neutral fraction of the oxidations. This is in accordance with observations on the analogous oxidation of *allo*-pregnanetriol-3,16,20 to 3-keto-*etio-allo*-bilianic acid.[5]

In all of the oxidation studies of the pseudo and dihydropseudo diacetates it is significant that none of the C_{22} keto acid[6] (IX) was encountered. This is in accordance with suggested structures of the pseudo and dihydropseudo compounds.



IX. C_{22} Keto Acid

The $\Delta^{16,17}$-pregnenol-3(β)-one-20 acetate obtained in the oxidation of acetylated pseudosarsasapogenin and dihydropseudosarsasapogenin was characterized by a study of its reduction products. With sodium and ethanol it yields pregnanediol-3-(β),20(α). Hydrogenation with Adams catalyst and subsequent oxidation with chromic anhydride yielded the acetate of pregnanol-3(β)-one-20. These transformations are in accordance with previous postulations concerning



the configuration of the C-3 hydroxyl group in sarsasapogenin.[7,8] $\Delta^{16,17}$-Pregnenol-3(β)-one-20 acetate on alkaline hydrolysis and subsequent mild oxidation with chromic anhydride readily yields $\Delta^{16,17}$-pregnenedione-3,20.

(4) Wieland and Dane, *Z. physiol. Chem.*, **212**, 263 (1932).
(5) Marker and Wittle, THIS JOURNAL, **61**, 855 (1939).
(6) Marker and Rohrmann, *ibid.*, **61**, 1285 (1939).
(7) Farmer and Kon, *J. Chem. Soc.*, 414 (1937).
(8) Marker and Rohrmann, THIS JOURNAL, **61**, 943 (1939).

We wish to thank Parke, Davis and Company for their generous help and assistance in the various phases of this work.

Experimental Part[9]

Pseudosarsasapogenin.—This was prepared as described in previous work. Pseudosarsasapogenin is very readily oxidized by selenium dioxide, a reaction which we have not investigated further as yet. It reacts readily with bromine but at present we have not isolated any definite crystalline products from this reaction. Pseudosarsasapogenin does not react with semicarbazide acetate under the usual conditions. The acetylated product is likewise unreactive.

Oxidation of Acetylated Pseudosarsasapogenin. (a) at 90°.—Pseudosarsasapogenin (2.5 g.) was refluxed for thirty minutes with 15 cc. of acetic anhydride. The acetic anhydride was evaporated *in vacuo* and the residual sirup dissolved in 60 cc. of acetic acid. The solution was heated on a steam-bath while 5 g. of chromic anhydride in 50 cc. of 80% acetic acid was added over a period of one hour. Ethanol (10 cc.) was then added and the solution evaporated *in vacuo* to a volume of about 50 cc. Water was added and the precipitated solid taken up in ether and the ethereal extract washed with 3% sodium hydroxide solution and water. The sodium hydroxide washing was heated on the steam-bath for twenty minutes to complete hydrolysis. The solution was then cooled, acidified with hydrochloric acid and the precipitated solid was taken up in ether and crystallized from chloroform to give 600 mg. of white crystals, m. p. 221–223°. This gave no depression with a sample of 3-hydroxy-*etio*-bilianic acid, m. p. 220–222°.

Anal. Calcd. for $C_{19}H_{30}O_5$: C, 67.4; H, 8.9. Found: C, 67.3; H, 8.9.

With hot acetic anhydride the acid gave an *acetate anhydride* which crystallized from aqueous acetone as flat white needles, m. p. 204.5–206.5°. This gave no depression with a sample of the acetate anhydride of 3-hydroxy-*etio*-bilianic acid, m. p. 205–207°.

Anal. Calcd. for $C_{21}H_{30}O_5$: C, 69.6; H, 8.3. Found: C, 69.5; H, 8.3.

The ethereal solution containing the material not extracted with alkali was evaporated and the residual sirup hydrolyzed with ethanolic potassium hydroxide. Water and dilute hydrochloric acid were added and the precipitate taken up in ether and crystallized from ether to give 30 mg. of small white crystals, m. p. 284–287°. This product has not been investigated further.

Anal. Calcd. for $C_{22}H_{34}O_4$: C, 72.9; H, 9.5; neut. equiv., 362. Found: C, 73.1, 73.1; H, 9.3, 9.5; neut. equiv., 358.

The filtrate from this acid was evaporated and crystallized from chloroform to give white crystals, m. p. 220–222°. This gave no depression with a sample of 3-hydroxy-*etio*-bilianic acid, m. p. 220–222°.

(b) At Room Temperature.—Pseudosarsasapogenin (3 g.) was treated with acetic anhydride as before and the residual sirup dissolved in 100 cc. of acetic acid. To this solution was added 3 g. of chromic anhydride in 30 cc. of 80% acetic acid. The mixture was allowed to stand at room temperature for one hour. Water was added and the precipitated solid taken up in ether. The ethereal extract was washed with water and 3% sodium hydroxide solution.

The alkaline water layer was acidified with hydrochloric acid and the precipitated acid was taken up in ether and crystallized from chloroform to give white crystals, m. p. 220–222°. This gave no depression with a sample of 3-hydroxy-*etio*-bilianic acid, m. p. 220–222°.

Anal. Calcd. for $C_{19}H_{30}O_5$: C, 67.4; H, 8.9. Found: C, 67.0; H, 8.8.

The neutral fraction was crystallized from aqueous methanol to give white plates, m. p. 144–146°. This product is the *acetate* of $\Delta^{16,17}$-pregnenol-3(β)-one-20.

Anal. Calcd. for $C_{23}H_{34}O_3$: C, 77.0; H, 9.6. Found: C, 76.8, 77.0; H, 9.5, 9.4.

When treated with semicarbazide acetate under the usual conditions the product gave a *semicarbazone* which crystallized from aqueous ethanol, m. p. 250–252°.

Anal. Calcd. for $C_{24}H_{37}O_3N_3$: C, 69.35; H, 9.0. Found: C, 69.2; H, 8.8.

The filtrate remaining after removal of most of the $\Delta^{16,17}$-pregnenol-3(β)-one-20 acetate upon hydrolysis with ethanolic potassium hydroxide yielded an acid which crystallized from chloroform as white crystals, m. p. 219–222°. This gave no depression with a sample of 3-hydroxy-*etio*-bilianic acid, m. p. 220–222°. This indicates that some of the 3-hydroxy-*etio*-bilianic acid is present in the oxidation mixture as the anhydride.

3-(β)-Hydroxy-*etio*-bilianic Acid from $\Delta^{16,17}$-Pregnenol-3(β)-one-20 Acetate.—The acetate of $\Delta^{16,17}$-pregnenol-3(β)-one-20 was oxidized in acetic acid solution with chromic anhydride for sixteen hours at room temperature. The acid fraction after alkaline hydrolysis was crystallized from chloroform to give small white plates, m. p. 221–223°. This gave no depression with a sample of 3(β)-hydroxy-*etio*-bilianic acid, m. p. 220–222°.

Anal. Calcd. for $C_{19}H_{30}O_5$: C, 67.4; H, 8.9. Found: C, 67.3; H, 8.9.

$\Delta^{16,17}$-Pregnenedione-3,20 from $\Delta^{16,17}$-Pregnenol-3(β)-one-20 Acetate.—The acetate of $\Delta^{16,17}$-pregnenol-3(β)-one-20 was hydrolyzed by refluxing for ten minutes with ethanolic potassium hydroxide solution. The product was crystallized from ethanol as white needles, m. p. 207–209°. The product evidently contains a molecule of ethanol, as indicated by the analysis.

Anal. Calcd. for $C_{23}H_{38}O_3$: C, 76.2; H, 10.6. Found: C, 76.2, 76.2; H, 10.6, 10.6.

When treated with semicarbazide acetate under the usual conditions the product gave a *semicarbazone* which crystallized from ethanol, m. p. 240° dec.

Anal. Calcd. for $C_{22}H_{35}O_2N_3$: C, 70.7; H, 9.5. Found: C, 70.6; H, 9.5.

Treatment with boiling acetic anhydride gave the acetate, m. p. 143–145°, which gave no depression with the original acetate, m. p. 144–146°.

To a solution of 150 mg. of the hydrolyzed product in 10 cc. of acetic acid was added 100 mg. of chromic an-

(9) Microanalyses by Dr. John R. Adams, Jr., of this Laboratory.

hydride in 5 cc. of 80% acetic acid. After standing for twenty minutes at room temperature, water was added and the products taken up in ether, and washed free from acid with sodium hydroxide. The neutral material was crystallized from acetone to give white plates, m. p. 199–201°. This gave no depression with a sample of $\Delta^{16,17}$-pregnenedione-3,20, m. p. 200–202°.

Anal. Calcd. for $C_{21}H_{30}O_2$: C, 80.2; H, 9.6. Found: C, 80.3; H, 9.5.

Reduction of $\Delta^{16,17}$-Pregnenol-3(β)-one-20 Acetate. (a) With Sodium and Ethanol.—To a boiling solution of 500 mg. of the acetate of $\Delta^{16,17}$-pregnenol-3(β)-one-20 in 100 cc. of absolute ethanol was added 6 g. of sodium over a period of one hour. The solution was diluted with water and extracted with ether. The product was crystallized from ether and finally from acetone to give compact white crystals, m. p. 180–183°. This gave no depression with a sample of pregnanediol-3(β),20(α), m. p. 182–184°.

Acetylation with hot acetic anhydride yielded an acetate which crystallized from aqueous ethanol as white needles, m. p. 138–140°. This gave no depression with a sample of the diacetate of pregnanediol-3(β),20(α), m. p. 139–141°.

(b) **With Adams Catalyst.**—A mixture of 300 mg. of $\Delta^{16,17}$-pregnenol-3(β)-one-20 acetate, 300 mg. of Adams catalyst and 120 cc. of absolute ethanol was shaken with hydrogen at 3 atm. at room temperature for three hours. No definite crystalline product was isolated. The entire product was oxidized in acetic acid (20 cc.) at room temperature with 300 mg. of chromic anhydride for one hour. The product was crystallized from aqueous ethanol as compact white crystals, m. p. 118–119.5°. This gave no depression with a sample of pregnanedione-3,20, m. p. 118–120°.

Anal. Calcd. for $C_{21}H_{32}O_2$: C, 79.7; H, 10.2. Found: C, 79.6; H, 10.2.

In another experiment the acetate of $\Delta^{16,17}$-pregnenol-3-(β)-one-20 (800 mg.) was reduced as above. The catalyst and solvent were removed and the residue dissolved in 25 cc. of acetic acid. To this solution was added a solution of 500 mg. of chromic anhydride in 10 cc. of 80% acetic acid. After standing for thirty minutes at room temperature, water was added and the precipitated solid taken up in ether and freed from acids by washing with water and sodium carbonate solution. The product was crystallized from aqueous ethanol as thick white needles, m. p. 116–118°. This gave no depression with a sample of pregnanol-3(β)-one-20 acetate, m. p. 118–120°.

Anal. Calcd. for $C_{23}H_{36}O_3$: C, 76.6; H, 10.1. Found: C, 76.6; H, 10.1.

Dihydropseudosarsasapogenin.—A mixture of 1 g. of pseudosarsasapogenin, 500 mg. of Adams catalyst and 120 cc. of acetic acid was shaken with hydrogen at 3 atm. at room temperature for fifteen hours. The catalyst was filtered and the filtrate evaporated *in vacuo*. The residual sirup was hydrolyzed with ethanolic potassium hydroxide and crystallized from acetone as small white plates, m. p. 168–170°. The mixture with the original pseudosarsasapogenin (m. p. 171–173°) melted at 150–155° and that with dihydrosarsasapogenin (m. p. 165–166°) at 154–162°. Similar results were obtained when the reduction was carried out in ethanol or in ethanol acidified with hydrochloric acid.

Anal. Calcd. for $C_{27}H_{46}O_3$: C, 77.4; H, 11.1. Found: C, 77.3; H, 10.9.

With boiling acetic anhydride the substance gave a **diacetate** which crystallized from pentane as white needles, m. p. 95–97°.

Anal. Calcd. for $C_{31}H_{50}O_5$: C, 74.1; H, 10.0. Found: C, 74.0, 74.1; H, 9.9, 10.0.

With *p*-nitrobenzoyl chloride in pyridine at 60° a **di-*p*-nitrobenzoate** was formed which crystallized from ethyl acetate as white needles, m. p. 196–197.5°.

Anal. Calcd. for $C_{41}H_{52}O_9N_2$: C, 68.7; H, 7.3. Found: C, 68.7; H, 7.1.

Dihydropseudosarsasapogenin does not react noticeably with selenium dioxide. It absorbs bromine slowly in acetic acid solution.

Reduction of Acetylated Pseudosarsasapogenin.—Pseudosarsasapogenin (2 g.) was refluxed with an excess of acetic anhydride and the anhydride evaporated *in vacuo*. The residual sirup was reëvaporated several times with acetic acid and finally dissolved in a mixture of 50 cc. of acetic acid and 75 cc. of absolute ethanol. The solution was shaken with 1 g. of Adams catalyst and hydrogen at 3 atm. pressure at room temperature for twelve hours. The catalyst was removed and the acetic acid evaporated *in vacuo*. The residue was crystallized from pentane as white needles, m. p. 95–97°. This gave no depression with a sample of the diacetate of dihydropseudosarsasapogenin, m. p. 95–97°.

Anal. Calcd. for $C_{31}H_{50}O_5$: C, 74.1; H, 10.0. Found: C, 74.2; H, 9.9.

Oxidation of Dihydropseudosarsasapogenin.—To a solution of 4 g. of dihydropseudosarsasapogenin in 200 cc. of acetic acid was added 6 g. of chromic anhydride in 50 cc. of 80% acetic acid. After standing at 15–18° for ninety minutes a large volume of water was added and the mixture shaken with ether. The ethereal solution was washed with water and 3% sodium hydroxide solution. The aqueous alkaline layer was acidified with hydrochloric acid and the precipitated acid taken up with ether and crystallized from acetone as small white needles, m. p. 233–236°. This is a diketo acid (VIII).

Anal. Calcd. for $C_{27}H_{42}O_4$: C, 75.3; H, 9.6. Found: C, 75.3, 75.1; H, 9.4, 9.6.

With semicarbazide acetate in the usual manner, the acid gave a **disemicarbazone** which crystallized from ethanol as small white crystals, m. p. 209° dec.

Anal. Calcd. for $C_{29}H_{48}O_4N_6$: C, 63.9; H, 8.9. Found: C, 63.7; H, 8.5.

With diazomethane in ether–methanol solution the acid gave a **methyl ester** which crystallized from pentane as white needles, m. p. 85–87°.

Anal. Calcd. for $C_{28}H_{44}O_4$: C, 75.6; H, 10.0. Found: C, 75.4; H, 9.8.

The ethereal extract containing the neutral fraction was evaporated and the residue crystallized from acetone to give $\Delta^{16,17}$-pregnenedione-3,20 as white plates, m. p. 199–201°. This gave no depression with an authentic sample of $\Delta^{16,17}$-pregnenedione-3,20, m. p. 200–202°.

Anal. Calcd. for $C_{21}H_{30}O_2$: C, 80.2; H, 9.6. Found: C, 80.3; H, 9.6.

$\Delta^{16,17}$-Pregnenedione-3,20 from Diketo Acid (VIII).—To a solution of 250 mg. of diketo acid in 20 cc. of acetic acid was added a solution of 250 mg. of chromic anhydride in 5 cc. of 80% acetic acid. After standing at 25° for seventy-five minutes water was added and the precipitated solid taken up in ether and washed with water and potassium hydroxide solution. Evaporation of the ether gave a product which crystallized from acetone as white plates, m. p. 199–201°. This gave no depression with a sample of $\Delta^{16,17}$-pregnenedione-3,20, m. p. 200–202°.

Anal. Calcd. for $C_{21}H_{30}O_2$: C, 80.2; H, 9.6. Found: C, 80.1; H, 9.5.

The acidic fraction yielded some unchanged diketo acid.

Oxidation of Diacetate of Dihydropseudosarsasapogenin. (a) **At 90°.**—To a solution of 4 g. of dihydropseudosarsasapogenin diacetate in 100 cc. of acetic acid heated at 90° was added with stirring over a course of one hour 8 g. of chromic anhydride in 40 cc. of 80% acetic acid. The mixture was heated for an additional hour after which ethanol was added and the mixture evaporated *in vacuo* to a volume of about 75 cc. Water was added and the precipitated solids taken up in ether. The ethereal solution was washed with water and 3% sodium hydroxide. The aqueous alkaline layer was heated on the steam-bath for twenty minutes and the acids precipitated with hydrochloric acid. The acidic product was crystallized from chloroform as white crystals, m. p. 220–223°. This gave no depression with an authentic sample of 3-hydroxy-*etio*-bilianic acid, m. p. 220–222°. The yield was 1.4 g.

Anal. Calcd. for $C_{19}H_{30}O_5$: C, 67.4; H, 8.9. Found: C, 67.3; H, 8.8.

Hydrolysis of the "neutral fraction" gave only additional amounts of the above bilianic acid. There was no noticeable neutral material.

(b) **At Room Temperature.**—To a solution of 2 g. of dihydropseudosarsasapogenin diacetate in 100 cc. of acetic acid was added 2 g. of chromic anhydride in 20 cc. of 80% acetic acid. After standing at 25–28° for two hours, water was added and the precipitated solid taken up in ether. The ethereal solution was washed with water and 3% sodium hydroxide solution. The acidic fraction was hydrolyzed and worked up as under (a). The product crystallized from chloroform as small white crystals, m. p. 219–222°. This gave no depression with a sample of 3-hydroxy-*etio*-bilianic acid, m. p. 220–222°.

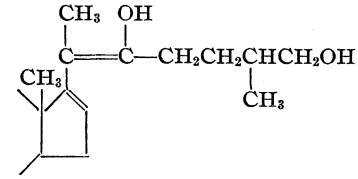
The neutral fraction was crystallized from aqueous methanol to give white plates, m. p. 143–145°. This gave no depression with a sample of pregnenol-3-(β)-one-20 acetate, m. p. 144–146°.

Anal. Calcd. for $C_{23}H_{34}O_3$: C, 77.0; H, 9.6. Found: C, 76.7; H, 9.4.

When the reaction was carried out below 20° the only neutral product which could be isolated (after alkaline hydrolysis) was dihydropseudosarsasapogenin.

Summary

Evidence has been presented indicating that pseudosarsasapogenin probably has the structure (or one of its equivalents)



STATE COLLEGE, PENNA. RECEIVED DECEMBER 26, 1939

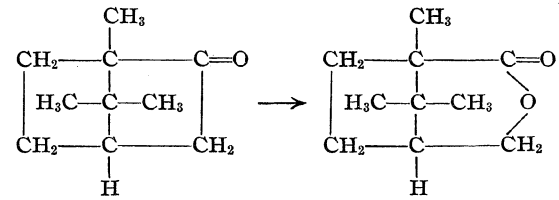
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. XC. Oxidation Products of Sarsasapogenin. Pregnanetriol-3,16,20

BY RUSSELL E. MARKER, EWALD ROHRMANN, HARRY M. CROOKS, EUGENE L. WITTLE, ELDON M. JONES AND D. L. TURNER

In a recent publication the conversion of sarsasapogenin to pregnane derivatives was described.[1] This degradation involved the isomerization of sarsasapogenin to pseudosarsasapogenin, the oxidation of this substance to $\Delta^{16,17}$-pregnenedione-3,20 and the subsequent reduction of this to pregnanedione-3,20 and the various pregnanediols.

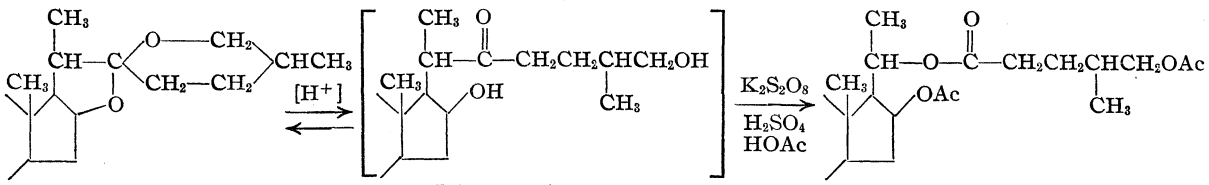
The fact that sarsasapogenin (III) appears to have a potential ketone group which is very reactive in the presence of acids[2] suggested a method of directly converting the substance to a pregnane derivative in one step, namely, by a persulfate oxidation. It is well known that persulfates in the presence of sulfuric acid readily react with polycyclic ketones to yield lactones. A typical example of this type of oxidation is the conversion of camphor (I) to α-campholide (II).[3] Ruzicka and Stoll[4] carried out similar oxidations in a lig-



I.

(1) Marker and Rohrmann, THIS JOURNAL, **62**, 518 (1940).
(2) Marker and Rohrmann, *ibid.*, **61**, 846 (1939).
(3) Baeyer and Villiger, *Ber.*, **32**, 3630 (1899).
(4) Ruzicka and Stoll, *Helv. Chim. Acta*, **11**, 1159 (1928).

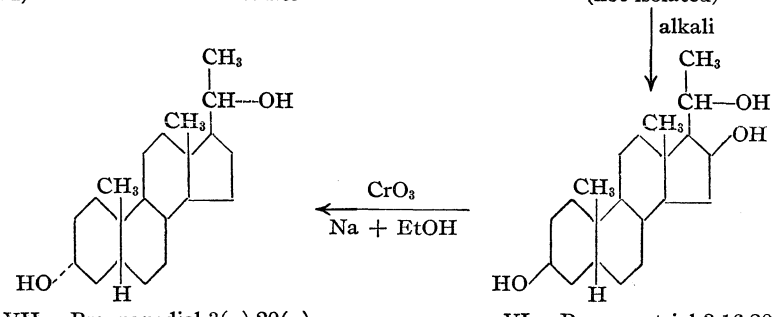
roin medium to obtain good yields of lactones. Rollett and Bratke[5] carried out the oxidations in an aqueous acetic acid medium in the presence of a small amount of sulfuric acid.



III. Sarsasapogenin (Marker and Rohrmann)

IV. Postulated intermediate

V. Ester (not isolated)



VII. Pregnanediol-3(α),20(α)

VI. Pregnanetriol-3,16,20

Using this latter procedure we have carried out the oxidation of sarsasapogenin acetate with potassium persulfate and have obtained a substance after alkaline hydrolysis of the composition $C_{21}H_{36}O_3$ (VI). This substance forms an acetate and a benzoate which appear to be *tris* derivatives. The substance contains no ketonic groups. Mild oxidation of the substance with chromic anhydride followed by removal of the acidic products with alkali and subsequent reduction of the neutral fraction with sodium and ethanol gave pregnanediol-3(α),20(α) (VII). This indicates that the original substance was pregnanetriol-3,16,20 (VI) since by a similar procedure *allo*-pregnanetriol-3,16,20 has been converted to *allo*-pregnanedione-3,20.[6,7] When the neutral fraction from the persulfate oxidation was oxidized with chromic anhydride (without prior alkaline hydrolysis), the only product which was obtained on subsequent hydrolysis was pregnanetriol-3,16,20. This indicates that all of the hydroxyl groups are esterified in the course of the oxidation.

The ease with which this conversion of sarsasapogenin to pregnanetriol-3,16,20 takes place raises many interesting questions in regards to the mechanism of the cleavage. It appears that all of the facts are in complete accordance with the ketone spiro acetal structure of the sapogenin side chain as is indicated in the suggested mechanism given in the accompanying chart. The postulated intermediates IV and V were not isolated.

epi-Sarsasapogenin acetate on oxidation with persulfate yielded a triol having the *epi* configuration at C-3. The persulfate oxidation of sarsasapogenin acetate yields an appreciable acidic fraction which we have not investigated as yet.

We wish to thank Parke, Davis and Company for their generous help and assistance in the various phases of this work.

Experimental Part[8]

Pregnanetriol-3(β),16,20 from Sarsasapogenin Acetate.—A mixture of 1 g. of sarsasapogenin acetate, 4 g. of potassium persulfate, 150 cc. of 90% acetic acid and 1 cc. of concentrated sulfuric acid was refluxed for two hours. Water was added and the precipitated solid taken up in ether and washed with water and 3% sodium hydroxide. The ether was evaporated and the residual material was hydrolyzed with ethanolic potassium hydroxide. Water was added to the alkaline solution and the precipitated solid taken up in ether and crystallized from ether–pentane as small white crystals, m. p. 223–226°. The yields varied from 20 to 40% in different runs.

Anal. Calcd. for $C_{21}H_{36}O_3$: C, 74.9; H, 10.8. Found: C, 75.0, 74.8; H, 10.6, 11.0.

With benzoyl chloride in pyridine the product gave a **benzoate** which was crystallized from methanol as white prisms, m. p. 185–187°.

Anal. Calcd. for $C_{42}H_{48}O_6$: C, 77.7; H, 7.5. Found: C, 77.9; H, 7.5.

With boiling acetic anhydride the substance gave a **triacetate** which crystallized from dilute ethanol as white crystals, m. p. 108–111°.

(5) Rollett and Bratke, *Monatsh.*, **43**, 685 (1922).

(6) Marker, Kamm, Wittle, Oakwood and Lawson, THIS JOURNAL, **60**, 1067 (1938).

(7) Marker and Wittle, *ibid.*, **61**, 855 (1939).

(8) Microanalyses by Dr. John R. Adams, Jr., of this Laboratory.

Anal. Calcd. for $C_{27}H_{42}O_6$: C, 70.1; H, 9.2. Found: C, 69.8; H, 9.1.

Pregnanetriol-3(α),16,20 from *epi*-Sarsasapogenin.—*epi*-Sarsasapogenin acetate was treated with potassium persulfate as described above. After hydrolysis with ethanolic potassium hydroxide the neutral fraction yielded a substance which crystallized from ether to give white crystals, m. p. 206–207°.

Anal. Calcd. for $C_{21}H_{36}O_3$: C, 74.9; H, 10.8. Found: C, 74.9; H, 10.7.

With benzoyl chloride in pyridine the product gave a **benzoate** which crystallized from aqueous acetone as small white needles, m. p. 153–155°.

Anal. Calcd. for $C_{42}H_{48}O_6$: C, 77.7; H, 7.5. Found: C, 77.3; H, 7.4.

Conversion of Pregnanetriol-3(β),16,20 to Pregnanediol-3(α),20(α).—To a solution of 900 mg. of pregnanetriol in 35 cc. of acetic acid was added slowly a solution of 400 mg. of chromic anhydride in 5 cc. of water and 15 cc. of acetic acid. The solution was allowed to stand at room temperature for twenty minutes and then diluted with water and the product taken up in ether. The ether solution was washed with sodium hydroxide solution and water and evaporated to dryness to give a colorless neutral oil which was dissolved in 200 cc. of boiling absolute ethanol and reduced with 10 g. of sodium. Water was then added and the neutral fraction extracted with ether. The ether solution was washed with water and evaporated to leave a yellow oily residue which was dissolved in 10 cc. of acetone and allowed to stand overnight. The product which crystallized from the solution was purified by further recrystallization from acetone to give pregnanediol-3(α),-20(α), m. p. 235–238°. It gave no depression with a sample of pregnanediol-3(α),20(α), m. p. 236–239°. It gave a depression of 20° with the original pregnanetriol.

Anal. Calcd. for $C_{21}H_{36}O_2$: C, 78.7; H, 11.3. Found: C, 78.7; H, 11.2.

Treatment with acetic anhydride gave the **diacetate of pregnanediol-3(α),20(α)**, m. p. 177–179°, which gave no depression of the melting point with the known diacetate, m. p. 178–180°.

Summary

Sarsasapogenin has been converted to pregnanetriol-3,16,20 by persulfate oxidation.

STATE COLLEGE, PENNA. RECEIVED DECEMBER 26, 1939

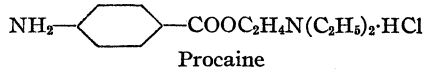
[CONTRIBUTION FROM THE LABORATORY OF G. D. SEARLE & CO., AND DEPARTMENT OF PHYSIOLOGY AND PHARMACOLOGY, UNIVERSITY OF LOUISVILLE]

Heterocyclic Local Anesthetics. Carbazole, Dibenzofuran and Dibenzothiophene Derivatives[1]

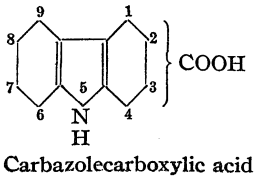
BY ROBERT R. BURTNER AND GERHARD LEHMANN

In any study of local anesthetics of the procaine type one is impressed by the fact that most of the structural variations have been focused upon the amino alcohol portion of the molecule. The effect of alkylation of the nuclear amino group has been studied, and in a few instances useful drugs have resulted, whereas the introduction of an aryl group in this position has received little or no attention.

The carbazole carboxylic acids offered a readily available group of starting materials of the latter type with the interesting variation involving the carbon–carbon bond between the two benzene nuclei.



Procaine

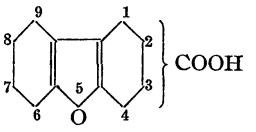


Carbazolecarboxylic acid

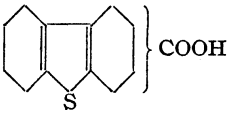
(1) Presented before the Medicinal Section of the American Chemical Society at the Baltimore Meeting, April, 1939.

Previous investigation of a series of esters of carbazole-N-(or 5)-carboxylic acid by Knoefel[2] led to some rather active compounds of low toxicity. In the present study a series of dialkylaminoalkyl esters of the isomeric carbazolecarboxylic acids was prepared with suitable variations involving the alcohol portion of the molecule as well as nuclear substituents.

Seeking to determine the effect of replacement of the heterocyclic element by oxygen and sulfur an analogous series of esters of dibenzofuran and dibenzothiophenecarboxylic acids was investigated.



Dibenzofurancarboxylic acid



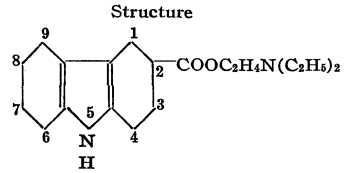
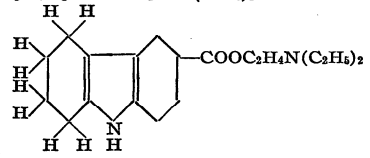
Dibenzothiophenecarboxylic acid

In order to study the effect of the carbon–carbon bond between the two benzene nuclei on the activity of compounds of this type, the correspond-

(2) Knoefel, *J. Pharmacol.*, **47**, 69 (1933).

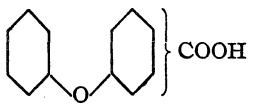
TABLE I

CARBAZOLE LOCAL ANESTHETICS

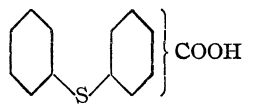
No.	Structure	Hydrochloride m. p., °C.	N analyses, % Calcd.	Obsd.	Min. duration of corneal anesthesia in rabbits[a] 0.1%	0.5%	1.0%	Av. subcutaneous toxicity in mice g./kg.[c]
1		195	8.1	8.3	14[e]+	27++		0.4[d]
2	3-$COOC_2H_4N(C_2H_5)_2$	127 (base)	8.97	8.91	10+	30++		.5
3	4-$COOC_2H_4N(C_2H_5)_2$	Viscous oil	Cl, 10.22	10.38	0		8−	2.0
4	2-$COOC_2H_4N(n\text{-}C_4H_9)_2$	187	6.95	6.99	7−	14−		1.0
5	2-$COOCH_2CH_2CH_2N(C_2H_5)_2$	169	7.96	7.77	17+	36++		0.15
6	5-C_2H_5 2-$COOC_2H_4N(C_2H_5)_2$	204	7.48	7.6	4[e]−		7+	.7
7	5-n-C_4H_9 2-$COOC_2H_4N(C_2H_5)_2$	Glass (sulfate)	6.74	6.5			0[b]	3.5
8	5-C_2H_5 3-$COOC_2H_4N(C_2H_5)_2$	174	7.48	7.40	36[e]+	43++		0.5[d]
9	5-n-C_4H_9 3-$COOC_2H_4N(C_2H_5)_2$	Viscous oil	Cl, 8.79	8.91				
10	8-NH_2 3-$COOC_2H_4N(C_2H_5)_2$	146–147 (base)	12.5	12.7				
11		234	8.0	8.0	12+	29++		0.08

[a] 0 = none, − = weak, + = full, ++ = deep. A 1% cocaine solution gave deep anesthesia lasting fifteen minutes. [b] A 5% solution of this compound gave weak anesthesia for three minutes. [c] Dose at which 50% of animals died. The fatal dose of cocaine is 0.08 g./kg. [d] Intravenous M. L. D. in rabbits = 20 mg./kg. [e] The duration of anesthesia for 5% solutions of compounds 1, 6, 8 and procaine applied intracutaneously in man is 69 min., 34 min., 24 hr. and 70 min., respectively.

ing derivatives of diphenyl ether and diphenyl sulfide also were prepared.



Phenoxybenzoic acid



Thiophenoxybenzoic acid

Experimental Part

Carbazole Derivatives.—The unsubstituted carbazolecarboxylic acids were prepared either by carbonation of the N-potassium derivative followed by pyrolytic rearrangement, or by alkali fusion of the corresponding methyl ketones according to known methods.[3,4] 5-Ethylcarbazole-2-carboxylic acid was obtained in good yield by alkylation of the acid with ethyl sulfate followed by saponification.[5]

5-*n*-Butylcarbazole-2-carboxylic Acid.—A mixture of 21 g. of carbazole-2-carboxylic acid, 47 g. of *n*-butyl sulfate, 42 g. of sodium hydroxide (dissolved in 28 cc. of water) and 146 cc. of acetone was shaken vigorously with intermittent cooling for ten minutes. The solid mass was poured into one liter of water containing 50 g. of sodium hydroxide and concentrated to a volume of 500 cc. The resulting solution was chilled, filtered and acidified. The crude product, which became granular on standing overnight, was filtered out, dried and crystallized from petroleum ether. The yield of white needles melting at 157° was 15 g.

Anal. Calcd. for $C_{17}H_{17}O_2N$: N, 5.24. Found: N, 5.36.

5-Ethylcarbazole-3-carboxylic Acid.—Repeated attempts to alkylate carbazole-3-carboxylic acid using ethyl sulfate or ethyl iodide were unsuccessful. The desired product, however, was obtained easily by alkali fusion of 5-ethyl-3-acetylcarbazole described below.

Fifteen grams of 3-acetylcarbazole, 15 cc. of ethyl sulfate, 15 g. of sodium hydroxide (dissolved in 10 cc. of water) and 100 cc. of acetone were shaken for fifteen minutes. Dilution with water gave the crude product, which was crystallized from petroleum ether to yield 15 g. of 5-ethyl-3-acetylcarbazole melting at 97°.

Anal. Calcd. for $C_{16}H_{15}ON$: N, 5.9. Found: N, 5.6.

Potassium hydroxide fusion gave a 40% yield of the desired acid melting at 248° after crystallization from toluene.

Anal. Calcd. for $C_{15}H_{13}O_2N$: N, 5.82. Found: N, 5.92.

5-*n*-Butylcarbazole-3-carboxylic Acid.—As with the ethyl derivative described above, this acid could not be prepared by direct alkylation but was obtained by alkali fusion of 5-*n*-butyl-3-acetylcarbazole.

A mixture of 28 g. of 3-acetylcarbazole, 70 g. of *n*-butyl iodide, 30 cc. of 66% potassium hydroxide and 140 cc. of acetone was refluxed for twenty-four hours. After dilution with water the acetone and excess butyl iodide were boiled off, the chilled mixture filtered and the crude product crystallized from petroleum ether to yield 28 g. of 5-*n*-butyl-3-acetylcarbazole melting at 74.5–75°.

Anal. Calcd. for $C_{18}H_{19}ON$: N, 5.28. Found: N, 5.41.

Fusion with potassium hydroxide gave an 8% yield of

(3) German Patent 442,609; British Patent 27,051.

(4) Meitzner, THIS JOURNAL, **57**, 2327 (1935); Plant and Williams, *J. Chem. Soc.*, 1142 (1934); Borsche and Fiese, *Ber.*, **40**, 378 (1907).

(5) Gilman and Kirby, *J. Org. Chem.*, **1**, 146 (1936).

the desired acid which was crystallized from benzene and melted at 198°.

Anal. Calcd. for $C_{17}H_{17}O_2N$: N, 5.24. Found: N, 5.6.

8-Nitrocarbazole-3-carboxylic Acid.—Two grams of sodium nitrite was added in portions, with stirring, to a solution of 5.5 g. of carbazole-3-carboxylic acid in 80 cc. of acetic acid at 90°. A solution of 4.5 cc. of acetic acid and 4.5 cc. of concentrated nitric acid was then added dropwise with stirring at 80–85°. Stirring was continued for one hour at 85°, the resulting mixture chilled and the yellow product filtered out and washed with 50 cc. of alcohol. Refluxing with 100 cc. of alcohol and 40 cc. of 40% sodium hydroxide for thirty minutes gave, after dilution with water and acidification, 6 g. of a yellow amorphous powder, m. p. 335° (dec.). Crystallization from nitrobenzene raised the melting point to 338°.

Anal. Calcd. for $C_{13}H_8O_4N_2$: N, 10.95. Found: N, 11.1.

Decarboxylation with copper bronze in the high boiling fraction (b. p. 300–350°) of technical pyridine gave 2-nitrocarbazole.

6,7,8,9-Tetrahydrocarbazole-2-carboxylic Acid.—Thirty-eight grams of *p*-hydrazinobenzoic acid[6] and 38 cc. of cyclohexanone were heated on a steam-bath for fifteen minutes and then refluxed gently with stirring for fifteen minutes with 400 cc. of 10% (by volume) sulfuric acid. The chilled mixture was filtered, the crude product dissolved in dilute alkali, decolorized with Darco and acidified. The yield of pure product melting at 279° was 40 g.

Anal. Calcd. for $C_{13}H_{13}O_2N$: N, 6.51. Found: N, 6.46.

The dialkylaminoalkyl esters were prepared by conversion to their respective acid chlorides (by means of phosphorus trichloride) followed by treatment with the desired alcohol (method A) or by way of the ω-chloroalkyl ester which was then treated with the appropriate amine (method B).

β-Chloroethyl Carbazole-2-carboxylate.—A slow stream of dry hydrogen chloride was passed into a refluxing solution of 10 g. of carbazole-2-carboxylic acid in 50 cc. of ethylene chlorohydrin for a period of six hours. After standing overnight at laboratory temperature the mixture was poured into 400 cc. of ice water, the crystalline product filtered out, washed with sodium bicarbonate solution and crystallized from benzene to yield 8 g. of the ester melting at 141°.

Anal. Calcd. for $C_{15}H_{12}O_2NCl$: Cl, 12.95. Found: Cl, 13.0.

γ-Chloropropyl Carbazole-2-carboxylate.—A procedure similar to that above starting with 20 g. of the acid and 80 cc. of trimethylene chlorohydrin gave 18 g. of pure product, m. p. 129°.

Anal. Calcd. for $C_{16}H_{14}O_2NCl$: Cl, 12.32. Found: Cl, 12.26.

β-Diethylaminoethyl 5-Ethylcarbazole-2-carboxylate (Method A).—Ten grams of 5-ethylcarbazole-2-carboxylic acid and 40 cc. of phosphorus trichloride were heated on a steam-bath for one and one-half hours. The excess phosphorus trichloride was distilled off under reduced pressure and the acid chloride cautiously treated with 50 cc. of β-diethylaminoethanol. When the initial reaction had subsided, the mixture was heated on a steam-bath for fifteen minutes and then let stand overnight at laboratory temperature. After dilution with 500 cc. of water containing 50 cc. of 10% sodium hydroxide the oily base was extracted with ether, the ethereal extract washed with water and dried over sodium sulfate. The solvent was removed and the excess amino-alcohol distilled off under reduced pressure. The crude base was dissolved in 300 cc. of dry ether, treated with Darco and the filtrate saturated with dry hydrogen chloride. The viscous hydrochloride was taken up in 150 cc. of warm acetone from which it soon precipitated in crystalline form. The acetone filtrate was concentrated to 50 cc. to yield an additional amount of material. Crystallization of the combined products from methanol gave 7 g. of the hydrochloride melting at 204°.

γ-Diethylaminopropyl Carbazole-2-carboxylate (Method B).—Seventeen grams of γ-chloropropyl carbazole-2-carboxylate and 11 g. of diethylamine were heated in a sealed tube at 110° for thirty-six hours. The base was isolated and converted to its hydrochloride in the same manner as described in method A to give 8 g. of the desired compound melting at 169°.

β-Diethylaminoethyl 8-Aminocarbazole-3-carboxylate.—Using the procedure described under method A, β-diethylaminoethyl 8-nitrocarbazole-3-carboxylate hydrochloride was obtained, melting at 225–227°, after crystallization from ethanol.

Anal. Calcd. for $C_{19}H_{22}O_4N_2Cl$: N, 11.8. Found: N, 11.5.

Reduction was effected by means of iron filings and acetic acid in the customary manner. When the reaction was complete, the mixture was poured into water, made alkaline and filtered. The precipitate was extracted with acetone, the extract treated with Darco and the solvent removed. The crude base was then dissolved in ether and precipitated as the hydrochloride. Addition of alkali to an aqueous solution of the salt precipitated the base in crystalline form, which was filtered out and recrystallized from petroleum ether to give yellow plates, m. p. 146–147°.

Dibenzofuran and Dibenzothiophene Derivatives. β-(*p*-Phenoxy)-acrylic Acid.—Thirty-five grams of *p*-phenoxybenzaldehyde,[7] 175 cc. of acetic anhydride and 28 g. of twice fused sodium acetate were refluxed for eight hours and then diluted with 1400 cc. of warm water to destroy excess acetic anhydride. The mixture was made alkaline to phenolphthalein and extracted with ether to remove any oily precipitate. Acidification precipitated the crude acid which was crystallized from petroleum ether to yield 10 g. of acid melting at 135°.

Anal. Calcd. for $C_{15}H_{12}O_3$: C, 75.0; H, 5.0. Found: C, 75.18; H, 4.89. The acid chloride was obtained by treatment with thionyl chloride in benzene solution and boiled at 225° (18 mm.).

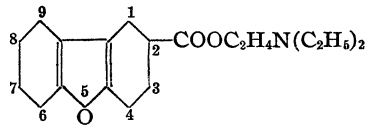
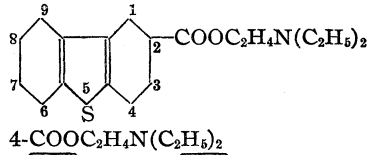
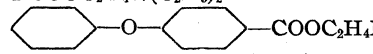
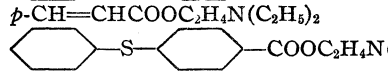
Since this paper was presented, *bis*-(β-diethylaminoethyl)-dibenzofuran-2,8-dicarboxylate dihydrochloride, m. p. 251–253°, has been prepared and found to be only faintly active at a concentration of 5%.

(6) Fischer, *Ann.*, **212**, 337 (1882).

(7) German Patent 650,430.

TABLE II

DIBENZOFURAN AND DIBENZOTHIOPHENE LOCAL ANESTHETICS

No.	Structure	Hydrochloride m. p., °C.	N analyses, % Calcd.	Obsd.	Min. duration of corneal anesthesia in rabbits[a] 0.1%	0.5%	1.0%	Av. subcutaneous toxicity in mice g./kg.[b]
12		185	4.03	4.09	4[d]+	11++	20++	0.45[c]
13	3-$COOC_2H_4N(C_2H_5)_2$	221	4.03	4.05	5+	25++	30++	.5
14	4-$COOC_2H_4N(C_2H_5)_2$	210	4.03	4.12	4−		11+	.45
15	2-$COOCH_2CH_2CH_2N(C_2H_5)_2$	185	3.38	3.51	8−	14+	35++	.3
16	2-$COOC_2H_4NHC_4H_9(i)$	212	4.03	4.2	0	14+	26+	.45
17	2-$COOC_2H_4NHC_5H_{11}(n)$	160	3.38	3.42	0	27+		.6
18	7-NH_2 2-$COOC_2H_4N(C_2H_5)_2$	255	7.72	7.8				
19	2-CH=CH$COOC_2H_4N(C_2H_5)_2$	185	3.75	3.75	0	10+	13+	.5
20		219	3.86	4.1		8−		1.0
21	4-$COOC_2H_4N(C_2H_5)_2$	213	3.86	4.01		9−		0.65
22		136	4.0	4.05	[d]	15++	22++	.15
23	*p*-CH=CH$COOC_2H_4N(C_2H_5)_2$	129–130	3.73	4.0				
24		137	S, 8.75	8.62	0	14+	34++	.35

[a] See (*a*) Table I. [b] See (*c*) Table I. [c] Intravenous M. L. D. in rabbits = 30 mg./kg. [d] The concentration and duration of anesthesia for solutions of compounds 12, 22 and procaine applied intracutaneously in man are, respectively: 0.5%, 60 min.; 0.2%, 53 min.; 0.5%, 70 min.

The other acids used in the preparation of the esters listed in Table II were prepared by known methods.[8,9] Although Courtot prepared dibenzothiophene-2-carboxylic acid by carbonation of the corresponding Grignard reagent,[8d] it also may be obtained by diazotizing the recently accessible 2-aminodibenzothiophene,[10] converting the diazonium halide to the nitrile and hydrolyzing according to the customary procedure.

The esters of the above acids were prepared by either of the two methods described in the case of the carbazolecarboxylic acids.

γ-Chloropropyl Dibenzofuran-2-carboxylate.—Twenty-three grams of dibenzofuran-2-carboxylic acid chloride and 50 cc. of trimethylene chlorohydrin were heated at 150° (bath temp.) for five hours, the excess trimethylene chlorohydrin distilled off under reduced pressure and the residual material poured into water. The crude product was washed with water and crystallized from petroleum ether to give 20 g. of ester melting at 85°.

Anal. Calcd. for $C_{16}H_{13}O_3Cl$: Cl, 12.27. Found: Cl, 12.25.

β-Diethylaminoethyl 7-Aminodibenzofuran-2-carboxylate.—7-Nitrodibenzofuran-2-carboxylic acid chloride, prepared by refluxing the nitro acid with thionyl chloride for ten hours, melted at 225° after crystallization from toluene. The acid chloride was treated in the usual manner with diethylaminoethanol to give an 85% yield of the nitro ester, m. p. 161°. Reduction of the nitro group was effected with iron filings and acetic acid in the usual manner. The crude oily product was dissolved in absolute ethanol and treated with one equivalent of alcoholic hydrogen chloride. Crystallization from ethanol gave the monohydrochloride, m. p. 255°.

β-Isobutylaminoethyl Dibenzofuran-2-carboxylate.—The β-isobutylaminoethanol is most conveniently prepared by the interaction of isobutyl bromide and ethanolamine.[11] The formation of the ester is best carried out in the manner of a Schotten–Baumann reaction according to the procedure of Goldberg and Whitmore.[12] The hydrochloride of this ester as well as the amyl derivative are somewhat unusual in that their aqueous solutions are slightly alkaline to litmus.

The β-*n*-amylaminoethanol and its ester are prepared in the same manner as described above.

Pharmacological Results

Anesthetic potency was determined on rabbits' cornea by applying the solutions for one minute and testing the reflex at each minute thereafter. At least six experiments were carried out for

(8) See the following references for preparation of these acids: (a) Borsche and Bothe, *Ber.*, **41**, 1940 (1908); (b) Kirkpatrick and Parker, THIS JOURNAL, **57**, 1126 (1935); (c) Hinkel, Ayling and Beynon, *J. Chem. Soc.*, 778 (1937); (d) Courtot and Pomonis, *Compt. rend.*, **186**, 1624 (1928); (e) Weedon and Doughty, *Am. Chem. J.*, **33**, 424 (1905).

(9) Dibenzofuran-2-carboxylic acid was prepared by hypochlorite oxidation of 2-acetyldibenzofuran, and 7-nitrodibenzofuran-2-carboxylic acid was obtained by chromic acid oxidation of 7-nitro-2-acetyldibenzofuran in essential accordance with directions kindly supplied by Professor Henry Gilman.

(10) Gilman and Jacoby, *J. Org. Chem.*, **3**, 108 (1938).

(11) British Patent 482,886.

(12) Goldberg and Whitmore, THIS JOURNAL, **59**, 2280 (1937).

each concentration and compared with a 1% solution of cocaine. In most instances the induction period varied from one to three minutes.

Toxicity was determined by subcutaneous injections in white mice. In the carbazole series lethal doses resulted in convulsions preceded by excitement, whereas with the sulfur compounds and no. 22 the symptoms were weakness and depression even in fatal doses. The dibenzofuran derivatives in small doses cause depression, while larger amounts give rise to convulsions. The lethal intravenous dose in rabbits for compounds no. 1, 8 and 12 is 20, 20 and 30 mg./kg., respectively, death being preceded in each instance by clonic-tonic convulsions and dyspnea. Death occurred in all cases through respiratory failure.

Discussion

Of the simple unsubstituted carbazole esters the 2- and 3-isomers (nos. 1 and 2) exhibit about the same degree of anesthetic potency, with the 4-isomer falling considerably behind. Among the analogous dibenzofuran derivatives the 3-isomer (no. 13) possesses the greatest anesthetic potency, while the 2- and 4-isomers follow in order of decreasing activity. This was rather unexpected, since in compounds of the procaine type the para position (corresponding to the 2-position in carbazole) of the carboxyl group with respect to the amino group has been regarded as the most favorable combination, the meta and ortho isomers following in order of decreasing activity. Furthermore, in the case of the dibenzofuran compounds the observed order is likewise at variance with the predictions one might make from a study of the alkoxybenzoic acid esters in which the compounds bearing the side chain para to the ether linkage are the most active. It is possible that the abnormally high activity of the 3-isomer in either series may be due to the fact that the side chain occupies a position para to the *carbon–carbon* bridge and that this position combination exerts a more profound influence than that resulting from the para relationship between the imino group or the ethereal oxygen and the carboxyl group. With the analogous dibenzothiophene derivatives it is evident that these compounds possess a much weaker anesthetic action, exhibiting not only a shorter duration of corneal anesthesia but also a much less profound effect.

In the carbazole series the order of toxicity is quite definitely 2>3>4-isomer, while among the dibenzofuran isomers there is little difference in toxicity, whereas with the dibenzothiophene derivatives the order is reversed, the 4-isomer being the most toxic.

Extending the carbon chain between the carbonyl group and the terminal nitrogen atom in the carbazole or the dibenzofuran series practically doubles the toxicity with a much less significant increase in anesthetic potency. Substitution of *n*-butyl groups for ethyl in the alcohol of the carbazole esters results in a proportional decrease in activity and toxicity. The effect of replacing hydrogen by an alkyl group on the ring nitrogen varies with the position of the side chain. With the carboxyl group in the 3-position the introduction of the N-ethyl group nearly doubles the anesthetic potency without increasing the toxicity. It is interesting to note that this compound (no. 8) is at least three times as potent as cocaine and only one-fifth as toxic. When the carboxyl group is in the 2-position both toxicity and activity are reduced by the introduction of the N-ethyl group and practically lost with the substitution of an N-butyl group. Partial hydrogenation of the carbazole nucleus increases the toxicity by more than two-fold without affecting the potency.

The β-mono-isobutylaminoethyl dibenzofuran-2-carboxylate (no. 16) offers no advantage over the diethylaminoethyl ester (no. 12) and does not exhibit any measurable degree of pressor action. This is somewhat surprising, since the corresponding derivative of the procaine type recently described by Goldberg and Abramson[13] is considerably more active than procaine and possesses definite pressor activity. The mono-*n*-amyl ester (no. 17) is somewhat better than no. 12, since it has a slightly lower toxicity and greater duration of corneal anesthesia. The introduction of an ethylenic linkage between the dibenzofuran nucleus and the carbonyl group as in compound no. 19 results in a slight decrease in toxicity but a much greater drop in activity. This also is at variance with the expected result, since the introduction of an ethylenic linkage at such a point generally enhances the efficacy of the parent compound.

In considering the effect of opening the carbon–carbon bond between the two benzene nuclei as in compounds nos. 22 and 24, it is evident that such a transition in the oxygen derivative results pri-

(13) Goldberg and Abramson, *J. Pharmacol.*, **62**, 69 (1938).

marily in a marked increase in toxicity with only a minor increase in activity. In the case of the diphenyl sulfide ester the toxicity is likewise greater than that of its dibenzothiophene analog, although in this instance the anesthetic potency is substantially enhanced both as to duration and quality.

None of these compounds had a mydriatic action in the concentrations used, whereas they all caused more or less irritation of the cornea and conjunctiva, the extent of the damage depending on the concentration. The pathological changes were conjunctivitis, chemosis, opacity of the cornea and intense secretion with consequent ectropion.

Effect on Blood Pressure and Respiration.—The action on blood pressure and respiration was determined for compounds no. 1, 8 and 12 by intravenous injection of 5 mg./kg. in dogs anesthetized with ether or without anesthesia. All three drugs caused depression of respiration and a sharp fall in blood pressure, the latter effect being only slightly diminished by the addition of epinephrine.

Action on Human Skin.—The anesthetic action of five of these compounds was further examined by means of wheal experiments on human skin under aseptic conditions. The solutions were prepared so as to contain 0.9% sodium chloride and a concentration of epinephrine of 1:250,000. Two-tenths cc. of this solution was used for intracutaneous injection. The duration, quality of anesthesia and side effects were observed and compared with procaine.

The same relative order of activity as was observed in the corneal studies is maintained in this instance. The unusual duration of compound 8 is worthy of note. As might have been predicted from the experiments on the rabbit cornea each of the compounds thus examined was more or less irritating and painful on injection.

The irritating effects of the entire group of compounds appear to be inherent to the nucleus involved, since meticulous purification, variation of the substituent groups and changing the method of synthesis does not materially alter the situation.

Acknowledgment.—The authors wish to express their appreciation to Mr. John W. Cusic for assistance with some of the experimental work.

Summary

The investigation of a series of alkylaminoalkyl esters of carbazole-, dibenzofuran- and dibenzothiophenecarboxylic acids led to some powerful local anesthetics. The best one of the series is β-diethylaminoethyl 5-ethylcarbazole-3-carboxylate hydrochloride (no. 8), which is more than thrice as potent as cocaine and only one-fifth as toxic. The activity of these compounds appears to be predominantly a function of the position of the carboxyl group rather than other structural variations. Opening of the carbon–carbon bridge in the dibenzofuran and dibenzothiophene derivatives does not improve the therapeutic efficiency. All of these compounds were more or less irritating to the rabbit's eye and to human skin, so that they cannot be regarded as useful anesthetics.

CHICAGO, ILLINOIS
LOUISVILLE, KENTUCKY
RECEIVED AUGUST 5, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF CALCO CHEMICAL DIVISION, AMERICAN CYANAMID CO.]

Sulfanilamide Derivatives. VI. Substituted N^1-Aliphatic Sulfanilamides[1]

BY M. L. CROSSLEY, E. H. NORTHEY AND M. E. HULTQUIST

A number of N^1-alkyl and hydroxyalkylsulfanilamides have been prepared by Kharasch, Mietzsch, Fourneau, Bauer and others.[2,3,4,5] As part of our program on N^1-substituted sulfanilamides, we have independently synthesized many of the derivatives reported by these authors, as well as a number of others which have not hitherto been published to our knowledge. The latter are sulfanilyl derivatives of aliphatic amines, amino-alcohols, diamino-alcohols, and amino-acids. Closely allied derivatives of morpholine and difurfurylamine are included.

The syntheses of these derivatives followed the

(1) Presented in part before the Division of Medicinal Chemistry, A. C. S., September, 1939.

(2) M. S. Kharasch and O. Reinmuth, U. S. Patents 2,097,414, and 2,097,415, October 26, 1937.

(3) F. Mietzsch and J. Klarer, U. S. Patent 2,085,037, June 29, 1937.

(4) E. Fourneau, J. and Mme. J. Trefouel, F. Nitti and D. Bovet, *Compt. rend. soc. biol.*, **122**, 258 (1936).

(5) S. M. Rosenthal, H. Bauer and S. E. Branham, *Public Health Reports, U. S. Treas. Dept.*, **52**, 662 (1937).

TABLE I

Name	Crystallized from	Crystalline form	Melting range, °C.	Calcd. mol. wt.	Assay by $NaNO_2$ Calcd.	Found
N^1-*n*-Octylsulfanilamide	Alcohol	Long prisms	114–119.5	284.4	N, 9.86	9.87
N^1-*n*-Dodecylsulfanilamide	Toluene	Leaves	118–124	340.5	N, 8.23	8.40
N^1-*n*-Octadecylsulfanilamide	60% alc.	Leaves	127–130	456.7	N, 6.13	6.06
N^1-(9-Octadecenyl)-sulfanilamide	60% alc.	Needles	118–122.5	454.7	N, 6.16	6.22
1,2-*bis*-Sulfanilamidoethane	H_2O as Na salt	Crystalline powder	229.4–231.2	370.2	99.9	
1,2-*bis*(N^4-Sulfanilylsulfanilamido)-ethane	60% acetone	Prisms	>118 dec.	680.8	100.6	
N^1,N^1-*bis*(2-Sulfanilamidoethyl)-sulfanilamide trihydrochloride	Water	Crystalline powder	241.5–244	678.1	99.4	
N^1-Methyl-N^1-2-hydroxyethyl sulfanilamide	Water	Prisms	124.5–126.3	230.2	100.2	
2-Methyl-2-sulfanilamido-1-propanol	95% alc.	Prisms	154–155.8	242.3	99.6	
2-Methyl-2-sulfanilamido-1,3-propanediol	95% alc.	Prisms	131.8–134.0	260.3	100.3	
1,3-*bis*-Sulfanilamido-2-propanol	50% alc.	Fine needles	184.2–186.5	400.3	100.0	
N^1-2-Hydroxyethyl-N^1-(2-sulfanilamidoethyl)-sulfanilamide	50% alc.	Short prisms	163.0–164.5	414.5	100.3	
N^1,N^1-Difurfurylsulfanilamide	95% alc.	Needles	134.0–136.5	334.38	99.0	
N-(2-Sulfanilamidoethyl)-morpholine	20% alc.	Needles	98–100.4	285.3	100.1	
Ethyl N-sulfanilylglycinate	30% alc.	Needles	90.4–92.0	258.2	100.3	
Di-*n*-butyl-N-sulfanilylglutamate hydrochloride	Dioxane–ether	Crystalline powder	138.4–141.6	451.0	100.2	
2-Sulfanilamidoethyl dodecanoate	60% alc.	Prisms	63.4–64.8	398.5	100.3	

general procedure used previously[6] except in the case of the amino-acid ester derivatives. The N-sulfanilylamino acids were first prepared.[7] These were then esterified by boiling with the corresponding alcohol in the presence of hydrogen chloride. Di-*n*-butyl-N-sulfanilylglutamate was difficult to crystallize, so was isolated and recrystallized as the hydrochloride.

Pharmacology.—The long chain N^1-alkylsulfanilamides were prepared with the object of obtaining lipoid solubility. The promising pharmacological properties of N^1-dodecanoylsulfanilamide[8] made the investigation of other lipoid soluble derivatives of particular interest. The available results indicate that the long chain N^1-alkylsulfanilamides are decidedly inferior to the corresponding N^1-acylsulfanilamides on experimental streptococcal infections in mice.

The derivatives of amino-alcohols, amino-acid esters and morpholine appeared to be almost inactive while the difurfurylamine derivative was toxic. The esters were also inactive.

The pharmacological work was done under the direction of D. R. Climenko and will be reported elsewhere.

Experimental

2-Sulfanilamidoethyl Dodecanoate.—4-Nitrobenzenesulfonyl chloride was heated with excess aqueous 2-hydroxyethylamine and the product recrystallized from 50% alcohol giving N-2-hydroxyethyl-4-nitrobenzenesulfonamide, m. p. 126–127°; 41 g. (0.166 mole) of this was dissolved in 40 cc. of pyridine at 80° and 40 g. of dodecanoyl chloride was added gradually at 90–100°. The temperature was maintained for twenty min., then the hot mixture was poured into 500 cc. of water. The product was recrystallized from 80% alcohol, giving 78.4 g. of yellow crystals of 4-nitrobenzenesulfonamidoethyl dodecanoate, m. p. 72.0–73.5°. The nitro group was reduced by adding a solution of the compound in 100 cc. of toluene to a hot mixture of 60 g. of iron powder, 200 cc. of water, and 4 cc. of hydrochloric acid, then boiling for fifteen hours under agitation. The mixture was neutralized to *p*H 8, filtered, and the cake washed with hot toluene. The toluene layer was dried over calcium chloride and distilled under reduced pressure. The residue was taken up in 60% alcohol and recrystallized three times, using activated charcoal.

Intermediates for this series were obtained as follows: "Lorolamine" from E. I. du Pont de Nemours & Company was fractionated giving *n*-octylamine, b. p. 183–188° (770 mm.), and *n*-dodecylamine, 135.5–138.5° (15 mm.), setting point 26.5°. *n*-Octadecylamine and 9-octadecenylamine were obtained from Armour & Company, and were used without purification. β-Hydroxyethylamine, ethylenediamine, diethylenetriamine and N-(β-hydroxyethyl)-ethylenediamine were obtained from Carbide & Carbon Chemical Corp. and were used without purification. Difurfurylamine was obtained from the B. F. Goodrich Tire & Rubber Company. 2-Methyl-2-amino-1-propanol and 2-methyl-2-amino-1,3-propanediol were obtained from Commercial Solvents Corp. 1,3-Diamino-2-propanol was obtained from Eastman Kodak Company. 4′-(2′-Aminoethyl)-morpholine was synthesized from ethylenediamine and *bis*-β-chloroethyl ether.[9]

Summary

1. Eighteen new sulfanilamide derivatives are reported. These are sulfanilyl derivatives of aliphatic amines, polyamines, amino alcohols, diamino alcohols and aminoacid esters. Closely allied derivatives of morpholine and difurfurylamine are included.

2. The available pharmacological results in-

(6) Crossley, Northey and Hultquist, THIS JOURNAL, **60**, 2217 (1938); see also for nomenclature.

(7) Hultquist, U. S. Patent 2,142,847, January 3, 1939.

(8) Crossley, Northey and Hultquist, THIS JOURNAL, **61**, 2950 (1939).

(9) Hultquist and Northey, *ibid.*, **62**, 447 (1940).

dicate that these compounds as a class are less effective than sulfanilamide against infections by beta hemolytic streptococci in mice.

BOUND BROOK, N. J. RECEIVED DECEMBER 13, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY AND UNIVERSAL OIL PRODUCTS COMPANY]

The Electrolysis of Some Higher Aliphatic Organomagnesium Halides in Ethyl Ether

BY WARD V. EVANS, DAVID BRAITHWAITE AND EDMUND FIELD

The electrolysis studies of the simple organomagnesium halides have been completed.[1] These studies indicated that the main course of the reaction was the liberation of the organic free radical, which then reacted by disproportionation to give the corresponding saturated and unsaturated hydrocarbons. In the electrolysis of *n*-propylmagnesium halide in ethyl ether[1d] it was found, however, that there was a marked tendency for the liberated free radical to combine to give the coupled product *n*-hexane. The isopropylmagnesium halide, on the other hand, showed very little or no tendency to couple upon electrolysis.

The present work is a continuation of this problem, electrolyzing some higher organomagnesium halides in ethyl ether, and attempting thereby to further our knowledge of the coupling tendency. To accomplish this the four isomeric butyl compounds were studied, as well as the *n*-hexyl compound.

Experimental

The same apparatus that has previously been described was used,[1b] and platinum electrodes were employed throughout the investigation.

***n*-Butylmagnesium Bromide.**—In this electrolysis the solution conducted the electric current so readily that even at 0.4 to 0.5 ampere there was not sufficient heat generated to cause the solvent to reflux. Since refluxing was the sole means of agitation, there was no great amount of disturbance in this electrolysis, and consequently the magnesium plated out and often bridged the gap between the electrodes. For the most part this was avoided by shaking the cell, but it undoubtedly accounts for the low efficiency found.

It was noted, however, that gas was liberated when the gap between the electrodes had nearly been closed, whereas otherwise no gas was liberated. Samples of this gas at different current densities were taken, and the analyses, made by the absorption method, are shown in Table I. Change in current density had no effect on the composition of the gas over a small range.

A quantity of 0.72 mole of Grignard reagent was decomposed during the electrolysis, and the efficiency was approximately 65% based on the number of coulombs passed through the solution. On the basis of the amount of octane isolated experimentally, approximately 85% of the butyl radicals liberated coupled. Because of loss in isolating and purifying the octane, the actual amount of coupling must be approximately 100%.

Isobutylmagnesium Bromide.—As in the case of *n*-butylmagnesium bromide, no gas was liberated except when magnesium nearly bridged the gap between the electrodes. There was not sufficient gas to fractionate, and all that could be done with this small amount of gas was to determine that the saturated hydrocarbon gas in the mixture was essentially C_4.

A 500-cc. sample of the original organomagnesium halide (1.36 *N*) was hydrolyzed and analyzed. About 5 cc. of diisobutyl was found, indicating a slight coupling during the formation of the Grignard reagent.

The efficiency of this electrolysis was found to be about 83% based on the number of coulombs passed through the solution. After electrolysis, 500 cc. (0.6 *N*) was hydrolyzed and analyzed. No alcohols were found, but approximately 35 cc. of diisobutyl was present. During the electrolysis 0.78 equivalent of Grignard compound was decomposed. Therefore, on the basis of the amount of diisobutyl found, approximately 96% of the liberated isobutyl free radical coupled.

***s*-Butylmagnesium Bromide.**—No gas was liberated during this electrolysis.

A 500-cc. sample (1.35 *N*) of the original Grignard was hydrolyzed and analyzed before electrolysis. A 2-cc. portion of this solution was identified as the coupled product, 3,4-dimethylhexane.

On the basis of the amount of 3,4-dimethylhexane found on analyzing the solution after electrolysis, about 43% of the liberated free radical coupled. This would appear to be a poor yield of the coupled product, but considerable difficulty was encountered in the isolation of the product.

No alcohols were found.

On a second electrolysis of *s*-butylmagnesium bromide, the solution was prepared 0.588 *N* and 825 cc. electrolyzed until 0.165 equivalent had been decomposed. On the basis of the amount of coupled product isolated from the original solution and the electrolyzed solution, coupling took place to about 49%. In this experiment an external heater was used to keep the solution in the vicinity of the electrodes refluxing vigorously. This heater accomplished two things. It stopped the magnesium from bridging

(1) (a) Evans and Field, THIS JOURNAL, 58, 720 (1936); (b) Evans and Field, *ibid.*, 58, 2284 (1936); (c) Evans and Lee, *ibid.*, 56 654 (1934); (d) Evans and Braithwaite, *ibid.*, 61, 898 (1939).

TABLE I

ANALYSIS OF GAS LIBERATED BY THE ELECTROLYSIS OF *n*-BUTYLMAGNESIUM BROMIDE

Amp./sq. dm.	CO_2	Other unsatd. hydrocarbons	O_2	H_2	CO	Unsatd. hydrocarbon (butylene)	Hydrocarbons	*n*
1.0	2.0	1.2	2.0	2.5	1.2	42	50	3.7
1.6	...	2.1	1.5	2.2	...	43	52	3.6
0.4 to 2.0 (range)	0.8	1.1	1.9	0.3	0.3	40	55	3.7

the gap between the electrodes, and also decreased the solubility of any gases formed during the electrolysis and aided them to escape by means of the refluxing. Gas was not liberated to the extent that it could be collected.

Two possible conclusions can be drawn from these results. First, the free radical liberated on electrolysis may be considered to couple 100% since no gas was given off. The explanation for the poor yield of the isolated coupled product could be offered on the basis that some of the product was lost in separating it from the large volume of ether used as a solvent. Second, the coupling can be considered to take place only to the extent indicated by the amount of coupled product isolated. The remainder of the products of the electrolysis, supposedly butane and butylene, could be thought of as dissolving in the ether solution and consequently being lost on analysis.

The first interpretation seems more plausible because of the ease of liberation of small amounts of butane and butylene in the *n*-butylmagnesium bromide electrolysis, and because of the unfavorable conditions for solution of the gases when the solution was in a state of reflux. On this basis, then, the *s*-butyl free radical takes its assigned place in Table II.

***t*-Butylmagnesium Bromide.**—In the electrolysis of this compound the gas liberated could not be analyzed by the absorption method due to the presence of ethyl ether vapors. Also, the coupled product, di-tertiary-butyl, is a very volatile hydrocarbon. Only approximations, therefore, could be made as to amounts present.

A 550-cc. sample (0.506 *N*) of the solution was analyzed before electrolysis, and about 1 g. of the coupled hydrocarbon estimated to be present. After electrolysis, upon hydrolyzing and analyzing the same quantity of solution (0.278 *N*), from 3 to 4 g. of di-tertiary-butyl was found.

No alcohols were found.

During this electrolysis gas was given off freely but, as has been stated, samples at different current densities could not be analyzed because of the nature of the mixture. Therefore, after the run was completed, a Podbielniak distillation was made on the gas collected. The fractionation was not very efficient, and the main result was merely the separation of the gaseous products from the ethyl ether vapors. With the elimination of the ethyl ether vapors, however, it was then possible to analyze the hydrocarbon mixture by means of absorption and combustion. The mixture was found to be essentially isobutylene and C_4 saturated hydrocarbon, probably isobutane.

***n*-Hexylmagnesium Bromide.**—No gas was given off during this electrolysis.

On analysis of 500 cc. of original solution (0.916 *N*) 4 to 5 cc. of dodecane was found. During the electrolysis 0.364 equivalent of Grignard compound was decomposed. From 500 cc. of the final solution (0.507 *N*) 23 cc. of dodecane was isolated. The yield of the coupled product then, on the basis of the material isolated, was 82.5%. Since no other products were found, it can be assumed that the coupling reaction is the only one, and the obvious discrepancy between 82.5 and 100% is due to experimental methods of isolation.

Discussion

From all the data obtained thus far on the electrolysis of various aliphatic organomagnesium halides, we are able to draw certain conclusions.

1.—In all cases studied the ionization of the Grignard reagent and the liberation of the organic free radical at the anode may be represented as follows

$$R_2MgMgX_2 \rightleftharpoons \left[R{:}\ddot{\underset{\cdot\cdot}{Mg}}{:}\ddot{\underset{\cdot\cdot}{X}}{:} \right]^- + [Mg{:}R]^+$$

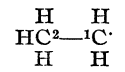
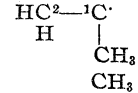
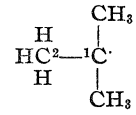
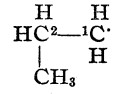
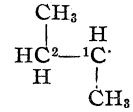
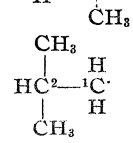
$$\downarrow -e \qquad\qquad \downarrow +e$$

$$R + MgX_2 \qquad {}^1/_2Mg + {}^1/_2MgR_2$$

2.—The reactions of the free radical with the solvent as represented in earlier papers[1b,d] seem to disappear, or at least become negligible as higher molecular weight organomagnesium halides are used for electrolytes.

TABLE II

GRADATION OF TENDENCY TO COUPLE WITH CHANGE OF STRUCTURE

Free radical		Coupling tendency
Ethyl		Trace
Isopropyl (mono-methyl substitution on C 1 of ethyl radical)		Trace
t-Butyl (dimethyl substitution on C 1 of ethyl radical)		Slight
n-Propyl (mono-methyl substitution on C 2 of ethyl radical)		Approximately 50%
s-Butyl (dimethyl substitution on C 1 and 2 of ethyl radical)		Approximately 100%
Isobutyl (dimethyl substitution on C 2 of ethyl radical)		Approximately 100%

3.—As higher molecular weight compounds are electrolyzed the main reaction seems to be one of coupling.

Certain generalizations can be made regarding structures necessary for nearly complete coupling.

A.—Straight chain free radicals of four carbon atoms or more will have approximately a 100% tendency to couple.

B.—Substituted *n*-propyl free radicals will have nearly a 100% tendency to couple.

It is interesting to consider the free radicals as substituted ethyl radicals, and it can be shown that there is a gradual increase in the tendency to couple as the ethyl radical becomes substituted with methyl groups. This is shown in Table II.

If we consider isopropyl and *t*-butyl as monomethyl and dimethyl substituted ethyl radicals, respectively, the effect of substitution on carbon number one is comparatively slight. If we consider *n*-propyl and isobutyl as mono-methyl and dimethyl substituted ethyl radicals, the effect on carbon number two is very marked. This analogy cannot be carried further, because, as has been stated, the higher molecular weight aliphatic radicals tend toward 100% coupling.

Summary

The products of electrolysis of the four butylmagnesium halides have been reported.

The products of the electrolysis of *n*-hexylmagnesium bromide in ethyl ether have been reported.

The relation between the structure of the free aliphatic radical liberated upon electrolysis and its tendency to couple has been presented.

EVANSTON, ILL. RECEIVED AUGUST 12, 1939

[COMMUNICATION NO. 752 FROM THE KODAK RESEARCH LABORATORIES]

Surface Conditions of Silver Halides and Rate of Reaction. I. Rate of Reduction of Precipitated Silver Chloride

BY T. H. JAMES

The effects of adsorption during and subsequent to the preparation of silver halide precipitates and sols are clearly shown, in both the physical and in the chemical behavior of the resulting product. The very important role played by adsorption of sensitizing dyes and gelatin in the photochemistry of the silver halides has been demonstrated by the work of several investigators.[1] The effects of adsorption on the chemical reduction of silver halide are less well understood, and the problem is clouded by lack of concrete evidence on the mechanism of the reduction process. The fact that gelatin markedly retards the reduction of unexposed silver halide by developing agents has been known since the early days of the gelatin dry plate, but the manner in which the gelatin acts has been the subject of conflicting views. Reinders and van Nieuwenburg[2] found that the reduction of silver chloride by ferrous citrate was definitely retarded by as little as 0.0012% gelatin in the solution, and an increase in the gelatin concentration resulted in a further decrease in the reaction rate. They assumed that three steps were involved in the over-all process: (1) solution of the silver chloride, (2) reduction of the silver ions in solution; and (3) crystallization of the silver. They attributed the effect of gelatin to a retardation of the crystallization process. Sheppard, however, viewed the protective action of gelatin as an adsorption effect, and showed that a layer of gelatin of approximately molecular thickness is tenaciously held to silver bromide grains which have been prepared in the presence of gelatin.

A decision between the conflicting points of view evidently rests upon a knowledge of the mechanism of the reduction process. Hydroxylamine is a reducing agent well adapted to an experimental investigation of the problem. The reaction between hydroxylamine and silver ions has been studied.[3] Reduction of silver chloride proceeds with quantitative formation of nitrogen, and this allows a convenient method of following the reaction. In addition, hydroxylamine is a photographic developing agent and results ob-

(1) *Cf.* review of G. Kornfeld, *J. Phys. Chem.*, **42**, 795 (1938); also, S. E. Sheppard, R. H. Lambert and R. D. Walker, *J. Chem. Phys.*, **7**, 265, 426 (1939); S. E. Sheppard, R. H. Lambert and R. L. Keenan, *J. Phys. Chem.*, **36**, 174 (1932).

(2) W. Reinders and C. J. van Nieuwenburg, *Kolloid Z.*, **10**, 36 (1912).

(3) T. H. James, THIS JOURNAL, **61**, 2379 (1939).

tained with it should be directly applicable to the theory of the development process.

Materials and Procedure

Silver chloride was prepared by precipitation. Purified samples of silver nitrate and potassium chloride were employed in the preparation of the primary solutions. In the precipitation, 5.00 ml. of 0.20 *M* potassium chloride was added from a buret to a solution of 5.00 ml. of 0.10 *M* silver nitrate plus 10.00 ml. of water. The tip of the buret dipped beneath the surface of the silver nitrate solution, and stirring was maintained by a glass paddle rotated at the rate of 600 r. p. m. The time of delivery of the potassium chloride solution was twenty seconds. By this procedure, results reproducible within 5% could be obtained from day to day.

The reaction between the silver chloride and hydroxylamine was carried out in the apparatus previously described.[3] The silver chloride precipitates were, in general, allowed to age for eighteen to twenty-two hours before use, and when additions such as gelatin, dye, or excess chloride were made, sufficient time was allowed for equilibrium before addition of the hydroxylamine. The time required varied from a few minutes to several hours, depending upon the addition in question. The solutions were buffered at *p*H 7.25, and a total volume of 60.0 ml. was employed in the rate measurements. The temperature was 20.0 ± 0.03°. All operations were carried out in a photographic dark room. When sensitizing dyes were employed, a no. 3 Wratten safelight was used. For all other cases, a no. 1 safelight sufficed.

The specific surface of the silver chloride precipitates was determined by the amount of dye IVa (3,3'-diethyl-9-methylthiocarbocyanine chloride) adsorbed. The dye solution was added in slight excess, and, after equilibrium had been attained, the excess dye in solution was determined by comparison with a series of standards. The dye adsorption is irreversible.[4]

Experimental Results

The general form of the reaction curve is given in Fig. 1. The shape of the curve suggests a strongly autocatalytic reaction, and this is confirmed by the fact that the introduction of colloidal silver into the silver chloride precipitate at the time of preparation markedly increases the rate of reduction. The shape of the reaction curve of the un-nucleated silver chloride is similar to that obtained for the reduction of silver ions by hydroxylamine in the presence of gold nuclei,[3] and, just as in that case, a plot of the cube root of the nitrogen volume against the time yields a straight line over one-fourth to one-third of the reaction course. This is illustrated by curve 2 of Fig. 1. In general, the points representing volumes of less than 0.3 fell definitely away from the straight line, and the line cut the "*t*" axis at finite values. Accordingly, the time, *T*, at which a nitrogen volume of 0.30 was obtained (representing 5% of the reaction course) was taken as a representation of the rate of formation of silver nuclei. In the following, the rate itself is expressed as the reciprocal, $1/T$. However, the relative results do not vary appreciably if any other sufficiently small value of the nitrogen volume is chosen for the determination of the rate. A measure of the rate of the silver-catalyzed reaction is given by the slope of the straight-line plot, and the values obtained are included in the subsequent tables. However, we are concerned here chiefly with the rate of the preliminary reaction. Discussion of the silver-catalyzed reaction will be reserved for a later paper in which results of an investigation of nucleated silver chloride precipitates will be presented.

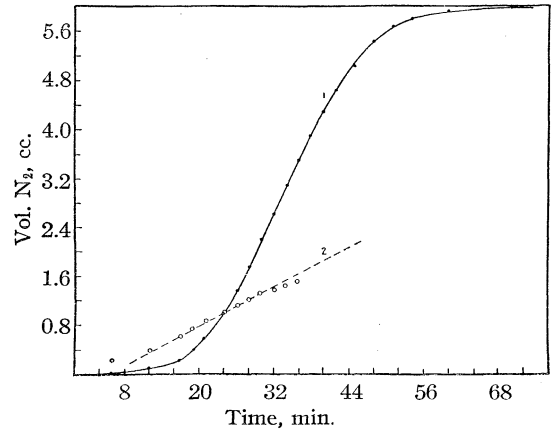


Fig. 1.—Reduction of AgCl by NH_2OH: Curve 1, *V*–*t* plot; Curve 2, $V^{1/3}$–*t* plot.

Effect of Age of the Precipitate on the Reaction Rate.—If a freshly prepared silver chloride precipitate is allowed to stand in contact with the mother liquor, the specific surface, as determined by dye adsorption, decreases at first and eventually attains a minimum value.[5] In the presence of excess chloride, the minimum is attained within a few hours. In the present investigation,

TABLE I

EFFECT OF AGE OF PRECIPITATE ON REACTION RATE

Age	*T*, min.	1/*T*	Slope
6 min.	2.4	0.415	0.142
12 min.	3.15	.317	.127
30 min.	4.05	.247	.127
95 min.	5.0	.200	.127
5 hr.	5.35	.187	.120
19 hr.	6.8	.147	.112

(4) S. E. Sheppard, R. H. Lambert and R. D. Walker, *J. Chem. Phys.*, **7**, 265 (1939).

(5) I. M. Kolthoff and H. C. Yutzy, THIS JOURNAL, **59**, 1215 (1937).

the aging of the precipitate is very well represented by the change in the rate of the initial reaction with hydroxylamine. The rate data are given in Table I. In Fig. 2, the curve represents the specific surface in arbitrary units as a function of age, and the crosses represent the reaction rates. The agreement is almost too good.

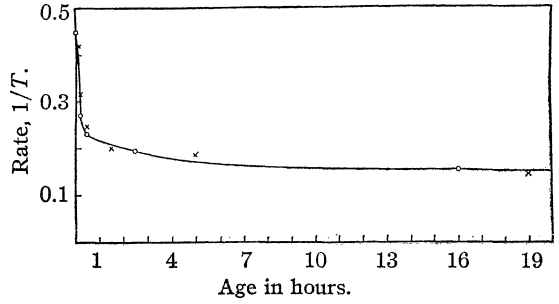


Fig. 2.—Effect of age of precipitate on rate of reaction: —○—○—, specific surface; × ×, reaction rate.

Variation of Rate with the Amount of Free Surface.—The well-aged silver chloride precipitate employed adsorbed 0.105 mg. of dye IVa at saturation, and the covered precipitate was attacked by hydroxylamine at a very low rate. An investigation was therefore carried out on a series of precipitates in which varying amounts of the surface were covered with the dye. The results are given in Table II. The calculated rates given in the last column are based upon the assumption that the rate of reaction is directly proportional to the available surface, and a small correction has been made for the finite "minimum" rate. The agreement between the experimental and calculated rates is quite good.

TABLE II

VARIATION OF RATE WITH AVAILABLE SURFACE

Fraction of surface covered by dye	T, min.	Slope	$1/T$	Calcd. rate
0	6.8	0.112	0.147	0.147
0.078	7.2	.110	.139	.136
.37	10.5	.082	.095	.095
.39	10.8	.078	.0925	.092
.50	13.2	.073	.076	.076
.50	14.0	.067	.071	.076
.75	25.0	.030	.040	.041
1.00	~200	..	~ .005	.005

Variation of Rate with the Amount of Gelatin.—The rate of the reaction decreases sharply as gelatin is added to the system, and attains a minimum value when the amount of gelatin employed is still quite small. This effect is shown in Fig. 3 and Table III.

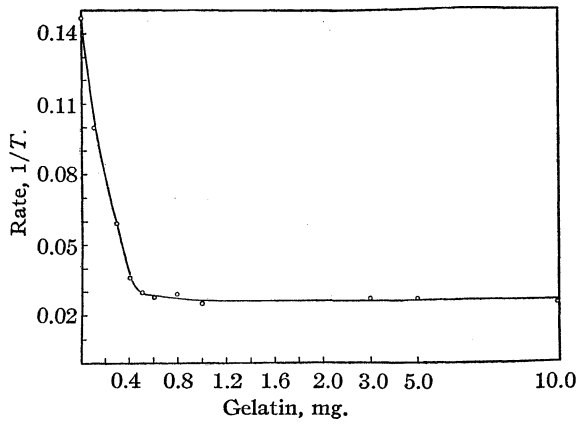


Fig. 3.—Variation of initial rate with amount of gelatin.

TABLE III

VARIATION OF RATE WITH AMOUNT OF GELATIN
GELATIN: EASTMAN DE-ASHED PURIFIED PRODUCT

Gelatin, mg.	T, min.	Slope	$1/T$
0	6.8	0.112	0.147
0.10	10.0	.058	.100
.30	16.9	.047	.059
.40	27.5	.047	.036
.50	33.5	.047	.030
.60	36.5	.043	.028
1.00	40	.038	.025
3.00	37	.043	.027
5.00	37	.038	.027
10.00	40	.038	.025

When a portion of the silver chloride surface was covered with dye IVa, the minimum reaction rate in the presence of gelatin was decreased by approximately the amount calculated on the basis of strict proportionality. The time required to attain equilibrium between the silver chloride and gelatin was increased, however. This is indicated by the data in Table IV. The time required for equilibrium in the absence of dye was, in general, not greater than one hour.

TABLE IV

EFFECT OF GELATIN ON THE REACTION OF SILVER CHLORIDE PARTLY COVERED BY DYE IVa

Fraction of surface covered by dye	Gelatin, mg./10	Time of agitation with gelatin	T, min.	$1/T$
0	0.50	2 hr.	37.0	0.027
0.33	.10	1 hr.	46.4	.0216
.33	.10	5 hr.	49.0	.0204
.33	.50	2 hr.	53.0	.0189
.33	.50	Calcd. for equil.		.0182

Gum arabic has a much smaller effect than gelatin. Moreover, no minimum rate was obtained in the experiments with gum arabic, as may be seen from an inspection of Table V.

TABLE V

EFFECT OF GUM ARABIC

Gum arabic mg.	T, min.	Slope	1/T
0	7.0	0.112	0.143
0.50	8.2	.079	.122
2.00	10.0	.076	.100
10.00	12.2	.073	.082
50.00	15.3	.060	.066

The rate of the initial reaction *varies directly with the hydroxylamine concentration.* This is evident from the constancy of the ratio, C/R, given in the last column of Table VI.

TABLE VI

VARIATION OF RATE WITH HYDROXYLAMINE CONCENTRATION

Hydroxylamine, mmole in 60 ml.	T, min.	Slope	$R = 1/T$	C/R
1.00	28.1	0.036	0.036	28.1
2.00	13.1	.067	.076	26.2
4.00	6.8	.112	.147	27.2

The rate varies *inversely as the excess chloride-ion concentration* under the experimental conditions employed. With the exception of the lowest concentration recorded in Table VII, the product $C \cdot R$ is reasonably constant.

TABLE VII

VARIATION OF RATE WITH EXCESS CHLORIDE ION

Added KCl in mmoles	Excess Cl^-, mmoles	T, min.	Slope	1/T	C.R
0	0.50	7.0	0.112	0.143	0.071
0.40	.90	17.0	.056	.059	.054
1.00	1.50	27.0	.038	.037	.0555
2.00	2.50	38.5	.016	.026	.052
3.00	3.50	66	.010	.105	.0525
5.00	5.50	110	.006	.009	.050

Discussion

The surface conditions of the silver chloride precipitate are of major importance in determining the rate of the initial stage of reduction by hydroxylamine. This is clearly shown by the close correlation between the specific surface and the reaction rate, both in the aging experiments and in the effect of an irreversibly adsorbed dye.

The effect of gelatin upon the reaction rate is of special interest. The curve representing rate as a function of the amount of gelatin breaks quite sharply, and additions of gelatin in excess of 0.5 mg. have little effect upon the reaction rate. The specific surface of the silver chloride, calculated from the adsorption of dye IVa (0.105 mg. per 0.50 mmole of AgCl) is approximately 9×10^2 sq. cm. The gelatin layer, therefore, exceeds molecular thickness.[6] Since gelatin in solution is not molecularly dispersed at the temperature employed in the present investigation (20°), it appears quite possible that the amount of gelatin required to produce the maximum effect upon the reaction rate will be smaller at higher temperatures. This point will be investigated later.

The failure of Reinders and Nieuwenburg[2] to obtain a minimum reaction rate at low gelatin concentrations might suggest a fundamental difference in the mechanism of the reaction which they studied. However, in their experiments, the gelatin was added to the reducing solution (Eder's ferrous citrate) preceding the addition of the silver chloride. Under these conditions, equilibrium between the gelatin and the silver chloride would not be obtained. Hence, rates of adsorption are involved in their experiments, and their results cannot be compared with those herein presented.

The form of the curve representing the effect of gelatin suggests that the gelatin is tenaciously held by the silver chloride and is probably irreversibly adsorbed. The decrease in reaction rate is to be attributed to this surface effect. These results do not support Reinders' suggestion that the effect is upon the rate of crystallization of silver from solution. In the present case, moreover, it is possible to measure the effect of gelatin on the reaction between hydroxylamine and silver ions in the presence of sodium sulfite,[3] and these measurements show a much smaller effect of gelatin than that encountered in the present work. The sharp minimum is not obtained. Thus, in one set of experiments in which silver ion was supplied by ionization of the silver sulfite complex, the rate, in the absence of gelatin, was 0.115. The addition of 1.0 mg. of gelatin reduced it to 0.071; of 5.0 mg. of gelatin to 0.051; and of 20 mg. of gelatin to 0.043.

The effect of gum arabic upon the reduction of silver chloride is much smaller than that of gelatin, and the form of the curve is different. The adsorption of gum arabic is probably reversible, and, in fact, the reaction rate data fit fairly well the expression derived from the Langmuir isotherm.

The adsorption of bromide ion[7] and iodide ion[8] by their respective silver salts does not follow the

(6) S. E. Sheppard, A. H. Nietz and R. L. Keenan, *Ind. Eng. Chem.*, **21**, 126 (1929).

(7) K. V. Astakhov and M. Suzdal'tzeva, *J. Phys. Chem. U. S. S. R.*, **6**, 1348 (1935).

(8) I. M. Kolthoff and J. J. Lingane, THIS JOURNAL, **58**, 1528 (1936).

Langmuir isotherm for small ion concentrations, and Kolthoff employs the equation

$$\Delta x = k\Delta \log a$$

for the adsorption of iodide ion to silver iodide. Such an expression obviously cannot hold for high ion concentrations where the surface is almost completely covered. Direct study of the adsorption in this region is beyond the power of ordinary analytical methods. It is of interest to note, therefore, that the reaction rate law suggested by the data in Table VII may be obtained directly from the Langmuir isotherm. The concentrations of chloride employed are such that the surface of the precipitate should be almost completely covered by the adsorbed monolayer, but the concentrations have not yet reached the values at which serious effects might be expected as the result of $AgCl_2^-$ formation.

The free surface, according to the Langmuir expression, is given by the equation

$$l - \alpha = \frac{l}{l + \beta c}$$

If c is relatively large, l may be neglected in comparison with βc, and the free surface will vary inversely as the chloride-ion concentration. Therefore, the rate, which varies as the free surface, varies inversely as the chloride-ion concentration.

The picture of the mechanism of the initial reaction suggested by the results of the present investigation is as follows. Hydroxylamine, in ionized form,[3] attacks those silver ions at the silver chloride surface which are not protected by adsorbed chloride ion or agents such as gelatin and adsorbed dye. It appears further that gelatin and possibly even the strongly held dye IV do not afford complete protection, but merely decrease the frequency of suitable contact between silver ions and hydroxylamine. Reduction of silver ions from solution may be definitely ruled out for the experimental conditions employed. At the end of the reaction, the silver is found in a white, spongy form which closely resembles the original chloride, whereas reduction of silver ions from solution yields silver powder or plating on the vessel walls. If reduction took place from solution, the effect of the gelatin and the dye could be explained only as an effect upon the rate at which the silver chloride dissolved. Solution, as the rate-controlling process, is not compatible with the catalytic action of silver and the direct proportionality between the rate and the hydroxylamine concentration.

Acknowledgment.—The author is indebted to R. H. Lambert and R. D. Walker of these Laboratories for information concerning the dye used in this investigation and for the calculation of the specific surface of the silver chloride precipitate.

Summary

1. The reduction of precipitated silver chloride by hydroxylamine has been studied with particular reference to the effects of aging of the precipitate, dye adsorption, gelatin adsorption and chloride-ion concentration upon the initial reaction rate.

2. The reaction rate closely parallels the change in specific surface with aging. The reaction is strongly inhibited by adsorption of the sensitizing dye, 3,3′-diethyl-9-methylthiocarbocyanine, to the silver chloride, and the reaction rate is approximately proportional to the free surface when the precipitate is only partly covered with the dye.

3. Gelatin markedly inhibits the reaction, and a minimum rate is obtained.

4. The kinetics of the process suggest that the initial reaction involves unprotected silver ions at the silver chloride surface. Under the conditions of this investigation, the silver ions do not pass into solution prior to reduction.

5. The effect of excess chloride-ion concentration upon the reaction rate suggests that, when the silver chloride surface is largely covered with chloride ions, further adsorption follows the Langmuir isotherm.

ROCHESTER, NEW YORK RECEIVED DECEMBER 8, 1939

[CONTRIBUTION FROM THE CHEMICAL INSTITUTE OF THE UNIVERSITY OF OSLO]

Inner Complex Salts of the 8-Hydroxyquinoline-5-sulfonic Acid

BY JACOB MOLLAND

When a solution of ferric sulfate is added to an aqueous solution of 8-hydroxyquinoline-5-sulfonic acid, the mixture is colored a deep green. If increasing amounts of copper sulfate are added to this mixture, the color gradually fades. If copper sulfate is added to a solution of the pure 8-hydroxyquinoline-5-sulfonic acid, no appreciable change of color occurs. The color reaction of iron has a considerable interest for analytical chemistry, as will be shown in papers which are to be published in the near future. The reaction is due to the formation of an inner complex iron salt, and the fading caused by the addition of copper must be explained by the formation of an equilibrium between the green iron salt and a colorless copper salt. The scope of this paper is to study the composition of these salts by means of a spectrophotometric investigation.

Supposing that the color reaction of iron is due to the formation of z molecules of an inner complex salt from x molecules of the 8-hydroxyquinoline-5-sulfonic acid and y ferric ions, the reaction can be represented by the equation

$$xR + yFe^{+++} = zRFe + sH^+$$

R denoting the 8-hydroxyquinoline-5-sulfonic acid and RFe the iron compound. Analogously the formation of the copper compound, RCu, can be represented by the equation

$$\xi R + \eta Cu^{++} = \zeta RCu + \sigma H^+$$

If the initial hydrogen-ion concentration is sufficiently large, the alteration caused by the reaction may be neglected, and the equilibrium condition for an aqueous solution of the 8-hydroxyquinoline-5-sulfonic acid containing iron and copper will be

$$\frac{[Fe^{+++}]^{y\xi}\ [RCu]^{x\zeta}}{[Cu^{++}]^{x\eta}\ [RFe]^{z\xi}} = \text{const.} \qquad (1)$$

Let the initial concentrations be $[R]_0 = a$, $[Fe^{+++}]_0 = b$, $[Cu^{++}]_0 = c$, $[RFe]_0 = 0$, $[RCu]_0 = 0$. In order to simplify the calculation, the concentrations of iron and copper are also kept so large that they may be considered as constant during the reaction. After establishment of the equilibrium, the concentration of the complex iron salt is measured by means of an extinction estimation. Let the observed Bunsen–Roscoe extinction coefficient be d. Further, let the extinction coefficient D be observed when a great excess of iron is added to a solution of the pure 8-hydroxyquinoline-5-sulfonic acid of the concentration A. In this case the 8-hydroxyquinoline-5-sulfonic acid is practically completely transformed to the complex iron salt, giving a concentration Az/x. The salt concentration corresponding to the extinction coefficient, d, is then $[RFe] = dzA/xD$.

On account of the great excess of iron and of copper, the concentration of the 8-hydroxyquinoline-5-sulfonic acid is vanishing. The amount of the acid which is not used for the formation of the iron salt, is used for the formation of the copper salt. This amount is

$$a - \frac{x}{z} \cdot [RFe] = a - \frac{A}{D} d$$

and the quantity of the copper salt formed is

$$[RCu] = \frac{\zeta}{\xi}\left(a - \frac{A}{D} d\right)$$

Finally, the concentrations of iron and of copper will remain practically constant, $[Fe^{+++}] = b$ and $[Cu^{++}] = c$. Introducing these values into equation (1), we obtain

$$\frac{b^{y\xi}\left(a - \frac{A}{D} d\right)^{x\zeta}}{c^{x\eta} d^{z\xi}} = \text{const.} \qquad (2)$$

The ratio x/y can be determined by the following experiment. The maximum concentration of the iron compound obtainable from a concentration p of the 8-hydroxyquinoline-5-sulfonic acid will be pz/x. This concentration can be obtained approximately if a great excess of iron is used. Let the extinction coefficient in this case be d_p. Further, the maximum concentration of the iron salt obtainable from a concentration q of iron will be qz/y, and this concentration is approximately reached if a great excess of 8-hydroxyquinoline-5-sulfonic acid is used. Let the extinction coefficient in this case be d_q. If now the same iron compound is formed in both cases, the molecular extinction coefficient ϵ must be the same in the two experiments, and we obtain the equation

$$\epsilon = \frac{d_p}{\frac{z}{x} p} = \frac{d_q}{\frac{z}{y} q}$$

giving $x/y = pd_q/qd_p$. An experiment gave the figures $p = 3.10^{-5}$, $q = 2.10^{-5}$, $d_p = 0.314$, $d_q = 0.630$. Substituting these figures, we obtain $x/y = 3.01$. The simplest formula giving this result is $(C_9H_6O_4NS)_3Fe$. If we accept this formula, we obtain $x = 3$, $y = 1$, $z = 1$.

If b and c are kept large and constant, and the extinction coefficient is measured for different values of a, equation (2) then can be written in the form

$$\left(a - \frac{A}{D}d\right)^{3\zeta/\xi} \Big/ d = \text{const.} \qquad (3)$$

allowing the determination of the ratio ζ/ξ. Let the extinction coefficient d_m correspond to the concentration a_m and d_n correspond to a_n. Then ζ/ξ is determined by the equation

$$\frac{\zeta}{\xi} = \frac{1}{3}\frac{\log d_m - \log d_n}{\log\left(a_m - \frac{A}{D}d_m\right) - \log\left(a_n - \frac{A}{D}d_n\right)} \qquad (4)$$

In order to determine ζ/ξ by means of equation (4), an experiment was carried out with a series of solutions containing 0.003 g. molecule of ferric sulfate, 0.01 g. molecule of copper sulfate, and increasing amounts from 0.00002 to 0.00014 g. molecule of 8-hydroxyquinoline-5-sulfonic acid per liter. The constant A/D for the wave length in question was determined to 0.0000685 by means of the observations given in Table I. The results are seen in Table I. These data should be combined two by two in equation (4). Generally q numbers can be combined in couples in $\frac{1}{2}q(q-1)$ different ways. In the present case with $q = 9$ we get 36 possible combinations. A mathematical investigation[1] will, however, show that a great part of these combinations will give a poor determination of ζ/ξ, as the mean square error of the extinction estimation in some cases will be greatly magnified by insertion into equation (4). Therefore we select ten combinations giving small mean square errors (Table II). The mean value of ζ/ξ is 0.509, showing that one molecule of the copper compound contains two molecules of 8-hydroxyquinoline-5-sulfonic acid.

TABLE I

10^5a	d
2	0.191
3	.300
4	.415
5	.525
6	.662
8	.875
10	1.152
12	1.370
14	1.624

TABLE II

10^5a_m	10^5a_n	ζ/ξ
14	2	0.509
14	3	.506
14	4	.499
14	5	.525
12	2	.494
12	3	.497
12	4	.488
10	2	.537
10	3	.559
8	2	.476

If a and b are kept constant, we are now able to write equation (2) in the form

$$\frac{\left(a - \frac{A}{D}d\right)^3}{c^{3\eta/\zeta}d^2} = \text{const.}$$

allowing the determination of η/ζ. Let the extinction coefficients d_m and d_n correspond to the concentrations c_m and c_n. Then

$$\frac{\eta}{\zeta} = \frac{\left(\log\left(a - \frac{A}{D}d_m\right) - \frac{2}{3}\log d_m\right) - \left(\log\left(a - \frac{A}{D}d_n\right) - \frac{2}{3}\log d_n\right)}{\log c_m - \log c_n} \qquad (5)$$

An experiment for the determination of η/ζ by means of equation (5) was carried out with a series of solutions containing 0.0025 g. molecule of ferric sulfate, 0.00013 g. molecule of 8-hydroxyquinoline-5-sulfonic acid, and increasing amounts of copper sulfate, from 0.01 to 0.1 g. molecule per liter. The extinction coefficients seen in Table III were observed (corrected for the extinction of the ferric sulfate and the copper sulfate). For the wave length used, A/D was determined to 0.0000786 by means of the data of Table III. Also in this case ten combinations with small mean square errors are collected (Table IV).

TABLE III

$100\,c$	d
0	1.654
1	1.407
2	1.202
3	1.025
4	0.902
5	.765
6	.681
7	.600
8	.553
9	.502
10	.481

TABLE IV

$100\,c_m$	$100\,c_n$	η/ζ
10	1	0.987
10	2	.972
10	3	.937
9	1	1.015
9	2	1.011
9	3	1.030
8	1	1.018
8	2	1.016
7	1	1.039
6	1	1.035
	Mean value	1.006

The copper compound thus contains one atom of copper and two molecules of 8-hydroxyquinoline-5-sulfonic acid.

Summary

The inner complex iron and copper salts of the 8-hydroxyquinoline-5-sulfonic acid were studied by means of extinction measurements, and the composition of the salts is found to correspond to the formulas $(C_9H_6O_4NS)_3Fe$ and $(C_9H_6O_4NS)_2Cu$.

OSLO, NORWAY RECEIVED JULY 24, 1939

(1) J. Molland, *Avhandl. Norske Videnskaps-Akad. i Oslo. I. Mat.-Naturv. Klasse*, **2** (1936).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, POLYTECHNIC INSTITUTE OF BROOKLYN]

Reaction between Ammonia and $SeO_2 \cdot 2HCl$ and $SeO_2 \cdot 2HBr$

BY JULIUS JACKSON[1] AND G. B. L. SMITH

The materials formed when selenium dioxide reacts with hydrogen chloride and bromide have been studied by several investigators.[2] Muehlberger and Lenher[2c] have shown that $SeOCl_2 \cdot H_2O$ is identical with $SeO_2 \cdot 2HCl$ of Ditte[2a] and that $SeO_2 \cdot 2HCl$ will give selenium oxychloride on dehydration. Latimer and Hildebrand[3] have listed this material as $H_2SeO_2Cl_2$. This paper presents a study of the reaction between ammonia and $SeO_2 \cdot 2HCl$ and $SeO_2 \cdot 2HBr$. The data obtained are in harmony with the postulation that these materials are mixtures of $2H^{++}(SeO_2X_2)^{--}$ and $(SeOXH_2O)^{+}X^{-}$.[4]

Experimental

Five g. of either $SeO_2 \cdot 2HCl$ or $SeO_2 \cdot 2HBr$, prepared by treating selenium dioxide with two equivalents of the respective halogen hydride, was dissolved in 100 ml. of the anhydrous solvent and ammonia passed into the solution for a period of two hours. The resulting precipitate was separated by filtration, washed with the solvent, dried in a vacuum desiccator, and analyzed for selenium, ammonia and the respective halogen. The data obtained are summarized in Table I.

TABLE I

DATA FOR THE REACTION BETWEEN $SeO_2 \cdot 2HCl$, $SeO_2 \cdot 2HBr$ AND NH_3 IN ETHER

Reactant	Temp., °C.	Analyses,[a] % Se	Cl or Br	N	Calculated composition $(NH_4)_2SeO_2X_2$	$(NH_4)_2SeO_3$	NH_4X	Total
$SeO_2 \cdot 2HCl$[b]	− 4	29.83	30.68	17.17	42.29	30.03	24.71	97.03
$SeO_2 \cdot 2HCl$	−10	29.37	30.08	17.49	38.22	32.21	26.90	97.13
$SeO_2 \cdot 2HCl$[c]	17	28.01	36.11	14.95	71.80	4.12	19.10	95.02
$SeO_2 \cdot 2HCl$[d]	2	10.41	53.49	23.65	14.06	11.00	75.14	100.02
$SeO_2 \cdot 2HCl$	12	25.56	39.43	16.25	64.59	4.49	27.79	96.87
$SeO_2 \cdot 2HBr$	5	27.96	42.20	12.17	62.11	24.81	12.11	99.03
$SeO_2 \cdot 2HBr$	− 5	25.17	47.33	12.31	63.35	18.36	18.04	99.75
$SeO_2 \cdot 2HBr$	−10 to −5	24.88	47.28	10.80	73.94	12.12	10.65	96.71

[a] Analyses represent mean values of two to four determinations. [b] Solvent was anhydrous ethyl acetate. [c] Solvent was anhydrous acetic acid and ammonia added as ammonium acetate. [d] Ammonia added for thirty minutes.

Discussion

Since the analyses indicated that the reaction products were mixtures, the composition of which varied with conditions, a number of arbitrary hypotheses were tested by computing the composition by the method of "indirect analysis." Reasonable material balances were obtained by assuming that the products were ammonium halide, ammonium selenite and ammonium dihalogenoselenite. These conclusions were confirmed by microscopic examination and X-ray diffraction measurements of several of the materials.

The formation of the ammonium salts of dichloroselenious acid and dibromoselenious acid shows that these acids are present in $SeO_2 \cdot 2HCl$ and $SeO_2 \cdot 2HBr$. However, the formation of the ammonium salts of selenious acid and of hydrogen halide indicates that no single structure can be assigned to $SeO_22 \cdot HCl$ or $SeO_2 \cdot 2HBr$. Accordingly, the authors suggest that these materials comprise an equilibrium (dynamic isomers) mixture as follows

$$H_2SeO_2X_2 \rightleftharpoons SeOXH_2O \cdot X$$

The water in the $SeOXH_2O \cdot X$ is replaced by ammonia forming $SeOXNH_3 \cdot X$ and this liberated water causes hydrolysis of the $SeO_2X^{=}_2$ ion yielding HX and H_2SeO_3. Further work is necessary, however, to establish definitely the presence of $SeOXNH_3 \cdot X$.

Summary

1. The products of the reaction of $SeO_2 \cdot 2HCl$ or $SeO_2 \cdot 2HBr$ with ammonia are ammonium selenite and the corresponding ammonium halide and ammonium di-halogeno-selenite.

2. $SeO_2 \cdot 2HCl$ or $SeO_2 \cdot 2HBr$ comprises an

(1) Research Fellow in Selenium Oxychloride Investigations. Presented before the Division of Physical and Inorganic Chemistry at the Baltimore meeting of the American Chemical Society, April, 1939. Original manuscript received June 1, 1939.

(2) (a) Ditte, *Compt. rend.*, **33**, 223 (1876); *Ann. chim. phys.*, (5) **10**, 82 (1877); (b) Lenher, THIS JOURNAL, **42**, 2499 (1920); (c) Muehlberger and Lenher, *ibid.*, **47**, 1842 (1925); (d) Henley and Sugden, *J. Chem. Soc.*, 1058 (1929); (e) Parker and Robinson, *ibid.*, 2853 (1929); 1316 (1931).

(3) Latimer and Hildebrand, "Reference Book of Inorganic Chemistry," The Macmillan Co., New York, N. Y., 1933, p. 205.

(4) See Smith, *Chem. Rev.*, **23**, 165 (1938), who regards water dissolved in selenium oxychloride as a base.

equilibrium mixture of dynamic isomers of which the di-halogenoselenious acid is one of the most probable constituents.

BROOKLYN, NEW YORK RECEIVED DECEMBER 15, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, POLYTECHNIC INSTITUTE OF BROOKLYN]

Selenium Oxychloro Compounds of Pyridine, Pyridinium Chloride and Related Substances

BY JULIUS JACKSON[1] AND G. B. L. SMITH

Introduction

The basic properties of pyridine and compounds of the same type have been demonstrated not only through the formation of salts, as pyridinium chloride, but also by the formation of series of pyridinates and analogous substances. It is to be expected, therefore, that pyridine and related substances will form definite compounds with selenium oxychloride which may be regarded as bases of the selenium oxychloro system.[2]

This paper presents a summary of the investigations into the nature of the reactions of pyridine, quinoline and isoquinoline in selenium oxychloride. Gordon[3] and Heimerzheim[4] have studied metathetical reactions in selenium oxychloride by conductometric and potentiometric titrations. Solutions of pyridine in selenium oxychloride (base[5]) have been allowed to react with solutions of stannic chloride, ferric chloride, sulfur trioxide and arsenic trichloride in selenium oxychloride (acids). The curves obtained when relative conductances or voltages were plotted against volume of reagent added showed that the acids and bases had reacted in definite stoichiometric ratios. Edgington and Firth[6] have demonstrated the formation of a dipyridinate of selenium oxychloride and found that the compound decomposes to $(C_5H_5N)_2SeCl_4$ and $(C_5H_5N)_2SeCl_2$ at temperatures above 145°.

The present studies have demonstrated the formation of well-defined compounds of selenium oxychloride with pyridine, quinoline and isoquinoline which may be characterized by the general formulas: $RSeOCl_2$; $(R)_2SeOCl_2$. The substances formed are very finely crystalline, or possibly amorphous, white to creamy white solids. The compounds in which two moles of the bases are combined with one mole of selenium oxychloride are not decomposed at 61° in the case of quinoline and isoquinoline but in the case of pyridine this compound loses the base and decomposes to the "monopyridinate" at 61° in 167 hours. Isoquinoline appears to have the greatest tendency to combine in 2-1 ratio and pyridine the least. The compounds of the type $RSeOCl_2$ are all stable at 61°. Attempts to recrystallize these materials from selenium oxychloride yield gelatinous products which cannot be separated from the excess solvent. An attempt to recrystallize the "monopyridinate" $C_5H_5N\cdot SeOCl_2$ from glacial acetic acid yielded a substance which gave the atomic ratios 1:3:1 for Se:Cl:N and for which the formula $C_5H_5NH\cdot SeOCl_3$ is suggested. Definitely crystalline compounds also were obtained by adding pyridinium, quinolinium and isoquinolinium chlorides to $SeOCl_2$. In the case of pyridinium chloride the product appears as beautiful cubical crystals. They all may be characterized by the general formula $(RHCl)\cdot(SeOCl_2)_2$, except in the case of isoquinoline which appears to be a mixture of $RHCl\cdot SeOCl_2$ and $(RHCl)(SeOCl_2)_2$.

Experimental

Materials.—Commercial carbon tetrachloride was purified by fractionation. C. p. pyridine, quinoline and isoquinoline were dried with potassium hydroxide, distilled and preserved in glass ampules. The corresponding chlorides were prepared by precipitation in benzene solution with hydrogen chloride.

Analyses.—Selenium was weighed as elementary selenium, which was precipitated by sulfurous acid from a solution containing 20% hydrochloric acid. Chlorine was weighed as silver chloride. Pyridine, quinoline and isoquinoline were separated by distilling from a solution containing 25% sodium hydroxide and then were absorbed in an approximately 0.1 *N* solution of hydrochloric acid.

(1) Research Fellow in Selenium Oxychloride Investigations. Presented at the Boston meeting of the American Chemical Society, September, 1939. Original manuscript received July 8, 1939.

(2) Smith, *Chem. Rev.*, **23**, 165 (1938).

(3) Gordon, Thesis, B.S. in Chem., 1937, Polytechnic Institute of Brooklyn.

(4) Heimerzheim, Thesis, M.S. in Chem., 1939, *ibid.*, also ref. (2).

(5) The concept of *acid–base* employed in these studies is that of Gilbert N. Lewis, "Valence and the Structure of Atoms and Molecules," A. C. S. Monograph, Reinhold Publishing Co., N. Y., 1923. See also reference 2, and *J. Franklin Inst.*, **226**, 293 (1938).

(6) Edgington and Firth, *J. Soc. Chem. Ind.*, **58**, 192T (1939).

TABLE I

DETAILS OF EXPERIMENTS ON REACTIONS OF SELENIUM OXYCHLORIDE AND PYRIDINE, PYRIDINIUM CHLORIDE AND RELATED SUBSTANCES

Compound employed	Approx. ratio base/$SeOCl_2$ taken	Atomic ratios found[a] Se	Cl	Base	Formula of compound formed	Analyses[b] Found, % Se	Cl	Base	Calcd., % Se	Cl	Base
Pyridine	1–1	1.000	1.986	1.027	$C_5H_5N \cdot SeOCl_2$	31.81	28.59	32.61	32.24	28.96	32.30
Pyridine	2–1	1.000	2.013	1.890	$(C_5H_5N)_2 \cdot SeOCl_2$	This material decomposed to the "mono-pyridinate" in 167 hours at 61°					
Quinoline	1–1	1.003	2.001	1.000	$C_9H_7N \cdot SeOCl_2$	25.55	23.74	43.75	26.77	24.05	43.75
Quinoline	2–1	1.000	1.981	2.030	$(C_9H_7N)_2 \cdot SeOCl_2$	18.05	18.46	60.13	18.62	16.73	60.88
Isoquinoline	1–1	1.000	1.969	1.070	$C_9H_7N \cdot SeOCl_2$	23.12	21.90	49.25	26.77	24.05	43.75
Isoquinoline	2–1	1.000	1.994	2.009	$(C_9H_7N)_2 \cdot SeOCl_2$	18.26	16.91	60.47	18.62	16.73	60.88
Pyridinium chloride	Crystallized from $SeOCl_2$	2.054	5.105	1.000	$C_5H_5NHCl \cdot (SeOCl_2)_2$	34.73	38.90	17.35	35.31	38.82	17.31
		2.100	5.059	1.000		35.87	38.80	17.10			
Quinolinium chloride	Crystallized from $SeOCl_2$	2.017	4.986	1.000	$C_9H_7NHCl \cdot (SeOCl_2)_2$	32.07	35.65	26.01	31.75	35.65	25.97
Isoquinolinium chloride	Crystallized from $SeOCl_2$	2.974	7.080	2.000	Probably mixtures of	29.39	31.42	32.33	Probably mixtures		
		2.910	7.678	2.000	the monosolvate	28.63	33.91	32.18			
		2.235	4.986	1.000	and disolvate	31.11	31.17	22.78			

[a] Atomic ratios are for the moist material for the first six compounds and are for the crystalline material for the chlorides. These values are all based on at least two determinations. [b] Analyses reported are based on two to four determinations.

The excess hydrochloric acid was titrated with standard sodium hydroxide using methyl orange as indicator, followed by a determination of the combined hydrochloric acid using phenolphthalein as indicator.

Reaction between Selenium Oxychloride and Pyridine Bases.—A weighed sample of selenium oxychloride was dissolved in 50 ml. of carbon tetrachloride. Either a one or two molar equivalent quantity of pyridine or other base was dissolved in 50 ml. of the same solvent and the two solutions were added dropwise to 50 ml. of carbon tetrachloride contained in a 500-ml. Wolf flask. The white solid which formed was separated by filtration and washed three times with fresh carbon tetrachloride. One portion of the material was analyzed immediately for selenium, chlorine and base. Another portion was freed of carbon tetrachloride by drying in an Abderhalden oven at 61° and 17 mm. pressure. The experimental details and analytical data obtained are presented in Table I.

Reaction between Selenium Oxychloride and the Chlorides of Pyridine Bases.—Ten ml. of selenium oxychloride was saturated with the respective chloride at a temperature of 70–80° and the resulting solution chilled to 0° or slightly lower and allowed to remain at this temperature for one hour. The resulting crystals were separated by filtration after adding 25 ml. of carbon tetrachloride, washed with the same liquid and dried in a vacuum desiccator. Table I presents the analytical data obtained.

Discussion

The experimental findings presented in this paper are in agreement with the thesis that selenium oxychloride is the parent solvent of a system of compounds.[2] The formation of $C_5H_5N \cdot SeOCl_2$ and $(C_5H_5N)_2SeOCl_2$ and the analogous compounds of quinoline and isoquinoline is suggestive of ammonium hydroxide and ammonium oxide. It is suggested that the pyridine type compounds act as bases, "electron pair donors" toward the solvent cation, $SeOCl^+$. This is a verification of the postulation that pyridine when dissolved in selenium oxychloride forms selenium oxychloro–pyridinium cation, $C_5H_5NSeOCl^+$, and chloride ion.

The isolation of definite selenium oxychloro compounds of pyridinium chloride and the other two chlorides, which we may term "solvates," indicates something about the solvation of the chloride ion in selenium oxychloride. Julien[7] found that hydrogen chloride is soluble in selenium oxychloride and that the resulting solution has a high electrical conductivity. Wise[8] isolated the mono-solvates of potassium chloride and believed that rubidium and cesium chlorides also formed "mono-solvates." Since potassium, rubidium and cesium ions are not likely to be solvated, it is probable that the molecule of selenium oxychloride is associated with the chloride ion and $KCl \cdot SeOCl_2$ is potassium trichloroselenite, $K^+(SeOCl_3)^-$. The data presented in this paper, however, for pyridinium chloride and related chlorides are indicative of a disolvated chloride ion, *i. e.*, $Se_2O_2Cl_5^-$. In each case selenium would have a covalent number of four.

Summary

1. Selenium oxychloride forms two series of compounds with pyridine, quinoline, and isoquinoline in which one and two moles of the base are combined with one mole of selenium oxychloride. These facts substantiate the view that pyridine and related substances act as bases in selenium oxychloride.

(7) Julien, THIS JOURNAL, **47**, 1799 (1925).
(8) Wise, *ibid.*, **45**, 1233 (1923).

2. Pyridinium chloride and quinolinium chloride crystallize from solutions in selenium oxychloride with two molecules of the solvent. Isoquinolinium chloride probably forms a mixture of the mono-solvate and the di-solvate. These facts indicate the possibility of disolvation of the chloride ion in selenium oxychloride.

BROOKLYN, N. Y. RECEIVED DECEMBER 29, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF CORNELL UNIVERSITY]

Chlorogermanic Acid and the Chlorogermanates. Properties and Crystal Structure of Cesium Hexachlorogermanate

BY A. W. LAUBENGAYER, O. B. BILLINGS AND A. E. NEWKIRK

The tendency of the elements of Group IV, exclusive of carbon and thorium, to form complex ions with the halogens is well recognized. Germanium is known[1] to form hexafluogermanates but no other halogen complexes of germanium have been studied. Pauling[2] has shown that it is possible to predict the type of aggregate which two ions can form by considering the ratio of the ionic radii. Using his values for the radii, the ratios of the univalent ionic radius of germanium to those of fluorine, chlorine, bromine, and iodine are 0.54, 0.42, 0.39, and 0.35, respectively. Since 0.41 is the minimum radius ratio which will permit hexacoördination it is evident that germanium should form hexahalogen complex ions with fluorine and chlorine but can only have a coördination number of four toward bromine or iodine. Because the ratio in the case of chlorine is so close to the limit between hexa- and tetra-coördination, it is to be anticipated that the hexachlorogermanate ion will not form except under the most favorable conditions.

In the present investigation the formation of chlorogermanic acid and its salts has been studied.

Experimental

Formation of Chlorogermanic Acid.—Germanium tetrachloride is slightly soluble in concentrated hydrochloric acid.[3] This indicates that chlorogermanic acid may be formed, but that it is not very stable in solution since its formation to any great extent would give rise to high solubility of the tetrachloride.

Chlorostannic acid crystallizes as the hexahydrate when a solution of stannic chloride in concentrated hydrochloric acid is chilled. A similar procedure was tried in an effort to isolate chlorogermanic acid. Germanium tetrachloride was added to an equal volume of 12 *N* hydrochloric acid to give a two liquid layer system and the mixture was chilled to −49°. No crystals appeared. When gaseous hydrogen chloride was bubbled through cold anhydrous germanium tetrachloride no solid formed above −49°, the freezing point of germanium tetrachloride. If chlorogermanic acid is formed under such conditions it is present in such small amounts that it will not crystallize out.

Migration studies of solutions of various concentrations of germanium tetrachloride in 6 *N* hydrochloric acid gave evidence that the small amount of germanium in solution is present in complex ions. The solutions were electrolyzed in a migration cell which had a capacity of 60 cc. The concentration of germanium in anolyte and catholyte was determined before and after electrolysis with a given current for a definite period of time. These experiments are summarized in Table I.

TABLE I

MIGRATION OF GERMANIUM DURING ELECTROLYSIS OF SOLUTIONS OF $GeCl_4$ IN 6 *N* HCl

Expt.	Time, min.	Current, m. amp.	Grams Ge per 1000 g. solution: Original	Anolyte finally	Catholyte finally
1	70	86	2.001	2.072	1.903
2	60	87	4.681	4.734	4.627

Both of these experiments show a small but significant migration of germanium toward the anode, indicating the presence of an anion of this element, presumably $GeCl_6^{=}$. The solutions contained such large concentrations of other ions that the concentration of chlorogermanate ions could not be calculated from the data.

Formation of Chlorogermanates.—The direct addition of ammonia to 12 *N* hydrochloric acid saturated with germanium tetrachloride gave only a precipitate of ammonium chloride with no evidence of chlorogermanate formation.

The reactions of the alkali chlorides with germanium tetrachloride were studied under a variety of conditions.

Anhydrous germanium tetrachloride was refluxed with a weighed amount of sodium chloride for several days, the mixture being protected from atmospheric moisture. No evidence of any reaction could be observed. Similarly the chlorides of lithium, potassium, cesium and calcium did not react when refluxed with anhydrous germanium tetrachloride.

The low solubility of germanium tetrachloride in concentrated hydrochloric acid makes it impossible to achieve any large concentration of germanium tetrachloride in an

(1) Winkler, *J. prakt. Chem.*, **36**, 177 (1887); Müller, *Proc. Am. Phil. Soc.*, **65**, 44 (1926); Dennis and Staneslow, THIS JOURNAL, **55**, 4392 (1933).

(2) Pauling, THIS JOURNAL, **49**, 765 (1927).

(3) Allison and Müller, THIS JOURNAL, **54**, 2833 (1932).

aqueous solution containing sufficient acid to prevent hydrolysis. Also the alkali chlorides are all rather insoluble in concentrated hydrochloric acid. It is impossible, therefore, to prepare the aqueous solution presumably the most ideal for the formation of chlorogermanates, namely, one high in concentration of chloride ion, germanium tetrachloride, and alkali ion. All attempts to obtain chlorogermanates from such systems failed.

Cesium chloride, however, is quite soluble in a mixture of one volume of ethyl alcohol and two volumes of 12 *N* hydrochloric acid. When germanium tetrachloride was added to such a solution a flocculent yellowish-white precipitate was formed. This was filtered off, washed with 12 *N* hydrochloric acid, and dried in air to a light yellow powder. It was found advisable to use less than the equivalent amount of germanium tetrachloride for the precipitation to avoid contamination of the precipitate by the tetrachloride. Analysis of the dry powder showed it to be cesium hexachlorogermanate, Cs_2GeCl_6. In the analysis the chlorine was determined as silver chloride and the germanium by precipitation as the sulfide and conversion to the oxide.[4] Cesium was determined by heating the cesium chlorogermanate with a low flame. The compound decomposes into cesium chloride and germanium tetrachloride and the latter volatilizes. The residual cesium chloride was finally heated to its melting point, 646°, and then cooled and weighed. It was found to retain only very slight traces of germanium.

Anal. Calcd. for Cs_2GeCl_6: Cs, 48.21; Ge, 13.18; Cl, 38.62. Found: Cs, 48.77; Ge, 12.54; Cl, 38.62.

Properties of Cesium Hexachlorogermanate.—Cesium hexachlorogermanate dissolves readily in water, undergoing rapid hydrolysis. It is insoluble in 12 *N* hydrochloric acid and in absolute ethyl alcohol, but 100 cc. of a 1:2 mixture dissolves 1.5 g. at 0° and 4.3 g. at 75°. It may readily be recrystallized from this mixed solvent.

Cesium chlorogermanate is stable in dry air at room temperature. Passage of a slow stream of nitrogen over it at various temperatures and then through a dilute solution of silver nitrate showed that decomposition, without melting, to cesium chloride and germanium tetrachloride became appreciable at 160° and was very rapid and in some hours complete at 200°.

The density of the compound at 25° was found to be 3.45 ± 0.01 by the pycnometric method, using toluene as the immersion liquid.

The crystals are well formed and are isotropic and, for the most part, octahedral. Their refractive index is 1.68.

Crystal Structure of Cesium Hexachlorogermanate.—A powder X-ray diffraction pattern for the compound was obtained, using Cu Kα radiation. The data fitted a face-centered cubic lattice, since only lines having all odd or all even indices appeared. The structure is probably of the ammonium chloroplatinate type, and the intensity calculations have been made on this basis. This type of structure is also shown by cesium fluogermanate.[5]

A value of a_0 was calculated for each line. The values for the last 20 lines were plotted against $\cos^2\theta$, and the best straight line through the points was extrapolated to $\cos^2\theta = 0$ to obtain $a_0 = 10.21$ Å. In this manner, correction was

TABLE II

h k l	*I*-obsd.	*I*-calcd.	*h k l*	*I*-obsd.	*I*-calcd.
111	20	28	10, 00	0	1.2
200	19	14	860		
220	105	91	10, 20	5	13
311	3	7	862		
222	86	77	951	0.8	4
400	75	72	773		
331	0	1	10, 22	1.6	6
420	8	11	666		
422	58	68	953	0.8	2
511	7	8	10, 40	.7	2
333			864		
440	46	49	10, 42	3	8
531	5	6	11, 11	0	0.04
600	5	6	775		
442			880	0.7	4
620	19	12	11, 31	.6	2
533	0	1	971		
622	17	28	955		
444	16	16	10, 44	.6	1.5
711	3	5	882		
551			10, 60	2.4	3.5
640	0.9	2	866		
642	13	24	11, 33	0	0.3
731	1.6	2.5	973		
553			10, 62	2.3	7
800	1.4	8	12, 00	3.4	8
733	0	1	884		
820	1.4	4	11, 51	0	0.2
644			777		
822	5	8	12, 20	0	1
660			12, 22	5	6.5
751	0.6	2	10, 64		
555			11, 53	0	3
662	5	12	975		
840	7	21	12, 40	1.5	5
911	0.6	2	991	0.5	0.9
753			12, 42		
842	1.1	4	10, 80	1.4	3
664	4	7	886		
931	1	2	10, 82	1.3	6.5
844	6	15	13, 11		
933			11, 71	0	0.5
771	0	1	11, 55		
755			993		
			10, 66	1	2.3

( ) Dennis and Johnson, THIS JOURNAL, 47, 790 (1925).

(5) Wyckoff and Müller, *Am. J. Sci.*, 13, 347 (1927).

made for incorrect centering of the specimen and for absorption in the powder rod.[6]

The density of cesium chlorogermanate as determined pycnometrically was 3.45. From this figure and the value of a_0 the number of molecules in the unit cell was calculated to be 3.96. The number of molecules in the unit cell is therefore four, and the density calculated from X-ray data is 3.48.

The values for the intensities of the powder lines were calculated from the formula

$$I = \text{constant}\left(\frac{1+\cos^2 2\theta}{\sin 2\theta \sin\theta}\right) jS^2 \text{ where}$$

$$S = f_{Ge} + 2f_{Cs}\cos 2\pi\left(\frac{h+k+l}{4}\right) + 2f_{Cl}(\cos 2\pi hx + \cos 2\pi kx + \cos 2\pi lx)$$

The atomic f-values of Pauling and Sherman[7] were used throughout these calculations. In order to determine the chlorine parameter, values of 0.22, 0.23 and 0.24 were used to calculate the intensities for the first ten lines. The value $x = 0.23$ gave the best agreement with the observed and was therefore used in the calculation of the remaining intensities. The observed intensities were corrected for absorption in the powder rod in the usual manner. The values for the observed and calculated intensities are given in Table II. The agreement is reasonable.

From the chlorine parameter of 0.23, the germanium–chlorine distance was calculated to be 2.35 Å. This is in good agreement with the value 2.34 Å. calculated from the ionic radii of Pauling.[2]

The authors wish to acknowledge the assistance of Professor J. L. Hoard who made available X-ray equipment and helped with the interpretation of the X-ray data.

Summary

1. The formation of chlorogermanic acid and its salts has been studied under a variety of conditions.

2. Evidence for the formation of negatively charged complex ions, presumably $GeCl_6^=$, when germanium tetrachloride is dissolved in concentrated hydrochloric acid has been obtained by migration experiments.

3. Cesium hexachlorogermanate has been prepared and its properties and crystal structure have been studied. It has a face-centered cubic lattice.

ITHACA, N. Y. RECEIVED SEPTEMBER 1, 1939

(6) "Internationale Tabellen zur Bestimmung von Krystallstrukturen," Gebrüder Borntraeger, Berlin, 1935, pp. 581–582.

(7) Pauling and Sherman, *Z. Krist.*, **81**, 1 (1932).

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 756]

The Dielectric Constants of Some Pairs of Diastereomers

BY SAUL WINSTEIN AND REUBEN E. WOOD

Pairs of diastereomeric substances show no very characteristic differences in physical properties such as boiling point, polarizability, etc.[1] However, owing to the lack of free rotation about carbon–carbon single bonds[2] there is the possibility that the dipole moments and thus the dielectric constants of *meso* and *dl* compounds or *erythro* and *threo* compounds may differ sufficiently to be useful analytically. Also, there is the possibility that there may be enough regularity in these differences to allow the formulation of rules for the assignment of configuration to diastereomers on the basis of dielectric constant measurements. To study these possibilities and in some cases to obtain data immediately useful in analysis and identification we have determined the dielectric constants of some pairs of diastereomers available to us.

Materials

***meso-* and *dl*-2,3-Diacetoxybutanes.**—The *meso* isomer, m. p. 2.5°, b. p. (13 mm.) 83.6°, was prepared[3] from *meso*-2,3-butanediol, m. p. 34.0°, and distilled through a 40-cm. Weston column.[4] The *dl* isomer, m. p. 42.1°, was prepared[3] from the *dl*-2,3-butanediol from pure *cis*-2,3-epoxybutane.[5]

***dl-erythro-* and *dl-threo*-2,3-Diacetoxypentanes.**—These materials were kindly furnished us by Professor H. J. Lucas and Mr. M. J. Schlatter of these Laboratories.

(1) Hückel, "Theoretische Grundlagen der organischen Chemie," Vol. II, Akademische Verlagsgesellschaft m. b. H., Leipzig, 1935, p. 125.

(2) See Weissberger, *J. Org. Chem.*, **2**, 245 (1937), for a review of configuration about single bonds.

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

(4) Weston, *Ind. Eng. Chem., Anal. Ed.*, **5**, 179 (1933).

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

Distillation through the Weston column yielded constant boiling materials; *erythro* isomer, b. p. (12 mm.) 90.4°; *threo* isomer, b. p. (12 mm.) 94.3°.

***dl-erythro-* and *dl-threo*-3,4-Diacetoxyheptanes.**—These materials were generously loaned us by Dr. W. G. Young of the University of California at Los Angeles. The *threo* isomer was pure while the *erythro* material needed redistillation. Distillation through the Weston column yielded constant boiling material, b. p. 114.2° (10 mm.).

***meso-* and *dl*-2,3-Dibromobutanes.**—These compounds were obtained as constant boiling materials from *meso*-2,3-diacetoxybutane and *trans*-2,3-epoxybutane[5,6] or the bromohydrin or 2-acetoxy-3-bromobutane derived from it. k_2 for the reaction of these dibromides with potassium iodide[7] in 99.00% methanol at 74.93° using synthetic methanol was 0.0553 for the *meso* preparation and 0.0298 for the *dl* compound.

***dl-erythro-* and *dl-threo*-2,3-Dibromopentanes.**—Very pure materials were generously made available by Mr. M. J. Schlatter.

***meso-* and *dl*-3,4-Dibromohexanes.**—These compounds were kindly supplied by Dr. W. G. Young.

***dl-erythro-* and *dl-threo*-2-Acetoxy-3-bromobutanes.**—These compounds were prepared as previously described[5,6] starting with pure *cis-* and *trans*-2,3-epoxybutanes.

Apparatus and Method

The dielectric constant measuring apparatus has been referred to in another paper.[8] As mentioned there the cell used was of the type described by Doborzynski.[9] For a cell of this type there may be derived an expression which relates approximately the cell's capacitance to the dielectric constant of the filling fluid. This will be of the form

$$\epsilon = \frac{l(C - m)}{1 - n(C - m)}$$

in which ϵ is the dielectric constant of the fluid, C the capacitance of the cell and l, m and n are constants characteristic of the cell. Such an equation was used to calculate the dielectric constants here reported. The values of l, m and n for the cell used were determined from measurements with fluids of known dielectric constant, *viz.*, air and the carefully purified liquids carbon tetrachloride, benzene, chlorobenzene, ethyl bromide, and ethylene dichloride. It was found possible to select values for l, m and n so that when the resulting equation was used to calculate the dielectric constants of the standard fluids ϵ's resulted which were on the average within 0.2% of the literature values we chose, namely, 1.001,[10a] 2.227,[10b] 2.272,[10c] 5.612,[10c] 9.21,[10d] 10.36.[10c]

(6) Winstein and Lucas, THIS JOURNAL, **61**, 1581 (1939).
(7) Dillon, Young and Lucas, *ibid.*, **52**, 1953 (1930).
(8) Wood and Dickinson, *ibid.*, **61**, 3259 (1939).
(9) D. Doborzynski, *Z. Physik*, **66**, 657 (1930).
(10) (a) "Int. Crit. Tab.," Vol. 6, p. 77; (b) Davies, *Phil. Mag.*, **21**, 1 (1936); (c) Sugden, *J. Chem. Soc.*, 768 (1933); (d) Smyth and Morgan, THIS JOURNAL, **50**, 1553 (1928).

Data and Discussion

Table I summarizes the dielectric constants, ϵ, we have obtained for the substances investigated. In the case of the *dl*-2,3-diacetoxybutane and *meso*-3,4-dibromohexane the values recorded are those obtained by linear extrapolation from the value for a mixture and the value for one pure diastereomer. These values are thus not as accurate as the others.

The values, in general, are listed to four significant figures to show the differences between the isomeric samples. The differences between the dielectric constant of the members of a pair of diastereomers are accurate enough to require so many figures even though the accuracy of the absolute values is only about 0.2%.

From a practical standpoint it is interesting to notice in Table I the very appreciable differences that exist in most cases between the dielectric constants of the isomeric substances. The dielectric constant is thus an excellent property for identification and even analysis in these cases that are usually otherwise quite difficult. An identification or analysis on the basis of a dielectric constant measurement is especially accurate if one or both of the pure isomers are available so that high accuracy for the absolute value of the dielectric constant is not necessary. Already the dielectric constants of the 2,3-dibromobutanes[5,6] and the 2,3-dibromopentanes[11] have proved very useful in these Laboratories.

TABLE I

PROPERTIES OF SOME PAIRS OF DIASTEREOMERS

Substance	Isomer	d^{25}_4	$n^{25}D$	ϵ at 25°
2,3-Diacetoxybutane	*meso*	1.0213	1.4121	6.644
	dl	1.0235[a]	1.4133[a]	5.10[a]
2,3-Diacetoxypentane	*dl-erythro*	1.0022	1.4147	6.734
	dl-threo	1.0073	1.4175	5.228
3,4-Diacetoxyheptane	*dl-erythro*	0.9758 (20°)	1.4207	6.684
	dl-threo	0.9829 (20°)	1.4241	5.029
2,3-Dibromobutane	*meso*	1.7747	1.5091	6.245
	dl	1.7836	1.5125	5.758
2,3-Dibromopentane	*dl-erythro*	1.6724	1.5062	5.430
	dl-threo	1.6745	1.5064	6.507
3,4-Dibromohexane	*meso*	1.5940	1.5049	4.67[b]
	dl	1.5896	1.5031	6.732
2-Acetoxy-3-bromobutane	*dl-erythro*	1.3327	1.4489	7.268
	dl-threo	1.3320	1.4490	7.414

[a] Obtained by linear extrapolation using the values for one pure isomer and for a mixture of *meso* and *dl* isomers. Mixtures were measured either due to lack of material or to be able to perform the measurement at 25°. Mixture of 58.5% *dl* and 41.5% *meso* exhibited dielectric constant of 5.740. [b] See *a*. Mixture of 60.7% *dl* and 39.3% *meso* exhibited a dielectric constant of 5.922.

(11) Lucas and Schlatter, unpublished work.

Dielectric constants have been reported previously for several of the compounds we have investigated. Sherrill and co-workers[12] have reported the dielectric constant of 2,3-dibromopentane prepared from 2-pentene obtained presumably by Boord's[13] synthesis as 5.43. This agrees with our value for *dl-erythro*-2,3-dibromopentane and indicates that the 2-pentene was pure *trans*-2-pentene. It is very interesting that the Boord synthesis gives essentially pure *trans*-2-pentene.

The 2,3-dibromobutanes have been previously investigated by Trieschmann,[14] but the materials employed by him were of doubtful purity. The dielectric constants 8.96 for the *meso* isomer and 8.72 for the *dl* compound reported by Trieschmann are about 50% larger than the values reported in this paper. In view of the values for the dielectric constants generally reported for substances of the type of the dibromobutanes it seems very unlikely that the dibromobutanes have dielectric constants as high as 8.96 and 8.72 and the finding of Trieschmann that *meso*- and *dl*-2,3-dibromobutane possess the same dipole moment possibly is incorrect also.

We had hoped that in a series of pairs of compounds such as the 2,3-diacetoxybutanes, 2,3-dibromobutanes, and 2-acetoxy-3-bromobutanes, there would be a regularity in the relative dielectric constants of the isomers. However, values obtained do not indicate a simple correspondence between relative dielectric constant and configuration. Since the *meso* isomer displays the higher dielectric constant in the case of both the dibromobutanes and the diacetoxybutanes, one might expect the *erythro*-2-acetoxy-3-bromobutane to exhibit a larger dielectric constant than the *threo* compound. Instead the last two compounds have nearly the same dielectric constant and that of the *threo* isomer is slightly larger.

In the case of the dibromobutanes, dibromopentanes, and dibromohexanes the situation is similar. The order of relative dielectric constants in the case of the dibromobutanes is different from the order obtaining for the other two pairs of dibromides. The greatest regularity observed was in the diacetoxyalkane series. For each of the three pairs of these compounds examined the *meso* or *erythro* isomer has the larger dielectric constant. In fact, the dielectric constants are nearly the same for corresponding members of the three different pairs of isomers.

Several expressions[15,16,17] relating the dielectric constant of liquids to the dipole moments of their molecules have been proposed. Using Onsager's equation

$$\mu^2 = \frac{(n^2 + 2\epsilon)(\epsilon - n^2)}{\epsilon(n^2 + 2)^2} \frac{M}{D}$$

Böttcher[18] calculated μ for a number of liquids and obtained values agreeing reasonably well on the whole with those reported for the gaseous molecules. It seemed worth while to subject our data to a similar treatment to estimate the dipole moments, and in particular the relative dipole moments, of the diastereomeric pairs we studied.

Since between the members of each pair of these isomers ϵ differs much more than the other parameters appearing in Onsager's equation, the difference in the calculated μ's between isomers is in the same direction as the difference between ϵ's. We used $n^{25}D$ for n; the dipole moment values thus calculated are tabulated below.

Compound	Dipole moment of the *meso* or *dl-erythro* isomer		Dipole moment of the *dl* or *dl-threo* isomer
2,3-Diacetoxybutane	2.35	>	1.95
2,3-Diacetoxypentane	2.48	>	2.07
3,4-Diacetoxyheptane	2.68	>	2.18
2,3-Dibromobutane	1.73	>	1.62
2,3-Dibromopentane	1.67	<	1.90
3,4-Dibromohexane	1.57	<	2.06
2-Acetoxy-3-bromobutane	2.23	≈	2.26

It has been pointed out by Dr. V. Schomaker that the dipole moment of ethylene dichloride calculated by means of Onsager's theory from the dielectric constant of the liquid is considerably greater than the dipole moment of a molecule in the gas at the same temperature, and that this fact probably indicates that the relative abundance of the *cis* and *trans* forms of ethylene dichloride in the liquid is quite different from the relative abundance in the gas. The same effect may be expected to occur in the liquids discussed in the present paper; the dipole moments which we have calculated may, for this reason, differ appreciably from those of the corresponding free molecules.

Moreover, it is conceivable, but not probable, that molecular association[17] in some of the liquids affects the dielectric constants of the members of

(12) Sherrill, Smith and Thompson, THIS JOURNAL, **56**, 611 (1934).
(13) Boord and co-workers, THIS JOURNAL, **52**, 651 (1930); **53**, 1505 (1931).
(14) Trieschmann, *Z. physik. Chem.*, **B33**, 283 (1936).
(15) Wyman, THIS JOURNAL, **58**, 1482 (1936).
(16) Onsager, *ibid.*, **58**, 1486 (1936).
(17) J. N. Wilson, *Chem. Rev.*, **25**, 377 (1939).
(18) Böttcher, *Physica*, **6**, 59 (1939).

a diastereomeric pair enough differently to lead to an erroneous conclusion as to which member has the higher dipole moment. Pertinent to this question are Stewart's findings[19] that in the cases of diethyl tartrate, pinene and camphene the *dl* mixtures possess the same dielectric constants as the corresponding *d* or *l* compounds.

Despite the uncertainties and approximations involved in computing dipole moments from the dielectric constants of pure liquids it seems probable that the values tabulated above indicate correctly both the approximate dipole moments of the diastereomers and the sense of the difference between the dipole moments of the members of a pair of isomers.

While any extended discussion of the significance of the relative dipole moments of the pairs of diastereomers we have investigated should await actual quantitative work on the dipole moments, several things may be pointed out at this time. It would seem that the order *meso* > *dl* and the analogous one *erythro* > *threo* are much more prevalent than has been indicated by the previous literature. The dipole moments of the diethyl tartrates, the dimethyl α,α'-dimethoxysuccinates, the dimethyl α,α'-dichlorosuccinates, the hydrobenzoins, and the stilbene chlorides have been reported previously.[20,21] In these cases only the diethyl tartrates exhibit the order of dipole moments *meso* > *dl*, and the difference in dipole moments is very large only for the stilbene chlorides. Judging from dielectric constants it would appear that in the cases investigated by us the differences between dipole moments of isomers are not very large. Except for the dibromobutanes, the compounds which exhibit the order *meso* > *dl* seem to be the ones with angular polar groups.[2]

The relative dipole moments of diastereomers such as the 2,3-dibromobutanes depend on both the equilibrium configurations about the central carbon–carbon bond and the vibrations or rotations about this bond. Thus, the customary expectation that the *meso* isomer will have the lower dipole moment seems difficult to justify. For example, in the case of the 2,3-dibromobutanes, electron diffraction studies[22] have shown that the equilibrium configuration for both the *meso* and *dl* isomers is that with the bromine atoms *trans* to each other. Thus, the equilibrium *meso* molecule has zero moment and the equilibrium *d* or *l* molecule has a small moment. The rather large moment of this type of molecule then arises chiefly from vibrations about the mean configuration. The shape of the potential curve is different for the *meso* and *dl* compounds because different interactions are involved in the vibration about the mean position. Thus, it is conceivable that either order, *meso* > *dl* or *dl* > *meso* is possible for diastereomeric pairs.

Acknowledgment.—We wish to acknowledge our gratitude to those already mentioned as having furnished chemicals, and also to Professor Linus Pauling and particularly to Dr. J. Norton Wilson for criticisms and suggestions.

Summary

The dielectric constants of seven pairs of diastereomers, namely, the 2,3-diacetoxybutanes, 2,3-diacetoxypentanes, 3,4-diacetoxyheptanes, 2,3-dibromobutanes, 2,3-dibromopentanes, 3,4-dibromohexanes, and 2-acetoxy-3-bromobutanes, have been measured. In general, the members of a pair of diastereomers differ sufficiently in their dielectric constants for the dielectric constant to be useful for analytical purposes.

From these dielectric constants dipole moments have been estimated using Onsager's equation. The ϵ's and μ's for *meso* and *erythro* compounds are compared with those for the corresponding *dl* and *threo* isomers.

PASADENA, CALIFORNIA RECEIVED DECEMBER 12, 1939

(19) Stewart, *J. Chem. Soc.*, **93**, 1059 (1908).

(20) Stefan Goldschmidt, "Hand- und Jahrbuch der chemischen Physik. 4. Stereochemie," Akademische Verlagsgesellschaft m. b. H., Leipzig, 1933, p. 52, for a summary.

(21) Eisenlohr and Hill, *Z. physik. Chem.*, **B36**, 30 (1937).

(22) Stevenson and Schomaker, THIS JOURNAL, **61**, 3173 (1939).

[CONTRIBUTION FROM THE HERCULES EXPERIMENT STATION, HERCULES POWDER CO.]

The Dehydration of Some Tertiary Alcohols Containing the Cyclohexane Ring

BY WILLIAM A. MOSHER

Although many tertiary alcohols containing the cyclohexane ring have been prepared, especially by Sabatier and Mailhe,[1] it appears that none has been subjected to a careful study of its dehydration products. In dehydration only one of the expected products has been reported. The properties of the olefins formed are such as to make physical separation extremely difficult, if not impossible, when only small amounts of materials are used.

In order to obtain data on the manner of dehydration of certain of these alcohols, as well as to gain some insight into the process as applied to the group as a whole, we have prepared and dehydrated 1-methylcyclohexanol, 1-ethylcyclohexanol, 1-isopropylcyclohexanol, and dimethylcyclohexylcarbinol. The alcohols were prepared by means of the Grignard reaction. The dehydration was effected by heating with iodine under a column so that the olefins and water distilled out of the mixture as formed. The use of ozonolysis offers a simple and satisfactory approach to the problem as it makes physical separation of the isomers unnecessary. If we assume that no shifting of the double bonds occurs after dehydration, one of the products of each dehydration will give rise to formaldehyde, acetaldehyde, or acetone; in the case of dimethylcyclohexylcarbinol both acetone and formaldehyde may be formed. These facts greatly simplify the problem as it is only necessary to ozonize the olefin mixture obtained by dehydration and analyze, both qualitatively and quantitatively, for the appropriate carbonyl compounds. From the analyses the ratios of the isomers in the dehydration products may be determined. The accuracy of such a method is approximately 10%. A very complete discussion of the technique of ozonolysis is given by Church, Whitmore and McGrew.[2]

The absence of isomerization concomitant with, or subsequent to, dehydration is indicated by the following facts. In the case of dimethylcyclohexylcarbinol the summation of acetone and formaldehyde was within 5% of the theoretical. In the case of 1-methylcyclohexanol, analysis for methyl ketone in the ozonolysis product gave a value of 93% of the theoretical. Finally, the method of dehydration used minimizes secondary reactions by removing the dehydrated product from the action of the dehydrating agent. The absence of polymerization is indicated by the recovery of yields of olefin always better than 97% having the properties of the monomer.

We may look upon dehydration as a competitive reaction indicating the relative affinities of structurally different carbon atoms for a proton. According to the concept of Whitmore[3] the hydroxyl group is removed leaving a carbon atom with only six electrons. To stabilize this organic fragment a proton may be lost from an adjacent carbon atom. The determination of the ratio in which different carbon atoms lose protons measures the affinities of the groups in question and gives a relative indication of the bond strengths.

In the dehydration of 1-methylcyclohexanol no formaldehyde was detected in the products of ozonolysis indicating that no methylenecyclohexane was formed and that only 1-methylcyclohexene was formed by the dehydration. In the case of 1-ethylcyclohexanol only a trace of acetaldehyde was found, indicating that less than 1% of ethylidenecyclohexane was formed. Presumably the other 99% was present as 1-ethylcyclohexene. An amount of acetone corresponding to approximately 5% of the theoretical was found in the products from 1-isopropylcyclohexanol, indicating this percentage of isopropylidenecyclohexane in the olefin mixture. The analysis of the products from dimethylcyclohexylcarbinol gave values of approximately 50% each for acetone and formaldehyde indicating equal amounts of isopropylidenecyclohexane and isopropenylcyclohexane in the mixture.

Dehydration apparently will take place in such a manner that the double bond occurs principally in the ring when this is possible. In other words the hydrogen atoms attached to the ring are less firmly bound than those of a more aliphatic nature. In the case of 1-isopropylcyclohexanol a cyclic hydrogen is lost in preference to the tertiary

(1) Sabatier and Mailhe, *Compt. rend.*, **138**, 1321 (1904); *Bull. soc. chim.*, (3) **33**, 75 (1905); *Ann. chim.*, (8) **10** 527 (1907).

(2) Church, Whitmore and McGrew, THIS JOURNAL, **56**, 176 (1934).

(3) Whitmore, *ibid.*, **54** 3274 (1932).

hydrogen of the isopropyl group. At first sight the case of dimethylcyclohexylcarbinol seems more unusual in that a primary hydrogen from a methyl group is lost in equality with a tertiary hydrogen from the ring. It must be remembered, however, that there are six primary hydrogens on adjacent carbons while only one adjacently attached tertiary hydrogen. On this basis the tertiary hydrogen is lost relatively more readily than a primary hydrogen.

Experimental

Apparatus and Methods.—The column under which the dehydrations were carried out was of the type described by Whitmore and Lux.[4] It was packed with single turn glass helices and had an efficiency equivalent to 12 theoretical plates. Its nichrome resistance windings were connected in series with a "variac" for temperature control of the column jackets.

The ozone was generated by passing dry oxygen through a generator obtained from the U. S. Ozone Co., Scottdale, Pa. The generator was calibrated so that a measured amount of ozone could be delivered by controlling the rate and time of oxygen flow. The ozonolyses of the olefin mixtures were conducted as described by Whitmore and Church.[5] In all cases the theoretical amount of ozone just saturated the olefin.

Preparation of Materials.—The cyclohexanol derivatives were prepared by the usual Grignard procedure; their boiling points, refractive indices ($n^{20}D$), and yields based upon the halides used were, respectively, as follows: 1-methyl- 70° at 25 mm., 1.4546, 60%; 1-ethyl- 78° at 20 mm., 1.4642; 1-isopropyl- 80° at 18 mm., 1.4579, 35%; dimethylcyclohexylcarbinol 96–98° at 18 mm., 1.4700, 40%. In the reaction of isopropylmagnesium bromide and cyclohexanone a 7% yield of cyclohexanol, α-naphthyl urethan m. p. 128°, was obtained. Cyclohexylidenecyclohexanone[6] amounting to 34% of the original cyclohexanone was isolated and identified through its semicarbazone, m. p. and mixed m. p. 177°.

Dehydration of the Alcohols.—In all cases the dehydrations were carried out by heating 0.15 to 0.20 mole of the alcohol with 0.05 to 0.1 g. of iodine. The jackets of the column under which the dehydrations were performed were set at a temperature which would allow water and olefin to distil out of the mixture but which prevented loss of undehydrated alcohol. In all cases dehydration was rapid and complete. Both the water and olefin obtained were weighed; the yields of water from all four alcohols were 95–95.5% and the yields of olefin were 97.5–99%. The olefin mixtures were dried over anhydrous sodium sulfate at 10°. The olefins were treated in no other way before ozonolysis.

Analysis.—The ozonolyses were conducted by the method referred to above.[5] Formaldehyde was detected by the resorcinol–sulfuric acid test; methyl ketone by the iodoform reaction; sodium nitroprusside was used to indicate acetone. In cases where acetone was expected it was isolated as such by distilling it out of the aqueous solution and identified by preparing the 2,4-dinitrophenylhydrazone. Formaldehyde was determined by iodimetric titration when no acetone or other methyl ketone was present. When acetone was present with formaldehyde the two were determined together by titration with iodine in basic solution and the formaldehyde determined separately on an aliquot part with hydrogen peroxide and standard base.[2] Acetone was determined by Messinger's method,[7] as was the methyl ketone from 1-methylcyclohexanol.

The aqueous distillate from the decomposition of the ozonide from 1-methylcyclohexanol gave no test for formaldehyde, nor methyl ketone. The solution failed to give a positive Schiff test. After removing the zinc from the residue in the decomposition flask iodimetric titration showed the presence of methyl ketone, 93% calculated as 6-ketoheptaldehyde.

In the case of 1-ethylcyclohexanol the aqueous distillate gave no test for aldehyde or methyl ketone. The contents of the dry-ice trap attached to the condenser outlet gave a positive test for aldehyde with Schiff reagent. Alcohol was added to the trap contents and then 2,4-dinitrophenylhydrazone and concd. hydrochloric acid. After refluxing, evaporating most of the low boiling solvent, water was added to effect a complete separation of the hydrazone. The dried product corresponded to a 0.5% yield of acetaldehyde. On recrystallizing twice from alcohol, the derivative melted at 163° and showed no depression when mixed with an authentic specimen of the 2,4-dinitrophenylhydrazone of acetaldehyde.

In the case of 1-isopropylcyclohexanol the distillate gave a positive iodoform test. Analysis showed a 2.5% yield of acetone. The distillate gave no test for aldehyde; the residue in the decomposition flask gave no iodoform reaction.

The presence of both formaldehyde and acetone was demonstrated in the products from dimethylcyclohexylcarbinol. Analysis showed yields of 53% formaldehyde and 42.5% acetone. Methyl cyclohexyl ketone, one of the products, would interfere with the acetone analysis. However, it was not allowed to distil over; water was allowed to distil out but the ketone, being an insoluble oil, was returned to the decomposition flask by proper adjustment of the take off stopcock on the decomposition apparatus. Acetone was distilled out of the aqueous solution using the 12-plate column; a 35% yield was obtained in this way, 2,4-dinitrophenylhydrazone m. p. and mixed m. p. 126°.

The author wishes to acknowledge the valuable assistance and advice of his colleagues, Dr. Paul H. Scrutchfield and Dr. Richard F. Cox.

Summary

1. 1-Methylcyclohexanol, 1-ethylcyclohexanol, 1-isopropylcyclohexanol, and dimethylcyclohexylcarbinol have been dehydrated with iodine and the resulting olefin mixtures ozonized. From the analysis of the ozonolysis products

(4) Whitmore and Lux, THIS JOURNAL, **54**, 3448 (1932).
(5) Whitmore and Church, *ibid.*, **54**, 3710 (1932).
(6) Kohler and Thompson, *ibid.*, **55**, 3822 (1933).
(7) Messinger, *Ber.*, **21**, 3366 (1888).

the ratios of dehydration have been determined.

2. Dehydration tends to take place in such a manner that the double bond formed enters the ring when this is possible.

3. It is noted that a proton is lost from the cyclohexane ring more readily than from a methyl, ethyl or isopropyl group.

WILMINGTON, DELAWARE RECEIVED OCTOBER 28, 1939

[CONTRIBUTION FROM THE PATHOLOGICAL DIVISION, BUREAU OF ANIMAL INDUSTRY]

Lupine Studies. XV.[1] The Alkaloids of *Lupinus sericeus* Pursh

BY JAMES FITTON COUCH

The silky lupine, *Lupinus sericeus*, occurs in the plains and canyons of the pinyon and yellow pine belts from Saskatchewan to South Dakota, Wyoming, Oregon, and Washington.[2]

A collection made by the late A. B. Clawson has been examined and found to contain two alkaloids, spathulatine previously isolated[3] and a new alkaloid now named nonalupine, $C_{15}H_{24}ON_2$, isomeric with lupanine and differing from it in important respects.

The discovery of spathulatine in another lupine presented an opportunity for a revision of the chemistry of the alkaloid, particularly in the light of new developments in our knowledge of the lupine alkaloids since spathulatine was first described. The formula then assigned to the alkaloid on the basis of analyses of the base and the mercuric iodide compound as well as the molecular weight determination is $C_{33}H_{64}O_5N_4$. This formula cannot easily be harmonized with the series of sparteine derivatives now known. The molecular weight is more than twice that of lupanine but is supported by the high melting point reported, 227° (uncor.). Moreover, the large content of hydrogen precludes a combination of structures with a sparteine skeleton and requires a largely aliphatic structure with not more than two 6-membered rings.

Analyses of both the anhydrous and the hydrated alkaloid for carbon, hydrogen, and nitrogen gave figures that agree with the previously assigned formula. The newly prepared compound with potassium iodide which is analogous to the mercuric iodide compound previously described also furnishes analytical evidence consistent with the previously assigned formula. In this study no evidence has been obtained to indicate that the formula requires revision.

The behavior of spathulatine suggests the presence of amine-oxide groups, possibly adjacent to a carbonyl group, for three of the nitrogen atoms, the function of the fourth being undetermined. This view is supported by the slight basicity of spathulatine and the inability to prepare crystalline salts with the usual acids and by its sparing solubility in acetone and ether. The formation of a compound with three molecules of potassium iodide also supports this view since compounds with one molecule of potassium iodide to each amine-oxide group are readily formed. When treated with sulfur dioxide spathulatine is converted into an unidentified base probably as a result of reduction of the amine-oxide groups.

When boiled with hydrochloric acid spathulatine is converted into an isomer of spartyrine, $C_{15}H_{24}N_2$, which is positive to the modified Grant's test.[4] This behavior indicates the probability of hydrolysis with subsequent ring closure to form the sparteine skeleton. This relates spathulatine to the other lupine alkaloids.

The other alkaloid in the plant, nonalupine, is of interest because of its non-basic character. When a solution of nonalupine and camphor-sulfonic acid is evaporated to dryness the free alkaloid may be dissolved out of the residue by ether. No salts with mineral acids have been obtained. This behavior is difficult to explain. Since the alkaloid contains two nitrogen atoms and but one oxygen atom it cannot have lost its basicity because of amine-oxide formation or because of ad-

(1) Paper XIV, THIS JOURNAL, **61**, 3327 (1939).

(2) W. W. Eggleston in I. Tidestrom, "Flora of Utah and Nevada," *Contr. U. S. Nat. Herbarium*, **25**, 297 (1925).

(3) J. F. Couch, THIS JOURNAL, **46**, 2507 (1924). The alkaloid was isolated from a lupine collected by the writer and identified by W. W. Eggleston as *L. spathulatus* Rydb. whence the name spathulatine given to the new base. Since that time there has arisen a difference in opinion among botanists as to the proper name of the species used, I. Tidestrom (personal communication) referring it to *L. marianus* Rydb. and being confirmed by C. P. Smith. Eggleston considered *marianus* a synonym of *spathulatus* and recombined the species. Material of a species identified by C. P. Smith as *L. spathulatus* collected near Puffer's Lake, Utah, has been examined and found free from spathulatine. The alkaloid has, it appears, been misnamed since, unless there is a reversal of botanical opinion, it does not occur in *L. spathulatus*.

(4) J. F. Couch, *Am. J. Pharm.*, **97**, 36 (1925).

jacent carbonyl groups. The possibility of an oxygen bridge between the nitrogen atoms involves assumptions of structure which are unacceptable. The alkaloid is unaffected by warming with sulfur dioxide in water. It reduces potassium permanganate in neutral solution forming a crystalline compound containing two atoms of oxygen more than the parent substance. This compound which may be an amine-oxide is also unaffected by hot sulfur dioxide in water.

These alkaloids differ from octalupine found in *L. sericeus* var. *flexuosus*[5] which is considered by botanists to be only a variety of *L. sericeus*. It appears that the dissimilarities between the two forms extend to the physiological processes and are deeper than mere varietal differences.

Experimental Part

Material Used.—The plant material used was collected by A. B. Clawson in the neighborhood of Meeker, Colo., on August 24, 1934, and was identified by C. P. Smith. The plant was air-dried and shipped to Washington, D. C., for examination. It then contained 11.36% of moisture.

Isolation of the Alkaloids.—The finely ground plant (5.55 kg.) was extracted with alcohol and the alkaloids were recovered by the process previously described.[6] The yield of crude alkaloids freed of solvent was 181 g. or 3.68% of the moisture-free plant. The sirupy mass was dissolved in acetone plus 10% of alcohol, filtered from a little resin, and the solvent was distilled off. The residue solidified to a mass of prismatic crystals embedded in a thick brownish sirup. The mass was negative to the modified Grant's test for sparteine.[7] It was only slightly soluble in ether.

Isolation of Spathulatine.—The alkaloidal mixture was treated with cold acetone which dissolved the sirup, leaving most of the crystals undissolved. These were recrystallized several times from hot acetone plus a little norit and then melted constantly at 233–234°.[8] Mixture with spathulatine from *Lupinus marianus* caused no change in the melting point. A sample was dried at 110° to constant weight.

Anal. Calcd. for $C_{33}H_{64}O_5N_4$: C, 66.39; H, 10.82; N, 9.39. Found: C, 66.11, 66.65; H, 11.14, 10.64; N, 9.54, 9.48. Undried sample: calcd. for $C_{33}H_{64}O_5N_4 \cdot 4^1/_2H_2O$: C, 58.45; H, 10.85; H_2O, 11.96. Found: C, 58.65; H, 10.91, averages of 6 analyses; H_2O, 12.01.

The picrate forms yellow needles, quite soluble in water and melting at 182–184°. A methiodide was obtained in scanty yield as diamond-shaped crystals melting at 250–252°. It did not depress the melting point of authentic spathulatine methiodide. Spathulatine decomposed when an attempt was made to distill it under reduced pressure.

Spathulatine Potassium Iodide.—Spathulatine (3 g.) in 5 cc. of water was mixed with 2.1 g. of potassium iodide in 2 cc. of water. There was an immediate precipitation of small crystals in good yield. These were recrystallized from hot water as large prisms of m. p. 260–261°. A test portion was moistened with sulfuric acid and ashed. It evolved iodine vapor and left a residue of potassium sulfate.

Anal. Calcd. for base·3KI: I, 34.81. Found: I, 34.85, 34.82.

Spathulatine and Sulfur Dioxide.—A stream of sulfur dioxide was passed through a solution of 2 g. of spathulatine in 10 cc. of water for two days. The product was alkalized with sodium hydroxide and the milky precipitate extracted with chloroform which on evaporation left a brownish oil from which nothing crystalline could be isolated. It has not yet been identified but it has been shown not to contain spathulatine.

Spathulatine and Hydrochloric Acid.—Spathulatine (3 g.) and 10 cc. of concd. hydrochloric acid and 25 cc. of water was maintained at the boiling point for six hours until fumes of hydrogen chloride were given off. The mixture turned dark brown. On cooling nothing crystallized. The mixture was alkalized with sodium hydroxide and extracted with chloroform. The chloroform extract was a yellow oil which was strongly positive to the modified Grant's test. It formed a crystalline perchlorate of m. p. 216–217°. When mixed with *d*-lupanine perchlorate (m. p. 214–216°) the mixture melted at 194–207° like a mixture.

Anal. Calcd. for $C_{15}H_{24}N_2HClO_4$: C, 53.98; H, 7.5; N, 8.42. Found: C, 54.15, 53.85; H, 7.51, 7.80; N, 8.61, 8.34.[9] The base was very slightly levorotatory.

The new base gave a precipitate with mercuric chloride like that given by sparteine and formed a picrate which was recrystallized from hot water, m. p. 214–216°. Mixed with spartyrine picrate (m. p. 206–207°) the mixture melted at 192–202°.

Isolation of a New Lupine Alkaloid, Nonalupine.—The acetone solution containing the sirup dissolved from the original alkaloidal residue was allowed to evaporate. It solidified to a mass of crystals. It was dissolved in hot acetone and filtered from the crystals that formed on cooling. The solution was evaporated and the brownish crystalline residue was recrystallized several times from methyl isobutyl ketone plus a little norit as colorless leaflets of m. p. 91.5–92.5°, b. p. 260–270° (18 mm.). Mixed with 16-keto sparteine (m. p. 85–86°) the mixture melted from 80 to 97°. Dried to constant weight at 110° the substance softened at 219° and was completely melted at 235°. On recrystallizing from water the substance took up solvent and then melted at 90–91°, regenerating the original hydrated base.

Anal. Calcd. for $C_{15}H_{24}ON_2 \cdot 2H_2O$: C, 63.34; H, 9.97; N, 9.85; H_2O, 12.68. Found: C, 63.11, 63.23; H, 9.39, 9.88; N, 9.71, 9.68; H_2O, 12.51.[9] In alcohol, $[\alpha]^{25}D$ $-21.3°$, $c = 5.15$, $l = 1$, $a = 2.19°$.

Nonalupine Gold Chloride.—The gold chloride double salt was recrystallized from hot water as small yellow needles, m. p. 177.5–178° decompn. It decomposed when heated to 110°.

(5) J. F. Couch, THIS JOURNAL, **61**, 1523 (1939).
(6) J. F. Couch, *ibid.*, **56**, 2434 (1934).
(7) J. F. Couch, *Am. J. Pharm.*, **97**, 36 (1925).
(8) Melting points are corrected.
(9) The analyses were made by the Arlington Laboratories, Vera A. Conard, Director.

Anal. Calcd. for base·2HAuCl$_4$·5H$_2$O: Au, 38.72. Found: Au, 38.71.

Nonalupine picrate recrystallized from 50% alcohol melted at 185–186°.

Oxidation of Nonalupine.—Nonalupine (5 g.) in 600 cc. of water was treated with a saturated solution of potassium permanganate in the cold until the pink color persisted for twenty-four hours. The filtrate was extracted with chloroform, which took out an oil (2.5 g.) that slowly crystallized. Recrystallized from a mixture of chloroform and petroleum ether the substance formed long flat crystals, m. p. 168.5–170.5°. On drying in the oven it slowly volatilized, losing 28% of its weight in fifteen days at 110°. A further crop (2 g.) of the substance was obtained by extracting the precipitated manganese dioxide with alcohol.

Anal. Calcd. for $C_{15}H_{24}O_3N_2$: C, 64.24; H, 8.63; N, 9.99. Found: C, 63.99, 64.18; H, 8.45, 8.58; N, 9.84, 9.94.

The substance was recovered unchanged after warming with sulfur dioxide in water. It is readily soluble in water and the solution is neutral to test papers.

Oxynonalupine Gold Chloride.—This compound is quite soluble in water. On slow evaporation it forms small yellow needles, m. p. 238–239°. Analysis indicated a partial reduction of the base on combination with gold chloride.

Anal. Calcd. for $C_{15}H_{24}O_2N_2$·HAuCl$_4$: Au, 32.61. For $C_{15}H_{22}O_2N_2$·HAuCl$_4$: Au, 32.72. Found: Au, 32.82.

Summary

Lupinus sericeus Pursh. collected in Colorado contained when dried 3.68% of alkaloids consisting of spathulatine, previously described, and nonalupine, a new lupine alkaloid. A reinvestigation of the chemistry of spathulatine has confirmed the empirical formula previously assigned to this base. Nonalupine is not basic enough to form salts with strong acids.

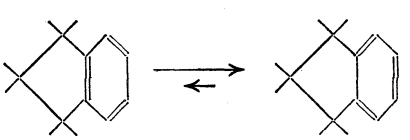
WASHINGTON, D. C. RECEIVED JANUARY 4, 1940

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

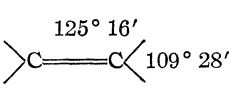
Aromatic Stabilized Double Bonds. Mills–Nixon Problem

BY RICHARD T. ARNOLD AND ROBERT L. EVANS

The fundamental stereochemical problem proposed by Mills and Nixon[1] can be summarized by the equilibrium



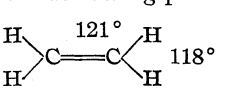
The assumptions in this interesting and clever proposal are: (a) that the structure of the olefinic double bond is represented by



and (b) that there exists a simple relation between bond types and bond angles.

Many experimental and theoretical approaches have been made toward a solution,[2,3,4] but the evidence submitted is most contradictory and leaves the problem completely unsolved. Objections have been raised to practically all of the experimental evidence thus far produced.[5]

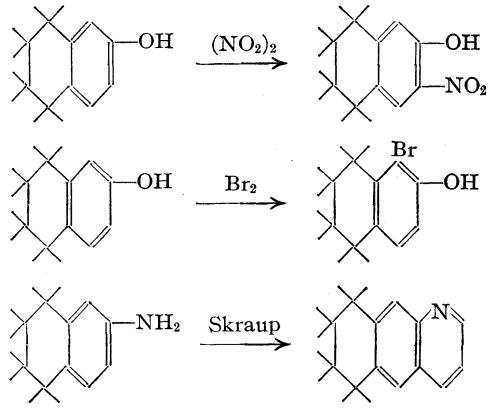
The structure of ethylene recently has been determined, apparently with some degree of accuracy, and gives the following picture:[6,7]



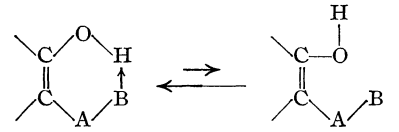
Pauling and Brockway[8] have shown however that the angles in tetramethylethylene are nearly tetrahedral. These models, if true, question the validity of a simple correlation between bond angles and bond types. The foremost use of this assumption lies at the basis of the Sidgwick–Springall experiments. The structural work just completed on formaldehyde again raises a serious objection to this correlation.[9]

The wave mechanical treatment of the Mills–Nixon problem leads to the conclusion that substitution reactions (with high activation energies) cannot be used to locate stabilized aromatic double bonds. That this conclusion is in accordance with the experimental evidence is shown by the following

(1) Mills and Nixon, *J. Chem. Soc.*, 2510 (1930).
(2) Sidgwick and Springall, *J. Chem. Soc.*, 1532 (1936).
(3) McLeish and Campbell, *ibid.*, 1103 (1937).
(4) Sutton and Pauling, *Trans. Faraday Soc.*, **31**, 939 (1935).
(5) Brockway and Taylor, *Brit. Ann. Reports*, **34**, 219 (1937).
(6) H. W. Thompson, *Trans. Faraday Soc.*, **35**, 697 (1939).
(7) Private communication from Professor Verner Schomaker of the California Institute of Technology.
(8) Pauling and Brockway, THIS JOURNAL, **59**, 1223 (1937).
(9) Stevenson, LuValle and Schomaker, *ibid.*, **61**, 2508 (1939).

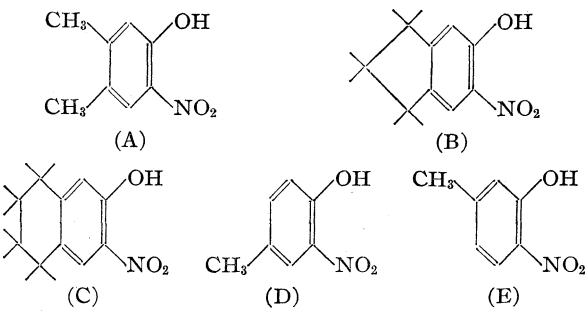


It is seen that the double bond can be placed in either of the two possible positions depending on the reaction chosen. During the past two years, an attempt has been made in this Laboratory to develop a physical method for locating double bonds which is free from objections. Using the naphthalene nucleus, the structure of which is well accepted, it has been shown[12] that if a hydroxyl and negative (electron attracting) group are placed around a stabilized double bond, an abnormally strong acid results. It has been proved[13] that chelate ring structures involving stabilized double bonds are unusually strong. In connection with correlations between the acidity of the hydroxy group and chelate rings involving stabilized double bonds, one must recognize two effects. This can be described by making use of a general equation



The inductive effect of (AB) is easily passed across the stabilized double bond. However, around this stabilized double bond the hydrogen bond is abnormally strong and, thermodynamically, results in a higher concentration of (1). Since it is easy for the proton to dissociate from (2) the overall effect of hydrogen bond formation is a slight diminution in the acidity. It must be recognized however that the inductive effect is usually the more important. This method has been extended, with a full realization of its limitations, to the Mills–Nixon problem by a careful study of the following molecules

(10) Thoms and Kross, *Archiv. Pharm.*, **265**, 336–347 (1927).
(11) Von Braun and Gruber, *Ber.*, **55**, 1710 (1922).
(12) Arnold and Sprung, THIS JOURNAL, **60**, 1163 (1938).
(13) Arnold and Sprung, *ibid.*, **61**, 2475 (1939).



The acidity of the hydroxyl group here has been found to depend on four factors: namely, (a) the type of activating group present; (b) the strength of the chelate ring; (c) the inductive effect of all the dipoles present; and (d) the carbon–carbon bond type between the hydroxyl and activating group. As far as possible the first three factors have been held constant in A, B and C. Differences in dissociation constants for these substances must then indicate a dissimilarity in bond type. Actually the acidities of A, B and C are almost identical. A study of any interaction (*ortho*-effect) between the two methyl groups in A has been made by determinations on D and E. Such interactions seem to be active but appear to be constant in A, B and C. This has been recognized in dipole moment studies.

The possibility of stabilization in hetero rings containing one or more oxygen atoms, which according to our calculations is more probable than in hydrindene, is being investigated intently. Table I summarizes the data upon which the above mentioned statements are based.

TABLE I

Solvent: Ethanol–Water (50% by weight)

Compound	*T*, °C.	*p*K
2-Nitrophenol	29	8.20
4,5-Dimethyl-2-nitrophenol	28	8.81
4,5-Dimethyl-2-nitrophenol	37	8.90
5-Hydroxy-6-nitrohydrindene	37	8.96
6-Hydroxy-7-nitrotetralin	37	9.05
4-Methyl-2-nitrophenol	28	8.57
5-Methyl-2-nitrophenol	28	8.43

Experimental

5-Hydroxyhydrindene.—Thirty-five grams of 5-acetamidohydrindene was hydrolyzed with concentrated hydrochloric acid in several treatments to give 31 g. of the amine. To this sample in 45 cc. of concentrated hydrochloric acid and 70 cc. of water was added 21 g. of sodium nitrite in a saturated solution. To the clear solution was added 50 cc. of borofluoric acid (40%), and the white crystals which formed were filtered immediately. Decomposition of the crystals and filtrate (separately) using 44 cc. of sulfuric acid in 177 cc. of water gave after

steam distillation 12.5 g. of the phenol; b. p. 148–152° (30 mm.).[14,15]

5-Hydroxy-6-nitrohydrindene.—(a) The above 5-aminohydrindene was diazotized and nitrated in one step according to Neunhoffer[16] but on steam distillation an impurity accompanied the product. This unknown material melted at 82–83°.

(b) Following Diepolder's general method,[17] 5-hydroxyhydrindene was nitrated directly. The impurity (m. p. 82–83°) was again obtained but it was found that the high solubility of the desired compound in petroleum ether (b. p. 60–68°) allowed it to be decanted away from the more insoluble impurity and then crystallized; m. p. 63.5–64.5°.

6-Hydroxy-7-nitrotetralin.—Raney nickel catalytic hydrogenation of β-naphthol gave 50–60% yields of 6-hydroxytetralin at 190° and 500 lb. pressure (33.3 atm.). This phenol was nitrated with nitrogen dioxide and after steam distillation gave a 21% yield of the product which was recrystallized from ethanol; m. p. 88.5–89°. The acetate prepared from acetyl chloride in pyridine melted at 100°.[10]

6-Methoxy-7-nitrotetralin.—Using two equivalents each of 2.0 *N* sodium hydroxide and methyl sulfate, we obtained from 3.05 g. of the phenol, 1.37 g. of the ether. The substance was pale yellow and melted at 50–51.5°.

Anal. Calcd. for $C_{11}H_{13}O_3N$: C, 63.73; H, 6.32. Found: C, 63.74; H, 6.54.

4,5-Dimethyl-2-nitrophenol.—This compound was prepared by the direct nitration of the phenol using Diepolder's method; m. p. 85–86°.[14]

5-Methyl-2-nitrophenol.—Technical *m*-cresol was nitrated in cooled glacial acetic acid with a small excess of nitric acid dissolved in glacial acetic acid. After steam distillation and recrystallization, it melted at 54.5–55°.[18]

4-Methyl-2-nitrophenol.—This substance was prepared in the usual manner from *p*-cresol.

(14) W. Baker, *J. Chem. Soc.*, 476 (1937).
(15) Smith and Haller, THIS JOURNAL, **61**, 143 (1939).
(16) Otto Neunhoffer, *Ber.*, **68**, 1774 (1935).
(17) Emil Diepolder, *Ibid.*, **42**, 2916 (1909).
(18) Staedel and Kolb, *Ann.*, **259**, 210 (1890).

MINNEAPOLIS, MINNESOTA RECEIVED OCTOBER 23, 1939

Summary

1. In the light of recent structural studies on ethylene and tetramethylethylene, some of the original assumptions of the Mills–Nixon postulate are questionable.

2. A set of physical measurements on nitrophenols indicates no appreciable stabilization of double bonds caused by ring structures.

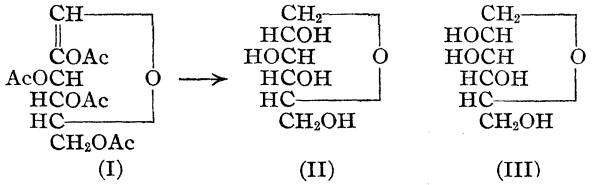
3. It has been pointed out that substitution reactions do not offer an acceptable method for locating double bonds.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, FORDHAM UNIVERSITY]

The Chemistry of Naturally Occurring Monoanhydrohexitols. II. Synthetic Tetramethylstyracitol[1]

BY WERNER FREUDENBERG AND JOHN T. SHEEHAN

In 1930 Zervas[2] reported the synthesis of styracitol, the naturally occurring monoanhydrohexitol in *styrax obassia*. Tetraacetyl oxyglucal (I) was hydrogenated and subsequently deacetylated to 1,5-anhydro-*d*-sorbitol (II) or 1,5-anhydro-*d*-mannitol (III) depending on whether a *cis* or a *trans* addition occurred at the double bond.



(I) (II) (III)

The synthetic material was identical with the natural product. The question, however, if styracitol should be classified as a sorbitol or a mannitol derivative was not answered.

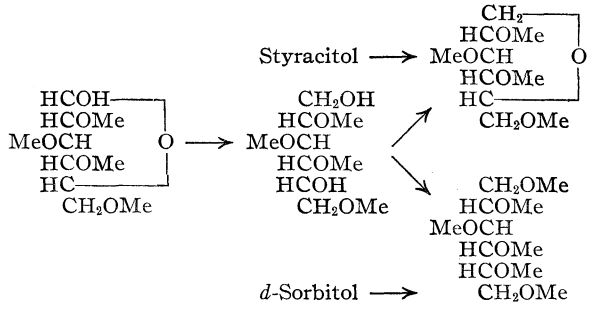
In a recent publication from this Laboratory we[3] attempted to ascertain the configuration of styracitol by a comparison of the rates of oxidation with lead tetraacetate and by an application of the isorotation rules to styracitol and its isomer polygalitol. These two substances were assumed to be epimeric since they formed on oxidation the same anhydrofructosazone[4] and glucosazone.[5] On the basis of this assumption the experimental results favored the mannitol structure for styracitol and the sorbitol structure for polygalitol.

To establish definitely the configuration of styracitol as a sorbitol or mannitol derivative, it was deemed necessary to devise a synthesis of a derivative of styracitol starting with glucose or mannose wherein all asymmetric centers are protected and remain unaltered throughout the series

(1) Reported before the Organic Division, A. C. S. Meeting, Boston, Mass., September, 1939.
(2) Zervas, *Ber.*, **63**, 1689 (1930).
(3) Freudenberg and Rogers, THIS JOURNAL, **59**, 1602 (1937).
(4) Bergmann and Zervas, *Ber.*, **64**, 2032 (1931).
(5) Shinoda, Sato and Sato, *Ibid.*, **65**, 1219 (1932).

of reactions. The tetramethyl ether of styracitol was the derivative chosen. It was synthesized from tetramethyl-*d*-glucopyranose by reducing the latter and then dehydrating the 2,3,4,5-tetramethylsorbitol obtained. The dehydrated product agreed in every respect with that obtained by methylating the natural styracitol isolated from the shells of *styrax obassia*. Styracitol therefore has the configuration of 1,5-anhydro-*d*-sorbitol as originally announced by Zervas.

To exclude the possibility of tetramethylmannitol being formed in the hydrogenation of tetramethylglucopyranose, the reduction was carried out in a neutral medium at high pressure. Furthermore a portion of the product obtained was completely methylated and its properties compared with an authentic sample of hexamethylsorbitol. The two compounds were found to agree completely, indicating that the hydrogenation and methylation had no racemizing or epimerizing effects.



When tetramethyl-*d*-mannopyranose was used as a starting material and methylated and dehydrated as described for the glucose derivative with the hope of synthesizing tetramethylpolygalitol, which as mentioned above was thought to be the epimer of tetramethylstyracitol, the resulting synthetic tetramethyl ether was not identical with that obtained from the natural product but differed considerably in physical properties. The configuration of 1,5-anhydro-*d*-mannitol therefore is excluded for polygalitol, and the two naturally occurring anhydro polyhydric alcohols are not epimeric.

The methylated derivatives herein described, while useful as reference compounds in establishing the presence of furanose and pyranose rings, may find other uses as they are high boiling limpid liquids quite soluble both in organic and inorganic solvents.

Experimental

Styracitol.—This compound was isolated from *styrax obassia* according to the method described by Asahina,[6] melting at 155°, $[\alpha]^{23}D$ −49.4° (H_2O, c = 1.6).

Anal. Calcd. for $C_6H_{12}O_5$: C, 43.89; H, 7.37. Found: C, 43.90; H, 7.32.

Tetramethylstyracitol.—Ten grams of styracitol was methylated according to the method of West and Holden.[7] The product obtained was a limpid, colorless sirup which distilled at a bath temperature of 110° under 1.5 mm. pressure; $[\alpha]^{23}D$ −36.5° (no solvent), n^{25} 1.4520, d. 1.0849.

Anal. Calcd. for $C_{10}H_{20}O_5$: C, 54.54; H, 9.13; CH_3O, 56.31. Found: C, 54.62; H, 9.14; CH_3O, 56.72.

Tetramethylsorbitol.—A solution of 30 g. of tetramethylglucose in 75 cc. of water and 15 cc. of alcohol was reduced for seven hours at 135° under a pressure of 1300 pounds (85 atm.) of hydrogen in the presence of Raney nickel. The filtered solution was evaporated *in vacuo* to a clear sirup which did not reduce Fehling's solution. The sirup was purified by distillation at a bath temperature of 145° under 2 mm. pressure; $[\alpha]^{23}D$ +10.3° (EtOH, c = 6.3), $[\alpha]^{23}D$ +4.7° ($CHCl_3$, c = 10.5), n^{20} 1.4612.

Anal. Calcd. for $C_{10}H_{22}O_6$: C, 50.40; H, 9.32; CH_3O, 52.03. Found: C, 50.36; H, 9.36; CH_3O, 52.35.

Tetramethyl-1,5-anhydrosorbitol.—Fifteen grams of tetramethylsorbitol and 2 cc. of 13% sulfuric acid solution were heated *in vacuo* for half an hour at 140°. The solution was neutralized with 0.4 g. of anhydrous sodium carbonate after which a small amount of decolorizing charcoal and 50 cc. of ether were added. The solution was filtered and dried over anhydrous sodium sulfate. After filtering, the ether was removed leaving a sirup which distilled colorless at a bath temperature of 115° under 2 mm. pressure; $[\alpha]^{23}D$ −36.2° (no solvent), n^{25} 1.4518, d. 1.0876.

Anal. Calcd. for $C_{10}H_{20}O_5$: C, 54.54; H, 9.13; CH_3O, 56.31. Found: C, 54.29; H, 9.08; CH_3O, 56.58.

Hexamethylsorbitol.—Ten grams of tetramethylsorbitol was methylated according to the method of West and Holden. The product obtained was a colorless sirup which distilled at a bath temperature of 100° under 1.5 mm. pressure; $[\alpha]^{23.5}D$ 1.93° (no solvent), n^{22} 1.4370, d. 1.0476. For comparison 10 g. of sorbitol was methylated in the above fashion. The resulting product was found to distil at 100° under 1.5 mm. pressure; $[\alpha]^{24}D$ 1.97° (no solvent), n^{22} 1.4367, d. 1.0334.

Anal. Calcd. for $C_{12}H_{26}O_6$: C, 54.14; H, 9.77; CH_3O, 69.92. Found: C, 54.17; H, 9.75; CH_3O, 70.02 (product from tetramethylsorbitol); C, 54.07; H, 9.94; CH_3O, 69.80 (product from sorbitol).

Polygalitol.—This compound was isolated from *polygala amara*, according to the method described by Shinoda.[5] Briefly, the pulverized drug was repeatedly extracted with methyl alcohol and the extract, after the addition of water, neutralized with magnesia, filtered and the filtrate then taken to dryness in the air. The residue of dark brown gum was extracted with absolute methyl alcohol and the combined extract concentrated. Through the careful ad-

(6) Asahina, *Ber.*, **45**, 2365 (1912).
(7) West and Holden, THIS JOURNAL, **56**, 930 (1934).

dition of ether the bulk of the saponin present in the extract was removed. The filtrate was concentrated with removal of ether and, after standing a few days in the ice-box, crystals appeared. These were filtered off and recrystallized from methyl alcohol, forming colorless plates, melting at 142–143°; $[\alpha]^{21}D$ +42.0° (H_2O, c = 1.8).

Anal. Calcd. for $C_6H_{12}O_5$: C, 43.89; H, 7.37. Found: C, 43.95; H, 7.44.

Tetramethylpolygalitol.—Ten grams of polygalitol was methylated according to the method of West and Holden. The product obtained was a limpid, colorless sirup which distilled at a bath temperature of 80° under 2 mm. pressure; $[\alpha]^{23}D$ +67.67° (no solvent); n^{22} 1.4444, d. 1.0571.

Anal. Calcd. for $C_{10}H_{20}O_5$: C, 54.54; H, 9.13; CH_3O, 56.31. Found: C, 54.54; H, 9.10; CH_3O, 56.55.

Tetramethylmannitol.—A solution of 30 g. of tetramethylmannose in 75 cc. of water and 15 cc. of alcohol was reduced for seven hours at 135° under a pressure of 1300 pounds (85 atm.) of hydrogen in the presence of Raney nickel. The filtered solution was evaporated *in vacuo* to a clear, thick sirup which did not reduce Fehling's solution. The sirup was purified by distillation at a bath temperature of 150° under 2 mm. pressure; $[\alpha]^{21}D$ +20.7° (EtOH, c = 10.15), $[\alpha]^{21}D$ +17.5° ($CHCl_3$, c = 10.6), n^{24} 1.4605.

Anal. Calcd. for $C_{10}H_{22}O_6$: C, 50.40; H, 9.32; CH_3O, 52.03. Found: C, 50.34; H, 9.27; CH_3O, 52.38.

Tetramethyl-1,5-anhydromannitol.—Fifteen grams of tetramethylsorbitol and 2 cc. of 13% sulfuric acid solution were heated *in vacuo* for a half hour at 140°. The solution was neutralized with 0.4 g. of anhydrous sodium carbonate, after which a small amount of decolorizing charcoal and 50 cc. of ether were added. The solution was filtered and dried over anhydrous sodium sulfate. After filtering off the sodium sulfate, the ether was removed leaving a limpid sirup which distilled colorless at a bath temperature of 95° under 2 mm. pressure; $[\alpha]^{22}D$ +30.6° (no solvent), n^{22} 1.4479, density 1.0435.

Anal. Calcd. for $C_{10}H_{20}O_5$: C, 54.54; H, 9.13; CH_3O, 56.31. Found: C, 54.21; H, 9.03; CH_3O, 56.24.

Hexamethylmannitol.—Ten grams of tetramethylmannitol was methylated according to the method of West and Holden. The product obtained was a colorless sirup which distilled at a bath temperature of 95° under 2 mm. pressure; $[\alpha]^{22}D$ +12.53° (no solvent), $n^{21}D$ 1.4403, density 1.0458. For comparison 10 g. of isolated mannitol was methylated in the above fashion. The resulting product was found to distil at 97° under 2 mm. pressure; $[\alpha]^{22}D$ +12.46° (no solvent), $n^{21}D$ 1.4400, d. 1.0410.

Anal. Calcd. for $C_{12}H_{26}O_6$: C, 54.14; H, 9.77; CH_3O, 69.92. Found: C, 54.28; H, 9.58; CH_3O, 69.90 (product from tetramethylmannitol); C, 54.28; H, 9.79; CH_3O, 70.07 (product from mannitol).

Acknowledgments.—The authors wish to express their thanks to Dr. P. A. Levene for permission to carry out the high pressure reductions in his laboratory, to Prof. S. Takei for the styrax used, and to the Atlas Powder Co. for a sample of natural mannitol. The microanalyses were made by J. F. Alicino of this Laboratory.

Summary

Styracitol has been proved to be 1,5-anhydro-*d*-sorbitol by the synthesis of its tetramethyl derivative.

Polygalitol has been shown not to be 1,5-anhydro-*d*-mannitol.

A new method is described for establishing the presence of furanose and pyranose rings by preparing the corresponding methylated anhydro sugar alcohols.

NEW YORK, N. Y. RECEIVED DECEMBER 20, 1939

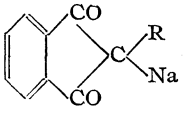
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

A Synthesis of Substituted α-Naphthoquinones

BY C. F. KOELSCH AND D. J. BYERS

The recent discovery that vitamin K is a substituted α-naphthoquinone adds importance to all reactions leading to substances of this class. The research described in the present paper is an investigation of a series of reactions by means of which 2-alkyl, 2-alkyl-3-hydroxy-, and 2-alkyl-3-carbalkoxy-α-naphthoquinones and hydroquinones can be prepared. The reactions may be formulated as

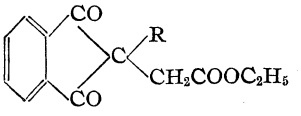
$$o\text{-}C_6H_4(COOC_2H_5)_2 + RCH_2COOC_2H_5 \xrightarrow{Na}$$



(1)

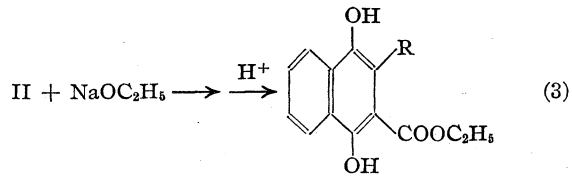
I

$$I + BrCH_2COO_2H_5 \longrightarrow$$



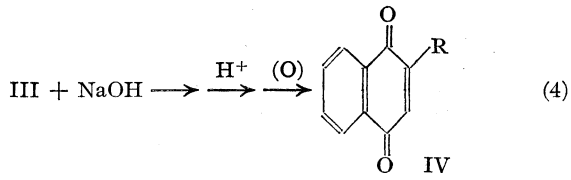
(2)

II



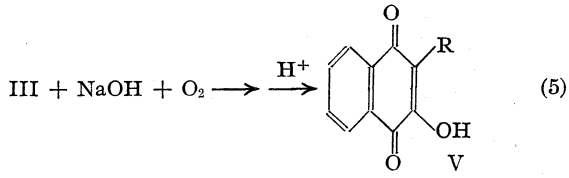
(3)

III



(4)

IV



(5)

V

Reaction (1) has been carried out previously by Wislicenus and Kötzle[1] for the case where R was methyl. In the present investigation it was carried out for the cases where R was methyl, ethyl, *n*-propyl and *n*-butyl.

Reaction (2) has been studied by Nathanson,[2] by Radulescu and Gheorgiu[3] and by Gheorgiu[4] for the cases where R was phenyl and methyl. In the present investigation the reaction was carried out for the cases where R was methyl, ethyl, *n*-propyl and *n*-butyl; the products in the latter two cases were not purified, but were used directly in reaction (3).

Reaction (3) was found to take place when R was phenyl by Radulescu and Gheorgiu,[3] and was later studied for the case where R was methyl by Gheorgiu.[5] The yield and the quality of the methyl quinone so obtained were reported to be inferior to those of the phenyl quinone prepared previously by the analogous method. The reaction was applied in the present research to the cases where R was methyl, ethyl, *n*-propyl and *n*-butyl, the expected hydroquinones being formed in fair yields.

The combination of reactions represented in (4) was believed feasible by analogy with the results of Nef[6] who showed that quinone acids lose carbon dioxide readily. It was carried out only in the case where R was ethyl, and yielded 77% of the theoretical amount of 2-ethylnaphthoquinone.

(1) Wislicenus and Kötzle, *Ann.*, **252**, 80 (1889).
(2) Nathanson, *Ber.*, **26**, 2577 (1893).
(3) Radulescu and Gheorgiu, *ibid.*, **60**, 186 (1927).
(4) Gheorgiu, *J. prakt. Chem.*, **146**, 193 (1936).
(5) Gheorgiu, *Compt. rend.*, **198**, 755 (1934).
(6) Nef, *Ber.*, **18**, 3496 (1885).

The reactions formulated in (5) were carried out in the cases where R was ethyl and *n*-butyl. They find an analogy in the work of Radulescu and Gheorgiu,[3] who discovered that when air was not excluded in the rearrangement of II (R = phenyl) to III, the product contained some 2-phenyl-3-hydroxynaphthoquinone.

Experimental

Since corresponding experiments involving compounds differing only in the size of the alkyl group R were quite similar, details are given for those only in which R was ethyl. Analytical data, yields, and melting points are given in Table I.

2-Ethylindanedione-1,3.—To a hot (115°) mixture of ethyl phthalate (55 g.) and sodium wire (10.5 g.) was added 30 g. of ethyl butyrate. Heating was continued for four hours; the mixture was then cooled and triturated with moist ether. The acidic products were removed by solution in dilute aqueous alkali. The quantity of dilute sulfuric acid necessary to precipitate all of the organic material was added in three portions, the mixture being extracted with ether after each addition. The third extract contained phthalic acid, while the diketone was in the first two. It distilled at 135–140° (7 mm.), and was recrystallized from benzene.

Ethyl 2-Ethylindanedionyl-2-acetate.—To a solution of the above diketone (13.6 g.) in absolute alcohol (25 ml.) was added a solution of potassium hydroxide (4.4 g.) in absolute alcohol (50 ml.) and then 13.0 g. of ethyl bromoacetate. The resulting mixture was boiled for two and one-half hours, distilled to a volume of 40 ml. and poured into water. The precipitated oil soon solidified and was then recrystallized from alcohol.

2 - Ethyl - 3 - carbethoxy - 1,4 - naphthohydroquinone.—The above diketo-ester (13.8 g.) was added to a solution of sodium (3 g.) in absolute alcohol (40 ml.) under a hydrogen atmosphere. The resulting reddish-brown solution was boiled for two hours, and then air-free water (50 ml.) was added through the condenser. The whole was poured into 600 ml. of air-free cold dilute sulfuric acid, and the precipitated pale yellow product was crystallized from alcohol.

2 - Ethyl - 3 - carbethoxy - 1,4 - naphthoquinone.—2-Ethyl-3-carbethoxynaphthohydroquinone was oxidized with chromic acid in cold acetic acid. The resulting yellow quinone was crystallized from a mixture of ether and petroleum ether.

2-Ethyl-3-hydroxy-1,4-naphthoquinone.—Sodium hydroxide (20 ml. of 1%) was added to 2-ethyl-3-carbethoxynaphthohydroquinone (1 g.) in warm alcohol (5 ml.). Air was bubbled through the solution at 50° for ten minutes, and then heating was continued for ten minutes without the air stream. The water solution was decanted from the yellow oil into cold dilute acetic acid, and the yellow product which separated was crystallized twice from alcohol.

2-Ethylnaphthoquinone.—A solution of 2-ethyl-3-carbethoxynaphthohydroquinone (1 g.) in 12 ml. of 5% sodium hydroxide containing 5 drops of alcohol was boiled under hydrogen for two hours. Acidification under hydrogen

TABLE I

MELTING POINTS, YIELDS AND ANALYSES

Compound	M. p., °C.	Yield, %	Formula	Analyses, % Calcd. C	Calcd. H	Found C	Found H
2-Methylindanedione	83–85[a]	31	$C_{10}H_8O_2$				
2-Ethylindanedione	53–55[b]	32	$C_{11}H_{10}O_2$				
2-*n*-Propylindanedione	48–49.5[c]	17	$C_{12}H_{12}O_2$				
2-*n*-Butylindanedione	35[d,e]	18	$C_{13}H_{14}O_2$				
Ethyl 2-methylindanedionyl-2-acetate	91–92[f]	62	$C_{14}H_{14}O_4$	68.3	5.7	68.5	6.0
Ethyl 2-ethylindanedionyl-2-acetate	77–78.5	68	$C_{15}H_{16}O_4$	69.2	6.2	69.3	6.3
Ethyl 2-*n*-propylindanedionyl-2-acetate	Oil	[g]	$C_{16}H_{18}O_4$				
Ethyl 2-*n*-butylindanedionyl-2-acetate	Oil	[g]	$C_{17}H_{20}O_4$				
2-Methyl-3-carbethoxynaphthohydroquinone	100–101	44	$C_{14}H_{14}O_4$	68.3	5.7	68.3	5.7
2-Ethyl-3-carbethoxynaphthohydroquinone	110.5–111	68	$C_{15}H_{16}O_4$	69.2	6.2	69.5	6.2
2-*n*-Propyl-3-carbethoxynaphthohydroquinone	125–126.5	14[h]	$C_{16}H_{18}O_4$	70.0	6.6	69.9	6.8
2-*n*-Butyl-3-carbethoxynaphthohydroquinone	98.5–100	24[h]	$C_{17}H_{20}O_4$	70.8	7.0	70.7	7.1
2-Methyl-3-carbethoxynaphthoquinone	99–100	92	$C_{14}H_{12}O_4$	68.8	5.0	69.0	5.2
2-Ethyl-3-carbethoxynaphthoquinone	47.5–48	88	$C_{15}H_{14}O_4$	69.7	5.5	69.6	5.3
2-Ethyl-3-hydroxynaphthoquinone	137.5–138.5[i]	36	$C_{12}H_{10}O_3$	71.3	5.0	71.5	5.4
2-*n*-Butyl-3-hydroxynaphthoquinone	100–101[j]	55	$C_{14}H_{14}O_3$				

[a] Reported [Wojack, *Ber.*, **71**, 1102 (1938)] m. p. 84–85°. [b] Reported (ref. *a*) m. p. 55.5°. [c] Reported (ref. *a*) m. p. 50.5°. [d] B. p. 155–160° at 1 mm. [e] Reported (ref. *a*) m. p. 33°. [f] Reported[4] m. p. 161–162°. Possibly Gheorgiu had a hydrolysis product rather than ester. [g] Not purified. [h] Over-all, including preceding step. [i] Reported [Hooker, THIS JOURNAL, **58**, 1178 (1936)] m. p. 138.2–138.5°. [j] Reported [Hooker, *ibid.*, **58**, 1167 (1936)] m. p. 101–101.5°.

gave a solid which was removed, dissolved in acetic acid (10 ml.) and treated with a solution of chromic acid (0.5 g.) in water. This mixture was heated on a water-bath for fifteen minutes and then diluted with water. The resulting precipitate was obtained in the form of yellow needles (0.55 g., 77%) that melted at 87–88° (literature[7] 88°) by crystallization from acetic acid.

Anal. Calcd. for $C_{12}H_{10}O_2$: C, 77.4; H, 5.4. Found: C, 76.9; H, 5.5.

We thank the Graduate School of the University of Minnesota for a grant from the Fluid Research Fund.

(7) Kruber and Schade, *Ber.*, **69**, 1722 (1936).

Summary

A series of reactions has been described which appears to constitute a general method for the preparation of 1,4-naphthoquinones and hydroquinones which contain a hydrocarbon residue in position 2 and which bear a hydrogen, a hydroxyl or a carbethoxyl in position 3.

MINNEAPOLIS, MINN. RECEIVED DECEMBER 22, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMICAL ENGINEERING, UNIVERSITY OF WASHINGTON]

p-Cymene Studies. IV. Mononitration of 2-Amino-*p*-cymene. Preparation of 3-Amino-*p*-cymene and *o*- and *p*-Cymylenediamine

BY THOMAS F. DOUMANI AND KENNETH A. KOBE

Of the three possible nitro-2-amino-*p*-cymenes, only one has been reported formed in the nitration of 2-amino-*p*-cymene liquid isomer obtained by Wheeler and Brooks.[1,2] We now find that the large amount of tarry by-product in this reaction consists almost exclusively of a solid isomer. Wheeler and Brooks claimed their liquid product to be 2-amino-5-nitro-*p*-cymene, which would make the solid product the 2-amino-3-nitro-*p*-cymene. In our investigation of these compounds the following proof is given that the liquid isomer (I) is 2-amino-3-nitro-*p*-cymene and the solid isomer (II) is 2-amino-5-nitro-*p*-cymene. Product I on reduction gave an unknown diamine in which the *ortho* position of the amino groups is proved by their ready condensation with benzil and phenanthraquinone, and by its conversion to a benzimidazole on heating with glacial acetic acid or atmospheric distillation of its diacetyl derivative. Product II when reduced to the diamine could be oxidized to thymoquinone.

The 2-acetamino-*p*-cymene is extremely diffi-

(1) Wheeler and Brooks, THIS JOURNAL, **49**, 2832–2834 (1927).
(2) Wheeler and Cutlar, *ibid.*, **49**, 2819–2822 (1927).

cult to purify for nitration purposes. Nitration of this acetyl derivative gave 52% 2-amino-3-nitro-*p*-cymene and 48% 2-amino-5-nitro-*p*-cymene. The nitration of 2-amino-*p*-cymene sulfate gave approximately 60% 2-amino-3-nitro-*p*-cymene and 40% 2-amino-5-nitro-*p*-cymene.

In this work 2-formylamino-*p*-cymene was used instead of the corresponding acetyl derivative, because of its ease of purification and subsequent ease of hydrolysis of the formyl groups from the isomeric nitroamines. Further, it gave the isomeric nitroamines in a practically pure state after fractionation, thus eliminating any purification through acyl derivatives. Nitration gave 70% of 2-amino-3-nitro-*p*-cymene and 30% of 2-amino-5-nitro-*p*-cymene.

Reduction of the nitroamines with zinc dust and sodium hydroxide gave the corresponding cymylenediamines in excellent yield. Statements as to the instability of *p*-cymylenediamine were found to be somewhat misleading. This compound was isolated in the pure state and found to deteriorate only very slowly in the presence of light. In aqueous ethanol solution this compound is more rapidly destroyed. The elaborate vacuum distillation apparatus employed by Wheeler and Bost[3] for the isolation of this diamine was found to be unnecessary.

Experimental[4,5]

2-Formylamino-*p*-cymene (I).—Nitration and reduction were carried out according to our published methods.[6] All *p*-toluidine was removed from the crude 2-amino-*p*-cymene by repeated fractionation *in vacuo*. A solution of 149 g. (1.0 mole) of 2-amino-*p*-cymene and 90 g. (1.76 moles) of formic acid (90%) was refluxed for two hours. (The excess of formic acid was used to prevent violent bumping.) The product after shaking with 300 ml. of water and cooling gave the formyl derivative as an oil which rapidly solidified. It was crystallized twice from ethanol, forming colorless needles of m. p. 108.8–109.4°. It is very soluble in cold concentrated sulfuric acid or chloroform, quite soluble in ether or acetone, slightly soluble in hot water, and practically insoluble in cold water.

Anal. Calcd. for $C_{11}H_{15}NO$: N, 7.90. Found: N, 7.95.

Nitration.—100 g. of I (0.565 mole) of m. p. 108.8–109.4° was dissolved in 400 g. of sulfuric acid (sp. gr. 1.84). To this solution at 0° was added drop by drop with stirring a previously cooled nitrating acid consisting of 56 g. (0.613 mole) of nitric acid (sp. gr. 1.42) and 100 g. of sulfuric acid (sp. gr. 1.84). After the addition of all the nitrating acid stirring was continued for ten minutes. The mixture was poured with efficient stirring into about 0.5 kg. of crushed ice in 0.5 kg. of water. The product was a yellow, sticky, amorphous mass which became hard and crystalline after several hours. It was filtered, washed with cold water and air dried. The filtrate was extracted with 50 ml. of chloroform and the latter evaporated; total yield, 113 g. (90%).

Hydrolysis.—The crude formyl-nitroamines (113 g.) were refluxed for one hour with 150 ml. of 30% sodium hydroxide solution. The red nitroamine layer was washed with water; the sodium hydroxide layer extracted with benzene (25 ml.), and the latter evaporated off; total yield, 98.2 g. (99%).

Separation of Isomeric Nitroamines.—The nitroamines (98.2 g.) were fractionated very slowly three times in a 150 ml. well-lagged Vigreux flask of 16-cm. column resulting in the following fractions: (1) 0.8 g. of a light yellow liquid of b. p. 65–67° (1 mm.); (2) 64.5 g. of an orange-red liquid of b. p. 114–116° (1 mm.); and (3) 26.6 g. of a yellow solid b. p. 144–148° (1 mm.), m. p. 57–60°. The residue in the flask was 4.5 g. At this low pressure superheating very easily occurs; consequently, to avoid this, fractionation must be executed slowly; approximately eight hours was used.

Fraction (1) was acetylated by refluxing with 5 ml. of acetic anhydride for one hour. The resulting product (after washing with water and refrigerating at 0°) remained liquid. It was boiled for one hour with 20 ml. of concentrated hydrochloric acid made alkaline with sodium hydroxide solution, and extracted with benzene. The free base was refluxed with 5 ml. of formic acid (90%) for one hour; it was crystallized once from ethanol and boiled with Norite in ethanol; m. p. 108.8–109.4° (mixed m. p. with authentic 2-formylamino-*p*-cymene was the same).

2-Amino-3-nitro-*p*-cymene (II).—Fraction (2), 64.5 g., was acetylated by refluxing with equivalent acetic anhydride for three hours. The product consisted of only one **acetylderivative,** as colorless needles of m. p. 167.6–167.8° from ethanol–ether mixture. It was crystallized by dissolving in ethanol, diluting with ether and cooling to 0°. A total of 65 g. of this acetyl derivative was isolated; the residue of crystallization amounted to 0.6 g. Thus the II taken for acetylation was practically pure.

Anal. Calcd. for $C_{12}H_{16}N_2O_3$: N, 11.86. Found: N, 11.82.

This acetyl derivative was hydrolyzed by refluxing with 100 ml. of concentrated hydrochloric acid for two hours. The mixture was made alkaline with sodium hydroxide solution and after washing with water was distilled. II is an orange-red liquid of sweet taste and of b. p. 142.9° (5 mm.), 158.8° (10 mm.), 175.6° (20 mm.) and at atmospheric pressure it is decomposed. The salts formed with hydrochloric, nitric, or sulfuric acid are all hydrolyzed by cold water.

Its **formyl derivative** was prepared by refluxing 5 g. of II with 10 g. of formic acid (90%) for five hours. (After

(3) Wheeler and Bost, THIS JOURNAL, **50**, 2000 (1928).

(4) All melting points are corrected and were determined using Brothcom total immersion thermometers graduated in 0.2° (immediately after crystallization and air drying); this was found to be necessary since many of the compounds, such as the acyl derivatives of the nitroamines, were found to be transformed upon standing into modifications which for some of the compounds have different melting points.

(5) Analyses for nitrogen by micro-Dumas using dry-ice as a source of pure carbon dioxide.

(6) Kobe and Doumani, *Ind. Eng. Chem.*, **31**, 257 (1939); Doumani and Kobe, *ibid.*, **31**, 264 (1939).

two hours refluxing there still remained unreacted amine.) It was crystallized from ethanol in colorless needles which soften at 128.0° and melt at 139.6–140.0°.

Anal. Calcd. for $C_{11}H_{14}N_2O_3$: N, 12.61. Found: N, 12.60.

Its **benzoyl derivative** was prepared by heating 5 g. of 2-amino-3-nitro-*p*-cymene with 10 g. of benzoyl chloride for five minutes at 90°. It crystallizes from ethanol as colorless needles of m. p. 193.4–193.8°.

Anal. Calcd. for $C_{17}H_{18}N_2O_3$: N, 9.39. Found: N. 9.33.

***o*-Cymylenediamine (III).**—Thirty-five grams of II, 35 ml. of ethanol, and 30 ml. of 30% sodium hydroxide solution was shaken with the addition of 50 g. of zinc dust in such portions that the solution gently refluxed. After the addition of all the zinc dust it was further refluxed for one hour giving a light brown solution. The excess zinc dust was filtered off in the hot, and the filtrate rapidly cooled, causing the diamine to crystallize out. (In alkaline solution upon standing in the presence of air this compound is slightly oxidized to a reddish dye very soluble in ethyl ether.) This *o*-diamine forms hard, well-defined, colorless, rhombic crystals from ethanol of m. p. 95.0–95.8°. It remains practically colorless on long standing in the presence of light. It is very soluble in acetone, ethyl ether, chloroform, or benzene, and practically insoluble in petroleum ether; yield 26 g. (88%).

Anal. Calcd. for $C_{10}H_{16}N_2$: N, 17.06. Found: N, 17.04.

***o*-Diacetylcymylenediamine (IV).**—Fifteen grams of III was dissolved in 30 ml. of acetic anhydride. The diacetyl derivative crystallized out upon cooling; colorless needles of constant m. p. 235.1–235.3° were obtained after one crystallization from ethanol. Refluxing 5 g. of III with 10 ml. of acetic anhydride for one hour gave a mixture of IV and the anhydro base (V).

Anal. Calcd. for $C_{14}H_{20}N_2O_2$: N, 11.28. Found: N, 11.23.

2,7-Dimethyl-4-isopropyl-benzimidazole (V). A.—Ten grams of IV was distilled at atmospheric pressure, b. p. 326–327° (uncor.). The distillate was crystallized by dissolving in the minimum volume of warm benzene and diluting with two volumes of warm petroleum ether. Upon cooling colorless crystals of m. p. 179.5–179.9° were obtained. This benzimidazole is very soluble in ethanol, ethyl ether, chloroform, or benzene, slightly soluble in hot water or petroleum ether, and practically insoluble in cold water. It readily forms salts with dilute hydrochloric, nitric, sulfuric, or acetic acid.

Anal. Calcd. for $C_{12}H_{16}N_2$: N, 14.88. Found: N, 14.81.

B.—2.5 g. of III was refluxed for one hour with 10 g. of glacial acetic acid. It was made alkaline with dilute sodium hydroxide solution, clarified by boiling with Norite in benzene, and recrystallized as in A, above. A mixed m. p. with the above compound in A was not depressed.

2,3-Diphenyl-5-isopropyl-8-methylquinoxaline.—3.3 g. of III, 4.2 g. of benzil, and 30 ml. of ethanol were refluxed together for fifteen minutes. The quinoxaline separated out and was recrystallized from benzene–ethanol mixture (1:2); colorless crystals, m. p. 136.7–137.3°. This compound gives a blood red coloration when treated with a drop of concentrated sulfuric acid; upon dilution, the color becomes yellow. Concentrated hydrochloric acid gives a yellow coloration.

Anal. Calcd. for $C_{24}H_{22}N_2$: N, 8.27. Found: N, 8.14.

10-Isopropyl-13-methyldibenzophenazine.—0.8 g. of III, 1 g. of phenanthraquinone, and 20 ml. of glacial acetic acid were refluxed for fifteen minutes. The product was insoluble and was crystallized from benzene as light yellow needles of m. p. 181.2–181.4°. This compound gives a purplish-red coloration when treated with a drop of concentrated sulfuric acid. Concentrated hydrochloric acid gives a yellow coloration.

Anal. Calcd. for $C_{24}H_{20}N_2$: N, 8.33. Found: N, 8.26.

2-Amino-5-nitro-*p*-cymene (VI).—Fraction (3), 26.6 g., was recrystallized from ethanol as canary yellow needles of m. p. 66.6–67.6°. A total of 24.8 g. of VI was isolated; only 1.1 g. of impure amine could not be purified in this manner; however, upon acetylation with acetic anhydride it proved to be the 2-acetamino-5-nitro-*p*-cymene. Thus, the 26.6 g. of nitroamine taken for crystallization was practically pure. Like II its salts with hydrochloric, nitric, or sulfuric acid are all hydrolyzed by cold water; unlike it, however, it is tasteless.

Anal. Calcd. for $C_{10}H_{14}N_2O_2$: N, 14.42. Found: N, 14.48.

The **acetyl derivative,** prepared by refluxing with equivalent acetic anhydride for three hours, was crystallized once from ethanol and boiled with Norite in ethanol, giving colorless needles of m. p. 142.8–143.2°.

Anal. Calcd. for $C_{12}H_{16}N_2O_3$: N, 11.86. Found: N, 11.81.

Its **formyl derivative** was prepared by refluxing 5 g. of the amine with 20 ml. of formic acid (90%) for four hours; yellow crystals from ethanol, m. p. 101.6–102.2°.

Anal. Calcd. for $C_{11}H_{14}N_2O_3$: N, 12.61. Found: N, 12.59.

Its **benzoyl derivative,** prepared by heating the amine with a 20% excess of benzoyl chloride at 90° for fifteen minutes, crystallized from ethanol as light yellow, monoclinic crystals of m. p. 139.0–139.4°.

Anal. Calcd. for $C_{17}H_{18}N_2O_3$: N, 9.39. Found: N, 9.42.

***p*-Cymylenediamine (VII).**—19.4 g. (0.1 mole) of VI dissolved in 50 ml. of ethanol was mixed with 25 ml. of 40% sodium hydroxide solution and treated with 30 g. of zinc dust in such portions that the solution gently refluxed when shaken. Refluxing was continued for one hour after the addition of all the zinc dust; the excess zinc dust was filtered off, the ethanol evaporated off, the brown amine layer separated from the caustic layer and the amine distilled, b. p. 120–125° (1 mm.) uncor. The colorless amine rapidly turned yellow. It was recrystallized by dissolving in the minimum benzene (1 vol.) in the hot, diluting with warm petroleum ether (2 vols.), and cooling, giving large yellow coarse crystals that rapidly turned brown; m. p. 50.0–50.5°; yield 14.1 g. (86%).

Anal. Calcd. for $C_{10}H_{16}N_2$: N, 17.06. Found: N, 17.01.

p-**Diacetylcymylenediamine.**—Two grams of VII was heated with 10 ml. of acetic anhydride at 90° for five minutes. Crystallization from benzene gave m. p. 262.0–262.2°.

Anal. Calcd. for $C_{14}H_{20}N_2O_2$: N, 11.28. Found: N, 11.27.

Thymoquinone.—Half a gram of finely crushed VII was shaken for five minutes with 50 ml. of 50% ferric chloride solution at room temperature. The thymoquinone was insoluble; it was filtered off and crystallized from petroleum ether; m. p. 45.6–46.0° mixed m. p. with thymoquinone[7] prepared from thymol was the same.

3-Nitro-*p*-cymene (**VIII**). A.—From II: 8 g. of powdered sodium nitrite was dissolved in 160 g. of sulfuric acid (sp. gr. 1.84) below 40°. Very slowly at 35–40° was added 20 g. of II to avoid the precipitation of the insoluble amine sulfate. Stirring was continued for fifteen minutes after which a drop when poured in water gave none of the colored nitroamine. To this mixture was slowly added 300 ml. of absolute ethanol with vigorous shaking; the resulting mixture was refluxed for one hour. Steam distillation gave some phenolic substance (removed by washing with dilute sodium hydroxide solution) and VIII; yield 9.7 g. (52%). VIII is a light yellow liquid of b. p. 116.7 (10 mm.), b. p. 133.5 (20 mm.), and at atmospheric pressure it is decomposed.

B.—From VI: 20 g. of VI was dissolved in 20 ml. of glacial acetic acid and diazotized exactly as in A. The product consisted mostly of a phenolic residue in the steam distillation flask. The yield of VIII was 2.3 g.

C.—Twenty grams of the mixture of isomeric nitroamines in the proportion as formed by the nitration of I was diazotized and treated as in A, with the further addition of 5 g. of freshly reduced copper as a suspension in the absolute ethanol; yield 9.8 g. (53%).

3-Amino-*p*-cymene (**IX**).—The VIII in A and B above, were separately reduced with iron powder and hydrochloric acid.[6] Both amines gave the same formyl derivative by refluxing with twice the volume of formic acid (90%) for two hours. **3-Formylamino-*p*-cymene** forms colorless needles from ethanol of m. p. 106.2–106.6°. There was a depression of the melting point when admixed with I.

Anal. Calcd. for $C_{11}H_{15}NO$: N, 7.90. Found: N, 7.83.

3-Amino-*p*-cymene is a colorless liquid of b. p. 105.7° (10 mm.), 122.1° (20 mm.), 240.2° (760 mm.).

Thymol.—Five grams of IX was dissolved in 50 ml. of 5% sulfuric acid and diazotized with the exact equivalent of sodium nitrite dissolved in 10 ml. of water. It was steam distilled, extracted with dilute sodium hydroxide, and acidified, giving thymol of m. p. 47–49° from petroleum ether. The m. p. was raised when mixed with synthetic thymol from *m*-cresol and isopropyl alcohol.

(7) Kremers, Wakeman, and Hixon, *Org. Syntheses*, **6**, 92 (1926).

Summary

1. Nitration of 2-formylamino-*p*-cymene gives 70% of 2-amino-3-nitro-*p*-cymene and 30% of 2-amino-5-nitro-*p*-cymene. Nitration of 2-acetylamino-*p*-cymene gives 52 and 48%, respectively, of the above nitroamines.

2. Quantitative separation of the isomeric nitroamines can be effected by fractionation *in vacuo*.

3. The isomeric cymylenediamines can be obtained in excellent yield from the nitroamines by reduction with zinc dust and sodium hydroxide solution.

4. The nitroamine that has previously been described as 2-amino-5-nitro-*p*-cymene has been proved to be 2-amino-3-nitro-*p*-cymene.

SEATTLE, WASHINGTON RECEIVED OCTOBER 30, 1939

[CONTRIBUTION NO. 181 FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, THE UNIVERSITY OF TEXAS]

Alkaline Hydrolysis of Condensation Products of Hydantoin with Aldehydes[1]

BY HENRY R. HENZE, WILLIAM B. WHITNEY AND MARGARET A. EPPRIGHT

The condensation of aldehydes with the methylene hydrogens in —X—CH_2—CO— has been a valuable reaction for synthetic purposes following Perkin's[2] condensation of salicylic aldehyde and sodium acetate in the presence of acetic anhydride. This reaction has since been modified and widely applied. Plöchl and Wolfrum[3] were the first to employ it in connection with condensations involving the —NH—CH_2—CO— grouping. Initially, Plöchl used glycine but later he found that hippuric acid, the benzoyl derivative of glycine, gave much better results. Erlenmeyer[4] studied the chemical behavior of these condensation products of hippuric acid and obtained alpha amino acids by their reduction and *subsequent* hydrolysis.

Wheeler and Hoffman[5] further modified the

(1) Presented before the Division of Organic Chemistry at the 96th meeting of the American Chemical Society at Milwaukee, Wis., Sept. 5–9, 1938.

(2) Perkin, *Chem. News*, **32**, 258 (1875).

(3) Plöchl, *Ber.*, **16**, 2815 (1883); Plöchl and Wolfrum, *ibid.*, **18**, 1183 (1885).

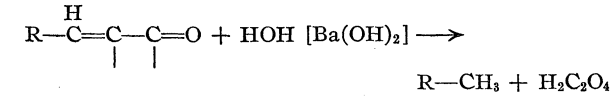
(4) Erlenmeyer, jun., *Ann.*, **271**, 137 (1892); **275**, 1 (1893); *Ber.*, **30**, 2976 (1897).

(5) Wheeler and Hoffman, *Am. Chem. J.*, **45**, 368 (1911).

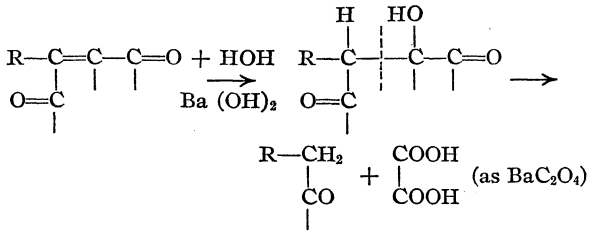
method by replacing hippuric acid with hydantoin, which contains the —NH—CH_2—CO— structure in a heterocycle. In only one instance, namely, that of anisalhydantoin, was the initial condensation product hydrolyzed by alkali *prior* to reduction, and Wheeler and Hoffman reported that "when it is boiled with alkali it gives *p*-methoxyphenylpyruvic acid." No details were recorded as to the yield and proof of identity of the latter, of the formation of by-products, or concerning the concentration and specific identity of the alkali used. Since either sodium hydroxide or barium hydroxide was utilized in hydrolyzing the reduced reaction products, it seems probable that one or the other of these bases was used in cleaving anisalhydantoin.

We have studied the effect of aqueous solutions of both sodium and barium hydroxide upon anisalhydantoin and believe that Wheeler and Hoffman utilized a dilute solution of barium hydroxide, for a 5% solution of sodium hydroxide liberates ammonia and forms some *p*-methoxyphenylpyruvic acid. However, some oxalic acid and *p*-methoxytoluene are formed, also. Concentrated solutions of either sodium or barium hydroxide when boiled with anisalhydantoin yield no *p*-methoxyphenylpyruvic acid; indeed, with barium hydroxide *p*-methoxytoluene and oxalate are the chief products although small amounts of anisaldehyde, anisyl alcohol and anisic acid are formed, too. It is of interest to note that concentrated solutions of either of these alkalies convert *p*-methoxyphenylpyruvic acid into oxalate and *p*-methoxytoluene.

The hydrolytic effect of barium hydroxide solution on *o*-chlorobenzalhydantoin, on *m*-nitrobenzalhydantoin, and on furfuralhydantoin has been studied. In each instance no substituted pyruvic acid was isolated; instead, the chief result was to convert the —CH= grouping into methyl.



The alkaline hydrolysis of these hydantoin condensation products is strictly analogous to the cleavage of the condensation products of hydantoin with isatin and 5-methylisatin reported by Henze and Blair[6] and for which the following mechanism had been proposed:



The essential steps in the mechanism of alkaline hydrolysis are: (a) the addition of a molecule of water to the ethylenic linkage in such a way that the HO— adds to the C atom of the hydantoin nucleus and the H— to the other C atom of the C=C linkage; (b) the double bond being saturated, the linkage between the two carbons breaks, either because of migration of a hydrogen atom in the reversal of enolization, or because of intermolecular change (bimolecular rather than monomolecular process).

Nicolet and Campbell,[7] as a result of a study of alkaline hydrolysis of benzalcreatinine (benzal-2-imino-1-methylhydantoin) and related compounds concluded that "It seems, however, to be well established that it is a matter of somewhat extreme difficulty to open the ring in any of the unreduced aldehyde condensation products of hydantoins by the action of alkali." That this statement is too broad is shown by the results of the present investigation.

Since *o*-chlorobenzalhydantoin and *m*-nitrobenzalhydantoin had not been synthesized previously, it was deemed desirable to reduce and hydrolyze the compounds in order to convert them into α-amino acids. By this process *o*-chlorophenylalanine and *m*-aminophenylalanine were obtained.

Experimental

Action of Sodium Hydroxide on Anisalhydantoin.—One gram of anisalhydantoin[5] was digested in 100 cc. of 5% sodium hydroxide solution for five hours at 80–90°; during this period ammonia was evolved and, in addition, the odor characteristic of *p*-methoxytoluene was detected in the reaction flask. The reaction mixture was neutralized with dilute hydrochloric acid causing the separation of a small amount of yellow solid. The latter did not contain nitrogen, and its solution in ethyl alcohol developed a fleeting blue-green color when treated with dilute, aqueous ferric chloride solution. A positive test for oxalate was obtained in the acid filtrate.

Action of Barium Hydroxide on Anisalhydantoin.—Thirty-five grams of anisalhydantoin, 300 g. of crystalline barium hydroxide and 400 cc. of water were digested under reflux in an oil-bath at 120–135° for one hundred hours.

(6) Henze and Blair, THIS JOURNAL, **55**, 4621 (1933).

(7) Nicolet and Campbell, THIS JOURNAL, **50**, 1155 (1928).

At intervals during the hydrolysis the cooling water was withdrawn from the condenser and distillation was permitted until a total volume of 150 cc. of distillate had been collected. The distillate was saturated with potassium carbonate and the oily layer was separated and dried. Upon distillation the product (7.5 cc.) proved to be a mixture, the chief constituent being *p*-methoxytoluene, b. p. 177.5–178°; d^{20}_4 0.9735; $n^{20}D$ 1.5140; M_R calcd. 37.19; M_R found, 37.73; a trace of anisic aldehyde was identified.

The mixture remaining after hydrolysis was cooled and filtered, the residue and filtrate being examined independently. The residue consisted largely of barium hydroxide and carbonate, but contained oxalate, also. The filtrate was treated with ether which served to extract 1 cc. of anisyl alcohol, b. p. 259° (cor.). From the filtrate upon acidification there separated 9 g. of curdy solid which was shown to be anisic acid, m. p. 184°; neutral equivalent 149 (in alcohol), 151 (in water); m. p. of mixture with authentic sample of anisic acid 184.5°; m. p. of mixture with *p*-methoxyphenylpyruvic acid showed a depression of twenty degrees.

Anal. Calcd. for $C_8H_8O_3$: C, 63.13; H, 5.30. Found: C, 63.50; H, 5.30.

Further confirmation of the identity of anisic acid was obtained by its conversion into the ethyl ester,[8] m. p. 7° (cor.); b. p. 264.5°; $n^{20}D$ 1.5238.

Converson of "Anisal-azlactone" [2-Phenyl-4-(*p*-methoxyphenyl)-oxazolone] into *p*-Methoxyphenylpyruvic Acid.—Following Dakin's[9] procedure, anisaldehyde was condensed with hippuric acid to form "anisal-azlactone," m. p. 158°. Fifty grams of the "azlactone" was heated for one hour with 750 cc. of 40% sodium hydroxide solution in an oil-bath at 110–115° following the directions of Wakeman and Dakin.[10] At the close of thirty minutes it was noticed that an oil, as well as water, was refluxing in the condenser; hence, during the next half hour distillation was permitted in order to collect the oily liquid. The reaction mixture was cooled and extracted with ether, the extract being combined with that of the distillate. After drying the extract over anhydrous potassium carbonate, and removing the ether, the residual liquid boiled at 177°; d^{20}_4 0.9702; $n^{20}D$ 1.5120; M_R calcd. for *p*-methoxytoluene, 37.19; M_R found, 37.74.

Continuing with the procedure 13 g. of *p*-methoxyphenylpyruvic acid,[11] melting at 185°, was obtained.

Action of Barium Hydroxide on *p*-Methoxyphenylpyruvic Acid.—Four grams of *p*-methoxyphenylpyruvic acid, 13 g. of crystalline barium hydroxide and 15 cc. of water were heated in an oil-bath for fifteen hours at 115–120°. The reaction mixture was subjected to steam distillation at intervals during the period of digestion. From the distillate there was isolated 0.8 cc. of an oil sparingly soluble in water. After drying over anhydrous potassium carbonate, the oil had b. p. 176.5°; d^{20}_4 0.9705; $n^{20}D$ 1.5130; hence, this product was *p*-methoxytoluene. Moreover, the presence of oxalate in the reaction mixture was established.

Action of Barium Hydroxide on Furfurylhydantoin.—Thirty grams of furfuralhydantoin, 320 g. of crystalline barium hydroxide and 350 cc. of water were digested under reflux in an oil-bath at 110–120° for sixty hours. After ten hours an oil, as well as water, was noticed in the condenser; therefore, the reaction mixture was subjected intermittently to steam distillation. From a total distillate of 500 cc. there separated 8 cc. of a yellow-green colored oil, sparingly soluble in and less dense than water, and of an aromatic odor strongly suggestive of the xylenes. After drying the oil was distilled and identified as being 2-methylfuran;[12] b. p. 63.2° (cor.); d^{20}_4 0.9032; $n^{20}D$ 1.4310; M_R calcd., 23.71; M_R found, 23.50. No organic matter other than oxalate was identified in the material remaining after hydrolysis.

Preparation of *o*-Chlorobenzalhydantoin.—*o*-Chlorobenzaldehyde (10 g.), hydantoin (10 g.), fused sodium acetate (8.2 g.) and glacial acetic acid (59 cc. to which 1 cc. of acetic anhydride had been added) were refluxed together for one hour in an oil-bath at 145°. Upon cooling some *o*-chlorobenzalhydantoin crystallized and additional material was obtained by dilution of the solution. The total yield of crude product was 10 g. (66%). After recrystallization from acetone and ethanol the silky needles melted at 275° (cor.). This derivative is soluble in glacial acetic acid, acetone and ethanol, but is nearly insoluble in water, ether and benzene.

Anal. Calcd. for $C_{10}H_7ClN_2O$: C, 53.94; H, 3.17; Cl, 15.92; N, 12.59. Found: C, 54.21; H, 3.36; Cl, 16.15; N, 12.87.

Action of Barium Hydroxide on *o*-Chlorobenzalhydantoin.—Ten grams of *o*-chlorobenzalhydantoin was refluxed with a mixture of 50 g. of barium hydroxide (octahydrate) and 50 cc. of water for fifty hours. The liquid refluxing in the condenser contained oily droplets; hence, the reaction mixture was steam distilled and the distillate extracted with ether. After drying and removal of the solvent, the residual liquid, by reason of the following data, was identified as being *o*-chlorotoluene: b. p. 155° (cor.); d^{20}_4 1.0890; $n^{20}D$ 1.5250; M_R calcd., 36.09; M_R found, 35.62.

Anal. Calcd. for C_7H_7Cl: Cl, 28.02. Found: Cl, 27.80.

Reduction of *o*-Chlorobenzalhydantoin.—Ten grams of *o*-chlorobenzalhydantoin, 45 g. of hydriodic acid (sp. gr. 1.7) and 10 cc. of glacial acetic acid were refluxed for two hours in an oil-bath at 120°. The solution was steam distilled until free from acid and cooled, thus causing the separation of 7.5 g. of white, crystalline solid material. The **5-(*o*-chlorobenzyl)-hydantoin** was recrystallized from glacial acetic acid in the form of white, glistening platelets melting at 240° (cor.).

Anal. Calcd. for $C_{10}H_9ClN_2O_2$: C, 53.45; H, 4.03; Cl, 15.79; N, 12.48. Found: C, 52.64; H, 3.77; Cl, 15.78; N, 12.09.

Hydrolysis of 5-(*o*-Chlorobenzyl)-hydantoin.—Ten grams of 5-(*o*-chlorobenzyl)-hydantoin, 50 g. of barium hydroxide (octahydrate) and 50 cc. of water were refluxed for about fifty hours. Most of the barium was removed

(8) Radcliffe and Brindley, *Perfumery Essentl. Oil Record*, **13**, 414 (1922), report m. p. 7–8°; b. p. 263°; $n^{18.5}D$ 1.5245.

(9) Dakin, *J. Biol. Chem.*, **8**, 18 (1910).

(10) Wakeman and Dakin, *ibid.*, **9**, 150 (1911).

(11) Wakeman and Dakin, ref. 10, report m. p. 190–192°, but Erlenmeyer and Wittenberg, *Ann.*, **337**, 294 (1904), report m. p. 186°.

(12) Paul, *Compt. rend.*, **200**, 1118 (1935).

from the solution by saturation with carbon dioxide, the remainder by exact neutralization with sulfuric acid. After filtration and concentration of the filtrate, 7.4 g. (88% yield) of white solid separated. After recrystallization from water and alcohol, **o-chlorophenylalanine** melts at 260–261° (cor.).

Anal. Calcd. for $C_9H_{10}ClNO_2$: C, 54.13; H, 5.05; Cl, 17.77; N, 7.02. Found: C, 55.14; H, 5.04; Cl, 17.30; N, 7.68.

Anhydrous hydrogen chloride was passed into an ethanol solution of *o*-chlorophenylalanine causing the separation of solid material. The latter was filtered, washed with a cold, saturated solution of hydrogen chloride in ethanol, and dried in a vacuum desiccator. The melting point of **o-chlorophenylalanine hydrochloride** is 255–256° (cor.).

Anal. Calcd. for $C_9H_{11}Cl_2N_2O_2$: Cl, 30.01. Found: Cl, 29.87.

Preparation of *m*-Nitrobenzalhydantoin.—Ten grams of hydantoin, 15 g. of *m*-nitrobenzaldehyde, 8.2 g. of fused sodium acetate, 60 cc. of glacial acetic acid and 2 cc. of acetic anhydride were heated together in an oil-bath at 145°; yellow solid material began to separate from solution after about three hours, but heating was continued for a total of eleven hours. Upon cooling and filtering, 14.5 g. (58% yield) of solid, with m. p. 250°, was obtained. After recrystallization from glacial acetic acid the bright yellow crystals of *m*-nitrobenzalhydantoin melted at 277° (cor.). This compound is quite sparingly soluble in all common solvents, the largest solubility being that (1.75–2 g./100 cc.) in boiling glacial acetic acid.

Anal. Calcd. for $C_{10}H_7N_3O_4$: C, 51.49; H, 3.03; N, 18.07. Found: C, 51.48; H, 3.18; N, 18.02.

Action of Barium Hydroxide on *m*-Nitrobenzalhydantoin.—Twenty grams of *m*-nitrobenzalhydantoin, 100 g. of barium hydroxide (octahydrate) and 100 cc. of water were placed in a distilling flask and heated in an oil-bath at 120° for about thirty hours. During this time a slow distillation occurred and oily droplets were collected in the receiver. After drying, the oil was identified as being *m*-nitrotoluene by its boiling point and refractive index.

The residue in the flask, to which water was added to replace that removed through distillation, was heated for an additional period of thirty hours before being examined for oxalate; the latter was present.

Reduction of *m*-Nitrobenzalhydantoin.—To 23.3 g. of *m*-nitrobenzalhydantoin were added 100 g. of tin and 500 cc. of concd. hydrochloric acid and the mixture was heated in an oil-bath for six hours at 120° while hydrogen chloride was passed into the well-stirred solution. The bright yellow crystals quickly changed to a flocculent light gray colored solid which dissolved after about five hours. The solution was concentrated, to remove much of the excess acid, diluted with water to adjust the *p*H, and saturated with hydrogen sulfide. After filtration and decolorization of the filtrate with Norite, further concentration in a vacuum desiccator over sulfuric acid caused separation of a crystalline solid. The latter was recrystallized from dilute hydrochloric acid and yielded the **hydrochloride of 5-(*m*-aminobenzyl)-hydantoin,** m. p. 270° (cor.). This salt is extremely soluble in water and alcohol, but is insoluble in acetone and ether.

Anal. Calcd. for $C_{10}H_{12}ClN_3O_2$: C, 49.68; H, 5.01; Cl, 14.67; N, 17.39. Found: C, 49.71; H, 5.27; Cl, 14.55; N, 17.11.

Action of Barium Hydroxide on 5-(*m*-Aminobenzyl)-hydantoin Hydrochloride.—The hydrolysis was accomplished in the usual manner with 17.5 g. of *m*-aminobenzylhydantoin, 87.5 g. of crystalline barium hydroxide and 87.5 cc. of water. The **dihydrochloride of *m*-aminophenylalanine,** m. p. 225° (cor.), was recrystallized from hydrochloric acid.

Anal. Calcd. for $C_9H_{14}Cl_2N_2O_2$: C, 42.69; H, 5.58; N, 11.06. Found: C, 43.02; H, 5.97; N, 11.29.

Summary

The behavior on alkaline hydrolysis of anisal-, furfural-, *o*-chlorobenzal-, and *m*-nitrobenzalhydantoin has been studied. The results are to be predicted on the basis of a mechanism advanced previously by Henze and Blair.

AUSTIN, TEXAS RECEIVED NOVEMBER 6, 1939

[CONTRIBUTION FROM THE DIVISION OF BIOCHEMISTRY, THE MAYO FOUNDATION, ROCHESTER, MINNESOTA]

The Preparation and Degradation of Lithocholic Acid

BY WILLARD M. HOEHN AND HAROLD L. MASON

The importance of desoxycorticosterone as the most active of the crystalline substances thus far isolated from the adrenal gland makes it desirable to develop methods for its preparation. Stigmasterol[1] and cholesterol[2] have been used as raw materials for its preparation by several procedures. It is the purpose of this note to describe some improved procedures for the conversion of bile acids into materials suitable for the preparation of desoxycorticosterone and related substances.

The first step was the conversion of cholic and desoxycholic acids to lithocholic acid. This conversion has been accomplished by a number of procedures[3] but the over-all yields have not been encouraging. By the action of benzoyl chloride and pyridine on methyl desoxycholate at 15° the 3-monobenzoate was obtained in good yield. Oxidation to methyl 3-benzoxy-12-ketocholanate with chromic acid proceeded smoothly as did the subsequent preparation of the semicarbazone. The over-all yield of semicarbazone from methyl desoxycholate was more than 80%. Reduction of the semicarbazone by the Wolff–Kishner method yielded an average of 60% of recrystallized lithocholic acid.

The degradation of lithocholic acid by the Wieland–Barbier method was performed as previously described for desoxycholic acid.[4] Reindel and Niederlander[5] and Sawlewicz and Reichstein[6] have described similar degradations. The melting points and specific rotations of the compounds so obtained are given in Table I since some of these values are not recorded in the literature. Oxidation of the acetylated diphenylethylenes was performed at 45–50° because of their insolubility in acetic acid at 15°. The other procedures require no comment.

TABLE I

DEGRADATION PRODUCTS OF LITHOCHOLIC ACID

Compound	M. p. °C.	$[\alpha]^{25}_{5461}$	Formula	Calcd., % C	Calcd., % H	Found, % C	Found, % H
3-Acetoxy-*bis-nor*-cholanyldiphenylethylene	158–160	+75.5 (in $CHCl_3$)	$C_{38}H_{50}O_2$	84.71	9.36		
3-Acetoxypregnanyldiphenylethylene	150–152	+140 ± 3° (in $CHCl_3$)	$C_{37}H_{48}O_2$	84.61	9.22		
1,1-Diphenyl-methyl-(3-acetoxy-*etio*-cholanyl)-ethylene	158–160	+398 ± 2° (in $CHCl_3$)	$C_{36}H_{46}O_2$	84.65	9.08	84.73	9.31
Pregnanol-3(α)-one-20	148–149	+129 ± 3° (in alcohol)	$C_{21}H_{34}O_2$	79.19	10.76	78.85	10.74
21-Benzalpregnanolone	228–230	+181 ± 3° (in alcohol)	$C_{28}H_{38}O_2$	82.71	9.42	82.34	9.51
3-Acetoxy-*etio*-cholanic acid	226–229	+86.4 ± 3° (in alcohol)	$C_{22}H_{34}O_4$	72.87	9.46	72.70	9.33
etio-Lithocholic acid	270–272		$C_{20}H_{32}O_3$	74.96	10.07	74.51	10.06

Ozonolysis of 1,1-diphenyl-methyl-(3-acetoxy-*etio*-cholanyl)-ethylene[7] followed by hydrolysis gave pregnanol-3(α)-one-20.[8] Further degradation proceeded as with the corresponding ketone derived from desoxycholic acid. The benzal ketone was isolated and its properties were found to agree with those given by Marker and Wittle[9] who have recently used this procedure for the preparation of *etio*-cholanic acids from the pregnanolones. The preparation of dehydro-*etio*-lithocholic acid and 4-bromo-3-keto-*etio*-cholanic acid by the usual methods offered no difficulties.

Experimental Part

Methyl 3-Benzoxy-12-hydroxycholanate.—A solution of 32 g. (0.08 mole) of methyl desoxycholate in 150 cc. of dry benzene was cooled to 5°, 10 cc. of dry pyridine was added, and then 9.3 cc. (0.081 mole) of benzoyl chloride in 20 cc.

(1) Steiger and Reichstein, *Helv. Chim. Acta*, **20**, 1164 (1937).

(2) Serini, Logemann and Hildebrand, *Ber.*, **72**, 391 (1939).

(3) Recent papers are (a) Bergström and Haslewood, *J. Chem. Soc. London*, 540 (1939); (b) Dutcher and Wintersteiner, THIS JOURNAL, **61**, 1992 (1939).

(4) Hoehn and Mason, THIS JOURNAL, **60**, 1493 (1938).

(5) Reindel and Niederlander, *Ber.*, **68**, 1969 (1935).

(6) Sawlewicz and Reichstein, *Helv. Chim. Acta*, **20**, 949 (1937).

(7) The Referee has pointed out that we have fallen into error in our previous paper[4] in naming the diphenylethylenes derived from desoxycholic and homologous acids. *3,12-Diacetoxy-bis-nor-cholanyldiphenylethylene* is correct for the compound called 3,12-diacetoxy-*nor*-cholanyldiphenylethylene; *3,12-diacetoxypregnanyl*diphenylethylene (or *3,12-diacetoxy-ter-nor-cholanyldiphenylethylene*) instead of 3,12-diacetoxy-*bis-nor*-cholanyldiphenylethylene; and *1,1-diphenyl-methyl-(3,12-diacetoxy-etio-cholanyl)*-ethylene instead of 3,12-diacetoxy-*ter-nor*-cholanyldiphenylethylene. The names previously applied included one carbon atom in both the ethylene group and the cholanyl radical.

(8) (a) Marker, Kamm and Jones, THIS JOURNAL, **59**, 1595 (1937); (b) Marker, Kamm and Wittle, *ibid.*, **59**, 1841 (1937); (c) Butenandt and Hildebrandt, U. S. Patent 2,156,275 (1939).

(9) Marker and Wittle, THIS JOURNAL, **61**, 1329 (1939).

of dry benzene was added at such a rate that no rise in temperature occurred. The mixture was allowed to come to room temperature and to stand for three hours. The benzene solution was washed with three 100 cc. portions of 0.5 *N* hydrochloric acid, then with 0.2 *N* sodium hydroxide and finally with water. After removal of water with anhydrous sodium sulfate, the benzene was distilled in a vacuum. The glassy residue was dissolved by warming with 200 cc. of dry ether. The etherate of methyl 3-benzoxy-12-hydroxycholanate crystallized from the solution on standing. It was air-dried and then melted at 78–80° with frothing; yield, 87–89%.

Anal. Calcd. for $C_{32}H_{46}O_5 \cdot {}^1/_2C_4H_{10}O$: C, 74.55; H, 9.39. Found: C, 74.35; H, 9.36.

When two molar equivalents of benzoyl chloride and pyridine were used, the dibenzoate of methyl desoxycholate was obtained, m. p. 145–146°.

Methyl 3-Benzoxy-12-ketocholanate.—A solution of 44 g. (0.08 mole) of methyl 3-benzoxy-12-hydroxycholanate etherate in 70 cc. of acetic acid was evaporated in a vacuum to remove the ether, and the residue was dissolved in 400 cc. of glacial acetic acid. To this solution, cooled to 15°, was added 8 g. of chromic acid in 100 cc. of 90% acetic acid. The mixture stood overnight in the refrigerator and was worked up in the usual manner for the neutral product. This substance usually was not isolated. It can be crystallized in the icebox from a large volume of absolute alcohol and then melts at 94–95°.

Semicarbazone.—The crude keto ester was dissolved in 250 cc. of alcohol and a solution of 19 g. (0.17 mole) of semicarbazide hydrochloride and 15 g. of sodium acetate in 100 cc. of 80% alcohol was added. This mixture was refluxed for fourteen hours. The bulk of the semicarbazone separated during the refluxing and was removed by filtration of the hot solution. A second crop, obtained by cooling, was purified by boiling with water. The total yield, after drying at 110° for eight hours, was 43 g. (95% based on the etherate). It melted at 160–162° after recrystallization from alcohol.

Lithocholic Acid (1).—A mixture containing 45 g. of sodium and 43 g. (0.076 mole) of the semicarbazone in 400 cc. of absolute alcohol was heated in an autoclave at about 200° for seven hours. The reaction product was dissolved in hot water and acidified to congo red with dilute hydrochloric acid. The precipitated acid was washed on the filter with hot water, dried and crystallized from acetone. The yield of lithocholic acid (m. p. 183–185°; $[\alpha]^{25}D$ +34°; $[\alpha]^{25}_{5461}$ +39°) was 18.4 g. (64.6%).

Anal. Calcd. for $C_{24}H_{40}O_3$: C, 76.55; H, 10.71. Found: C, 76.36; H, 10.68.

Lithocholic Acid (2).—Seventy grams (0.110 mole) of the disemicarbazone of methyl 3-benzoxy-7,12-diketocholanate (prepared by procedures similar to those used for the preparation of the semicarbazone of methyl 3-benzoxy-12-ketocholanate) was added to a solution of 70 g. of sodium in 700 cc. of methyl alcohol and heated in an autoclave at 174 ± 5° for six hours. After solution of the reaction products in warm water the methyl alcohol was removed in a vacuum. The aqueous fraction was warmed until all solids were dissolved and was then poured with stirring into an excess of dilute hydrochloric acid. The precipitated acid, which was often somewhat gummy, was suspended in 0.8 *N* sodium hydroxide solution and heated to 40–50° on the water-bath. The sodium lithocholate which separated under these conditions was filtered out, resuspended in 1 *N* sodium hydroxide and again isolated. It was then dissolved in hot water and the solution was poured into a slight excess of dilute hydrochloric acid. The lithocholic acid was filtered off and washed well with water. Dried at 110° and crystallized from dry acetone, the yield was 25.9 g. (62.5%) of lithocholic acid (m. p. 183.5–185°).

Dehydro-*etio*-lithocholic Acid.—A solution of 390 mg. (0.00124 mole) of *etio*-lithocholic acid in 20 cc. of glacial acetic acid was cooled to 15° and 100 mg. of chromic acid in 1 cc. of 90% acetic acid was added. After one hour the excess of chromic acid was reduced with alcohol. The solvents were removed in a vacuum and the residue was extracted with 200 cc. of ether and 100 cc. of water. The ether layer was separated, washed with water until colorless and dried over anhydrous sodium sulfate. The acid, after crystallization from acetone, weighed 330 mg. (84%). Crystallization from benzene gave a product which melted at 246–248°. Marker and Wittle[9] report a melting point of 246–249° but no analytical figures are given.

Anal. Calcd. for $C_{20}H_{30}O_3$: C, 75.43; H, 9.49. Found: C, 75.46; H, 9.70.

4-Bromo-dehydro-*etio*-lithocholic Acid.—To a solution of 784 mg. (0.00246 mole) of dehydro-*etio*-lithocholic acid in 30 cc. of glacial acetic acid at 18° was added 6.3 cc. of 0.82 *N* bromine in glacial acetic acid solution. After standing ten minutes the solvents were removed in a vacuum. The residue was taken up in ethyl acetate from which crystallized 620 mg. (63.5%); m. p. 190–192°.

Anal. Calcd. for $C_{20}H_{29}O_3Br$: C, 60.45; H, 7.19. Found: C, 60.30; H, 7.40.

Summary

Lithocholic acid has been prepared from cholic and desoxycholic acids with an over-all yield of 50%. Some of the intermediate compounds of the Wolff–Kishner degradation of lithocholic acid have been described.

ROCHESTER, MINNESOTA RECEIVED DECEMBER 18, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF BIOLOGICAL CHEMISTRY, COLUMBIA UNIVERSITY, AND FROM THE DEPARTMENT OF CHEMISTRY, THE CITY COLLEGE, COLLEGE OF THE CITY OF NEW YORK]

The Synthesis of the Sodium Salt of Tetradecamethylene Disulfonic Acid

BY GILBERT C. H. STONE

In a previous paper by the author,[1] a method for the synthesis of the sodium salts of alkane-α,ω-disulfonic acids by means of the Strecker reaction[2] was described. In each run the reaction had been followed by means of an argentometric titration of aliquot portions of the reaction mixture. And in each case the reaction was found to go to completion if given sufficient time. Table I gives the number of carbons in the alkane-α,ω-disulfonate and a rough estimate of the time for complete conversion.

TABLE I

Carbons	Time for complete conversion, hrs.
2	12
3	18
4	24
5	36
6	60
10	168

It can be inferred that for the preparation of higher members of this series, by means of the same method, an unduly long period of heating would be required. Reactions of this nature have been carried out successfully in short periods of time by using an autoclave to obtain high temperatures.[3,4,5] In order to obviate the use of the autoclave, which is inconvenient in the preparation of large quantities of material, other methods were sought.

A solvent in which both the initial materials are soluble was employed. The dibromide reacted with various simple sulfur-containing compounds yielding terminal carbon–sulfur linkages. In most cases such substances can be oxidized to the sulfonic acid stage. Because of the possibility of forming sulfides, which would yield sulfones upon oxidation, the synthesis of mercaptans was avoided. Preparation of a dithiocyanate met with no success. A dixanthate, however, could be made and oxidized to the sulfonic acid. The following synthesis of the sodium salt of tetradecamethylene disulfonic acid serves as an example of the method whereby the higher homologs of this series may be prepared.

(1) Stone, THIS JOURNAL, **58**, 488 (1936).
(2) Strecker, *Ann.*, **148**, 90 (1868).
(3) Reed and Tartar, THIS JOURNAL, **57**, 570 (1935).
(4) Norris, *J. Chem. Soc.*, **121**, 2161 (1922).
(5) Collins, Hilditch, Marsh and MacLeod, *J. Soc. Chem. Ind.*, **52**, 272T (1933).

Experimental Part

Tetradecamethylene Glycol.—This was prepared by means of the Grignard reaction from decamethylene dibromide[1] and ethylene oxide, by an adaptation of the method of Dreger.[6] After washing, drying and then vacuum distilling the crude glycol, the properties checked fairly well with those reported by P. Chuit.[7] The yield was 40% of the theoretical amount.

Tetradecamethylene Dibromide.—290 g. (1.26 moles) of the above glycol was treated with gaseous anhydrous hydrogen bromide according to the method of Ruhoff, Burnett and Reid.[8] The resulting dibromide, dissolved in twice its weight of ethylene chloride, was washed and then dried over calcium chloride. After decolorizing with Norite and then removing the solvent, the residue was distilled *in vacuo* and the fraction coming over at 172–175° under 2–3 mm. pressure was collected. The yield was 65% of the theoretical.

Anal. Calcd. for $C_{14}H_{28}Br_2$: C, 47.18; H, 7.93. Found: C, 47.60; H, 7.78.

Sodium Tetradecamethylene Disulfonate.—A solution of 402 g. (one mole) of tetradecamethylene dibromide in 2 liters of hot ethyl alcohol was added slowly to a solution of 480 g. (3 moles) of potassium ethylxanthate in 2 liters of ethanol. The mixture was refluxed with stirring for twenty-four hours. After completely removing the alcohol by distillation, the residual yellow liquid was dissolved in a minimum quantity of ether, well washed with water, and dried with calcium chloride. After removal of the ether, the residual yellow liquid was taken up in redistilled dioxane, and water added until a slight turbidity resulted; 2720 g. (17 moles) of bromine and 1000 ml. of water were added in alternate small portions with shaking. After several hours, excess bromine was removed on a steam-bath, and finally hydrogen bromide and other volatile substances were driven off under reduced pressure by repeated distillations. The liquid remaining was diluted with water and an aqueous solution of silver nitrate added until no more silver salts precipitated. The suspension was brought to a boil and filtered hot. In order to remove any of the silver disulfonate, which is soluble in hot water, from the silver bromide, the precipitate on the Buchner funnel was extracted repeatedly with boiling water. After combining the filtrates and evaporating down to incipient precipitation, the solution was allowed to cool. The silver salt was filtered off and washed with cold water. Further evaporation of the resulting filtrate gave another crop of crystals.

(6) Dreger, "Organic Syntheses," Coll. Vol. I, p. 299.
(7) Chuit, *Helv. Chim. Acta*, **9**, 264 (1926).
(8) Ruhoff, Burnett and Reid, THIS JOURNAL, **56**, 2784 (1934).

The silver disulfonate was suspended in water, and the silver removed as the sulfide. The yellowish brown filtrate was evaporated down to 2000 ml., exactly neutralized with sodium hydroxide, and concentrated to incipient crystallization. The sodium salt of tetradecamethylene disulfonic acid crystallized out in the ice-box overnight. Several crops of the salt were so obtained. The crystals were purified by dissolving them in a minimum of hot water and adding twice the volume of redistilled acetone. This process of purification was repeated five times. The resulting crystals were white with a slight grayish cast and were not very soluble in water. A solution of the salt was neutral to alizarin. Like the other sodium disulfonates,[1] it showed no tendency to hydrolyze. The yield was 54% of the theoretical.

Anal. Calcd. for $NaO_3S(CH_2)_{14}SO_3Na$: C, 41.76; H, 7.01; Na, 11.43. Found: C, 41.74; H, 6.99; Na, 11.48.

The author wishes to express his thanks to Prof. H. T. Clarke of Columbia University for his kind advice and help during the course of this work; and to Mr. W. Saschek for performing the analyses.

Summary

A method for the preparation and purification of the sodium salts of the higher members of the series of the alkane-α,ω-disulfonic acids has been described. Details were given in regard to the synthesis and properties of the sodium salt of tetradecamethylene disulfonic acid.

NEW YORK, N. Y. RECEIVED NOVEMBER 20, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE CITY COLLEGE, COLLEGE OF THE CITY OF NEW YORK, AND FROM THE DEPARTMENT OF BIOLOGICAL CHEMISTRY, COLUMBIA UNIVERSITY]

The Activity Coefficient of Thallous Iodate in Solutions of Alkane-α,ω-disulfonates

BY GILBERT C. H. STONE

The alkane-α,ω-dicarboxylic acids have been studied extensively by Gane and Ingold,[1] Greenspan,[2] and others, with the view of ascertaining the fine structure and dimensions of the aliphatic chain in such molecules. Their results, which indicate that the chain has a rigidly extended zigzag configuration, check well with X-ray data.[3,4,5] These compounds are weak acids, not completely dissociated in aqueous solution. They do not lend themselves to studies, such as activity coefficient measurements from solubility data, which are made on the basis of theories developed on the assumption of complete dissociation. Strong dibasic acids of similar structure would be necessary. With this in mind, a series of alkane-α,ω-disulfonic acids with from one to fourteen carbons were prepared by the author.[6,7] Titration curves of these acids indicated that they are at least as strong as sulfuric acid.

It was desired to determine the qualitative and, if possible, the quantitative effect which would be obtained by increasing the distance between the two strongly polar groups; and the saturated straight aliphatic chain seemed ideal as a separating medium, especially since its normal length and diameter are known. It was hoped that by increasing the distance of separation of these polar groups a point might be found where the molecule ceased to behave as bivalent or dibasic and perhaps functioned as two univalent ions. A study of this nature might throw some light on the structure of large-sized multicharged ions, such as the proteins, which behave as multivalent ions despite the relatively large distances which separate the charged groups.[8]

By taking advantage of the Debye–Hückel relationship

$$-\log \gamma_{\pm} = \frac{0.5056\sqrt{\mu}}{1 + a \times 0.3286 \times 10^{8}\sqrt{\mu}} \text{ at } 25°$$

and that $\log S/S_0 = -\log \gamma_{\pm}$, solubility measurements seemed one way of attacking the problem. The "a" value gives an estimate of the *average* ion parameter. While the *average* distance of closest approach might not be expected to check with the actual size of the alkane-α,ω-disulfonate ion, as other ions are present in the solution, nevertheless, since these other ions remain the same, qualitatively and quantitatively, throughout the series of measurements, the a value should increase as the chain length increases.

In the calculations of the ionic strength

$$\mu = \frac{1}{2}\Sigma m_i z_i^2$$

(1) Gane and Ingold, *J. Chem. Soc.*, 1594 (1928); 2267 (1928); 1691 (1929); 1375 (1930).

(2) Greenspan, *Chem. Rev.*, **12**, 339 (1933).

(3) Bragg and Bragg, "X-Ray and Crystal Structure," G. Bell and Sons, Lockerbie, Scotland, 1925, p. 294.

(4) Muller, *Proc. Roy. Soc.* (London), **114**, 542 (1927).

(5) Caspari, *J. Chem. Soc.*, 3289 (1928).

(6) Stone, THIS JOURNAL, **58**, 488 (1936).

(7) Stone, *ibid.*, **62**, 571 (1940).

(8) Stone and Failey, *J. Phys. Chem.*, **37**, 935 (1933).

if the valence of the disulfonate ion is two, then for a molar solution, μ would be 3. On the other hand, if the ion were so long that it functioned as two moles of a univalent substance, μ would be 2. In other words, the tangent of the limiting law in the former case would be 0.5056, and in the latter case it would be 0.6193. With a decrease in the effective valency due to an increase in chain length, or increase in the separation of the charged groups, the tangents of the curves should be expected to increase. On the other hand, if the effective valency does not decrease and an effect is obtained due only to the increasing size of the molecule, the limiting tangent of the curve should remain the same, 0.5056, but the curves should diverge from this tangent to a greater and greater extent as the size of the ion increases.

Unfortunately, the solubility of the sodium salt of the alkane-α,ω-disulfonates reaches a maximum at the fourth or fifth carbon stage and then decreases rapidly. The salt of the fourteen carbon member of the series is just sufficiently soluble that these measurements could be made on it. To continue lengthening the chain in an attempt to achieve the above-mentioned effect seemed fruitless.

Experimental

The sodium salt of methanedisulfonic acid was prepared according to Schroeter.[9] The salt was recrystallized several times and the analysis checked with the theoretical values.

The synthesis and purification of the other sodium salts of the alkane-α,ω-disulfonic acids, as well as their titration curves, have been described.[6,7]

TABLE I

SOLUBILITY OF $TlIO_3$ IN THE PRESENCE OF SODIUM ALKANE α,ω-DISULFONATES

Soly. of $TlIO_3$ in water = S_0 = 1836 × 10^{-6} mole per liter at 25°

$$-\log \gamma_0 = \frac{0.5056\sqrt{0.001836}}{1 + 3 \times 10^{-8} \times 0.3286 \times 10^{8}\sqrt{0.001836}} = 0.0208^{b} \quad -\log \gamma_{\pm} = 0.0208 + \log S/S_0$$

Molarity of solvent salt	Soly. × 10^6	$-\log \gamma_{\pm}$	$\sqrt{\mu}$	a, Å.
	[a]$NaO_3S(CH_2)SO_3Na$			
0.0200	2300	0.1199	0.249	2.0
.0100	2138	.0881	.179	2.1
.0050	2036	.0669	.130	2.0
.0020	1937	.0453	.089	2.1
.0010	1897	.0362	.070	1.7
.0005	1867	.0293	.058	1.9
				Av. 1.9
	$NaO_3S(CH_2)_2SO_3Na$			
.0200	2220	.1033	.249	3.3
.0100	2094	.0779	.179	3.5
.0050	2009	.0599	.130	3.2
.0020	1927	.0418	.089	3.6
.0010	1887	.0327	.070	(4.3)
.0005	1868	.0283	.058	2.8
				Av. 3.3
	$NaO_3S(CH_2)_3SO_3Na$			
.0200	2216	.1025	.249	3.4
.0100	2094	.0779	.179	3.5
.0050	2007	.0595	.130	3.1
.0020	1924	.0411	.089	(4.1)
.0010	1890	.0334	.070	3.5
.0005	1868	.0283	.058	(2.8)
				Av. 3.4
	$NaO_3S(CH_2)_4SO_3Na$			
.0200	2207	.1008	.249	3.6
.0100	2093	.0777	.179	3.5
.0050	2003	.0586	.130	3.7
.0020	1921	.0405	.089	(4.5)
.0010	1891	.0336	.070	3.4
.0005	1860	.0265	.058	(6.0)
				Av. 3.5
	$NaO_3S(CH_2)_5SO_3Na$			
.0200	2198	.0990	.249	3.8
.0100	2079	.0748	.179	4.1
.0050	1997	.0573	.130	4.2
.0020	1915	.0391	.089	(5.9)
.0010	1884	.0320	.070	(5.2)
.0005	1860	.0264	.058	(6.1)
				Av. 4.0
	$NaO_3S(CH_2)_6SO_3Na$			
.0200	2196	.0986	.249	3.9
.0100	2084	.0759	.179	3.9
.0050	1995	.0569	.130	4.3
.0020	1920	.0402	.089	4.8
.0010	1890	.0334	.070	(5.2)
.0005	1860	.0264	.058	(6.1)
				Av. 4.2
	$NaO_3S(CH_2)_{10}SO_3Na$			
.0200	2176	.0946	.249	4.4
.0100	2071	.0731	.179	4.5
.0050	1994	.0567	.130	4.4
.0020	1924	.0411	.089	4.1
.0010	1885	.0322	.070	4.9
.0005	1861	.0267	.058	(5.5)
				Av. 4.5
	[a]$NaO_3S(CH_2)_{14}SO_3Na$			
.0200	2135	.0875	.249	5.5
.0100	2054	.0707	.179	5.2
.0050	1977	.0541	.130	5.7
.0020	...	...	...	...
.0010	1873	.0307	.070	...
.0005	1856	.0267	.058	5.5
				Av. 5.5

[a] In the cases of the one carbon and the fourteen carbon sodium disulfonate solutions, a different sample of the saturating salt was used. An average of 30 solubility determinations on this thallous iodate resulted in S_0 = 1831 × 10^{-6} mole per liter. [b] An a value of 3 Å. was assumed for $TlIO_3$.

(9) Schroeter, *Ann.*, **418**, 246 (1918).

The preparation of thallous iodate and the method of analysis were those of La Mer and Goldman.[10]

Solutions of the sodium salts of the disulfonic acids were made up with conductivity water and of the strengths shown in Table I. These solutions were rotated with the solid thallous iodate in glass-stoppered Pyrex bottles in a water-bath for twenty-four hours at a temperature of 25.00 ± 0.01°. The solid was allowed to settle and the supernatant solution filtered at 25.0° and then analyzed.

Discussion

From Curve I, which is a plot of the data given in Table I, it can be seen that despite the lengthening of the aliphatic chain or the greater separation of the sulfonate groups, all the curves approach the same theoretical limiting tangent of 0.5056. However, these curves deviate from the limiting tangent more and more as the chain length increases. This would indicate that the sodium salts of the alkane-α,ω-disulfonic acids behaved in solution as bivalent compounds, there being no indication in these experiments that even with a separation of fourteen carbons the two terminal negative groups ceased to have an effect upon each other.

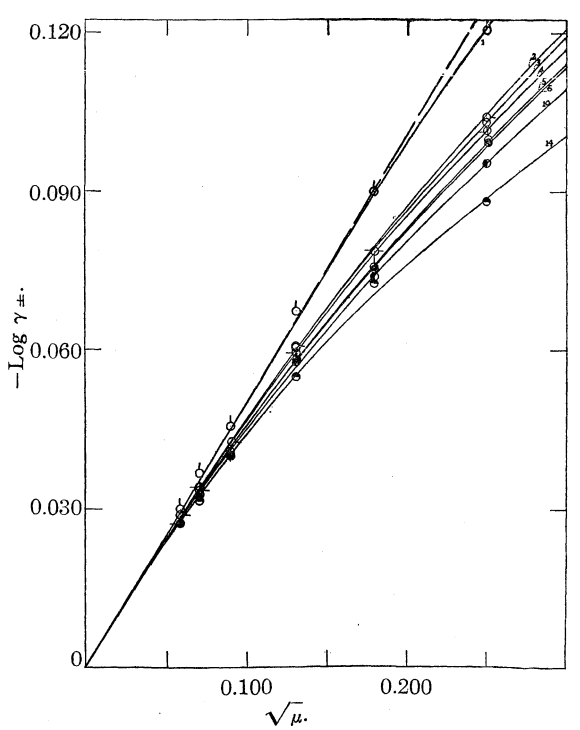


Fig. 1.—Curve 1, Ò, $NaO_3S(CH_2)SO_3Na$; Curve 2, O-, $NaO_3S(CH_2)_2SO_3Na$; Curve 3, Ọ, $NaO_3S(CH_2)_3SO_3Na$; Curve 4, -O, $NaO_3S(CH_2)_4SO_3Na$; Curve 5, ◑, $NaO_3S(CH_2)_5SO_3Na$; Curve 6, ◒, $NaO_3S(CH_2)_6SO_3Na$; Curve 10, ◐, $NaO_3S(CH_2)_{10}SO_3Na$; Curve 14, ◓, $NaO_3S(CH_2)_{14}SO_3Na$.

(10) La Mer and Goldman, THIS JOURNAL, **51**, 2632 (1929).

The continuous deviation of the curves from the theoretical limiting tangent with increasing chain lengths may be attributed to the increasing size of the ion involved. As can be seen from the table of data, the average distance of closest approach becomes greater as the chain becomes longer. These values of a were calculated by means of the La Mer, Gronwall and Greiff extended formula of the Debye–Hückel relationship.[11] The calculated values of a for any one series of measurements on any one disulfonate do not vary very much. As might be expected, the values obtained for a on the most dilute solutions showed the greatest deviation from the average; in these cases the accuracy of the measurements was at its lowest.

An attempt was made to correlate the average values of a with an increase in one CH_2 group. Approximately 0.25 Å. corresponded to the size of the methylene group. This value is far from that obtained by measurements of other kinds. However, the a values calculated on the basis of the Debye–Hückel equation do not check well with, for example, the size of the ion found by X-ray measurements. The value of a is not the absolute size of the ion, but the distance of nearest approach. Hydration, the presence of other ions, etc., will affect this value greatly.

Notwithstanding all this, the effect of separating the two charged groups of the ion is not as great as one might have expected. However, the long disulfonate ion, with a negative charge at either end, in all likelihood would bend around in the presence of an ion of opposite charge, both negative groups being attracted by the positive ion. Such a bending would greatly decrease the effective size of the disulfonate ion and account for the results obtained. This bending would not take place in the solid state nor in the case of the corresponding dicarboxylic acids, which are not greatly dissociated. Such a distortion would also explain why, even with a distance equivalent to fourteen carbon atoms between two charged groups, the bivalent disulfonate ion shows no unusual effect and behaves like a small ion of equal charge.

The author wishes to express his gratitude to Professor H. T. Clarke of Columbia University for his kind help and coöperation in the work on this problem.

(11) La Mer, Gronwall and Greiff, *J. Phys. Chem.*, **35**, 2245 (1931).

Summary

The solubility of thallous iodate was measured at 25° in aqueous solutions of the sodium salt of alkane-α,ω-disulfonic acids with from one to fourteen carbons in the separating chain. The results were considered on the basis of the Debye–Hückel equation.

All of the above-mentioned salts functioned as bivalent compounds, despite the great separation of the sulfonate groups in the case of the latter members of the series.

The values for the mean effective ionic diameters were calculated for each salt of the series of the alkane-α,ω-disulfonates. These values increased with increasing chain length. However, this increase in effective size was equivalent to only 0.25 Å. for each additional CH_2 group in the chain.

The small increment in effective size due to the addition of a methylene group to the aliphatic chain, as well as the bivalency of the disulfonate ion, was accounted for on the assumption that the molecule bent in the presence of a positive ion, both negative groups of the disulfonate ion being attracted to the oppositely charged particle.

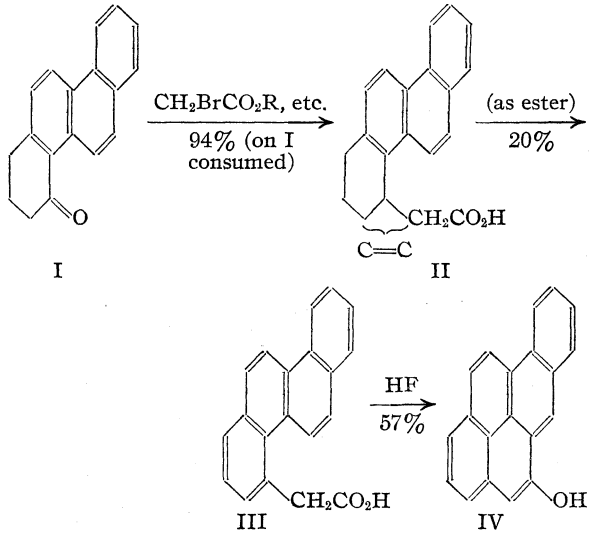
NEW YORK, N. Y. RECEIVED NOVEMBER 20, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Synthesis of 6-Hydroxy-3,4-benzpyrene and 8-Isopropyl-1,2-benzanthracene from 9,10-Dihydrophenanthrene

BY LOUIS F. FIESER AND WILLIAM S. JOHNSON

In extension of previous work[1] in which a satisfactory method was developed for obtaining 4-keto-1,2,3,4-tetrahydrochrysene (I) starting with 9,10-dihydrophenanthrene,[1b] this ketone has been utilized for the synthesis of the hitherto undescribed 6-hydroxy-3,4-benzpyrene (IV) by the process outlined.



I II III IV

The Reformatsky reaction at first seemed unpromising because of the separation of an insoluble complex which stopped the reaction. While no way was found for pushing the reaction to completion, it proved quite satisfactory to operate under mild conditions permitting the easy recovery of the unchanged starting material in a pure form after saponification of the ester. After dehydration with formic acid, the crude acidic product, possibly consisting of a mixture of isomers, was esterified and the ester dehydrogenated with sulfur, which gave better results than palladium charcoal. The product was contaminated with a small amount of high melting material which appeared to be a hydrocarbon, but this was separated easily after saponification of the ester.

Cyclization of 4-chryseneacetic acid (III) proceeded well under the influence of anhydrous hydrogen fluoride[2] giving pure 6-hydroxy-3,4-benzpyrene (IV) in good yield. It seemed interesting to determine whether an intermediate ketone could be detected, for in the formation of anthrones by cyclization, the use of hydrogen fluoride provides a particularly advantageous means of isolating the material in the ketonic condition and avoiding enolization. Even with highly sensitive anthrones which have not been isolated as such, it has been possible to effect a Grignard addition by adding the reagent directly to the crude residue remaining after evaporation of the hydrogen fluoride.[2b,3] This technique was applied in the present case and the mixture examined care-

(1) Fieser and Johnson, (a) THIS JOURNAL, **61**, 168 (1939); (b) *ibid.*, **61**, 1647 (1939).

(2) Fieser and Hershberg, (a) *ibid.*, **61**, 1272 (1939); (b) **62**, 49 (1940).

(3) Fieser and Cason, *ibid.*, **62**, 432 (1940).

fully for the presence of a carbinol or hydrocarbon. Aside from a trace of fluorescent material, no such product was found and it is concluded that the intermediate has no appreciable stability in the ketonic form.

Another series of synthetic experiments afforded 8-isopropyl-1,2-benzanthracene, desired as a further member of the series described[1] and for comparison with the carcinogenic 6-isopropyl compound[4] and with the 7[4]-(inactive) and 5[5]-isomers. The 8-keto-3,4,5,6,7,8-hexahydro-1,2-benzanthracene required as starting material was obtained from γ-(9,10-dihydro-2-phenanthryl)-butyric acid by cyclization with hydrogen fluoride in 89.5% yield (pure). A careful investigation of other cyclization methods was previously reported[1a] and the yields of pure ketone may be summarized for comparison: 85% sulfuric acid, 22%; zinc chloride and acetic acid-anhydride, 45%; phosphorus pentachloride-aluminum chloride, 63.5%. The ketone reacted satisfactorily with isopropylmagnesium bromide, giving after dehydration a hydrocarbon mixture which was dehydrogenated successfully with sulfur at 250°. Pure 8-isopropyl-1,2-benzanthracene was isolated through the picrate in 35% yield in the dehydrogenation step. It has been observed that an isopropyl group is eliminated from the 5[6]- and 10[7]-positions in dehydrogenations conducted with selenium but that a 10-isopropyl[7] or a 4-methyl[8] group can be retained at least in part by the use of sulfur.

Experimental Part[9]

4-Chryseneacetic Acid (III).—The Reformatsky condensation of methyl bromoacetate with 4-keto-1,2,3,4-tetrahydrochrysene[1b] (I) under a variety of conditions was subject to the difficulty that a sparingly soluble zinc complex separated as an oil which coated the zinc and stopped the reaction. Expedients tried with little success included vigorous stirring, the use of various special solvents, and suspension of the zinc in a basket to keep it away from the walls of the vessel. After numerous trials it was found most satisfactory to allow the reaction to proceed to a stopping point under moderate conditions and work up the mixture in such a way as to recover unchanged starting material in a pure condition.

Highly active metal for the reaction was prepared by immersing 30-mesh zinc in hot (100°) concentrated sulfuric acid containing a few drops of concentrated nitric acid. There was little evident reaction except that after about fifteen minutes the zinc surface became very bright. The acid was largely decanted and water added; a vigorous reaction with the dilute acid was allowed to proceed for a few minutes and the metal was then collected, washed thoroughly with water and then with acetone, and dried.

In a typical run 4 g. of activated zinc was added to a solution of 2 g. of the ketone (I) and 1.2 cc. of methyl bromoacetate in 40 cc. of dry benzene. The mixture was heated in a water-bath almost to boiling and a crystal of iodine was introduced, when the reaction promptly started and soon became vigorous. After heating for one hour the zinc had become completely coated over with oily complex, the mixture was cooled, enough methanol was added to dissolve the oil, and the solution was decanted from the metal, shaken with 10% hydrochloric acid, water, and saturated salt solution, and filtered through sodium sulfate. After removal of the solvent, the residual oil was boiled for fifteen minutes with excess 1 *N* alcoholic potassium hydroxide; water was added to the hot solution to the point of incipient cloudiness and on cooling 1.0 g. of unchanged ketone of good quality crystallized. Acidification of the alkaline liquor brought down a dark amorphous product which lost no weight when heated with anhydrous formic acid and which therefore was already in a dehydrated condition; yield 1.1 g. (94%, based on ketone consumed).

A solution of 1.7 g. of the crude acid in 250 cc. of methanol was saturated in the cold with hydrogen chloride, refluxed for twelve hours, diluted and extracted with ether. Vacuum distillation gave 1.44 g. of the ester as a yellow oil; this was heated with 0.18 g. of sulfur for two hours at 210°, and after heating with a pinch of zinc dust for five minutes, the product was distilled in vacuum. The distillate was dissolved in hot acetone–methanol and the solution filtered from about 80 mg. of high melting, unsaponifiable material (chrysene?). On cooling, 0.59 g. of product separated as glistening prisms (m. p. 109–111°) consisting of methyl 4-chryseneacetate contaminated with some of the above by-product. This was readily removed after saponification with 0.22 g. of potassium hydroxide in 7 cc. of boiling alcohol. The potassium salt of the chryseneacetic acid separated on cooling as glistening blades and was obtained colorless by washing with acetone. The salt dissolved readily in water and after filtration from a trace of the high-melting solid 4-chryseneacetic acid was precipitated in a high state of purity, m. p. 206.5–207.5°; yield 0.34 g. (20.1%, based on the crude unsaturated acid). A sample, crystallized once from benzene–acetone, formed colorless needles, m. p. 207–208°.

Anal.[10] Calcd. for $C_{20}H_{14}O_2$: C, 83.89; H, 4.93. Found: C, 84.12; H, 5.00.

From a number of variations tried in the dehydrogenation step it appeared that the reaction with sulfur proceeded better at the temperature specified than at higher or lower temperatures. With palladium charcoal the higher temperature required seemed to favor the formation of the high melting by-product and the yield was lower.

6-Hydroxy-3,4-benzpyrene (IV).—The following experiment was designed to detect any ketonic material

(4) Cook, *J. Chem. Soc.*, 456 (1932).
(5) Cook and de Worms, *ibid.*, 268 (1939).
(6) Cook, *ibid.*, 1592 (1933).
(7) Fieser and Hershberg, THIS JOURNAL, **59**, 1028, 2331 (1937).
(8) Fieser and Jones, *ibid.*, **60**, 1940 (1938).
(9) All melting points are corrected.
(10) Microanalysis by Herbert S. Wight.

resulting from the cyclization of 4-chryseneacetic acid. Three-tenths gram of the acid was treated with 20 g. of chilled liquid hydrogen fluoride in a platinum cylinder and after thirty minutes the excess reagent was removed in a stream of air and the chilled residue was treated with the Grignard reagent from 1.5 g. of magnesium and excess methyl chloride. After three hours the mixture was worked up as usual, giving a yellow, highly fluorescent ethereal solution. Evaporation left a solid residue which was sublimed at 150–155° and 0.001 mm. Sublimation occurred rapidly at first and then stopped, apparently because of encrustation of the residual solid, but after dissolving this in ether and evaporating to dryness, a further sublimate was obtained. The operation was repeated once more and the combined sublimate was crystallized from toluene, giving 0.16 g. (57%) of light yellow needles, m. p. 193–194°, decompn. Recrystallization raised the m. p. to 195–196°, decompn.

Anal.[10] Calcd. for $C_{20}H_{12}O$: C, 89.53; H, 4.51. Found: C, 89.12; H, 4.56.

The substance couples readily with diazotized *p*-nitroaniline to give a sparingly soluble, red azo compound. Like 4'-hydroxy-3,4-benzpyrene,[11] the phenol gives a red color in concentrated sulfuric acid and on adding a drop of concentrated nitric acid the solution acquires a transient green color changing to deep blue.

In search of a possible hydrocarbon the mother liquors were combined with the residue from the sublimation and submitted to chromatographic adsorption, but only a trace of fluorescent material could be washed through the tower with benzene and this was not identified.

8-Keto-3,4,5,6,7,8-hexahydro-1,2-benzanthracene.—γ-(9,10-Dihydro-2-phenanthryl)-butyric acid (7.1 g.) was treated with hydrogen fluoride (100 g.) at room temperature for two hours, the reagent was largely removed with a stream of air and the residue neutralized with sodium carbonate solution and extracted with benzene. No unchanged acid was detected and distillation in vacuum gave 6.2 g. (94%) of nearly colorless ketone. One crystallization from ligroin yielded 5.92 g. (89.5%) of colorless prisms, m. p. 89.5–90.5°, remelting at 96.5–97.5° (see ref. 1a).

8-Isopropyl-1,2-benzanthracene.—A benzene solution of 3 g. of the above ketone was added to a stirred solution of the Grignard reagent from 3 g. of magnesium and 15 g. of isopropyl bromide (transient red color). After refluxing for two hours and standing overnight, the product was worked up in the usual way and heated at 220° for several minutes to effect dehydration and distilled in vacuum from a small amount of high boiling residue. The pale yellow distillate (2.56 g.) when treated with petroleum ether gave 0.73 g. of crystallizate, consisting of pure starting ketone. The hydrocarbon fraction recovered from the mother liquor was an oil amounting to 1.83 g. (73.5%, based on ketone consumed). A mixture of 1.47 g. of the crude material and 0.34 g. of sulfur was heated at 205–250° for forty-five minutes, when the evolution of hydrogen sulfide had practically ceased, heated with a pinch of zinc dust, and distilled. The distillate, which partially solidified, was clarified by passage through an alumina tower in benzene solution and treated with 1.5 g. of picric acid in alcohol solution. One recrystallization from alcohol gave 0.94 g. (35%) of the **picrate** as shiny red blades, m. p. 151–153°. After three recrystallizations, a sample melted at 155.5–156.5°.

Anal.[12] Calcd. for $C_{21}H_{18}\cdot C_6H_3O_7N_3$: N, 8.41. Found: N, 8.38.

Filtration of a benzene solution of 0.6 g. of the picrate through an alumina tower gave a yellow solution fluorescent in ultraviolet light. Crystallization of the hydrocarbon from alcohol gave 0.27 g. (83.5%) of glistening yellow prisms, m. p. 95–97.5°. Recrystallized from petroleum ether, the compound melted at 97–98°.

Anal.[12] Calcd. for $C_{21}H_{18}$: C, 93.29; H, 6.71. Found: C, 93.32; H, 6.74.

Summary

4-Keto-1,2,3,4-tetrahydrochrysene has been converted by Reformatsky reaction and dehydrogenation into 4-chryseneacetic acid and the latter cyclized with hydrogen fluoride to 6-hydroxy-3,4-benzpyrene.

8-Isopropyl-1,2-benzanthracene was synthesized by a process requiring a dehydrogenation in the last step; this was accomplished successfully with sulfur without loss of the alkyl group.

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RECEIVED JANUARY 20, 1940

(11) Fieser, Hershberg and Newman, THIS JOURNAL, **57**, 1509 (1935).

(12) Microanalysis by Lyon Southworth.

[A CONTRIBUTION FROM THE PEARSON MEMORIAL LABORATORY OF TUFTS COLLEGE]

Aryl Isothiocyanates and Ethyl Acetonedicarboxylate

BY DAVID E. WORRALL

It has been shown[1] that a piperidone is obtained by the action of *p*-tolyl isothiocyanate on ethyl acetonedicarboxylate. The product, which is readily methylated, may be converted into a benzothiazole derivative through the action of bromine. These reactions have been studied with phenyl isothiocyanate itself and some of the more common derivatives.

TABLE I

DERIVATIVES OF 2,4-DIOXO-5-CARBETHOXY-6-SULFOPIPERIDINE-3-THIOFORMO-

	M. p., °C.	Formula	Analyses, % Calcd. C	Calcd. H	Found C	Found H
(1-Phenyl) anilide	188–189	$C_{21}H_{18}N_2O_4S_2$	59.1	4.2	59.0	4.1
6-Sulfomethoxy	148–149	$C_{22}H_{20}N_2O_4S_2$	60.0	4.5	59.8	4.6
(1-*m*-Tolyl) *m*-toluide	125–126	$C_{23}H_{22}N_2O_4S_2$	60.8	4.9	60.8	4.6
6-Sulfomethoxy	137–138	$C_{24}H_{24}N_2O_4S_2$	61.5	5.1	61.8	5.0
(1-*p*-Anisyl) aniside	162–163	$C_{23}H_{22}N_2O_6S_2$	56.8	4.5	56.4	4.7
6-Sulfomethoxy	152–153	$C_{24}H_{24}N_2O_6S_2$	57.6	4.8	57.3	4.8
(1-*p*-Phenetyl) phenetide	195–197	$C_{25}H_{26}N_2O_6S_2$	58.4	5.1	58.1	5.1
6-Sulfomethoxy	114–115	$C_{26}H_{28}N_2O_6S_2$	59.1	5.3	58.8	5.5
(1-*p*-Bromo) *p*-bromoanilide	179–181	$C_{21}H_{16}Br_2N_2O_4S_2$	43.2	2.8	43.0	2.8
6-Sulfomethoxy	152	$C_{22}H_{18}Br_2N_2O_4S_2$	44.1	3.0	43.9	3.1

TABLE II

DERIVATIVES OF (2,4-DIOXY-5-CARBETHOXY-6-SULFOPIPERIDYL)-BENZOTHIAZOLE

	Formula	Analyses, % Calcd. C	Calcd. H	Found C	Found H
(1-Phenyl)	$C_{21}H_{16}N_2O_4S_2$	59.4	3.8	59.5	3.8
(1-*m*-Tolyl) 4 (or 6)-methyl	$C_{23}H_{20}N_2O_4S_2$	61.1	4.4	60.8	4.3
(1-*p*-Anisyl) 5-methoxy	$C_{23}H_{20}N_2O_6S_2$	57.0	4.1	56.8	4.2
(1-*p*-Phenetyl) 5-ethoxy	$C_{25}H_{24}N_2O_6S_2$	58.6	4.7	58.2	4.8
(1-*p*-Bromo) 5-bromo	$C_{21}H_{14}Br_2N_2O_4S_2$	43.3	2.4	43.6	2.5

Experimental

To 0.1 g. mole of pulverized sodium suspended in ether was added 0.05 g. mole of the ester and then a similar amount of the isothiocyanate. After several hours the mixture, dissolved in water containing crushed ice, was carefully decomposed by addition to cold dilute hydrochloric acid. The pasty product using hot alcohol or alcohol–benzene mixture yielded yellow plates and prismatic needles varying in amount from 3–8 g. All melted with decomposition. Tars were obtained with *o*-tolyl and *β*-naphthyl isothiocyanates. Prepared by short heating with methyl iodide in alcohol solution the sulfomethoxy derivatives separated as bright yellow slender needles. The benzothiazoles, yellow crystalline powders precipitated from glacial acetic acid solution by the action of bromine, were thoroughly washed with alcohol and used directly for analysis. They may be crystallized from aniline. The melting points were too high to be recorded with a sulfuric acid-bath.

Summary

Several piperidones have been prepared by the interaction of representative aryl isothiocyanates with ethyl acetonedicarboxylate. The corresponding sulfomethoxy and benzothiazole derivatives were synthesized.

(1) Worrall, THIS JOURNAL, **61**, 2966 (1939).

MEDFORD, MASS. RECEIVED JANUARY 20, 1940

[CONTRIBUTION FROM THE AVERY LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF NEBRASKA]

The Ternary System: Isopropyl Alcohol, Toluene and Water at 25°

BY E. ROGER WASHBURN AND ALBERT E. BEGUIN[1]

Continuing a series of previously described investigations[2] of similar systems, solubility and distribution studies have been carried out with the system isopropyl alcohol, toluene and water at 25.0°.

Materials.—Carefully purified water was used. It was prepared by the partial condensation of steam from an alkaline permanganate solution.

The toluene was the better of the two grades obtainable from the Eastman Kodak Company. As efforts to purify this material further failed to alter its physical constants it was used as received. The specific gravity d^{25}_4 was 1.4938.

The isopropyl alcohol, from Eastman Kodak Company, was refluxed for many hours with fresh lime. It was then distilled into a carefully dried all glass still from which it was fractionally distilled. The middle portion of the distillate, boiling from 81.7 to 81.9° was used. It had a specific gravity d^{25}_4 of 0.78087 and a refractive index n^{25}_D of 1.3748.

Procedure and Results.—The details of the experimental work which seem to different workers to be most suitable for different ternary systems differ so that it is hardly possible to state that one system was studied by a previously described procedure and give an entirely truthful impression. The procedure followed in this investigation was like that described previously[3] with the following modifications. The titrations were carried out at 25.0° in small Erlenmeyer flasks which were shaken mechanically in the constant temperature bath except when additions of water or toluene were made from weight pipets. The values obtained with toluene as a titrant agreed with those obtained with water as the added liquid as closely as the water titrations agreed with each other. Preliminary titrations were carried out with materials not of the highest purity so that in the final titrations dropwise addition of all but the last few tenths of a gram of titrant was avoided.

The appearance of the end-point varied with different proportions of alcohol and toluene in the liquid titrated. At the lower end of the water rich part of the binodal curve relatively large droplets of the second phase appeared at the end-point; both phases appeared perfectly clear even after separation. As points further up on the curve were determined the droplets of the toluene rich phase separating out at the end-point became smaller and smaller until at an alcohol concentration of about 35% the mixture had the appearance of a fine mist. Above about 43% alcohol across the top of the curve and down to about 42% alcohol on the toluene rich side a still finer state of subdivision, a "milkiness," appeared at the end-point. In this region the first indication that the end-point was being approached was an opalescence, probably like that noted on cooling certain two component systems just before they separate into two liquid phases at the critical temperature. The remainder of the toluene rich side presented end-points similar to those on the lower part of the water rich side.

The end-points consisting of droplets and mists were easily observed by looking through the solution at a light bulb behind the bath. The "milky appearing" end-points were studied by light reflected from smooth black background suspended back of the titration flask. It was necessary to have the water-bath filled with very clear water when these titrations were carried out.

A special technique was developed in order to obtain reproducible results for the extreme lower ends of the solubility curve or more particularly for the important first and last parts of the refractive index–concentration curves used for the analysis. Flasks presenting a very small air space were employed since the amount of titrant used to saturate the air was important. The amounts of the first two liquids added to the small flasks were determined by weight, and the third liquid was added drop by drop from a fine pipet. The weight was determined from the number of drops added. The flask was carefully stoppered and if after about an hour the third liquid had all dissolved the process was repeated with one more drop of titrant.

The refractive indices of these saturated solu-

(1) Present address: Eastman Kodak Company, Rochester, New York.

(2) See THIS JOURNAL, **61**, 1694 (1939).

(3) THIS JOURNAL, **54**, 4217 (1932); **56**, 361 (1934); **61**, 1694 (1939).

tions were determined with an Abbe refractometer at a temperature of 25.00 ± 0.01°. Representative values are listed in Table I. The concentrations determine the solubility curve in Fig. 1. Only the values marked with an asterisk are plotted.

TABLE I

SOLUBILITIES AND REFRACTIVE INDICES AT 25.0°

Wt. % toluene	Wt. % alcohol	Refractive indices	Wt. % toluene	Wt. % alcohol	Refractive indices
0.13	4.25	1.3359	27.73	50.89	1.4032
* .18	10.76	1.3419	*33.50	49.61	1.4102
.30	16.50	1.3473	37.36	48.14	1.4148
* .38	23.40	1.3530	*42.70	45.59	1.4213
*1.07	30.16	1.3583	47.09	42.55	1.4266
1.88	34.38	1.3616	*52.63	39.05	1.4332
*4.22	39.44	1.3669	59.28	34.30	1.4415
6.75	43.64	1.3724	*68.72	27.45	1.4525
*10.74	47.53	1.3789	75.50	21.76	1.4619
14.13	49.57	1.3845	*82.43	15.97	1.4703
*18.27	51.01	1.3906	*88.48	10.64	1.4784
*22.55	51.17	1.3963	95.30	4.31	1.4878
		Toluene saturated with water			1.4937
		Water saturated with toluene			1.3322

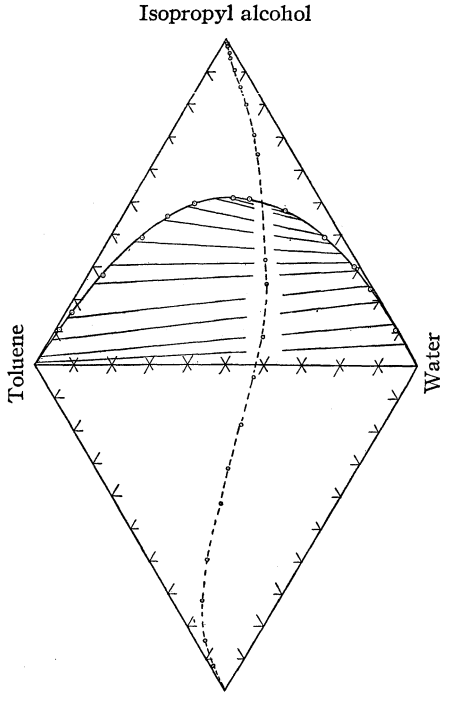

Fig. 1.

The tie lines were determined by adding varying amounts of alcohol to two liquid phase water–toluene mixtures. The amounts of alcohol were kept below that necessary to bring about complete miscibility. The mixtures were shaken from time to time during the twenty-four hours they were kept in the constant temperature bath. The deep but narrow flasks used for this work were constructed from 25-mm. test-tubes and 6-mm. glass tubes fitted with glass stoppers. The refractive index of each of the layers in the equilibrum mixture was determined. The concentration of these solutions was then read from large curves obtained by plotting refractive index against concentration for each of the three components in the saturated solutions. The fact that the sum of the percentages of the three components in each of the layers equaled 100.0 ± 0.1 indicates something of the precision of the analysis. Similar precision by these methods is not possible in several of the ternary systems that we have studied. Typical values are given in Table II and the marked values are used in locating the tie lines and the conjugation curve in Fig. 1. The intersection of the conjugation curve with the solubility curve locates the plait point.

TABLE II

REFRACTIVE INDICES AND CONCENTRATIONS OF ALCOHOL IN CONJUGATE SOLUTIONS AT 25.0°

Water layer			Toluene layer		
Refractive index	Wt. % alcohol	Wt. % water	Refractive index	Wt. % alcohol	Wt. % toluene
1.3383	6.87	93.12	*1.4925	0.89	99.14
1.3433	12.16	87.54	*1.4905	2.27	97.64
1.3501	19.77	79.95	*1.4829	7.45	91.84
1.3537	24.14	75.34	*1.4729	14.34	84.30
1.3574	29.00	69.98	*1.4570	24.90	71.90
1.3591	31.40	67.35	*1.4477	30.62	64.35
1.3616	34.34	64.20	*1.4351	37.90	54.20
1.3646	37.40	59.64	*1.4234	44.23	44.35
1.3675	39.92	55.75	*1.4137	48.57	36.35
1.3702	42.10	52.32	1.4088	49.95	32.60
1.3730	44.13	48.78	*1.4023	51.00	27.16
1.3739	44.73	46.80	1.4013	51.05	26.40
1.3769	46.50	44.00	*1.3972	51.20	23.56

If the solubility curve for this system is compared with those for the systems containing methyl alcohol[4] and ethyl alcohol[2] in place of isopropyl alcohol, certain interesting differences will be observed. The isopropyl alcohol is the most efficient and the methyl alcohol is least efficient in bringing about miscibility in toluene–water systems. The maximum amounts (wt. %) of the alcohols necessary to bring about homogeneity are isopropyl 51, ethyl 57, methyl 67.5. When the curves are plotted with mole % instead of wt. % the differences become even greater, isopropyl 41, ethyl 47, methyl 68.

(4) L. S. Mason and E. Roger Washburn, THIS JOURNAL, **59**, 2076 (1937).

Beech and Glasstone[5] came to the same conclusion in regard to the relative efficiency of these alcohols in bringing about miscibility of ethyl acetate and water although a simple study of their binodal curves alone does not indicate the relation.

Methyl alcohol has the highest values for internal pressure, dielectric constant and dipole moment, and isopropyl alcohol has the lowest values for these constants among these alcohols. Since water has very high values and toluene very low values we may consider that the above solubility studies support the idea that liquids of high internal pressure and polarity tend to "squeeze out" relatively non-polar liquids.

A comparison of the tie lines is also interesting. The alcohols dissolve chiefly in the water layer, especially when they are present in relatively small proportions. As the amounts of the alcohols increase, increasing proportions are found in the toluene layer. The proportion of ethyl alcohol in the toluene layer increases more rapidly with increasing proportions of alcohol than is noted with methyl alcohol, but the proportion of isopropyl alcohol increases most rapidly of all.

This increase in the case of isopropyl alcohol continues to such an extent that a horizontal tie line finally results, after which more alcohol is found in the toluene layer than in the water layer.

Inasmuch as the alcohols have values of internal pressure, etc., nearer to the values for toluene than to the values for water, we might expect more alcohol to be found in the toluene layer. The isopropyl alcohol, however, is most like toluene, and the relatively greater tendency which it has to enter the toluene is what would be expected.

(5) D. G. Beech and S. Glasstone, *J. Chem. Soc.*, 67 (1938).

Summary

The solubility relationships for the ternary system toluene, isopropyl alcohol and water have been determined at 25.0°.

The refractive indices of these saturated solutions have been determined and used to study the distribution of isopropyl alcohol between toluene and water at 25.0°.

This system has been briefly compared with similar systems containing methyl and ethyl alcohols in place of isopropyl alcohol.

LINCOLN, NEBRASKA RECEIVED JANUARY 8, 1940

[CONTRIBUTION FROM COLUMBIA UNIVERSITY]

The Vapor Pressures, Heats of Vaporization and Melting Points of N^{14} and N^{15} Ammonias

BY HARRY G. THODE*

It has been observed previously[1,2] that the nitrogen isotopes are concentrated to a slight extent by the distillation of liquid ammonia, indicating that the N^{14} ammonia has the higher vapor pressure. However, the vapor pressure difference between N^{14} and N^{15} ammonia can now be measured directly since high concentrations of N^{15} have been obtained.[3] In this paper a simple apparatus is described for measuring the vapor pressure difference between two isotopic samples of liquid ammonia. With this apparatus the vapor pressure difference, and the difference in melting points between ordinary NH_3 and 70.6% $N^{15}H_3$, have been measured and the results reported.

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(1) M. K. Wahl, J. R. Huffman and J. Hipple, *J. Chem. Phys.*, **3**, 434 (1935).

(2) H. C. Urey and A. H. W. Aten, Jr., *Phys. Rev.*, **50**, 575 (1936).

(3) H. G. Thode and H. C. Urey, *J. Chem. Phys.*, **7**, 34 (1939).

Experimental

The ammonia used in this investigation was prepared by the action of a saturated solution of potassium hydroxide on C. P. ammonium chloride. The gas was subjected to preliminary drying by passing it through a vertical glass column containing potassium hydroxide pellets. The ammonia was then condensed over sodium in one of a series of distillation bulbs. About 1 g. of NH_3 was treated in this way. Following each distillation the sample was cooled to the temperature of liquid nitrogen and the apparatus was then evacuated to 10^{-4} mm. or better. The 70.6% $N^{15}H_3$ samples were treated in a similar manner, except that the original samples had to be recrystallized from ethyl alcohol to remove traces of amines which concentrated along with the N^{15} in the chemical separation process. The samples were considered pure when further purification produced no change, within experimental error, in the vapor pressure difference between the two samples.

The apparatus is shown diagrammatically in Fig. 1. It consists of an 8-mm. glass tube C, divided into two com-

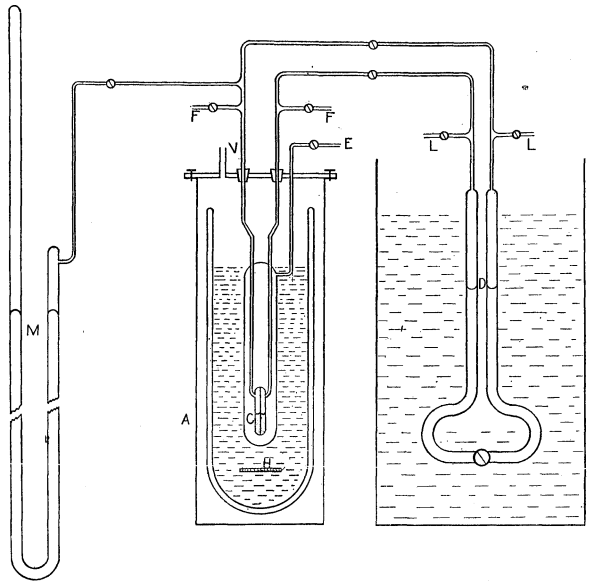


Fig. 1.

partments by a platinum partition, with each compartment partially filled with coiled platinum wire. The platinum partition and the coiled platinum serve to equalize the temperature between the two samples of ammonia whose vapor pressures are to be compared. The sample cells and the lead tubes are enclosed in a glass jacket which can be evacuated at E, and the whole apparatus is immersed in a liquid ammonia cryostat. The temperature of the cryostat is varied by regulating the pressure under which the liquid ammonia boils, with a vacuum pump and pressure regulator at V. A small heater H serves to stir the ammonia bath. The temperature of the cryostat could be controlled to 0.1°. Both the dewar flask and the steel container of the cryostat have windows through which the samples can be observed. However, during measurements the windows and lead tubes are covered with aluminum foil to keep out radiation. The two compartments at C can be connected by lead tubes to the arms of a differential oil (Apiezon) manometer D, thermostated at 27.2°, and one compartment can also be connected to a mercury manometer M. The two samples of ammonia, about half a gram of each, are condensed into the two compartments of C. The cryostat is regulated to the desired temperature and the glass jacket enclosing the two samples is evacuated. The differential manometer is then connected to the two samples and after twenty minutes readings are made with a cathetometer. The absolute vapor pressure of ordinary ammonia is measured on the mercury manometer before and after each reading of the vapor pressure difference on the differential oil manometer. From the absolute vapor pressure of ordinary ammonia the absolute temperature is deduced, using the vapor pressure data of Overstreet and Giauque for liquid ammonia.[4] With the above apparatus the measured vapor pressure difference between two samples of ordinary ammonia was found to be less than ±0.0005 cm. at 239°K. This corresponds to a difference in temperature between the two samples of ±0.00013°.

(4) Roy Overstreet and W. F. Giauque, THIS JOURNAL, **59**, 254 (1937).

The Vapor Pressure Difference.—The vapor pressure data for the liquids can be represented by the equation

$$\log_{10}(P_1/P_2) = (0.9593/T) - 0.003252 \qquad (1)$$

where P_1 is the vapor pressure of ordinary NH_3 (0.38% N^{15}), P_2 that of 70.6% $N^{15}H_3$, and T is the absolute temperature. The assumption is made that the differences in the vapor pressures of the two samples follow an equation of the type

$$\log_{10}(P_1/P_2) = (A/T) + B$$

and equation 1 is obtained by the application of least squares to the data in Table I. The ratio P_1/P_2 is obtained from the difference $(P_1 - P_2)$.

TABLE I

P_1, cm.	Temp., °K.	$P_1 - P_2$, cm. oil	$P_1 - P_2$, cm.	$(P_1 - P_2)$ (calcd.) − $(P_1 - P_2)$ (obsd.)	P_1/P_2, calcd.
5.488	197.7	0.320	0.0202	−0.00002	1.00369
9.060	204.4	.475	.0299	+ .00001	1.00332
12.593	208.8	.583	.0368	+ .00200	1.00310
21.570	217.2	.916	.0578	+ .00020	1.00268
41.030	228.2	1.462	.0922	− .00220	1.00219
41.550	228.4	1.478	.0933	− .00280	1.00218
59.560	234.9	1.797	.1134	+ .00060	1.00192
75.340	239.5	2.095	.1322	− .00170	1.00173

Table I includes the vapor pressure P_1 as determined on the mercury manometer, the temperature corresponding to the pressure P_1, and the vapor pressure difference $(P_1 - P_2)$ in cm. of oil as measured on the differential oil manometer. The table also includes the difference between calculated and observed $(P_1 - P_2)$, and the calculated ratios P_1/P_2.

Although the absolute temperature as deduced from the observed absolute vapor pressure of the ordinary ammonia is given to the nearest 0.1°, the difference in temperature between the two samples, as pointed out above, was probably less than 0.0002° at 239°K. Each arm of the oil manometer was read to the nearest 0.001 cm. with a probable error of ±0.003 cm. The mean difference between calculated and observed values of the vapor pressure difference $(P_1 - P_2)$ is ± 2%.

If the simple assumption is made that the vapor pressure of an isotopic mixture is a linear function of the mole fractions, we get the equation

$$\log_{10}\frac{P_{N^{14}H_3}}{P_{N^{15}H_3}} = \frac{1.3665}{T} - 0.004632 \qquad (2)$$

The Difference in Heats of Vaporization.—If the vapor pressures of each of the samples of am-

monia follow an equation of the form

$$\log_{10} P_n = \frac{\Delta H_n}{2.303RT} + C$$

then

$$\log_{10} P_1/P_2 = (\Delta H_2 - \Delta H_1)/2.303RT + C' \quad (3)$$

The subscripts 1 and 2 refer to ordinary ammonia and 70.6% N^{15} ammonia, respectively. The difference in the heats of vaporization of the two isotopic samples of ammonia can be calculated from the experimental data by comparing equation 3 with equation 1

$$\Delta H_2 - \Delta H_1 = 4.39 \text{ cal.} \quad (4)$$

where ΔH_1 is given in the literature[4] as 5581 ± 9 cal. By simple extrapolation, the heat of vaporization of pure N^{15} ammonia is calculated to be 6.25 cal. higher than the heat of vaporization of N^{14} ammonia.

The normal boiling point difference for the two forms of ammonia can be calculated from equation 1 by successive approximations, when T = 239.720°K., P_2 = 759.99 mm. or the n. b. p. difference. is 0.040°K., giving 0.055° for the pure N^{15} form.

The Difference in Melting Points.—A sample of ordinary ammonia was condensed into one cell of the apparatus and frozen with a liquid nitrogen bath. The jacket around the samples was then evacuated and the liquid nitrogen bath removed. A cooled dewar was placed around the apparatus to prevent the sample from warming up too fast. The vapor pressure of the sample was followed and a time–vapor pressure curve plotted. It was found that the sharp break in this curve, which occurs at the melting point, could be reproduced from experiment to experiment with great accuracy. The same procedure was followed for a sample of 70.6% $N^{15}H_3$; the results obtained are given in Table II.

TABLE II

V. P. at triple point in cm.

Sample 1, Ordinary NH_3 (0.38% N^{15})	Sample 2, 70.6% $N^{15}H_3$
4.560	4.574
4.562	4.572
4.561	4.576
Av. 4.561	4.574

From these data, and from the vapor pressure difference equation, the melting point difference between the two samples can be deduced. With the two samples at the same temperature, the triple point of ordinary ammonia (195.36°K., 4.558 cm.),[3] the vapor pressure of sample 1 will be 0.0173 cm. higher than the vapor pressure of sample 2 (from equation 1). However, from Table II it is seen that sample 2 has a higher vapor pressure at its melting point than sample 1 has at its melting point (0.013 cm.). Therefore sample 2 must melt at a higher temperature than sample 1, and the two effects must be additive. From the relation between temperature and pressure for liquid ammonia given by Overstreet and Giauque,[4] we find that dP/dT equals 0.365 cm./deg. at the triple point of N^{14} ammonia. Thus we calculate the melting point difference between ordinary and 70.6% N^{15} ammonia to be

$$(0.0173 + 0.013)/0.365 = 0.083°\text{K.}$$

If we make the simple assumption that the difference in triple points for isotopic mixtures is proportional to the mole fraction of one constituent, we find that N^{15} ammonia melts at a temperature 0.118° higher than N^{14} ammonia. The experimental error in this result may be as high as 10%.

The author is indebted to Professor H. C. Urey for making this experiment possible and for helpful suggestions.

Summary

The vapor pressure difference between 70.6% $N^{15}H_3$ and ordinary ammonia has been measured for the liquids over a range of temperatures by means of a differential oil manometer. The vapor pressure data for the liquids can be represented by the equation: $\log_{10} (P_1/P_2) = 0.9593/T - 0.00325$, where P_1 is the vapor pressure of ordinary ammonia and P_2 that of the 70.6% material. The vapor pressure of ordinary ammonia is 0.371 and 0.174% higher than the heavy ammonia sample at 195°K. (triple point of ammonia) and 239.68°K. (n. b. p.), respectively. The heavier sample of ammonia has a heat of vaporization 4.39 cal. per mole higher than that of ordinary ammonia. The triple points of the two samples differ by 0.081°, that of the 70.6% material being higher.

NEW YORK, N. Y. RECEIVED NOVEMBER 23, 1939

[CONTRIBUTION FROM THE STERLING CHEMISTRY LABORATORY OF YALE UNIVERSITY]

The Heat of Dilution of Aqueous Hydrochloric Acid at 25°

BY JULIAN M. STURTEVANT

In connection with some projected calorimetric experiments with amino acids and proteins, it became necessary to have reliable values for the integral heats of dilution of aqueous hydrogen chloride. Since very considerable discrepancies exist between the calorimetric heats available in the literature and those calculated from electromotive force measurements, it seemed advisable to redetermine these quantities.

Experimental Part

The calorimeter used in these measurements will be described elsewhere. Because of the limited size of the dilution cup, three different types of dilution were made:

Type 1. Varying amounts of the stock solution of hydrochloric acid were diluted with water.

Type 2. The stock solution of hydrochloric acid was diluted with less concentrated acid. The heat effect in an experiment of this type is due to diluting the stock solution to the final concentration and concentrating the weaker solution to this concentration.

Type 3. A solution composed of appropriate quantities of stock solution and water was diluted with water.

The hydrochloric acid used was a J. T. Baker analyzed product. The stock solution was analyzed gravimetrically at the start and finish of the measurements, and its concentration is considered to be known within $\pm 0.05\%$. All weighings were corrected for the buoyancy of the air.

The thermometer used to measure the temperature of the oil thermostat was calibrated against a platinum resistance thermometer certified by the Bureau of Standards. The standard cell used in the measurement of electrical energy input into the calorimeter was checked against the laboratory standard set of six calibrated cells. All timing was done with a synchronous clock furnishing audible signals and driven by a precision tuning fork. The over-all sensitivity of the thermometric system was 0.05 joule per mm. on the galvanometer scale.

Experimental Results.—The observed heats of dilution are summarized in Table I. The first and second columns in this table give the initial and final molalities, respectively. In the third column are listed, for dilutions of Type 2, the molalities of the diluting solutions. In the fourth column are the heats of dilution, expressed in international joules per mole of hydrogen chloride. In the case of dilutions of Type 2 these values are calculated according to the formula

$$\Delta H = \frac{\Delta q + a_2 \Delta H_1}{a_1 + a_2} \qquad (1)$$

where Δq is the observed heat absorption in joules, a_1, a_2 are the number of moles of hydrogen chloride in the dilution cup and in the calorimeter before the dilution, and ΔH_1 is the heat of the dilution, per mole of solute, of the stock solution to the molality of the solution originally present in the calorimeter. This latter quantity was obtained by graphical interpolation in the results of the pre-

TABLE I

INTEGRAL HEATS OF DILUTION OF HYDROCHLORIC ACID SOLUTIONS AT 25°

Square root of concentration (moles per 1000 g. H_2O)$^{1/2}$			Heat of dilution, $-\Delta H$ joules (int.) per mole
Initial	Final	Diluent	
1.8267	0.4463	0	3039
1.8267	.1919	0	3448
1.8267	.2676	0	3317
1.8267	.3272	0	3179
1.8267	.5377	0.3050	2899
1.8267	.6128	.4214	2781
1.8267	.7604	.6264	2529
1.8267	.8623	.7651	2357
1.8267	.9695	.8917	2165
1.8267	.1339	0	3533
1.8267	.3367	0	3212
1.8267	.1132	0	3566
1.8267	.3454	0	3194
1.8267		Dilution cup leaked	
1.8267	.2230	0	3397
1.8267	.2332	0	3369
1.8267	.3349	0	3227
1.8267	.3836	0	3140
1.8267	.0678	0	3605
1.8267	.0943	0	3617
1.8267	.9628	0.8345	2175
1.8267	1.0647	0.9800	1976
1.8267	1.2179	1.1470	1654
1.8267	0.4748	0	2997
1.8267	.5434	0	2882
1.7783	.4528	0	2889
1.7214	.4757	0	2664
1.4840	.4229	0	2069
1.2513	.3541	0	1617

vious runs, a method of successive approximations being employed if necessary. The heats of dilution have been corrected to 25.00° using the following temperature coefficient which is based on the data of Rossini[1] for the apparent molal heat capacity of the solute

$$d(\Delta H)/dt = 30.1(m_2^{1/2} - m_1^{1/2}) \qquad (2)$$

where m_1, m_2 are the initial and final molalities, respectively. Since the heat capacity used to evaluate the energy change during the dilution was that of the products plus the calorimeter, the observed heat of dilution corresponds to the initial temperature of the experiment. The initial temperatures deviated on the average about ±0.1° from 25°.

It should be noted that according to the work of Gucker and Schminke[2] the factor in equation (2) is about 21. However, the temperature correction amounts to only 0.1 to 0.2%, so that no serious uncertainties are introduced from this source.

Measurements of the heat capacity of the empty calorimeter, and of the calorimeter filled with water, were made. From these additional data the specific heat of the final solution in each run can be calculated. However, no attention was paid to keeping constant the amount of gold foil, vaseline and paraffin used to seal the dilution cup, so that the specific heats are not sufficiently precise to allow the calculation of the apparent molal heat capacities of the solute, since these quantities are very sensitive to errors in the specific heats for dilute solutions. The observed specific heats showed an average deviation of ±0.2% from those calculated from Rossini's values of Φ_C, and a slightly smaller deviation when Gucker and Schminke's values were used.

Treatment of Results.—The heats of dilution of the stock solution to molalities of 0.3 or lower were plotted against the square root of the molality on a large scale, and extrapolated to infinite dilution with the slope required by the limiting law of Debye and Hückel

$$\Phi_H - \Phi_H^0 = 1997\, m^{1/2} \qquad (3)$$

where $\Phi_H - \Phi_H^0$ is the apparent relative molal heat content of the hydrochloric acid. The slope was calculated according to the constants given by Harned and Ehlers.[3] The uncertainty in this extrapolation does not seem to exceed 10 joules per mole. The extrapolated value is the value of the apparent heat content of the stock solution. It is then a simple matter to evaluate this quantity for the solutions obtained by dilution. The values obtained are plotted against the square root of the molality in Fig. 1, the experimental points showing an average deviation from the smooth curve of ±5 joules per mole, corresponding to about ±0.15% of the observed dilution heats. Values read from the smooth curve at round values of $m^{1/2}$ are listed in the second column of Table II. These values are satisfac-

(1) Rossini, *Bur. Standards J. Research*, **9**, 679 (1932).
(2) Gucker and Schminke, THIS JOURNAL, **54**, 1358 (1932).
(3) Harned and Ehlers, THIS JOURNAL, **55**, 2179 (1933).

TABLE II

APPARENT AND PARTIAL RELATIVE MOLAL HEAT CONTENT OF SOLUTE AND PARTIAL RELATIVE MOLAL HEAT CONTENT OF SOLVENT IN HYDROCHLORIC ACID SOLUTIONS AT 25°

Square root of molality of hydrochloric acid	Heat content, joules (int.) per mole $\Phi_H - \Phi_H^0$	$\bar{L}_2$	$\bar{L}_1$
0.0000	0	0	0
.0500	97		
.1000	189	276	− 0.0157
.1500	273		
.2000	354	515	− .116
.2500	434		
.3000	515	753	− .386
.3500	594		
.4000	672	985	− .902
.4500	749		
.5000	827	1223	− 1.784
.5500	907		
.6000	988	1480	− 3.191
.6500	1070		
.7000	1154	1737	− 5.147
.7500	1237		
.8000	1320	2001	− 7.852
.8500	1406		
.9000	1494	2307	− 11.86
.9500	1587		
1.0000	1682	2647	− 17.39
1.0500	1779		
1.1000	1880	3015	− 24.74
1.1500	1986		
1.2000	2096	3432	− 34.66
1.2500	2210		
1.3000	2326	3842	− 46.16
1.3500	2442		
1.4000	2564	4314	− 61.80
1.4500	2690		
1.5000	2819	4789	− 79.86
1.5500	2952		
1.6000	3090	5348	−104.1
1.6500	3235		
1.7000	3384	5959	−134.1
1.7500	3538		
1.8000	3698	6631	−171.2
1.8267	3785		

torily represented at concentrations up to $m^{1/2} = 1.2$ by the expression

$$\Phi_H - \Phi_H^0 = \frac{1997m^{1/2}}{1 + 1.123m^{1/2}} + 747m \qquad (4)$$

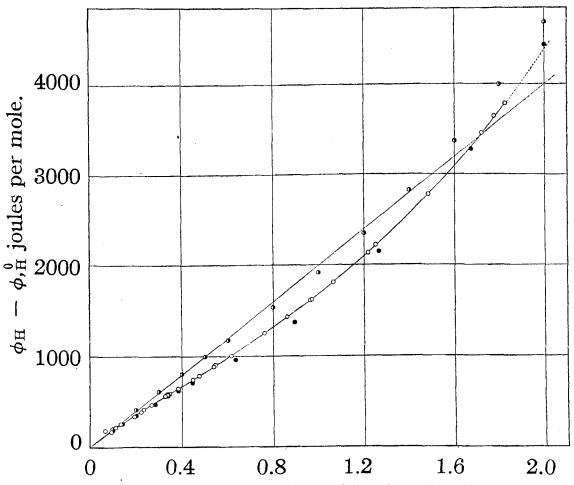


Fig. 1.—Relative apparent molal heat content of hydrochloric acid. The straight line is the Debye–Hückel limiting law. Open circles, this research; half-inked circles, Rossini; inked circles, Harned and Ehlers.

Values of $\bar{L}_2$, the partial relative molal heat content of the solute, were calculated according to the equation

$$\bar{L}_2 = \Phi_H - \Phi_H^0 + {}^1/_2 m^{1/2} \frac{d(\Phi_H - \Phi_H^0)}{dm^{1/2}} \qquad (5)$$

the necessary slopes being read from the large-scale plot of the original heat data. These quantities are listed in the third column of Table II, and are plotted in Fig. 2. An idea of the accuracy of the reading of the slopes is given by the closeness with which the calculated values fall on a smooth curve, the average deviation being of the order of ±5 joules per mole.

The relative partial molal heat content of the solvent is readily calculated from the relation

$$\Phi_H - \Phi_H^0 = \bar{L}_2 + \frac{55.506}{m}\bar{L}_1 \qquad (6)$$

The last column of Table II gives the values obtained in this way.

Estimate of Accuracy.—As mentioned above, all due care has been taken in the calibration of the instruments used in this research. It is therefore considered, since no sources of systematic error are believed to have been overlooked, that a reasonable estimate of the reliability of the results can be based on their internal consistency and the reliability of the extrapolation to infinite dilution.

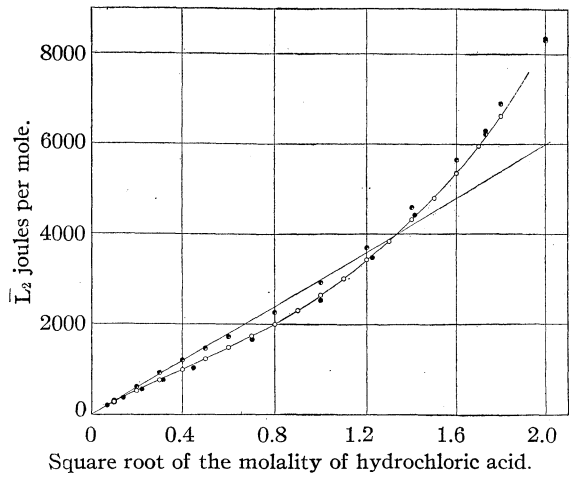


Fig. 2.—Relative partial molal heat content of hydrochloric acid. The straight line is the Debye–Hückel limiting law. Open circles, this research; half-inked circles, Åkerlöf and Teare ($m^{1/2} = 1.732$ and 2.0 only); three-quarters-inked circles, Rossini; full-inked circles, Harned and Ehlers. In the plot, Rossini's points at $m^{1/2} = 0.1$ and 2.0 are obscured by those of Harned and Ehlers.

On this basis it is concluded that the smoothed values of the apparent molal heat content should be reliable to about ±20 joules per mole, with considerably smaller limits of error associated with differences between these quantities. Since the values of the partial molal heat content involve slopes read from a graph, they are subject to somewhat larger uncertainties.

Discussion of Results

Several previous calorimetric determinations of the heat of dilution of aqueous hydrochloric acid have been made at various temperatures. These data have been summarized and calculated to 25° by Rossini,[1] who used the Debye–Hückel theory to extrapolate them to infinite dilution, and tabulated values of the apparent and partial relative molal heat contents at round values of the square root of the molality. The values given by Rossini are plotted in Figs. 1 and 2. Part of the relatively large discrepancy between these values and the ones found in the present research is due to the fact that the older values scatter rather badly below $m^{1/2} = 0.5$, so that the extrapolation to infinite dilution is somewhat arbitrary. Thus, if the values given by Rossini for $\Phi_H - \Phi_H^0$ are brought into coincidence with the present values at $m^{1/2} = 0.5$, the differences between the values thus obtained and the present ones gradually increase to a value of 130 joules per mole at $m^{1/2} =$

1.8, as compared with a difference of 300 joules per mole before making this change.

A small part of the discrepancy is due to the fact that the limiting Debye–Hückel slope used by Rossini is a little larger than the correct one, because of omission of the term involving the change of density with temperature. This fact can account for about 30 joules per mole difference.

One source of systematic error in calorimetric observations on hydrochloric acid might be corrosion of the various metallic parts of the calorimeter. It is believed that errors from this source are eliminated in the present research since the calorimeter is composed of tantalum, platinum–iridium, and pure gold solder, while the dilution cup is closed by pure gold foil. Whether corrosion is a cause of the remaining differences between the older work and the present work cannot, of course, be definitely established. Some of the discrepancy to be accounted for may arise in the fact that most of the older work was done at temperatures other than 25°, so that corrections based on the heat capacities of hydrochloric acid solutions are involved.

Doehlemann and Lange[4] have measured the heat of dilution of hydrochloric acid in concentrations up to 0.09 molal. It seems impossible to reconcile their data below 0.0025 molal with the requirements of the Debye–Hückel theory, since these data lie on a curve which is apparently approaching an infinite slope at infinite dilution. Their data from 0.0025 to 0.02 molal fall on a straight line having the limiting Debye–Hückel slope; the intercept of this line gives values of the relative apparent molal heat content which are 20 to 30 joules per mole above the values found in the present research. Also the present values indicate definite divergence from the limiting slope at concentrations below 0.01 molal, while the values of Doehlemann and Lange follow this slope to 0.02 molal, except at the very lowest concentrations, as mentioned above.

Values of the relative partial molal heat content have been calculated by Harned and Ehlers, and by Åkerlöf and Teare,[5] from their measurements of the temperature coefficient of the electromotive force of the cell

$$H_2/HCl\ (m)/AgCl/Ag$$

Harned and Ehlers measured this cell in the concentration range up to 4 molal, and reported values of $\overline{L}_2$ from infinite dilution up to this concentration. By graphical integration (counting squares, and checking the result with a planimeter) values of the apparent heat content have been calculated from their values of $\overline{L}_2$. These quantities are plotted in Fig. 1, and are seen to agree more closely with the present calorimetric values than do the earlier calorimetric data. This agreement is especially satisfactory when it is considered that an error of 1 microvolt per degree in the temperature coefficient of electromotive force causes an error of about 30 joules per mole in $\overline{L}_2$.

Harned and Ehler's values of $\overline{L}_2$ are compared with the present ones in Fig. 2. They show a maximum deviation, at 3 molal, of about 130 joules per mole, which is within the estimated accuracy of the e. m. f. measurements. It should be noted that the value obtained by Åkerlöf and Teare at this concentration shows a deviation of only about 60 joules per mole. Further comparison with their values is impossible since this is the lowest concentration at which they worked.

Summary

The heat of dilution of aqueous solutions of hydrogen chloride at 25° has been measured up to a concentration of 3.3 molal. From these data have been calculated the apparent and partial relative molal heat content of the solute, and the partial relative molal heat content of the solvent.

NEW HAVEN, CONN. RECEIVED DECEMBER 28, 1939

(4) Doehlemann and Lange, "Landolt–Börnstein Tabellen," 5th edition, Ergänzungsband IIIc, p. 2800.

(5) Åkerlöf and Teare, THIS JOURNAL, **59**, 1855 (1937).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

The Iodine-Sensitized Decomposition of Methyl Alcohol

BY G. K. ROLLEFSON AND WARREN GARRISON

Some years ago it was found by Bairstow and Hinshelwood[1] that the rates of decomposition of a number of simple organic compounds were greatly increased by the addition of iodine and in some cases the nature of the products was changed. Later, Rollefson and Faull[2] found that under the experimental conditions prevailing in these experiments the concentration of free iodine is extremely low during most of the reaction but returns to its original value as the decomposition of the organic compound approaches completion. They also showed that in mixtures of acetaldehyde or propionaldehyde with iodine the decomposition is the net result of a reaction of the iodine with the aldehyde to give carbon monoxide, hydrogen iodide, and alkyl iodide followed by the reaction of the alkyl iodide with hydrogen iodide to form the corresponding hydrocarbon and iodine. The latter reaction is the rate determining step. In this paper we wish to present a study of the iodine-sensitized decomposition of methyl alcohol which differs from that of the aldehydes in that the products are not the same as are obtained in unsensitized decomposition. In this case also we have found that the action of the iodine can be expressed in terms of ordinary chemical reactions.

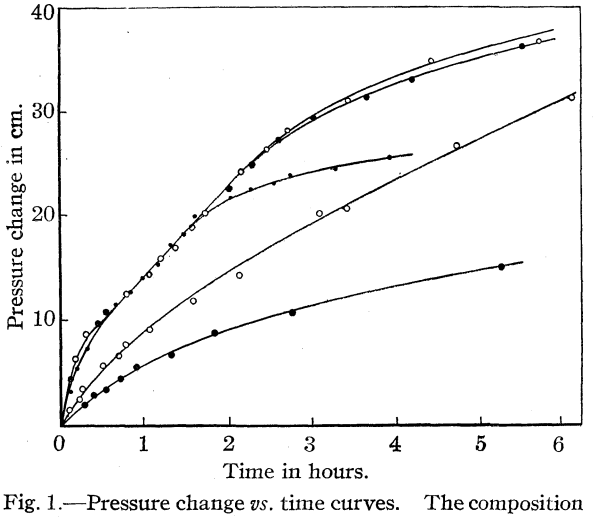


Fig. 1.—Pressure change *vs.* time curves. The composition of the reaction mixtures for the various curves is:

Curve	Iodine added, mole	Alcohol added, mole
1	1.67×10^{-4}	29.4×10^{-4}
2	2.66	29.4
3	4.00	20.0
4	4.00	28.6
5	4.00	30.9

(1) Bairstow and Hinshelwood, *Proc. Roy. Soc.* (London), **A142**, 77 (1933); *J. Chem. Soc.*, 1147 (1933).

(2) Rollefson and Faull, THIS JOURNAL, **58**, 1755 (1936); **59**, 625 (1937).

In order to obtain the maximum amount of information concerning conditions which affect the rate, it is desirable to have the iodine concentration measurable during the course of the reaction. Preliminary tests showed that at 325° the unsensitized decomposition was negligible and the sensitized reaction proceeded at a convenient rate with appreciable amounts of free iodine present at all times. All of the quantitative measurements were made at this temperature.

The reaction vessel was made of Pyrex, cylindrical in shape, and of approximately 250 cc. capacity. It was connected through a click gage to a mercury manometer and through another tube, which was sealed off during the reaction, to vacuum pumps and a supply of methyl alcohol. The vessel was mounted in an electric furnace which was kept within a degree of the desired temperature by hand regulation. The temperature was measured by a chrome–alumel thermocouple placed in a small glass tube which was sealed into the reaction vessel.

The alcohol was distilled over anhydrous potassium carbonate; the middle fraction with a boiling range of less than one degree was used (boiling range, 64.0–64.6°). The iodine was resublimed Merck reagent.

The procedure followed in filling the reaction vessel was to introduce sufficient alcohol vapor to give the desired pressure at 325°, and seal the reaction vessel off from the vacuum system and alcohol supply. The temperature of the system was raised to 325° and then a bulb containing a weighed quantity of iodine was broken in the vessel. The curves obtained by plotting the pressure against the time were found to be very reproducible and showed no anomalies which might be attributed to slowness of mixing of the iodine and alcohol vapors. A few typical curves are shown in Fig. 1.

It was found that the pressure–time curves were quite reproducible for any given mixture.

Consequently we found it more convenient to carry out most of the determinations of the composition of the reaction products at different degrees of completion of the reaction by heating a mixture of alcohol and iodine vapors for various definite times in sealed bulbs identical in size and shape with the one used in the pressure measurements. When the bulbs had been heated long enough to bring the reaction to the desired degree of completion the bulbs were removed from the furnace and cooled rapidly. Different rates of cooling were tried but were not found to affect the results appreciably. In order to analyze the reaction mixture the tip of the reaction vessel was broken under the surface of a known volume of potassium iodide solution and this solution was used to force the gases into an Orsat gas analyzer. A sample of the iodide solution was titrated for iodine using 0.05 *N* thiosulfate solution. The hydrogen ion concentration was determined by adding excess of potassium iodate to the same sample of the iodide solution and titrating again with the thiosulfate. The gases were analyzed for carbon monoxide, carbon dioxide, hydrogen and methane by conventional methods. Carbon dioxide and hydrogen were found to be negligible. The amounts of carbon monoxide and methane present at various states of the reaction are shown in Table I.

TABLE I

METHANE AND CARBON MONOXIDE PRESENT DURING THE REACTION

CH_3OH added = 25×10^{-4} mole. I_2 added = 3.9×10^{-4} mole.

Hours	Moles $\times 10^4$ CH_4	CO	CH_4/CO
0.75	2.40	3.40	0.71
.75	2.30	3.40	.68
1.25	4.20	4.50	.93
1.25	4.25	4.30	.99
2.5	8.30	6.00	1.38
2.5	8.45	6.15	1.37
3.0	9.30	6.76	1.38
3.0	9.30	6.70	1.39
4.25	13.40	7.30	1.84
4.25	13.60	7.45	1.83
5.5	15.10	7.50	2.01
5.5	15.0	7.50	2.00
9.0	15.8	7.56	2.08
9.0	15.9	7.56	2.10
18.0	16.0	7.60	2.10

The condition of the iodine during that part of a run corresponding to the relatively straight section of the pressure–time curve is shown by the data in Table II.

TABLE II

DISTRIBUTION OF IODINE DURING A REACTION

I_2 added = 1.67×10^{-4} moles. CH_3OH added = 25.0×10^{-4} moles.

Hours reacted	$I_2 \times 10^4$ mole	HI $\times 10^4$ mole	Other iodides $\times 10^4$ mole
1	0.314	0.340	2.38
1.5	.348	.360	2.228
2	.308	.340	2.38
3	.394	.368	2.20

The presence of hydrogen iodide was demonstrated by shaking water and carbon tetrachloride in a bulb filled with the gases to be analyzed. In this way hydrogen iodide and iodine were extracted from the gases. The water and carbon tetrachloride were separated, the water layer extracted again with carbon tetrachloride and then titrated for hydrogen and iodide ions. The iodide was found to be about 1% higher than the hydrogen ion but this slight discrepancy was attributed to incomplete removal of the iodine by the carbon tetrachloride.

The data which have been obtained show that the net over-all reaction may be represented by the equation

$$3CH_3OH = 2CH_4 + CO + 2H_2O \qquad (1)$$

Additional support for this equation is found in that the total pressure change observed in reaction mixtures which were run to completion was two-thirds the original methyl alcohol pressure. However, the variation of the methane–carbon monoxide ratio in the course of the reaction shows that this net reaction must be the resultant of two parallel reactions, one an oxidation of the alcohol to carbon monoxide, the other a reduction to methane. Iodine is the oxidizing agent for the first and hydrogen iodide the reducing agent for the second. The equations representing the changes are

$$CH_3OH + 2I_2 = CO + 4HI \qquad (2)$$

$$CH_3OH + 2HI = CH_4 + I_2 + H_2O \qquad (3)$$

The preponderance of carbon monoxide in the early stages of the reaction is caused by the first of these reactions proceeding faster than the second until the steady state is reached. During the steady state the methane and carbon monoxide are formed in the proportions of two to one as required by the over-all reaction as written above. In the final stages of the reaction when the iodine is regenerated methane is produced thus compensating for the excess carbon monoxide produced in the initial stage. This behavior is apparent from an inspection of the data in Table I.

The formation of methyl iodide in the reaction mixture can be accounted for by

$$CH_3OH + HI = CH_3I + H_2O \qquad (4)$$

which may be one of the steps in the mechanism of (3). The net change in the reaction mixture from the time of mixing is given by a combination of the equations (2), (3), (4). When the reaction is carried to completion the contribution from (4) is zero and the net effect is the combination of (2) and (3) so as to give (1).

No mechanisms which we have devised for the reactions (2) and (3) will account for all the experimental observations. The possibility that methane is formed from methyl iodide and hydrogen iodide was considered. Assuming that the iodine not in the form of hydrogen iodide or free iodine was all methyl iodide, we calculated the rate of formation of methane from Ogg's data. The observed rate during the steady state was 12.6×10^{-7} mole/cc./hr. and the calculated rate was 18.5×10^{-7} mole/cc./hr. The agreement is not sufficiently good to warrant the conclusion that the methane must be formed by this reaction but it seems to be a reasonable possibility at these temperatures. The constancy of the rate of formation of methane during a large percentage of the reaction could be accounted for by this reaction since the concentrations of methyl iodide and hydrogen iodide are constant over the same range.

Summary

The iodine sensitized decomposition of methyl alcohol has been studied at 325°. It has been shown that although the net effect in systems in which the reaction was carried to completion may be represented by the equation $3CH_3OH = 2CH_4 + CO + 2H_2O$ this is the resultant of two other reactions. One of these is the oxidation of the alcohol to carbon monoxide by the iodine, the other the reduction of the alcohol to methane by hydrogen iodide.

BERKELEY, CALIFORNIA RECEIVED DECEMBER 6, 1939

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, NO. 747]

The Dilituric (5-Nitrobarbituric) of Some Physiologically Important Bases

BY C. E. REDEMANN AND CARL NIEMANN

The qualitative or quantitative isolation of basic compounds from natural sources is, in general, most satisfactorily accomplished when the base in question can be obtained as the salt of a suitable acid.[1] Of the acidic reagents that have been employed in the past, it is certain that compounds such as picric acid, styphnic acid, picrolonic acid, nitranilic acid[2] and 3-nitrodiketohydrindene[3] have found the greatest application and it is noteworthy that all of these compounds are characterized by the presence of a contiguous nitrophenolic (or enolic) array in an ensemble of atoms capable of forming a resonating system.

We have found that dilituric acid (5-nitrobarbituric acid) surpasses the above nitro-enolic compounds as a reagent for the isolation of many naturally occurring bases and it is the purpose of this communication to call attention to the properties of some of the salts of this acid and their use in isolation problems.

Dilituric acid[4] prepared by the direct nitration of barbituric acid[4b,c,f,h,i] is readily purified. The solubility of the acid, in millimoles per liter of solution at 25°, in methanol is 99; in 95% ethanol, 85; in water, 63; in absolute ethanol, 35; in acetone, 25; in ethyl ether, 0.9; and in benzene, 0.4. Dilituric acid behaves like a strong monobasic acid and from the electrometric titration of a 0.00904 *N* aqueous solution it appears that the acid strength of dilituric acid is intermediate between that of picric acid and hydrochloric acid.[5]

Examination of Table I reveals that dilituric acid is a satisfactory reagent for the separation of potassium from binary mixtures containing so-

(1) (a) M. Bergmann and C. Niemann, *J. Biol. Chem.*, **122**, 577 (1937); (b) W. H. Stein, C. Niemann and M. Bergmann, THIS JOURNAL, **60**, 1703 (1938); (c) M. Bergmann and W. H. Stein, *J. Biol. Chem.*, **128**, 217; **129**, 609 (1939); (d) H. R. Ing and M. Bergmann, *ibid.*, **129**, 603 (1939).

(2) B. W. Town, *Biochem. J.*, **30**, 1833 (1936).

(3) (a) G. Wanag, *Ber.*, **69**, 1066 (1936); (b) G. Wanag and A. Lode, *ibid.*, **70**, 547 (1937).

(4) (a) A. Schlieper, *Ann.*, **56**, 23 (1845); (b) A. Baeyer, *ibid.*, **127**, 209 (1863); **130**, 140 (1864); (c) M. Grimaux, *Ann. chim.*, (5) **17**, 278 (1879); (d) M. Ceresole, *Ber.*, **16**, 1134 (1883); (e) R. Bartling, *Ann.*, **339**, 39 (1905); (f) A. F. Holleman, *Rec. trav. chim.*, **16**, 168 (1897); (g) H. Biltz and K. Sedlatscheck, *Ber.*, **57**, 339 (1924); (h) *Org. Syntheses*, **12**, 58 (1932); (i) H. Fredholm, *Z. anal. Chem.*, **104**, 400 (1936).

(5) P. A. Trübsach, *Z. physik. Chem.*, **16**, 718 (1895).

dium,[4i,6] and is an excellent reagent for the isolation of magnesium.[7]

TABLE I

INORGANIC SALTS OF DILITURIC ACID

Diliturate Metal	Mol. wt.	Solubility[a] Mmoles/l.	Appearance
Mg	476.5	0.1	Plates
Ba	517.5	1.3	Powder
Sr	442.7	1.7	Platelets
Cu	461.7	1.8	Needles
K	211.1	3.9	Prisms
Ca	402.2	5.7	Needles
Ag	352.0	12	Platelets
Na	195.0	38	Needles or prisms

[a] In water at 25°.

TABLE II

ORGANIC SALTS OF DILITURIC ACID

Diliturate Amine	Mol. wt.	Solubility[a] Mmoles/l.	Appearance
Simple Amines			
Ethylenediamine	406.2	0.6	Powder
Ammonia	190.1	7.3	Flakes
Ethylamine	218.1	13	Needles
Dimethylamine	218.1	15	Powder
Phenylisopropylamine	326.2	15	Needles
n-Butylamine	246.1	17	Scales
n-Amylamine	260.2	24	Scales
Aniline	266.1	26	Plates
Methylamine	204.1	37	Powder
Tri-*n*-butylamine	358.3	51	Prisms
Simple Heterocyclic Bases			
Quinoline	302.1	23	Needles
Imidazole	242.1	36	Prisms
Pyridine	252.1	54	Needles
d(+)Glucobenzimidazole	441.3	65	Needles
Morpholine	260.1	80	Platelets
Alkanolamines			
dl-Ephedrine	338.2	8.7	Platelets
β-Hydroxyphenyl ethylamine	319.2	13	Flat spears
l-Ephedrine	338.2	30	Platelets
d-Pseudoephedrine	365.2	32	Leaves
l-Epinephrine	374.2	37	Flakes
Ethanolamine	234.1	53	Plates
d-Glucosamine	387.2	85	Needles
Triethanolamine	322.2	132	Prisms
1-Amino-2-hydroxypropane	248.1	134	Flakes
Alkaloids			
Quinine	697.3	1.6	Plates
Brucine	812.4	3.7	Plates
Strychnine	734.4	3.9	Needles
Cinchonine	658.3	9.0	Needles
Nicotine	508.2	12.3	Needles
Caffeine	385.2	68	Plates
Amino Acids			
l-Diiodotyrosine	606.0	2.2	Powder
dl-Lysine	492.2	6.4	Scales
l-Histidine	501.2	7.9	Needles
l-Lysine	492.2	9.0	Powder
l-Tyrosine	372.2	10.0	Needles
l-Arginine	347.2	10.2	Needles
l-Cystine	586.3	15	Needles
dl-Phenylalanine	356.2	16	Scales
dl-α-Aminoisobutyric acid	276.1	20	Needles
l-Tryptophan	337.2	20	Needles
dl-α-Aminophenylacetic acid	324.1	28	Prisms
Sarcosine	262.1	34	Needles
Betaine	290.1	34	Needles
dl-α-Amino-*n*-butyric acid	294.2	40	Plates
l-Alanine	281.1	43	Needles
Glycine	248.1	49	Plates
dl-Alanine	281.1	50	Needles
dl-Aspartic acid	306.1	61	Powder
l-Glutamic acid	320.1	67	Powder
dl-γ-Amino-*n*-butyric acid	276.1	77	Scales
dl-Glutamic acid	320.1	90	Needles
l-Cysteine	303.2	92	Needles
l-Aspartic acid	306.1	94	Needles
dl-Leucine	304.2	94	Scales
l-Proline	288.1	100	Scales
l-Asparagine	305.1	103	Powder
l-Leucine	322.2	105	Needles
dl-Valine	290.1	107	Needles
dl-Isoleucine	304.2	107	Needles
dl-Norleucine	304.2	109	Plates
dl-Norvaline	290.1	110	Rosets
dl-Methionine	331.2	112	Plates
dl-Serine	278.1	112	Plates
l-Hydroxyproline	304.1	141	Scales
Proteinogenic Amines			
Guanidine	232.1	7.0	Needles
Tyramine	310.2	8.7	Plates
Histamine	284.1	17	Needles
Phenylethylamine	303.2	19	Needles
Creatinine	286.1	23	Powder
Urea	233.1	36	Powder

[a] In water at 25°.

In Table II we have tabulated the properties of salts formed by the interaction of dilituric acid with seventy-one organic bases. The dilliturates of the primary aliphatic amines are surprisingly insoluble in water at 25° and, within limits, the solubility in water increases with increasing chain length. The transition from a primary amine to a secondary amine diliturate is accompanied by a decrease in solubility; however, the salts of the tertiary amines are much more soluble than those of the corresponding secondary amines. The heterocyclic bases, quinoline, imidazole, and pyridine form sparingly soluble dilliturates but in con-

(6) (a) H. Frediani, Meeting of the American Chemical Society, Boston, September, 1939; (b) O. C. Dermer and V. H. Dermer, THIS JOURNAL, **61**, 3302 (1939).

(7) With the aid of dilituric acid we have been able to establish the presence of magnesium in the crude phospholipids obtained from bovine spinal cord.

trast to morpholine it was found that ethylmorpholine dilituratе was very soluble in water.

The isolation of ethanolamine from the hydrolyzates of phospholipids by the methods hitherto available has been a very laborious task and, still more serious, the methods are not capable of being developed to the point of yielding quantitative data.[8] The observation that ethanolamine dilituratе possesses but limited solubility in water has not only offered a means for the qualitative isolation of this base but in addition has provided a reagent that can be used for the quantitative estimation of ethanolamine and other alkanolamines by the so-called solubility product method of analysis.[1,9] Dilituric acid is also a suitable reagent for the isolation and estimation of glucosamine.

An extensive study of the dilituratеs of the amino acids has been made and in Table II are listed the properties of thirty-four salts. The dilituratеs of the aliphatic monoamino monocarboxylic acids present an interesting situation in that as the length of the side chain increases from zero to three carbon atoms the solubility of the dilituratе increases in a regular manner. Exactly the opposite is observed when one considers the solubility of the amino acids themselves. In addition it was noted that a branching of the side chain resulted in a decrease in the solubility of the dilituratе. Examination of Table II can leave no doubt that there are many amino acid mixtures that can be separated with the aid of dilituric acid. The dilituratеs of the proteinogenic amines are only slightly soluble in water at 25° and it is clear that dilituric acid is a suitable reagent for their isolation.

The fact that dilituric acid is not exceedingly soluble in water at 25° creates a demand for a more soluble form of this reagent. Fortunately the trimethylamine and the ethylmorpholine dilituratеs are very soluble in water and these salts may be used in lieu of the acid.

One of the advantages of isolating bases in the form of their salts is that the base can be easily regenerated. We have found that the regeneration of bases from their dilituratеs can be achieved in the majority of cases by simply replacing the base in question by either ethylenediamine, magnesium or ammonium, as the salts of these three substances are exceedingly insoluble in water. Thus in a typical case, the decomposition of glycine dilituratе with ammonia gave an 89% yield of crystalline glycine.

In conclusion it can be stated that dilituric acid possesses many of the characteristics of the ideal acidic precipitant in that: (a) it is readily available at low cost; (b) in aqueous solution it behaves as a strong monobasic acid thereby diminishing the possibility of forming mixed salts; (c) it is moderately soluble in water and the alcohols; (d) several very soluble salts are known; (e) all of the dilituratеs that were prepared were well-defined crystalline substances thereby facilitating their isolation; (f) the salts were characterized by a wide variation in solubility, thereby permitting fractionation of mixtures; (g) both the acid and the salts possess a high temperature coefficient of solubility which allows ready purification by recrystallization and enhances the possibility of resolving mixtures whose dilituratеs have similar solubilities at any one temperature; and (h) in the majority of cases the base can be obtained easily from the salt by a simple double decomposition.

Experimental

Dilituric Acid (5-Nitrobarbituric Acid).—The acid was prepared according to the directions given in Organic Syntheses.[4h] A solution of 0.2317 g. of thrice recrystallized anhydrous dilituric acid in 150 ml. of water (*p*H 2.03) was titrated electrometrically and examination of the titration curve revealed that the strength of this acid was intermediate between that of picric acid and hydrochloric acid.

Preparation of the Dilituratеs.—A solution of 5 millimoles of dilituric acid and 5 millimoles of the base[10] (2.5 millimoles for a diacidic base) was prepared with the minimum amount of boiling water and allowed to cool to 25°. The salts were recrystallized one or more times before determining their composition and solubility.

Analysis of the Dilituratеs.—Fifteen to twenty mg. samples of the inorganic salts, dried at 80°, were ignited in the presence of sulfuric acid and the average deviation of the percentage metal found from that calculated was ±0.11. In order to obtain satisfactory values for the carbon and hydrogen content of the organic dilituratеs it was necessary to replace the ordinary Pregl copper oxide–lead chromate combustion zone filling[11] by copper oxide and all of the silver plugs, in front of the combustion zone, by 10% platinized asbestos. In addition the sample, (20–30 mg.) dried at 80°, was mixed with powdered cupric

(8) (a) H. Thierfelder and E. Klenk, "Die Chemie der Cerebroside und Phosphatide," J. Springer, Berlin, 1930; (b) E. Chargaff, *J. Biol. Chem.*, **118**, 417 (1937).

(9) Unpublished observations of the authors taken from a study on the nature of the water soluble bases present in mammalian phospholipids.

(10) We wish to thank Dr. G. Alles for supplying a number of the alkanol- and proteinogenic amines.

(11) F. Pregl, "Die quantitative organische Mikroanalyse," 3rd ed., J. Springer, Berlin, 1930.

oxide prior to ignition. The average deviation of the percentages found from those calculated was ±0.15; the maximum in any case did not exceed 0.3 except for the following salts: ethylamine, % H, calcd. 4.6, found 4.2; *m*-amylamine, % H, calcd. 6.2, found 5.8; *l*-aspartic acid, % H, calcd. 3.3, found 3.7; *dl*-leucine, % C, calcd. 39.4, found 38.9; guanidine, % H, calcd. 3.5, found 3.1.

Determination of Solubilities.—The saturated solutions were approached from the supersaturated side by placing samples saturated at 40–50° and containing an excess of the solid phase in a thermostat at 25.0 ± 0.5° and allowing forty-eight or more hours, with shaking, for the attainment of equilibrium.[12] 10.00-ml. aliquots were withdrawn, evaporated to dryness at 80° and the residues weighed. The solubilities of the various dilituratates, in water at 25°, are given in Tables I and II and those of dilituric acid, in a number of different solvents at 25°, in the text. The over-all accuracy (*i. e.*, reproducibility) of the solubility data in these tabulations is ±4%.

Recovery of Glycine from its Dilituratate.—To 8.4 g. of glycine dilituratate in 100 ml. of hot water was added 3 ml. of 15 *N* ammonium hydroxide. The solution was cooled to room temperature, the precipitate removed and the filtrate evaporated to 20 ml. Upon adding 100 ml. of ethanol to the concentrate, glycine began to precipitate. After cooling to 5° the pure white product was recovered and dried *in vacuo*. The weight was 2.30 g. or 89% of the theoretical amount.

(12) Preliminary experiments with a monovalent salt, soluble in water at 25° to the extent of 50 millimoles per liter, gave identical results, within the limits of experimental error (±2%), when the saturated solution was approached from both sides.

Summary

A number of salts of dilituric acid (5-nitrobarbituric acid) have been prepared and a study of their properties has shown that dilituric acid is a satisfactory reagent for the isolation and determination of many organic and inorganic bases.

PASADENA, CALIF. RECEIVED NOVEMBER 3, 1939

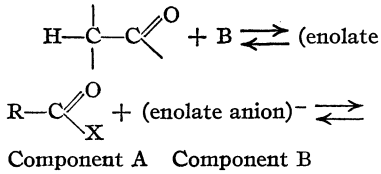
[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF DUKE UNIVERSITY]

Condensations Brought about by Bases. IX. The Relationship between the Claisen and Perkin Types of Condensations[1,2]

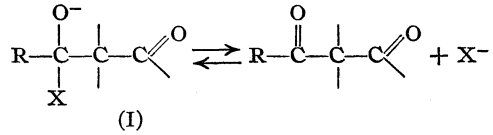
BY CHARLES R. HAUSER AND DAVID S. BRESLOW

The mechanisms for the Claisen[3] (acetoacetic ester) and Perkin[4] types of condensations in the presence of a base B have been represented by the following ionic equations.

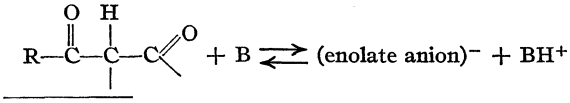
Claisen Type



Component A Component B



(I)



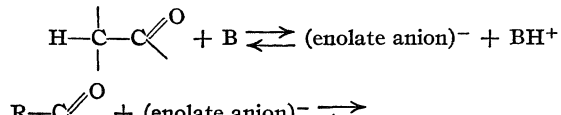
(1) Paper VIII, THIS JOURNAL, **62**, 62 (1940).

(2) This paper was presented before the Division of Organic Chemistry at the Baltimore meeting of the American Chemical Society, April, 1939.

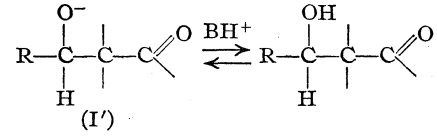
(3) Two types of reaction are known as Claisen condensations, the acetoacetic ester type and the condensation of a ketone with benzaldehyde by means of alkali. In the present paper the Claisen condensation refers only to the acetoacetic ester type. See (a) Hauser and Renfrow, THIS JOURNAL, **59**, 1823 (1937); (b) Hauser, *ibid.*, **60**, 1957 (1938).

(4) See Hauser and Breslow, *ibid.*, **61**, 793 (1939).

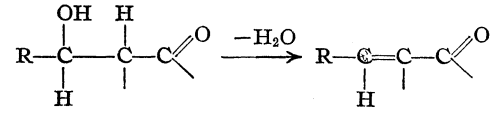
Perkin Type



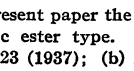
Component A Component B



(I′)



The purpose of this paper is to compare these two types of condensation and to discuss certain experiments in which it is possible for either or both types to occur.

It is evident from the above equations that in both the Claisen and Perkin reactions component B is the enolate anion of a compound of the type  (ester, anhydride, aldehyde, ketone, etc.). Component A, however, is different in the two condensations. In the Claisen reaction

component A is a compound of the type R—C(=O)—X (ester, anhydride, acid chloride, etc.), where X is an atom or group that is released as an anion during reaction; whereas in the Perkin reaction component A is an aldehyde, which contains the hydrogen atom in place of X.

A further inspection of the above equations shows that the first two steps of the Claisen and Perkin reactions are analogous. In both types of condensation a compound of the type H—C(—)—C(=O)— is converted by a base into its enolate anion (component B) which condenses with the carbonyl group of component A, giving the anions (I) and (I′) with the negative charge on the oxygen atom, but here the analogy ends. The anion (I) formed in the second step of the Claisen reaction releases X as an anion, forming the β-keto compound (which may or may not be converted into its enolate anion), whereas in the Perkin reaction this is not possible, as there is no X present in the aldehyde; instead, the corresponding anion (I′) takes up a proton from the medium to give the "aldol," which may eliminate water to form an unsaturated compound.

Certain experiments in which it is possible for both the Claisen and Perkin types of condensation to occur now will be considered. Whenever the Perkin reaction is carried out using the enolate of an ester or anhydride as component B, the Claisen type of condensation also is possible, since the ester or anhydride may serve as component A for the latter type of condensation. Thus the fact, noted by Perkin,[5] that carbon dioxide and a ketone are formed when an anhydride is heated with its sodium salt, is best explained on the basis that the anhydride undergoes self-condensation (Claisen type) to give an acetoacetic ester type of intermediate; it is well known that acetoacetic acid gives carbon dioxide and acetone on heating. In this Laboratory we have observed that phenylacetic anhydride[6] (in which the hydrogen on the α-carbon is reactive), when heated with sodium acetate, gives dibenzyl ketone. The latter is formed presumably by the decomposition of an acetoacetic ester type of intermediate. Actually, however, when benzaldehyde is present, an ester or anhydride undergoes very little self-condensation (Claisen type) on treatment with a base, the main reaction being the Perkin condensation giving cinnamic acid or one of its derivatives. Thus, for example, benzaldehyde with acetic anhydride and a base (sodium acetate or a tertiary amine) gives mainly cinnamic acid, and with ethyl acetate and a base (sodium ethoxide or sodium triphenylmethyl), mainly ethyl cinnamate.

It is rather striking that while ethyl acetate when treated with sodium triphenylmethyl is converted to acetoacetic ester within a few minutes,[7] a mixture of ethyl acetate and benzaldehyde when treated with this base gives mainly ethyl cinnamate; if the latter reaction is stopped within one minute the intermediate "aldol," ethyl β-phenyl-β-hydroxypropionate, is obtained in fair yield (20%).[4] Thus, although the Claisen type of condensation occurs very rapidly in the presence of the strong base, sodium triphenylmethyl, the Perkin type of reaction occurs even more rapidly. This is what might be expected, however, since the carbonyl group of benzaldehyde is more active than that of the ester[8] (or anhydride); moreover, when equimolar quantities of ethyl acetate, benzaldehyde and sodium triphenylmethyl are used, most of the ester is probably rapidly converted into its enolate, which cannot serve as component A in the condensation.

The reaction in which component B is a compound of the type H—C(R)(R)—C(=O)—, such as ethyl isobutyrate, is of especial interest. Scheibler reported[9] that ethyl isobutyrate condenses with benzaldehyde in the presence of sodium ethoxide to give the "aldol," ethyl β-phenyl-β-hydroxypi-

(5) Perkin, *J. Chem. Soc.*, **49**, 322 (1886).

(6) Actually, in this experiment sodium phenylacetate and acetic anhydride were used, but under the experimental conditions phenylacetic anhydride and sodium acetate were formed by double decomposition. See Breslow and Hauser, THIS JOURNAL, **61**, 786 (1939).

(7) Hudson, Dick and Hauser, *ibid.*, **60**, 1960 (1938).

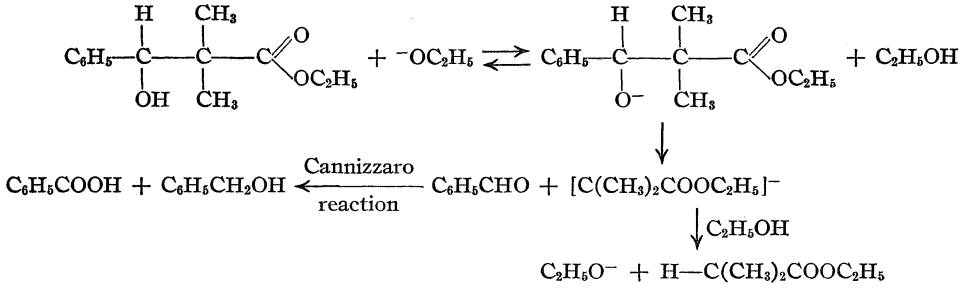
(8) The relative order of activity of the carbonyl group has been indicated by the reaction with the Grignard reagent; the following order is found

$$R-C(=O)-H > R-C(=O)-Cl > R-C(=O)-OC_2H_5$$

(See Gilman, "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1938, p. 418). This order may be explained on the basis of the tendency for the T effect; the positive charge on the carbon atom that would result from the change C=O is partially neutralized in the last two compounds, thus, R—C(=O)—X: .

(9) Scheibler and Friese, *Ann.*, **445**, 158 (1925).

valate, but Müller, Gawlick and Kreutzmann[10] were unable to confirm this result. In agreement with Müller and co-workers, we have obtained the Cannizzaro reaction products, benzyl alcohol and benzoic acid, when benzaldehyde and ethyl isobutyrate were allowed to stand with sodium ethoxide and we were unable to isolate any of the hydroxy-ester reported by Scheibler. We have shown further that when this ester, ethyl β-phenyl-β-hydroxypivalate, is allowed to stand with sodium ethoxide, it is decomposed practically completely giving benzaldehyde (most of which undergoes the Cannizzaro reaction forming benzoic acid and benzyl alcohol) and ethyl isobutyrate. This reaction may be illustrated by the following ionic equations in which the enolate anion is represented by a non-committal formula.



Müller and co-workers reported that ethyl isobutyrate does not condense with benzaldehyde even in the presence of the stronger base, sodium triphenylmethyl. Recently, however, we have shown[4] that condensation does occur in the presence of this base, and that the "aldol," ethyl β-phenyl-β-hydroxypivalate, can be isolated if the reaction is stopped by acidification within a short time (twenty minutes). We have now shown that this hydroxy ester on standing with sodium triphenylmethyl is partly decomposed, as is illustrated above with the ethoxyl anion from sodium ethoxide, into benzaldehyde (most of which undergoes the irreversible Cannizzaro reaction) and, presumably, the enolate of ethyl isobutyrate. This enolate then condenses with ethyl isobutyrate (formed from some of the enolate and triphenylmethane) to give ethyl isobutyryl-isobutyrate, which seemed to be present in small amounts among the reaction products.

Experimental

Preparation and Purification of Materials.—Benzaldehyde and ethyl isobutyrate were purified as previously described.[4,6]

Ethyl β-phenyl-β-hydroxypivalate was prepared according to the method of Blaise and Herman.[11] The zinc complex was hydrolyzed with cold 20% sulfuric acid until an extraction with dilute sodium carbonate gave no precipitate. The ester was collected at 153–158° at 11 mm. and recrystallized by dissolving it in an equal volume of petroleum ether (30–60°) and chilling the resulting solution for several days; m. p. 38.5–39°.

Sodium ethoxide was prepared from a weighed amount of sodium wire and excess absolute alcohol. The last traces of alcohol were removed by heating the sodium ethoxide for a half-hour at 150° at 20 mm., the flask being flushed out with nitrogen.

Sodium triphenylmethyl was prepared from Eastman Kodak Co. triphenylchloromethane according to the method previously described.[3a]

Attempted Condensation of Benzaldehyde with Ethyl Isobutyrate in the Presence of Sodium Ethoxide.—Sodium ethoxide (prepared from 4.6 g. of sodium) was covered with 100 cc. of dry ether and 17.4 g. (0.15 mole) of ethyl isobutyrate and 15.9 (0.15 mole) of benzaldehyde was added. The mixture was stirred mechanically. Heat was evolved, the ether refluxing, and the mixture turned a dark brown. After standing at room temperature for a week, the mixture was acidified with 30 cc. of glacial acetic acid, extracted with sodium carbonate until alkaline and dried over Drierite. The alkaline solution was acidified and the precipitate that formed recrystallized from hot water; in this way 1.0 g. of benzoic acid, m. p. 120–121°, was obtained. The ether was distilled off from the dried ethereal solution and the deep red residue distilled up to 120° at atmospheric pressure to remove ethyl isobutyrate. The residue was then collected up to 120° at 12 mm. A small residue was left behind, which started decomposing at 120° and gave only a small amount of dark red distillate up to 160°, showing the absence of ethyl phenylhydroxypivalate (b. p. 155–156° at 11 mm.[11]). The fraction boiling up to 120° at 12 mm. presumably consisted mostly of benzyl alcohol. This fraction yielded 7.2 g. of benzyl 3,5-dinitrobenzoate, m. p. 111–112°.[12] This is equivalent to 2.6 g. of benzyl alcohol.

The experiment was also run in the absence of any solvent, the mixture being allowed to stand for twenty-four hours before acidification. Essentially the same results were obtained.

(10) Müller, Gawlick and Kreutzmann, *Ann.*, **516**, 97 (1934).

(11) Blaise and Herman, *Ann. chim. phys.*, [8] **23**, 532 (1911).

(12) This is the melting point recorded in the literature for this compound. See Shriner and Fuson, "Systematic Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1935, p. 87.

Decomposition of Ethyl β-Phenyl-β-hydroxypivalate with Sodium Ethoxide.—Sodium ethoxide (prepared from 2.3 g. of sodium) was covered with 500 cc. of dry ether and 22.2 g. (0.10 mole) of ethyl phenylhydroxypivalate added. The mixture was shaken mechanically for several hours. No heat was evolved but the mixture turned a dark red-brown. It was allowed to stand for sixteen days with occasional shaking. The mixture, which still contained a precipitate, was acidified with 20 cc. of glacial acetic acid in 75 cc. of ether, extracted with dilute sodium carbonate until alkaline and dried over Drierite. The alkaline solution, on acidification and subsequent recrystallization of the precipitate from hot water, yielded 1.1 g. of benzoic acid, m. p. 120–121°.

The ether was distilled off from the dried solution through a long Widmer column and the residue was transferred to a 125 cc. Claisen flask, using as little ether as possible. The ether was carefully distilled off and the residue distilled at atmospheric pressure. The fraction boiling at 105–115° was collected (3.0 g.), most of it coming over at 108–112°. It was identified as ethyl isobutyrate (b. p. 111°) by converting it to isobutyramide, m. p. 127.5–128.5°.[13] The residue from the atmospheric distillation was distilled at 11 mm. The first fraction (5.6 g.) was collected at 75–96°. The second fraction (0.5 g.) boiled at 101–130°, and the third (1.1 g.) at 130–165°. A deep red residue was left weighing 3.0 g.

The first fraction was treated with a saturated solution of sodium bisulfite. No precipitate was formed, showing the absence of any benzaldehyde. The mixture was extracted with ether, the ether evaporated and the residue refluxed with 25 cc. of 25% sodium hydroxide solution for six hours in order to hydrolyze any ethyl benzoate present.[14] The mixture was extracted with ether and the alkaline solution acidified. The precipitate formed was recrystallized from hot water, 0.24 g. of benzoic acid, m. p. 121–122°, being obtained. The ether solution was dried, the ether distilled off and the residue distilled at atmospheric pressure; 3.4 g. boiling at 203–204° was obtained. It was identified as benzyl alcohol by its 3,5-dinitrobenzoate, m. p. 110–111°.

The second fraction (mid-fraction) was discarded. The third fraction, which was an oily solid at room temperature, was water-insoluble. This was presumably recovered ethyl phenylhydroxypivalate, but it would not yield a crystalline solid even after several recrystallizations from 30–60° ligroin. A previous duplicate run yielded no recovered ester.

The yield of ethyl isobutyrate was 3.0 g. (25.9%). The yield of benzaldehyde, based on benzoic acid, benzyl alcohol and the benzoic acid formed by the hydrolysis of the small amount of ethyl benzoate in fraction one, was 4.5 g. (42.5%).

Decomposition of Ethyl β-Phenyl-β-hydroxypivalate with Sodium Triphenylmethyl.—Sodium triphenylmethyl was prepared from 41.8 g. (0.15 mole) of triphenylchloromethane dissolved in a liter of ether and 1000 g. of 1% sodium amalgam. The resulting solution was analyzed according to the method of Hudson, Dick and Hauser.[7] To the solution, containing 0.10 mole of sodium triphenylmethyl, was added an equivalent amount (22.2 g., 0.10 mole) of ethyl phenylhydroxypivalate. No appreciable amount of heat was evolved, but the resulting solution was colored a much lighter red than the original. A copious precipitate formed on standing. After standing sixteen days at room temperature, the mixture was acidified with 20 cc. of glacial acetic acid in 75 cc. of ether, extracted with sodium carbonate until alkaline and dried over Drierite. The carbonate extract on acidification gave a precipitate which, after recrystallization from hot water, yielded 0.14 g. of benzoic acid, m. p. 121–122°.

The dried ethereal solution was distilled from a water-bath through a short Widmer column. After the ether had been removed, the liquid remaining in the flask was heated to 120° at atmospheric pressure, but no distillate was obtained; evidently no appreciable amount of ethyl isobutyrate (b. p. 111°) was present in the reaction mixture. The residue was distilled at 12 mm. collecting everything up to 190°. A large residue remained, consisting at least partly of triphenylmethane. The distillate was then redistilled at 10 mm. Two fractions were collected, the first boiling up to 120° (3.9 g.) and the second at 140–165° (5.4 g.). The second fraction was chilled for several days with 5 cc. of petroleum ether (30–60°), the petroleum ether decanted off and the resulting precipitate dried *in vacuo*. In this manner 4.4 g. of ethyl phenylhydroxypivalate, m. p. 38.5–39.5°, was recovered unchanged.

The first fraction (3.9 g.) boiling up to 120° at 10 mm. consisted of a mixture of benzaldehyde, benzyl alcohol and apparently ethyl isobutyryl-isobutyrate. The benzaldehyde was first removed as the sodium bisulfite addition complex (0.05 g.). The mixture was then heated with alkali in an attempt to hydrolyze the ethyl isobutyryl-isobutyrate, but no di-isopropyl ketone could be isolated; however the alkaline solution on acidification gave a strong odor of isobutyric acid. It should be mentioned that hydrolysis of this β-keto ester usually gives a poor yield of di-isopropyl ketone. The organic liquid left after the attempted hydrolysis consisted mostly of benzyl alcohol, which was identified as the 3,5-dinitrobenzoate, 2.1 g. of the latter being obtained.

Summary

1. The mechanisms for the Claisen and Perkin types of condensation are compared and reactions in which both types of condensation are possible are discussed.

2. It has been shown that in the presence of sodium ethoxide ethyl isobutyrate does not condense with benzaldehyde. The condensation product that would be formed, ethyl β-phenyl-β-hydroxypivalate, is decomposed by sodium ethoxide to give benzaldehyde and ethyl isobutyrate.

3. Although ethyl isobutyrate condenses with benzaldehyde in the presence of sodium triphenyl-

(13) Shriner and Fuson, ref. 12, p. 131.

(14) Claisen reported the presence of methyl benzoate when benzaldehyde was treated with sodium methoxide. See Claisen, *Ber.*, **20**, 646 (1887).

methyl to give ethyl β-phenyl-β-hydroxypivalate, the latter on standing in the presence of this base is again decomposed.

4. The mechanisms of the above decompositions are discussed.

DURHAM, NORTH CAROLINA RECEIVED NOVEMBER 9, 1939

[CONTRIBUTION FROM THE UNITED STATES DEPARTMENT OF AGRICULTURE, BUREAU OF ENTOMOLOGY AND PLANT QUARANTINE]

The Constituents of Certain Species of Helenium. III. The Ester Nature of Tenulin

BY E. P. CLARK

A description of tenulin and some of its derivatives was given in the second paper of this series.[1] No attempt was made to interpret the reactions reported, but as work on the material has progressed facts have emerged that warrant comment.

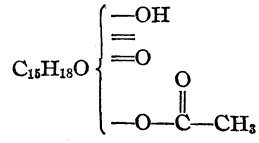
From the data already recorded the following conclusions may be drawn: Tenulin has a double bond, as two atoms of bromine *add* to form a dibromotenulin and hydrogenation with Adams catalyst yields a dihydro compound. Dihydrotenulin, as well as its isomer, dihydroisotenulin, readily forms phenylhydrazones, whereas the unhydrogenated materials do not. It is inferred, therefore, that both tenulin and isotenulin have a carbonyl group, which is sterically hindered by the presence of the double bond. Although tenulin does not give ordinary reactions for hydroxyl groups, the fact that heating it to 300° for a very short time produces an anhydro derivative is a reasonable indication that a sterically hindered hydroxyl group is present.

The work reported at this time shows that tenulin has also another hydroxyl group esterified as an acetate. This information was obtained in experiments having two different lines of approach. First it has been found that alkaline hydrogen peroxide oxidizes both tenulin and isotenulin to a monocarboxylic acid, $C_{15}H_{20}O_7$, which has been named "tenulinic acid." If potassium permanganate is used as the oxidizing agent, another acid, which crystallizes as $C_{17}H_{22}O_8 \cdot {}^1/_2H_2O$, is obtained. The difference between these two acids, aside from the water of crystallization, is C_2H_2O, which should result from the hydrolysis of an acetyl compound. Furthermore, tenulinic acid may be acetylated readily to give a quantitative yield of the second acid, and on hydrolysis it gives back tenulinic acid. The acid obtained by permanganate oxidation of both tenulin and isotenulin is therefore acetyltenulinic acid. The correctness of the formulas of the two acids was checked by the analysis of the acids themselves as well as by the analysis of their methyl esters.

The second approach was to apply hydrolytic reactions to isotenulin. When isotenulin is dissolved in concentrated sulfuric acid and heated for a short time, a substance, $C_{15}H_{20}O_4$, m. p. 255°, is obtained. This has the composition that would result from the hydrolytic loss of an acetyl group from isotenulin. At the same time exactly one mole of acetic acid is formed. The compound $C_{15}H_{20}O_4$, m. p. 255°, is identical with the by-product obtained by the action of 0.1 *N* sodium hydroxide or by prolonged action of 5% sodium carbonate solution on tenulin,[1] and this fact explains its formation as a by-product in the more drastic methods of preparing isotenulin. Further proof that the $C_{15}H_{20}O_4$ compound is deacetylated isotenulin is furnished by its ready reacetylation to isotenulin.

The same hydrolytic action takes place when concentrated sulfuric acid reacts on dihydroisotenulin. The deacetylated product $C_{15}H_{22}O_4$ melts at 203°. Alkali does not have the deep-seated action on dihydroisotenulin that it does on tenulin, and the hydrolysis may be brought about with little loss when aqueous alkali is employed. Both 10 and 50% potassium hydroxide solutions were used, and in each case the desacetyldihydroisotenulin, m. p. 203°, was obtained.

These facts constitute sufficient evidence of the presence of an acetoxy group in tenulin. It thus follows that tenulin may be represented as

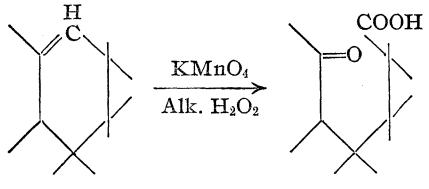


In further consideration of the acetyl group at-

(1) Clark, THIS JOURNAL, 61, 1836 (1939).

tention is directed to the fact that it is more firmly bound than ordinary *o*-acyls. Thus tenulin gave 10.1% acetyl by the standard acetyl method[2] and 12.8% when it was boiled with the alkali reagent for half an hour. The theoretical value is 14.05%. Again the standard procedure for the determination of acetyl in acetyltenulinic acid gave only 3.3% acetyl, and acetyltenulinic acid methyl ester was prepared in good yield by refluxing a solution of the acid in a methanolic hydrochloric acid mixture for one and one-half hours. This phenomenon may be interpreted in several ways, but it seems best to withhold comment until more pertinent facts are accumulated.

Likewise the reaction involving the formation of tenulinic acid is significant aside from the interpretation placed upon it in connection with the ester nature of tenulin. Since neither permanganate nor alkaline hydrogen peroxide attacks desacetyldihyroisotenulin, it is obvious that, in the reaction under consideration, the double bond is involved. The most likely mechanism to account for the addition of three oxygen atoms is the breaking of a double bond in an alicyclic ring to form a ketonic acid. This may be shown schematically as follows



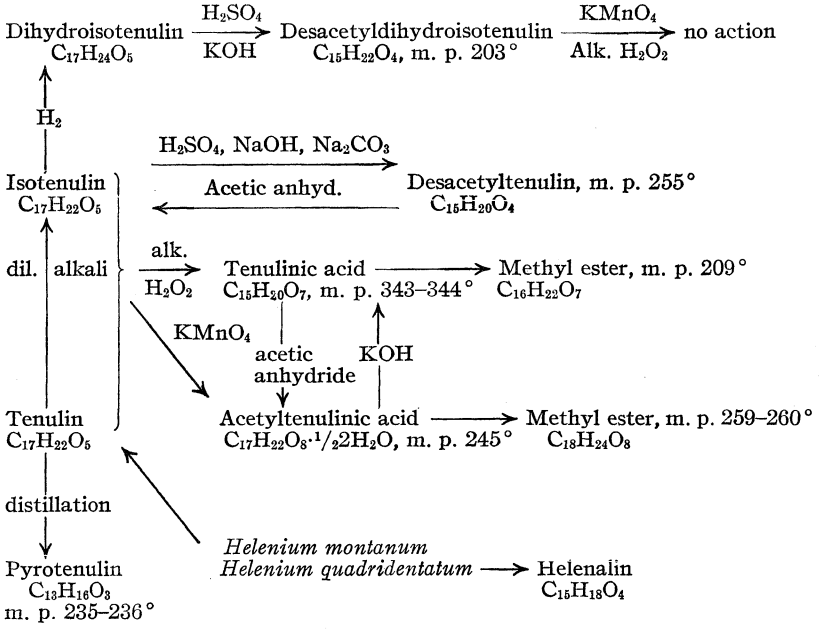
Attempts to prove such a reaction, however, have led to difficulties and further comment is therefore withheld until more information is available.

Another reaction, presented at this time for record only, is that when tenulin is distilled rapidly at atmospheric pressure, it yields a small quantity of a white crystalline compound whose composition is $C_{13}H_{16}O_3$. This has been named "pyrotenulin."

(2) Clark, *Ind. Eng. Chem., Anal. Ed.*, **9**, 539 (1937).

Two hitherto unexamined species of *Helenium*, *H. quadridentatum* and *H. montanum*, also were investigated for bitter and sternutative substances. The procedure followed was the same as that previously used.[1] It was found that *H. quadridentatum* contains helenalin and *H. montanum* yields tenulin.

DIAGRAM SHOWING THE INTERRELATIONS OF PREVIOUSLY UNRECORDED MATERIALS UNDER DISCUSSION



Experimental

Tenulinic Acid.—A solution of 1 g. of tenulin in 10 cc. of acetone, 10 cc. of water, and 8 cc. of 30% hydrogen peroxide was heated to boiling and treated portion-wise with 5 cc. of 10% sodium hydroxide solution. As the reaction and boiling proceeded, 10 cc. of water was added. After all the alkali had been added and the frothing had subsided, the solution was filtered and acidified with sulfuric acid (congo red). Crystallization began at once and yielded 0.57 g. of material which melted at 338–339°. This was recrystallized by acidifying a solution of its sodium salt with sulfuric acid until it had a constant melting point of 343–344°.

The purified product consisted of six-sided rods, many of which were broken into angular fragments. Its refractive indices as determined by the immersion method[3] were η_α, 1.507; η_β, indeterminate; η_γ, 1.595. In parallel polarized light (crossed nicols) the birefringence was extremely strong. Extinction on rods was usually inclined, and the elongation was negative. In convergent polarized light (crossed nicols) no interference figures were observed. The refractive indices were therefore determined by the statistical method. Those rods and fragments showing the maximum double refraction were se-

(3) The optical data recorded in this communication were determined by George L. Keenan, of the Food and Drug Administration of the U. S. Department of Agriculture.

lected for measuring the lowest and the highest indices of refraction.

Anal. Calcd. for $C_{15}H_{20}O_7$: mol. wt., 312.3; C, 57.68; H, 6.46.

Found: mol. wt. (by titration, calcd. to one COOH group), 311; C, 57.65; H, 6.50.

Isotenulin reacted in the same manner as tenulin. The resulting acid was obtained in the same yield as from tenulin, its melting point and composition were identical with those of tenulinic acid, and when the two substances were mixed there was no depression of the melting point.

Anal. C, 57.61; H, 6.63.

Tenulinic Acid Methyl Ester.—This material was made by two procedures. An acetone solution of the acid (0.5 g. in 10 cc.) was treated with an excess of diazomethane. The reaction took place at once, and the resulting solution was evaporated to dryness under reduced pressure. The residue was dissolved in 10 cc. of methanol, and then 30 cc. of water was added. The ester immediately crystallized. It had a m. p. of 208°. Upon recrystallization from methanol–water (1–4), long colorless rods that melted at 209° were obtained.

Anal. Calcd. for $C_{16}H_{22}O_7$: C, 58.88; H, 6.80; OCH_3(1), 9.51. Found: C, 58.94; H, 6.83; OCH_3, 9.55.

The second procedure for preparing the ester consisted in refluxing for one and one-half hours a solution of 0.2 g. of the acid in 5 cc. of methanol and 0.25 cc. of concentrated hydrochloric acid. Upon diluting the reaction mixture with water, long colorless rods were obtained (m. p. 207°). After recrystallization this material did not depress the melting point of the ester made with diazomethane.

Acetylation of Tenulinic Acid.—Tenulinic acid was acetylated by allowing a solution of 0.2 g. of the acid in 2 cc. of pyridine and 1 cc. of acetic anhydride to stand at room temperature overnight. The solution was then diluted with water and acidified with sulfuric acid (congo red). Crystallization began at once, and a quantitative yield of the acetate was obtained. It melted at 243°, and further recrystallizations did not alter the melting point. When mixed with acetyltenulinic acid obtained by permanganate oxidation of tenulin (see below), the melting point was not depressed.

Acetyltenulinic Acid.—A well-stirred solution of 3 g. of tenulin dissolved in 50 cc. of acetone and 25 cc. of water was slowly treated with 330 cc. of 1% aqueous solution of potassium permanganate, and then 3.3 g. of crystalline potassium permanganate was added portionwise. When the reaction was finished, the manganese dioxide was removed by filtration and the filtrate was evaporated, under reduced pressure, to about 60 cc. The concentrate was acidified with sulfuric acid (congo red) and allowed to crystallize. The yield was 1.8 g. of dense colorless crystals, usually joined together in fern-like aggregates. The material melted at 236°. It was recrystallized from its solution in acetone by adding three volumes of water. It then melted at 245°, with the evolution of gas. When it was recrystallized from other liquids its melting point varied from 234 to 245° depending upon the solvent used. Judged from analysis of the various preparations the material was pure, but slight variations in the water of crystallization influenced the melting points. Material crystallized from glacial acetic acid melted at 234–235°. It consisted of sphenoids belonging to the tetragonal system. Many of them broke into irregular fragments. Their refractive indices as determined by the immersion method were as follows: η_ω, 1.544; η_ϵ, 1.552; both ± 0.002. In parallel polarized light (crossed nicols) the fragments invariably extinguished sharply, and birefringence was weak. In convergent polarized light (crossed nicols) no interference figures were observed. The refractive indices, therefore, were determined for two positions of extinction on a number of grains in random orientation. One of the values, η_ω, was the same in all grains, while the other of maximum numerical magnitude was designated as η_ϵ.

Anal. Calcd. for $C_{17}H_{22}O_8 \cdot {}^1/_2H_2O$: mol. wt., 363.4; C, 56.19; H, 6.38; acetyl, 11.84. Found: material recrystallized from acetone–water, m. p. 245°; mol. wt. (by titration, calcd. to one COOH group), 363; C, 56.69; H, 6.66; acetyl (standard procedure), 3.3.

As with tenulin, isotenulin also gave acetyltenulinic acid. The identity of the material thus obtained was established by its melting point, mixed melting point and analysis.

Anal. C, 56.53; H, 6.74.

Hydrolysis of Acetyltenulinic Acid.—A solution of 0.1 g. of acetyltenulinic acid in 5 cc. of 10% sodium hydroxide solution was boiled for fifteen minutes. The reaction mixture was then made acid with sulfuric acid (congo red) and allowed to crystallize. This material, after two recrystallizations, melted with decomposition at 343–344°, and there was no depression of the melting point when it was mixed with an authentic sample of tenulinic acid.

Acetyltenulinic Acid Methyl Ester.—This compound was prepared by the two methods used to obtain tenulinic acid methyl ester except that it was crystallized from acetone by adding three volumes of water. When recrystallized to a constant melting point of 259–260°, preparations obtained in both ways consisted of thick plates and prisms.

Anal. Calcd. for $C_{18}H_{24}O_8$: C, 58.69; H, 6.57; OCH_3, 8.42. Found: C, 58.95; H, 6.58; OCH_3, 8.48.

Desacetylisotenulin.—A solution of 1 g. of isotenulin in 4 cc. of concentrated sulfuric acid was heated for one minute in a water-bath at 90°. Crushed ice and water were then added to dilute the mixture to about 50 cc. In a short time crystallization began, and on completion 0.3 g. of white crystals, m. p. 175–183°, was obtained. This product was recrystallized from *n*-butanol to a constant melting point of 255°. When mixed with the compound melting at 255° previously obtained as a by-product from the preparation of isotenulin, there was no depression of the melting point.

Anal. Calcd. for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 68.32; H, 7.78.

The acid mother liquors from the above experiment contained a volatile acid, which was recovered by distillation and estimated and identified by the Dyer procedure.[4]

(4) Clark and Hillig, *J. Assoc. Official Agr. Chem.*, **21**, 684 (1938).

The distillation curve for the recovered acid was a straight line with a distillation constant characteristic of acetic acid. The acid was therefore acetic, and the quantity recovered corresponded to one mole of acid from a mole of isotenulin.

Acetylation of Desacetylisotenulin.—A solution of 0.1 g. of the $C_{15}H_{20}O_4$ compound in 1 cc. of pyridine and 0.5 cc. of acetic anhydride was allowed to react overnight. Water was then added, causing the liquid to crystallize. Long colorless rods that melted at 160° were obtained. Recrystallization of these from methanol and water (1–3) raised their melting point to 161°. The product was identified as isotenulin by its melting point, mixed melting point with an authentic sample of isotenulin, and its optical crystallographic properties.

Hydrolysis of Dihydroisotenulin.—Dihydroisotenulin was hydrolyzed with concentrated sulfuric acid by the procedure used with isotenulin. Several days were required for complete crystallization from the reaction mixture. The product was purified by recrystallization from its methanol solution by adding water. It melted at 203°.

Anal. Calcd. for $C_{15}H_{22}O_4$: C, 67.64; H, 8.33. Found: C, 67.88; H, 8.61.

Sodium hydroxide was also used as a hydrolyzing agent. A mixture of 0.5 g. of dihydroisotenulin and 10 cc. of 10% sodium hydroxide was heated and stirred until a homogeneous solution resulted. This was then diluted with water to *ca.* 50 cc. and acidified to congo red with sulfuric acid. Colorless crystals (240 mg.) separated. They melted at 202°, and when they were mixed with the compound obtained above with sulfuric acid there was no depression of the melting point. The acid mother liquors were examined for acetic acid as reported under isotenulin. The results were identical.

Pyrotenulin.—A half gram of purified tenulin was heated until the first violent evolution of gas ceased. The resulting melt was then placed in a strong Bunsen flame and rapidly distilled. The distillate was caught in a thin-walled bulb blown close to the bottom of the test-tube. This was broken, and its contents dissolved in chloroform. The solution was filtered through Norit and diluted with several volumes of methanol. The liquid was distilled until the chloroform was removed, whereupon the methanol concentrate crystallized. The product consisted of colorless hexagonal plates, m. p. 235–236°.

Anal. Calcd. for $C_{13}H_{16}O_3$: C, 70.88; H, 7.32. Found: C, 70.90; H, 7.22.

Summary

Evidence has been presented to show that tenulin contains a double bond, an acetoxyl group, and a hydroxyl and a carbonyl group, both of which are sterically hindered.

A summary of the reactions of tenulin which have been used in this discussion and which have hitherto been unrecorded is shown diagrammatically in a chart.

Two hitherto unexamined species of *Helenium*, *i. e.*, *H. quadridentatum* and *H. montanum*, have been investigated for bitter and sternutative substances. *H. quadridentatum* contains helenalin, while *H. montanum* contains tenulin.

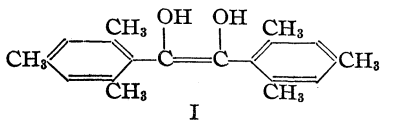
WASHINGTON, D. C. RECEIVED JANUARY 4, 1940

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

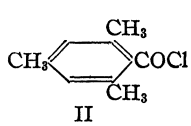
Enediols. III. 1,2-Dimesitylacetylene Glycol

BY REYNOLD C. FUSON, C. H. MCKEEVER[1] AND JOSEPH CORSE

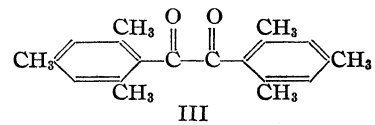
The isolation of a stable enediol, 1,2-dimesitylacetylene glycol (I), was reported recently.[2] The present paper presents the experimental details upon which the earlier communication was based. The enediol was obtained by the action of the binary mixture, Mg + MgI_2,[3] on mesitoyl chloride (II) or mesitil (III). The products from the two sources were identical. Both reverted to the benzil when exposed to the air or other oxidizing agents, and both rearranged to mesitoin (IV) under the influence of hydrochloric acid.



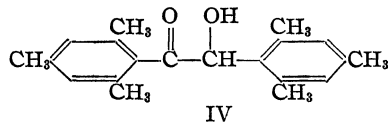
I



II



III



IV

Treatment of this enediol with acetic anhydride gave a diacetate (m. p. 164–165°) accompanied by a very small amount of a second diacetate (m. p. 218°). Mesitil and the acetate of mesitoin were also isolated.

Benzoylation with benzoyl chloride in the presence of pyridine converted the enediol into a dibenzoate melting at 188.5–189.5°.

By hydrogenation of mesitil in methanol,

(1) Röhm and Haas Research Assistant.
(2) Fuson and Corse, THIS JOURNAL, **61**, 975 (1939).
(3) Gomberg and Bachmann, *ibid.*, **49**, 236 (1927).

Thompson[4] obtained an enediol which gave a dibenzoate melting at 235°, and concluded that he had a stereoisomer of the enediol of Fuson and Corse. We have shown that the enediol made by Thompson's method yields chiefly the high-melting diacetate when treated with acetic anhydride. However, a small amount of the low-melting diacetate is formed also along with a large amount of the acetate of mesitoin.

In view of this result, the benzoylation was repeated and the mother liquors from the crystallization of the high-melting dibenzoate were examined with great care. A small amount of the low-melting dibenzoate was found. The very remarkable discovery was then made that this dibenzoate was the sole product when the catalytic hydrogenation was carried out in low-boiling petroleum ether instead of methanol. It is, therefore, not entirely clear what relationship obtains between the source of the enediol and its behavior toward acylating agents. However, it can be said that any given sample of enediol, regardless of its history, yields predominantly one form or the other of the expected diester. The second diester if produced at all is always in small amount. This observation supports Thompson's conclusion that the enediol exists in two stereoisomeric forms. However, it implies that the samples which have been described may be mixtures. The alternative is to assume partial isomerization during esterification. This question is being studied.

Experimental

Action of the Binary Mixture on Mesitoyl Chloride.—The binary mixture was prepared according to the directions of Gomberg and Bachmann.[3] To 3 g. of magnesium turnings, 60 cc. of dry ether and 120 cc. of dry benzene was added 15.3 g. of iodine in several small portions. When the reaction mixture had become colorless and cooled to room temperature, the air in the flask was swept out by a stream of dry, oxygen-free nitrogen. A solution of 11 g. of the chloride in 10 cc. of dry ether was then added over a period of fifteen minutes by means of a dropping funnel. Stirring was continued for sixteen to eighteen hours, in a nitrogen atmosphere. At the end of this time the magnesium had nearly disappeared and the solution was dark red.

The reaction mixture was filtered through folded cheesecloth into a separatory funnel containing 8 cc. of acetic acid and 100 cc. of ice water. The ether–benzene layer was separated and washed *rapidly* with water, with 5% sodium thiosulfate solution, again with water, then with 10% potassium bicarbonate solution and finally once more with water. The solution was then dried for a few minutes over calcium chloride, filtered and evaporated to a thin sirup as rapidly as possible with the aid of the water pump. Dilution of the brown sirup with 50 cc. of petroleum ether and cooling, precipitated the enediol as a white crystalline material which was separated and washed with petroleum ether. The yield amounted to 3.1 g. or 35% of the theoretical.

The enediol was unstable in the presence of oxygen, being rapidly autoxidized to the benzil. It was soluble in ether, benzene and alcohol but insoluble in petroleum ether and aqueous alkali. It immediately decolorized solutions of 2,6-dichlorobenzeneoneindophenol; Tollens' reagent and cold cupric acetate solutions were also immediately reduced.

The mother liquors from the enediol yielded 3 g. of mesitil or 34% of the theoretical. A little tarry material also was isolated.

When only 1.5 g. of iodine was used instead of the usual 15.3 g., and the procedure carried out as before, no reaction was apparent; only mesitoic acid was isolated.

In one run out of thirteen mesitoin was isolated (28% yield) instead of the enediol.

Action of the Binary Mixture on Mesitil.—To the binary mixture, made from 1.5 g. of magnesium and 7.6 g. of iodine in 60 cc. of benzene and 30 cc. of ether, was added 4.4 g. of mesitil. Stirring was continued for twenty-four hours, the mixture being kept under a nitrogen atmosphere. When the mesitil was added the solution turned dark red-brown, probably because of the liberation of iodine.[3] After a few hours, a dark red-brown precipitate formed which later disappeared. At the end of the reaction the mixture had the same appearance as that obtained from mesitoyl chloride and the binary mixture; it was decomposed and treated in the same manner as in the preceding experiment. Two and seven-tenths grams of the enediol was obtained, a yield of 60% of the theoretical. In addition, mesitil was recovered.

Hydrogenation of Mesitil.—The enediol also was made by the hydrogenation of mesitil in low-boiling petroleum ether.

One and one-half grams of mesitil was almost completely dissolved in 50 cc. of low-boiling petroleum ether. Approximately 0.02 g. of platinum oxide catalyst was added and the mixture reduced at room temperature under a pressure of one and one-half atmospheres. The enediol precipitated as it was formed and the reduction was complete when the solution became colorless. The reaction mixture was filtered, the enediol dissolved in ether, this solution filtered to remove the catalyst, the ether evaporated to a small volume and the enediol precipitated by addition of low-boiling petroleum ether. The yields varied from 85 to 95% of the theoretical amount.

Ketonization of the Enediol.—A solution of 1.3 g. of the enediol and 6 cc. of methanol which previously had been saturated with dry hydrogen chloride was refluxed for forty-five minutes, allowed to cool and poured into 70 cc. of water. A white crystalline compound separated. It was collected on a filter and recrystallized from 70% aqueous methanol; yield 1.2 g. The compound melted at 130–131°, and a mixed melting point with an authentic sample of mesitoin[5] showed no depression.

(4) Thompson, THIS JOURNAL, **61**, 1281 (1939).

(5) Fuson, Emerson and Weinstock, *ibid.*, **61**, 412 (1939).

The Acetate of Mesitoin.—A solution of 1.2 g. of mesitoin in 5 cc. of acetyl chloride was refluxed for two hours. It was poured into water, extracted with ether and the ether extracts were washed with water, 10% potassium bicarbonate and again with water. The ether solution was dried over calcium chloride and after filtration the ether was removed by an air blast. The solid which remained crystallized as long white needles from ether–petroleum ether and melted 106–107°; the yield was 1.2 g.

Anal. Calcd. for $C_{22}H_{26}O_3$: C, 78.07; H, 7.75; acetyl no., 12.7. Found: C, 78.11; H, 7.28; acetyl no., 10.6, 11.5.

Refluxing a solution of 0.085 g. of the acetate in 2.1 cc. of methanol and 0.2 cc. of concentrated hydrochloric acid for two hours gave mesitoin in good yield.

The Diacetates of the Enediol.—A solution of 1 g. of the enediol, prepared by the bimolecular reduction of mesitoyl chloride, and 5 cc. of acetic anhydride was refluxed for three hours and poured into water; the mixture was warmed to decompose the excess acetic anhydride and extracted with ether. The ether extracts were washed twice with a 10% solution of potassium bicarbonate, then with water and dried over calcium chloride; the ether was allowed to evaporate at room temperature. There was obtained a mixture of four compounds, which were separated as follows. The mixture was taken up in methyl alcohol; the very small amount of a diacetate which was insoluble was removed by filtration. After recrystallization from a benzene–low-boiling petroleum ether mixture it melted at 218°. It could be hydrolyzed to mesitil with dilute alcoholic potassium hydroxide.

Anal. Calcd. for $C_{24}H_{38}O_4$: C, 75.76; H, 7.43. Found: C, 75.69; H, 7.48.

When the methyl alcohol solution cooled to room temperature there precipitated a second diacetate, m. p. 156–160°, which after several recrystallizations from methyl alcohol melted at 164–165°.

Anal. Calcd. for $C_{24}H_{28}O_4$: C, 75.76; H, 7.43; acetyl no., 22.6. Found: C, 75.41; H, 7.61; acetyl no., 20.7.

When the methyl alcohol solution was evaporated to dryness, there was obtained the acetate of mesitoin contaminated with a small amount of mesitil. The structure of these compounds was proven by mixed melting point determinations with known samples.

All four compounds were obtained no matter how the enediol had been prepared. The enediol prepared by bimolecular reduction of the acid chloride and the one prepared by reduction of mesitil in low-boiling petroleum ether behaved exactly alike. They gave only a trace of the high-melting diacetate, a 30–40% yield of the diacetate melting at 164–165° and a mixture of mesitil and acetate of mesitoin.

In the case of the enediol prepared by catalytic reduction in methyl alcohol,[4] the amounts of the products were very different; the product consisted of a 20–30% yield of the high-melting diacetate, a trace (and sometimes none) of the diacetate which melted at 164–165° and a good yield of the acetate of mesitoin contaminated with small amounts of mesitil.

If mesitil is reduced in acetic anhydride according to the method of Thompson[4] a 90% yield of the diacetate, m. p. 164–165°, is obtained. This compound was also obtained when mesitil was treated with sodium according to the method of Kohler and Baltzly[6] with subsequent treatment with acetyl chloride rather than benzoyl chloride.

When acetyl chloride was used instead of acetic anhydride, the enediol yielded the acetate of mesitoin in 70–80% yield, together with only small amounts of the diacetates.

The Benzoates of the Enediol.—To 2 cc. of benzoyl chloride and 10 cc. of pyridine was added 0.3 g. of the enediol prepared by the bimolecular reduction of mesitoyl chloride. The mixture was refluxed gently for two hours, poured into water, acidified with dilute hydrochloric acid and extracted with ether. The ether extract was washed thoroughly with a 10% solution of potassium bicarbonate, water, dilute hydrochloric acid and water; it was then dried over calcium chloride and the ether was evaporated. The dibenzoate crystallized from ether–petroleum ether mixture, m. p. 188.5–189.5°. A second dibenzoate could not be found. The enediol prepared by catalytic reduction of mesitil in low-boiling petroleum ether, when treated as above, yielded the same compound, m. p. 188–189°. The enediol prepared from catalytic reduction in *methyl alcohol* yielded a dibenzoate, m. p. 235°.[2] Upon evaporation of the solvent, there was precipitated a second compound which after two recrystallizations from absolute alcohol melted at 188–189°. A mixed melting point determination proved it to be identical with the dibenzoate prepared above.

Summary

1,2-Dimesitylacetylene glycol has been prepared in three different ways. It has been caused to rearrange to the benzoin. The enediol gives two diacetates and two dibenzoates, presumably pairs of *cis-trans* isomers.

URBANA, ILLINOIS RECEIVED DECEMBER 29, 1939

(6) Kohler and Baltzly, THIS JOURNAL, **54**, 4015 (1932).

[CONTRIBUTION NO. 213 FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Identification of Organic Compounds. III. Chlorosulfonic Acid as a Reagent for the Characterization of Aromatic Ethers[1,2]

BY ERNEST H. HUNTRESS AND FREDERICK H. CARTEN

The use of chlorosulfonic acid as a tool for the characterization of organic compounds whose application to the identification of aryl halides was reported in the first paper[3] of this series has now been extended to thirty-six aromatic ethers. The principle employed is twofold: first, introduction of one sulfonyl chloride group into each aromatic nucleus by direct treatment with chlorosulfonic acid, and, second, conversion of the resultant sulfonyl chlorides into the corresponding sulfonamides. The sulfonyl chlorides were generally obtained in excellent yields and their conversion to sulfonamides was nearly quantitative. The resultant products crystallize well and possess sharp and characteristic melting points. Data expressing the results of this study are given in Table I.

TABLE I

SULFONAMIDES[a] FROM AROMATIC ETHERS

Original compound	Sulfonamide	Yield, %	M. p. obsd. uncor., °C.
A. Substituted benzenesulfonamides			
Anisole	*p*-Methoxy-	53	110–111[b]
Phenetole	*p*-Ethoxy-	78	149–150[c]
n-Propyl phenyl ether	*p*-(*n*-Propoxy)-	68	116–117
n-Butyl phenyl ether	*p*-(*n*-Butoxy)-	35	103–104
o-Tolyl methyl ether	3-Methyl-4-methoxy-	84	137[d,e,f]
m-Tolyl methyl ether	2-Methyl-4-methoxy-	69	129–130[g]
p-Tolyl methyl ether	5-Methyl-2-methoxy-	86	182[h]
o-Tolyl ethyl ether	3-Methyl-4-ethoxy-	71	148–149[i]
m-Tolyl ethyl ether	2-Methyl-4-ethoxy-	61	110–111[b]
p-Tolyl ethyl ether	5-Methyl-2-ethoxy-	77	138–138.5[j,f]
n-Propyl *p*-tolyl ether	2-(*n*-Propoxy)-4-methyl-	54	126–127
n-Butyl *o*-tolyl ether	4-(*n*-Butoxy)-5-methyl-	44	95–96
Catechol dimethyl ether	3,4-Dimethoxy-	89	135–136[k]
Resorcinol dimethyl ether	2,4-Dimethoxy-	53	166–167[l]
Hydroquinone dimethyl ether	2,5-Dimethoxy-	53	148[i,m]
Catechol diethyl ether	3,4-Diethoxy-	81	162–163
Resorcinol diethyl ether	2,4-Diethoxy-	59	184–185
Hydroquinone diethyl ether	2,5-Diethoxy-	47	154–155[m]
Pyrogallol trimethyl ether	2,3,4-Trimethoxy-	29	123–124
o-Chloroanisole	3-Chloro-4-methoxy-	85	130–131[n]
p-Chloroanisole	5-Chloro-2-methoxy-	82	150–151[o]
o-Bromoanisole	3-Bromo-4-methoxy-	78	139–140[p]
p-Bromoanisole	5-Bromo-2-methoxy-	81	147–148
p-Fluoroanisole	5-Fluoro-2-methoxy-	86	174–175
o-Chlorophenetole	3-Chloro-4-ethoxy-	73	132–133[q]
p-Chlorophenetole	5-Chloro-2-ethoxy-	71	134–134.5[q]
o-Bromophenetole	3-Bromo-4-ethoxy-	76	134–135[p]
p-Bromophenetole	5-Bromo-2-ethoxy-	68	144–144.5
p-Bromodiphenyl ether	4-(*p*-Bromophenoxy)-	67	130–131[r]
B. Substituted naphthalene sulfonamides			
α-Naphthyl methyl ether[s]	4-Methoxynaphthalene-	55	156–157[t]
β-Naphthyl methyl ether[s]	7-Methoxynaphthalene-	65	150–151[t]
α-Naphthyl ethyl ether[s]	4-Ethoxynaphthalene-	64	164–165[u]
β-Naphthyl ethyl ether[s]	7-Ethoxynaphthalene-	58	161–163[v]
C. Miscellaneous Disulfonamides			
Diphenyl ether	Diphenyl ether 4,4′-di-	86	159[w]
Ethylene glycol diphenyl ether	α,β-Diphenoxyethane-4,4′-di-	74	228–229
Trimethylene glycol diphenyl ether	α,γ-Diphenoxypropane-4,4′-di-	44	245–255

[a] Duplicate combustion analyses were carried out on every sulfonamide in Table I. Their results gave values agreeing closely with each other and with the theoretical values. [b] A mixed melting point of *p*-methoxybenzenesulfonamide (m. p. 110–111°) with 2-methyl-4-ethoxybenzenesulfonamide (m. p. 110–111°) was depressed to 99–103°. [c] Recorded m. p. 149°, Schober and Bowers, *Am. Chem. J.*, 25, 72 (1901). [d] Recorded m. p. 137°, Kolhatkar and Bokil, *J. Indian Chem. Soc.*, 7, 845 (1930). [e] Bromwell, *Am. Chem. J.*, 19, 573 (1897). [f] A mixed melting point of 3-methyl-4-methoxybenzenesulfonamide (m. p. 137°) with 5-methyl-2-ethoxybenzenesulfonamide (m. p. 138°) was depressed to 129–131°. [g] Recorded m. p. 129–130°, Haworth and Lapworth, *J. Chem. Soc.*, 123, 2988 (1923). [h] Recorded m. p. 183°, Stewart, *ibid.*, 121, 2558 (1922). [i] A mixed melting point of 3-methyl-4-ethoxybenzenesulfonamide (m. p. 148°) with 2,5-dimethoxybenzenesulfonamide (m. p. 148°) was depressed to 141–143°. [j] Recorded m. p. 138–139°, Metcalf, *Am. Chem. J.*, 15, 307 (1893). [k] Recorded m. p. 136°, Brown and Robinson, *J. Chem. Soc.*, 111, 953 (1917). [l] Recorded m. p. 166–167°, Suter and Hansen, THIS JOURNAL, 55, 2082 (1933). [m] A mixed melting point of 2,5-dimethoxybenzenesulfonamide (m. p. 148°) with 2,5-diethoxybenzenesulfonamide (m. p. 154°) was depressed to 142–144°. [n] Recorded m. p. 130° cor., Child, *J. Chem. Soc.*, 718 (1932). [o] Recorded m. p. 154°, Gauntlett and Smiles, *ibid.*, 127, 2745 (1925). [p] A mixed melting point of 3-bromo-4-methoxybenzenesulfonamide (m. p. 139–140°) with 3-bromo-4-ethoxybenzenesulfonamide (m. p. 134–135°) was depressed to 128–130°. [q] A mixed melting

(1) This paper is constructed from part of a dissertation submitted by Frederick H. Carten to the Faculty of the Massachusetts Institute of Technology in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1939. Original manuscript received August 23, 1939.

(2) This work was assisted by a grant to one of us (E. H. H.) from the Warren Fund of the American Academy of Arts and Sciences for which grateful acknowledgment is hereby made.

(3) Huntress and Carten, THIS JOURNAL, 62, 511 (1940).

point of 3-chloro-4-ethoxybenzenesulfonamide (m. p. 132–133°) with 5-chloro-2-ethoxybenzenesulfonamide (m. p. 134–134.5°) was depressed to 129–130°. [r] Recorded m. p. 131–132°, Suter, THIS JOURNAL, **53**, 1115 (1931). [s] With these compounds use of the usual quantity (5.0 g.) of chlorosulfonic acid yielded mainly water-soluble products. Upon reduction of the chlorosulfonic acid to two grams, however, the sulfonamides were obtained readily in the indicated yields. [t] A mixed melting point of 4-methoxynaphthalenesulfonamide-1 (m. p. 156–157°) with 7-methoxynaphthalenesulfonamide (m. p. 150–151°) was depressed to 146–147.5°. [u] Recorded m. p. 167°, Witt and Schneider, *Ber.*, **34**, 3182 (1901). [v] Recorded m. p. 155°, Lapworth, *Chem. News*, **71**, 206 (1895). [w] Recorded m. p. 158–160°, ref. *r*.

Experimental

The melting points reported in this paper are uncorrected. They were determined on a standard rod form 360° melting point thermometer in a copper melting point block of the Berl and Kullmann type. Observation of the sample was facilitated by means of a small twenty-five power microscope permanently attached to the apparatus.

The purification of all materials used in this work was the same as stated in our earlier paper. The chlorosulfonylation procedure was identical with Procedure I of the earlier paper. Since with the ethers the intermediate sulfonyl chlorides were sometimes difficult to purify, their chloroform solution (resulting from Procedure I) was treated directly with dry powdered ammonium carbonate (2.0 g.) and the mixture evaporated to dryness. After washing the dry residue with several 10-cc. portions of cold distilled water (to remove ammonium chloride), the crude sulfonamide was recrystallized from dilute alcohol. If desired the sulfonamides may be purified by solution in 6 *N* alkali and reprecipitation with acid (removal of traces of sulfonamides).

The color usually observed during the reaction of chlorosulfonic acid with aromatic ethers varies from pale yellow to brown. In a few cases, however, other colors were noted which appear to have diagnostic value. A red color was observed in three cases, *viz.*, *o*-tolyl methyl ether, *o*-tolyl *n*-butyl ether and trimethylene glycol diphenyl ether. A blue color was observed in one case, *viz.*, *p*-methoxybiphenyl. Shades of green were noted with eight compounds, *viz.*, *o*- and *p*-chloroanisole, *o*- and *p*-chlorophenetole, α- and β-naphthyl methyl ether, and α- and β-naphthyl ethyl ether.

Satisfactory monochlorosulfonylation could not be obtained with six other compounds which were studied, *viz.*, *o*- and *p*-methoxybiphenyl, methyl and ethyl benzyl ether, diphenylene oxide, and 4,4′-dibromodiphenyl ether.

Summary

1. A method for the identification of aromatic ethers by chlorosulfonylation with chlorosulfonic acid has been shown to yield excellent results.

2. Of forty-two aromatic ethers examined, thirty-six yield monosulfonyl chlorides readily converted to characteristic sulfonamides.

3. Eighteen previously unreported sulfonamides prepared in the course of this work have been characterized and structures tentatively assigned.

CAMBRIDGE, MASS. RECEIVED JANUARY 23, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

Some Fluorine and Chlorine Derivatives of Sulfanilamidobenzenesulfonic Acids

BY C. M. SUTER AND ARTHUR W. WESTON[1]

Recently it has been reported that the three isomeric sulfanilamidobenzenesulfonic acids[2] have a marked therapeutic effect against β-hemolytic streptococcus infections in mice, the ortho compound being superior to sulfanilamide. In an extension of the investigation on fluorine derivatives of aromatic medicinals in progress in this Laboratory,[3] several fluorine and chlorine derivatives of sulfanilamidobenzenesulfonic acid have been prepared.

4-Fluoroaniline-2-sulfonic acid was obtained readily by sulfonation of *p*-fluoroacetanilide with 100% sulfuric acid, whereas *p*-fluoroaniline remains unchanged under the same conditions. When 15% oleum was employed as the sulfonating agent the anilide gave the isomeric 3-sulfonic acid. 4-Chloroacetanilide behaved in similar fashion.[4] This convenient method for obtaining the isomeric 4-haloanilinesulfonic acids was developed by Kreis[5] for the case of *p*-bromoacetanilide. Both acids have been obtained[6] by direct sulfonation of *p*-chloroaniline with 15% oleum. The structures of the sulfonic acids were determined by bromination in aqueous solution, sulfonic acid groups ortho to amino groups under-

(1) Sharp and Dohme Fellow, 1938–1939.

(2) Crossley, Northey and Hultquist, THIS JOURNAL, **60**, 2220 (1938). References to previous literature on sulfanilamide are listed here.

(3) Suter, Lawson and Smith, THIS JOURNAL, **61**, 161 (1939); Suter and Weston, *ibid.*, **61**, 2317, 2556 (1939).

(4) Scott and Cohen, *J. Chem. Soc.*, **123**, 3190 (1923); see also Paal, *Ber.*, **34**, 2753 (1901).

(5) Kreis, *Ann.*, **286**, 381 (1895).

(6) Claus and Mann, *Ann.*, **265**, 93 (1891); see also Fischer, *Ber.*, **24**, 3196 (1891); Armstrong, *ibid.*, **25R**, 752 (1892).

going replacement with halogen[7] whereas in meta sulfonic acids the sulfo substituent is unaffected.[8]

The sulfonic acids were condensed with *p*-acetaminobenzenesulfonyl chloride in alkaline solution,[2] and the acetyl group removed by alkaline or acid[9] hydrolysis, the latter giving the better results.

The sodium salts of the sulfanilamidobenzenesulfonic acids and also N-sulfanilyl-4-fluoroaniline were tested for their therapeutic action against Streptococcus infections in white mice.[10]

None of the compounds evidenced any therapeutic effect when administered orally in daily doses of 10 mg. per 20 g. mouse for four days, except the N-sulfanilyl-4-fluoroaniline and this was much less effective than sulfanilamide. The sodium sulfonates were further tested against Type I Pneumococcus infections, also in white mice, employing 20 mg. per dose. Doses were administered simultaneously with the inoculation of the organisms, seven hours later and then at 24-hour intervals for a total of six doses in five days.

Here also the results showed an absence of therapeutic effect. Crossley, Northey and Hultquist[2] have shown that the presence of a methyl, ethoxyl or hydroxyl attached to the ring bearing the sulfonic acid group nullifies the therapeutic activity of otherwise active compounds. Fluorine and chlorine are in the same category.

Experimental

Materials.—*p*-Fluoroacetanilide[11] melting[12] at 150–151° and *p*-chloroacetanilide were obtained in 80% yields by acetylation of *p*-fluoroaniline in aqueous solution with acetic anhydride at 50°. The *p*-acetaminobenzenesulfonyl chloride was the crude product obtained in the usual manner.

4-Fluoro- and 4-Chloroaniline-2-sulfonic Acids.—A mixture of 10.7 g. (0.07 mole) of *p*-fluoroacetanilide and 7 g. (0.07 mole) of 100% sulfuric acid was heated until the solid melted and kept at this temperature until acetic acid was no longer evolved. The thick paste was then heated in an oil-bath at 170–180° for two hours, cooled and mixed with water. Recrystallization from hot water (Darco) gave 8.6 g. (64%) of white flaky crystals which decomposed above 310°.

Anal. Calcd. for $C_6H_6O_3NSF$: neut. equiv., 191.1. Found: neut. equiv., 190.8.

4-Chloroaniline-2-sulfonic acid[4,6] was obtained in a 49% yield by a similar procedure as fine white needles which decomposed above 325°.

Anal. Calcd. for $C_6H_6O_3NSCl$: neut. equiv., 207.5. Found: neut. equiv., 206.9, 206.6.

Bromination of 0.5 g. of 4-fluoroaniline-2-sulfonic acid in aqueous solution with excess 5% aqueous bromine gave 0.6 g. of a slightly pink solid which crystallized from dilute acetic acid as white needles melting at 64–65°. A mixture of this with the 2,6-dibromo-4-fluoroaniline obtained from *p*-fluoroaniline, m. p. 63–64°, showed no depression of the melting point.

Anal.[13] (Kjeldahl) Calcd. for $C_6H_4NBr_2F$: N, 5.21. Found: N, 5.09.

Bromination of 4-chloroaniline-2-sulfonic acid similarly gave 2,6-dibromo-4-chloroaniline, m. p. 94.5–95.5°. This melting point is about the average of those given in the literature for this compound.[14]

4-Fluoro- and 4-Chloroaniline-3-sulfonic Acids.—A mixture of 10.7 g. (0.07 mole) of 4-fluoroacetanilide and 65 ml. of 15% oleum was heated to 130° where frothing occurred and the temperature rose to 145°. After fifteen minutes at 140–145° the mixture was allowed to cool, poured on ice and the solid crystallized from hot water using decolorizing carbon. The yield of fine white needles was 8.4 g. (63%). These decomposed above 310°.

Anal. Calcd. for $C_6H_6O_3NSF$: neut. equiv., 191.1. Found: neut. equiv., 190.7.

4-Chloroaniline-3-sulfonic acid was obtained in 30–34% yield. It crystallized in white needles which decomposed above 310°.

Anal. Calcd. for $C_6H_6O_3NSCl$: neut. equiv., 207.5. Found: neut. equiv., 206.6.

Bromination of an aqueous solution containing 0.5 g. of the 4-fluoroaniline-3-sulfonic acid gave no precipitate. Evaporation of the solution to dryness gave a solid which was very soluble in water and alcohol but crystallized from concentrated hydrochloric acid. It was not obtained in a high state of purity. The basic properties of the amine group are here so completely lost that internal salt (dipolar ion) formation does not occur.

Anal. Calcd. for $C_6H_4O_3SNBr_2F$: neut. equiv., 349. Found: neut. equiv., 342.

Bromination of the 4-chloroaniline-3-sulfonic acid likewise gave no precipitate, confirming its structure. The anhydrous bromosulfonic acid was hygroscopic but the nature of the resulting hydrate was not determined. The compound crystallized as fine white needles which decomposed above 310°.

Anal. Calcd. for $C_6H_4O_3NSClBr_2$: neut. equiv., 365.5. Found: neut. equiv., 370, 372.

N-Sulfanilyl-4-fluoroaniline.—To a well-stirred mixture of 8.9 g. (0.08 mole) of *p*-fluoroaniline, 1.6 g. (0.015 mole)

(7) Limpricht, *Ann.*, **181**, 193 (1876); *Ber.*, **9**, 474 (1876).

(8) The two sulfonating agents lead to different products even though acetic acid is lost in both reactions. One explanation for this is that when the theoretical amount of 100% sulfuric acid is employed the first-formed phenylaminosulfonic acid rearranges when heated to 170–180°, while with the excess oleum the phenylaminosulfonic acid is sulfonated by the excess reagent. This is substantiated by the fact that *p*-fluoroaniline sulfate remains unchanged at 170–180° as already mentioned.

(9) Kolloff, THIS JOURNAL, **60**, 950 (1938); Bauer, *ibid.*, **61**, 613 (1939).

(10) We are much indebted to Dr. Maurice L. Moore and Mr. G. W. Webster of the Technical Division of Sharp and Dohme for these tests.

(11) Schiemann and Pillarsky, *Ber.*, **62B**, 3041 (1929).

(12) All melting points are corrected.

(13) Analysis by Mr. E. Washburn of this Laboratory.

(14) Chattaway and Orton, *J. Chem. Soc.*, **79**, 825 (1901); Zincke, Heuser and Möller, *Ann.*, **333**, 338 (1904); Reed and Orton, *J. Chem. Soc.*, **91**, 1552 (1907); Gilbert, THIS JOURNAL, **48**, 2242 (1926).

of sodium carbonate and 60 ml. of water, was added simultaneously and gradually 18.7 g. (0.08 mole) of *p*-acetaminobenzenesulfonyl chloride and enough 30% sodium hydroxide to maintain a *p*H of about 10. Stirring was continued for thirty minutes after the additions were complete and then 8 g. of solid sodium hydroxide was added and the mixture refluxed for ninety minutes. Exact neutralization gave 10 g. (47%) of the anilide which after crystallization from dilute methanol melted at 163–164°. Considerable unchanged *p*-fluoroaniline was recovered.

Anal. (Kjeldahl) Calcd. for $C_{12}H_{11}O_2SN_2F$: N, 10.53. Found: N, 10.8.

Sulfanilamidofluoro- and -chlorobenzenesulfonic Acids.—*p*-Acetaminobenzenesulfonyl chloride was condensed with the aminosulfonic acids essentially according to the procedure of Crossley, Northey and Hultquist,[2] and the sulfanilamido compounds were isolated as the free acids. The sodium salts of these were very soluble in water. The yields and analyses are summarized in Table I.

TABLE I

Compound, -benzenesulfonic acid	Yield,[a] %	Decompn. temp., °C.	Neutral eq.[b] Calcd.	Found
2-Sulfanilamido-5-fluoro-	14[c]	285	346	343
5-Sulfanilamido-2-fluoro-	42	260	346[d]	345
2-Sulfanilamido-5-chloro-	20[c]	300	380.5[e]	383
5-Sulfanilamido-2-chloro-	57	310	362.5	360

[a] These percentages do not take into account unreacted starting materials which were recovered. [b] The indicator used was methyl red–methylene blue. [c] The low yields were partly due to the low solubilities of the original sodium sulfonates. [d] This compound crystallized as the monohydrate. *Anal.* Calcd. for $C_{12}H_{11}O_5N_2S_2F \cdot H_2O$: neut. equiv., 364. Found: neut. equiv., 361.2. [e] This compound crystallized as the monohydrate. *Anal.* Calcd. for $C_{12}H_{11}O_5N_2S_2Cl \cdot H_2O$: H_2O, 4.72. Found: H_2O, 4.89. The dry material absorbed water rapidly when exposed to the air.

Summary

The isomeric 4-fluoroaniline- and 4-chloroaniline-sulfonic acids have been prepared. The sulfanilamidohalobenzenesulfonic acids prepared from these did not exhibit therapeutic action against Streptococcus and Type I Pneumococcus infections in white mice. N-Sulfanilyl-4-fluoroaniline showed a slight effect against Streptococcus infections.

EVANSTON, ILLINOIS RECEIVED DECEMBER 16, 1939

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF COLORADO]

A Series of 2-Methyl-5-alkyl-4,6-dihydroxypyrimidines

BY LIVINGSTON P. FERRIS II* AND ANTHONY R. RONZIO

E. L. Pinner[1] prepared 2-phenyl-4,6-dihydroxypyrimidine by the condensation of benzamidine with malonic ester. Dox and Yoder[2] continued this investigation obtaining more members of the same series. At this time they pointed out that the condensation using aliphatic amidines had not been tried. Remfry[3] discovered a reaction in which malonamide condensed with substituted malonic esters to give pyrimidines, identical in structure to those which theoretically should form if aliphatic amidines successfully condensed with substituted malonic esters.

We have investigated this reaction using acetamidine and substituted malonic esters in the presence of sodium alcoholate and have found that the expected pyrimidines are formed. The first six members of the series have been prepared for the purpose of a pharmacological study. Absorption spectra data were taken for the first member of the series.

(*) Now at Colorado Experiment Station, Ft. Collins, Colo.

(1) E. L. Pinner, *Ber.*, **41**, 3517 (1908).

(2) A. W. Dox and L. Yoder, THIS JOURNAL, **44**, 361 (1922).

(3) F. G. P. Remfry, *J. Chem. Soc.*, **99**, 610 (1911).

Experimental Part

Acetamidine hydrochloride, one-eighth mole, and either the redistilled malonic ester or the redistilled monoalkyl substituted malonic ester, one-twentieth mole, were added in the order given, to about 150 cc. of absolute alcohol in which had been dissolved 3.3 g. of sodium (slight excess over one-eighth mole). After standing for two to three days, the solution was exactly neutralized with concentrated hydrochloric acid. Enough water to dissolve the precipitated sodium chloride was then added. The un-

TABLE I

2-METHYL-5-ALKYL-4,6-DIHYDROXYPYRIMIDINES

5 Occupied by	Yield, %	Empirical formula	% C Calcd.	% C Found	% H Calcd.	% H Found	% N Calcd.	% N Found
H	43	$C_6H_6N_2O_2$	47.62	47.61	4.79	5.07	22.22	22.22
				47.64		4.99		22.14
Methyl	18	$C_6H_8N_2O_2$	51.42	51.45	5.75	6.08	19.99	20.00
				51.40		6.03		19.90
Ethyl	15	$C_7H_{10}N_2O_2$	54.53	54.52	6.54	6.62	18.17	18.09
				54.49		6.72		18.28
n-Propyl[a]	22	$C_8H_{12}N_2O_2$	57.13	57.17	7.19	7.29	16.66	16.79
				57.21		7.33		16.73
n-Butyl	33	$C_9H_{14}N_2O_2$	59.32	59.52	7.74	7.80	15.38	15.32
				59.51		7.86		15.49
n-Amyl	26	$C_{10}H_{16}N_2O_2$	61.20	61.28	8.22	8.40	14.28	14.32
				61.30		8.32		14.33

[a] First prepared by Remfry, ref. 3.

dissolved pyrimidine was filtered, decolorized in boiling glacial acetic acid, and reprecipitated by the addition of ether. After several reprecipitations in this manner, the pyrimidines left no residue when ignited and, after drying over phosphorus pentoxide *in vacuo* at 100°, gave correct analyses.

The pyrimidines prepared, as well as experimental and analytical data, are shown in Table I.

The pyrimidines are colorless compounds, slightly soluble in water, the solubility decreasing with increase in molecular weight. Definite melting points were not shown by any member of the series but sublimation took place between 260–350°. In a sealed tube they decomposed without melting.

The pyrimidines required a special Dumas method for correct nitrogen analyses.

The absorption spectra curves for 2-methyl-4,6-dihydroxypyrimidine in neutral, acid and basic solution are shown in Fig. 1. The curves show a maxima at about 2600 Å. The absorption spectrum curve for this pyrimidine in neutral solution shows a slight break at 2700 Å.

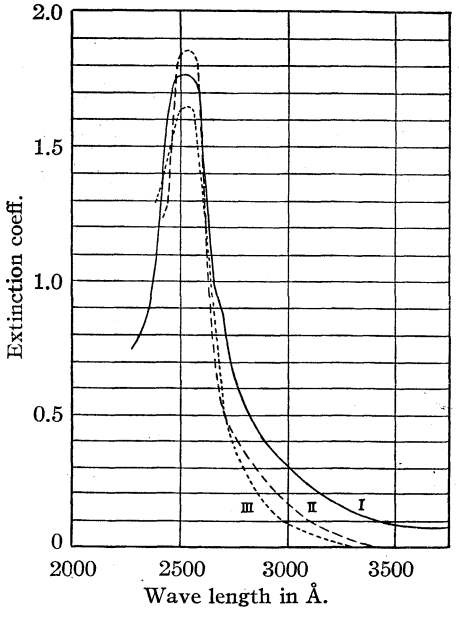


Fig. 1.—2-Methyl-4,6-dihydroxypyrimidine: I, 1.06 mg./50 cc. H_2O; II, 1.01 mg./50 cc. H_2O, 1 cc. concd. HCl; III, 2.06 mg./50 cc. H_2O, 1 cc. 50% KOH. 1-Cm. cell used throughout.

For purposes of comparison the absorption spectrum of 2-phenyl-5-*n*-butyl-4,6-dihydroxypyrimidine in alcoholic solution was taken (Fig. 2). A slight break in the curve at 3350 Å. not reported by Dox and Yoder[2] was observed.

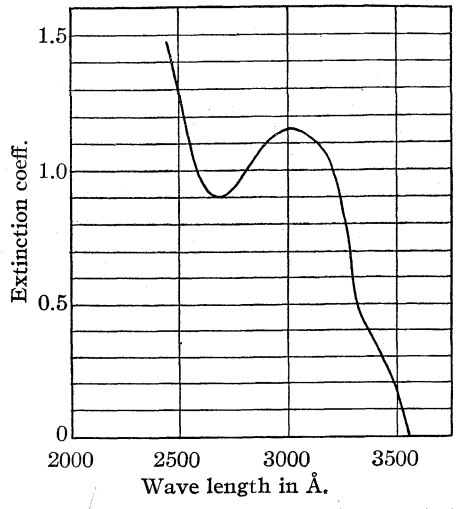


Fig. 2.—2-Phenyl-5-*n*-butyl-4,6-dihydroxypyrimidine: 1.61 mg./50 cc. ethyl alcohol, 1-cm. cell.

These data were obtained using a Hilger E3 spectrograph, Hilger sector photometer and Eastman Panchromatic plates. An under water spark served as light source.

Summary

A series of 2-methyl-5-alkyl-4,6-dihydroxypyrimidines has been prepared.

Absorption spectra curves of 2-methyl-4,6-dihydroxypyrimidine in neutral, acid and basic solution are shown.

The absorption spectrum curve of 2-phenyl-5-*n*-butyl-4,6-dihydroxypyrimidine in neutral solution has been retaken.

BOULDER, COLO. RECEIVED JANUARY 2, 1940

[CONTRIBUTION FROM THE AMMONIA DEPARTMENT OF E. I. DU PONT DE NEMOURS & COMPANY, INC.]

Analytical Procedures Employing Karl Fischer Reagent.[1] IV. The Determination of Acid Anhydrides

BY DONALD MILTON SMITH, W. M. D. BRYANT AND J. MITCHELL, JR.

Many of the older methods of determining anhydrides of carboxylic acids do not distinguish sharply between anhydride and free acid. A procedure developed by the senior authors[2] avoids this difficulty by a scheme based on separate titrations with sodium hydroxide and sodium methylate. This method, however, is subject to interference by easily hydrolyzed esters and certain acidic inorganic compounds.

Recent studies of the versatile Karl Fischer reagent have led to the development of new quantitative procedures for hydroxyl[3] and carboxyl[4] compounds, and now a similar method for anhydrides has been completed. This application depends on the hydrolysis of the anhydride in acetic acid solution under the influence of boron trifluoride. Introduction of a known quantity of water, somewhat in excess of stoichiometric requirements, and determination of the residual water by titration with Karl Fischer reagent permit an exact correlation of anhydride content with water removal according to the equation, $RCOOCOR + H_2O = 2RCOOH$.

Unlike the acidimetric procedures free acids do not react and easily hydrolyzed esters remain unchanged due to the relatively low water concentration and the great excess of acid present. Substances interfering with the hydroxyl procedure[3] also affect the new anhydride method.

A group of thirteen anhydrides were analyzed by this method and checked by the sodium hydroxide–sodium methylate procedure.[2] The precision and accuracy are usually within ±0.3%. Experimental results are given in Table I.

Although glutaric anhydride hydrolyzed quantitatively, other anhydrides derived from dibasic acids failed to react completely. Results with maleic, phthalic and succinic anhydrides showed 0, 11 and 91% hydrolysis, respectively.

Changes in catalyst concentration had a marked effect on these anhydrides, as indicated by data given in Table II.

TABLE I

ANALYTICAL DATA FOR ANHYDRIDES

Anhydride		% of theoretical —CO—O—CO— Catalytic hydrolysis	NaOH–NaOCH₃
Acetic	(6)[a]	100.0 ± 0.2	99.9
Propionic	(4)	97.0 ± 0.3	97.2
n-Butyric	(2)	85.5 ± 0.5	85.4
Crotonic	(2)	89.6 ± 0.0	
n-Valeric[b]	(2)	2.0 ± 0.4	1.9
Caproic	(2)	78.6 ± 0.4	78.4
Heptylic	(2)	92.0 ± 0.3	92.1
Glutaric	(2)	95.3 ± 0.3	95.5
Benzoic	(4)	99.0 ± 0.3	99.2
Furoic	(4)	95.1 ± 0.5	94.8

[a] Figures in parentheses indicate number of individual determinations. [b] Old sample, mainly *n*-valeric acid, used to test method in low anhydride range.

TABLE II

HYDROLYSIS OF ANHYDRIDES USING CATALYST SOLUTIONS OF VARIOUS CONCENTRATIONS[a]

Anhydride	% Hydrolysis[b] 100 g.	50 g.	25 g.	15 g.	5 g.	0 g.
Acetic	100.0		98.0			
Caproic	100.0		97.0			
Succinic	91.2	95.4	99.5	93.2	63.9	27.1
Maleic	0.0	1.0	2.3	42.0	36.5	24.5
Glutaric	100.0	100.0	100.0	100.0	93.7	47.6
Phthalic	10.9	13.8	15.5	18.7	16.9	14.0

[a] Catalyst concentration expressed as grams per liter of solution. [b] All results corrected for inert diluents.

From an examination of Table II it is evident that in isolated cases a procedure could be devised for distinguishing between certain anhydrides. For such cases control experiments should be run as a means of fixing the relative error.

Although the anhydrides in dioxane solution react only partially with the carboxyl catalyst,[4] the aliphatic acid anhydrides in methanol solution react quantitatively. The probable reactions

$(RCO)_2O + CH_3OH \longrightarrow RCOOCH_3 + RCOOH$ and
$RCOOH + CH_3OH \longrightarrow RCOOCH_3 + H_2O$

liberate one mole of water per mole of anhydride. Representative results, after correction for free acidity, are given in Table III.

It is interesting to note that maleic and succinic anhydrides react stoichiometrically under these conditions, whereas hydrolysis, as stated

(1) This reagent, discussed in detail in the first paper of the series (Smith, Bryant and Mitchell, THIS JOURNAL, **61**, 2407 (1939)), consists of a solution of iodine, sulfur dioxide and pyridine in methanol. It is specific for water.

(2) Smith and Bryant, *ibid.*, **58**, 2452 (1936).

(3) Bryant, Mitchell and Smith, *ibid.*, **62**, 1 (1940).

(4) Mitchell, Smith and Bryant, *ibid.*, **62**, 4 (1940).

TABLE III

ANALYTICAL DATA FOR ANHYDRIDES

Anhydride	% of Theoretical —CO—O—CO Carboxyl catalyst[4]	NaOH–NaOCH$_3$
Acetic	100.3 ± 0.3	99.9
Propionic	97.1 ± 0.3	97.2
Succinic	94.2 ± 0.4	94.5
Maleic	90.0 ± 0.2	90.0

above, is incomplete. As would be expected, the aromatic anhydrides only partially react.[4]

In the course of the present research several nitrogen bases, including pyridine and tri-*n*-butylamine, were substituted for the acid catalyst solution. It was previously thought that hydrolysis of acid anhydrides in the presence of slightly more than the theoretical quantity of water would be complete where large excesses of these bases are used. However, the anhydrides studied, with one exception, failed to react completely on heating at 100° for periods up to four hours. The exception was acetic anhydride, which hydrolyzed quantitatively in one hour at 60° using pyridine as the base.

Some experiments on the dehydration of glacial acetic acid by means of the anhydride without any catalyst or acid acceptor are of interest. The acid containing about half a per cent. of water was mixed with slightly more than the calculated amount of acetic anhydride required to produce anhydrous acid. The mixture was allowed to stand at room temperature and was analyzed at intervals by the Karl Fischer procedure. The following results were obtained.

Wt. % H_2O	Time, standing at room temperature
0.54	0
.52	4 min.
.47	1.5 hrs.
.36	4.5
.08	21
.015	48

The reaction is slow but proceeds to completion without a catalyst.

Experimental

Compounds Investigated.—With two exceptions all of the anhydrides studied in the present investigation were Eastman Kodak Co. products, and were used without further purification. The *n*-valeric anhydride was an old sample which was used primarily to determine the precision of the method for small quantities of anhydride.

Phthalic anhydride ("Aero" Brand) was obtained from American Cyanamide Corp., and glutaric anhydride was prepared from the acid by the method of Mol.[5] In order to prevent adsorption of water vapor, a simple "dry manipulator" was used to dispense the solid anhydrides.[2]

Analytical Procedure.—Five to 10 ml. of sample is weighed into a 100-ml. g. s. volumetric flask about one-third filled with Merck C. P. glacial acetic acid. The solution is adjusted to volume with more acetic acid, after thermostating at 25 ± 1°. Five ml. (using calibrated pipet) of this solution is transferred to a 250 ml. g. s. volumetric flask and 20 ml. of catalyst solution added.[6] The flask together with a blank containing 5 ml. of acetic acid and 20 ml. of catalyst solution is placed in a water-bath at 60 ± 1°. The stopper is loosened momentarily to allow for expansion of included air, tightened and heated for two hours. After the flasks have been allowed to cool spontaneously to room temperature and 5 ml. of Baker C. P. pyridine is added, the excess water is titrated with Karl Fischer reagent. The total anhydride is measured by the difference between the water added, *i. e.*, the water content of the blank, and the water found by titration after reaction.

Summary

1. A quantitative procedure for the determination of carboxylic acid anhydrides has been described. The method depends on complete hydrolysis of the anhydride in the presence of excess water and subsequent titration of the residual water with Karl Fischer reagent. It is best suited for the determination of acyclic aliphatic anhydrides.

2. Analytical data for ten anhydrides are tabulated.

WILMINGTON, DELAWARE RECEIVED JANUARY 9, 1940

(5) Mol, *Rec. trav. chim.*, **26**, 373 (1907).

(6) The catalyst solution is prepared by dissolving 100 g. of boron trifluoride gas and 4 ml. of water in sufficient Merck C. P. glacial acetic acid to make one liter of solution. Boron trifluoride of suitable quality can be obtained in cylinders from the Ohio Chemical Company, Cleveland, Ohio.

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, UNIVERSITY OF WASHINGTON]

Solubility of Sulfur Dioxide in Water

BY W. L. BEUSCHLEIN AND LOUIS O. SIMENSON

A knowledge of the equilibrium solubilities of sulfur dioxide in water is essential in connection with calculations and research work on absorption. In 1925, Sherwood[1] presented some values calculated from the data of previous workers and in 1928 the "International Critical Tables"[2] published some values. W. Boyd Campbell and O. Maass[3] have determined the solubility of sulfur dioxide in water for the temperature range 25–120° and the concentration range 1.00–7.40%. O. M. Morgan and O. Maass[4] have reported the solubility of sulfur dioxide in water at temperatures between 0 and 25°. This investigation was undertaken to check and extend existing data.

Experimental

The investigation was carried out with the apparatus shown in Fig. 1, consisting of a vertical glass solution tube containing a buoyant stirrer C and a mercury relay G attached to the upper part of the tube. The stirrer contained an iron core B and was activated by means of a solenoid A circumscribing the solution tube, the solenoid being intermittently energized. The whole apparatus was immersed below the oil level E of the temperature controlling bath. The solutions to be run were prepared by passing sulfur dioxide through freshly boiled, distilled water until saturated and then diluting to the desired concentration.

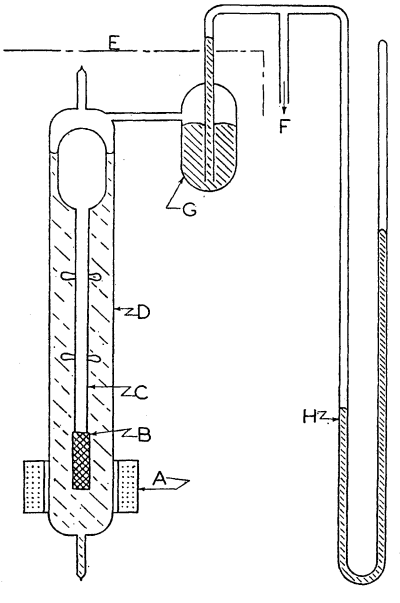


Fig. 1.

The solution was run into the apparatus through the small bottom tube shown in Fig. 1. The inflowing solution was allowed to fill completely all the free space in the solution tube and mercury pressure relay, displacing all the air through the small tube at the top. The end of the upper small tube, previously having been drawn to a hair-like capillary, was sealed with a small flame. The absence of air in the apparatus was indicated by the liquid completely filling the sealed capillary after the latter had cooled. Next, some of the solution was drawn out of the apparatus through the bottom tube by which it entered, great care being taken to maintain equal pressures on each side of the mercury pressure relay. This was done by branching the suction line, running one branch to the external side of the relay and drawing the solution out of the other. Just enough solution was removed to form a vapor space such that the stirrer could function. At this time, a sample of the solution was taken for analysis as to concentration and density. The bottom filling tube was flamed quickly and drawn to a seal at a point where it had previously been drawn to a very fine capillary.

The whole apparatus was then immersed into a thermostated oil-bath maintained to within ±0.2° and held constant for ten minutes before a pressure reading was recorded. The pressures were read to within ±0.5 mm. of mercury on a mercury, sealed in manometer H.

The external pressure on the relay was balanced in such a manner that the mercury head in the relay was constant throughout the whole run. This head, as shown in Fig. 1, was measured with a cathetometer. No particular temperature was selected for a reading, but approximately equal intervals were taken to ensure equilibrium conditions; the temperature of the bath was raised very slowly, one run consuming five hours in going from 20 to 110°.

The pressures were checked by taking measurements as the bath cooled. At the end of the run, a sample of the solution was withdrawn, analyzed and found to check with that at the beginning.

The sulfur dioxide used in this work was "refrigeration dry" and warranted by the manufacturer to be 99.99% pure. No trace of trioxide was found and freshly boiled, distilled water was used in making up the solutions.

The method of analysis consisted of running the sulfur dioxide solution into an excess of iodine with constant agitation and back titrating with sodium thiosulfate.[5] A check was made on the method of pressure measurement by determining the vapor pressure of water. The results

(1) T. K. Sherwood, *Ind. Eng. Chem.*, **17**, 745–747 (1925).

(2) "International Critical Tables," Vol. III, McGraw-Hill Book Co., New York, N. Y., p. 302 (1928).

(3) W. Boyd Campbell and O. Maass, *Can. J. Res.*, **2**, 42–64 (1930).

(4) O. M. Morgan and O. Maass, *Can. J. Res.*, **5**, 162–179 (1931).

(5) F. P. Treadwell and W. T. Hall, "Analytical Chemistry," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1935, pp. 88–89.

agreed with accepted values[6] within the limits of accuracy of the thermometer and manometer.

Experimental Results

In Table I are given the densities at 23° of the sulfur dioxide solutions used for the vapor pressure determinations. In Table II are given the partial vapor pressure data for the four concentrations, which are expressed as grams of sulfur dioxide in 100 g. of water. The partial vapor pressure of sulfur dioxide above the solution was calculated as the total pressure minus the vapor pressure of pure water at the temperature of the experiment.

TABLE I

DENSITIES OF SULFUR DIOXIDE SOLUTIONS

Temp., °C.	Concn., g. SO_2 per 100 g. H_2O	Density, g./cc.
23.0	0.51	1.0019
23.0	1.09	1.0043
23.0	4.36	1.0199
23.0	7.45	1.0338

TABLE II

PARTIAL VAPOR PRESSURE OF THE SYSTEM SULFUR DIOXIDE–WATER

Temp., °C.	SO_2 press., mm.	Temp., °C.	SO_2 press., mm.
0.51 g. SO_2/100 g. H_2O		1.09 SO_2/100 g. H_2O	
35.6	49.0	26.8	70.5
41.0	57.0	33.6	96.0
47.0	70.0	39.4	124.5
52.0	80.0	44.2	147.0
62.6	118.0	50.6	178.0
71.0	150.0	61.6	245.0
78.6	185.0	67.4	280.5
85.0	215.5	73.4	327.5
92.2	250.0	79.2	372.0
99.0	285.5	86.4	445.5
105.2	320.5	98.4	510.0
111.8	358.0	100.6	600.0
113.0	367.5	106.6	668.0
4.36 g. SO_2/100 g. H_2O		7.45 g. SO_2/100 g. H_2O	
23.2	332.0	25.2	647.0
27.2	373.0	31.4	780.5
30.0	420.0	34.2	838.0
33.0	465.5	37.4	915.5
36.0	513.0	41.0	989.0
38.2	551.5	44.0	1069.0
42.2	619.0	47.2	1152.5
45.2	680.5	50.4	1255.5
48.2	741.0	54.4	1391.0
52.0	818.0	55.6	1443.5
55.3	896.0		
58.4	970.5		
61.2	1036.5		
63.0	1085.5		
67.2	1200.5		
70.8	1292.0		
72.4	1323.5		

(6) "International Critical Tables," Vol. III, McGraw-Hill Book Co., New York, N. Y., p. 212.

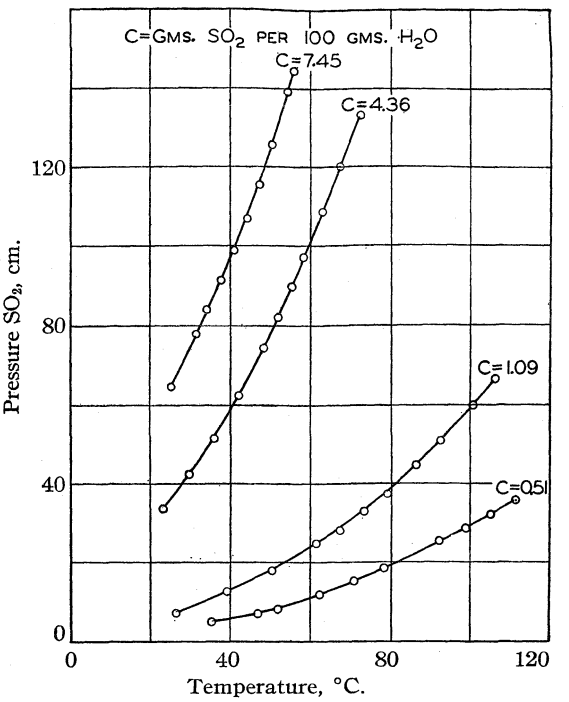


Fig. 2.

In the "International Critical Tables" the partial pressure of the water was calculated using Fulda's values for the ionization constant of sulfurous acid; however, this was neglected in this work because the effect is within the experimental error of the apparatus.

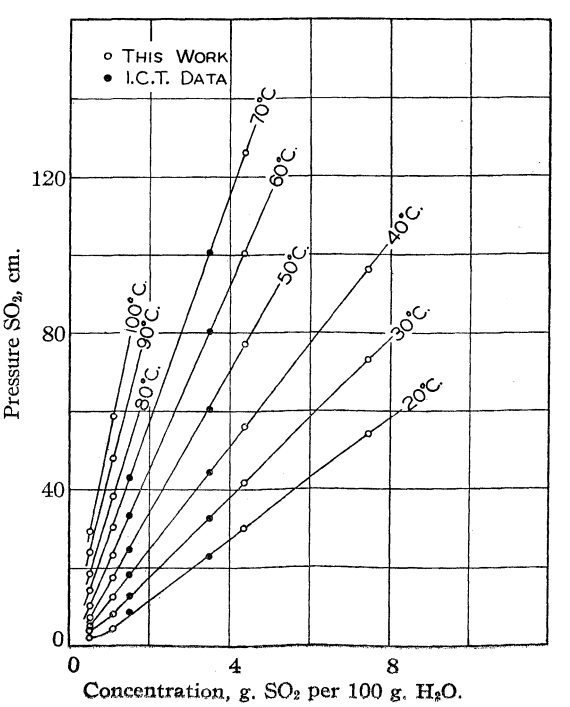


Fig. 3.

The vapor pressure data are shown graphically in Fig. 2 and Fig. 3 shows the isotherms plotted by taking values from Fig. 2. According to the results of Fig. 3, the concentration is a linear function of the sulfur dioxide content except at the lower temperatures of the low concentrations.

Summary

1. Partial vapor pressures for sulfur dioxide in the system sulfur dioxide in water have been determined over the temperature range 20–110° and total pressure range of 10 to 150 cm. of mercury for concentrations of 0.51, 1.09, 4.36 and 7.45 grams of sulfur dioxide in 100 grams of water.

2. These data extend the values of the International Critical Tables and show excellent agreement over the coincident ranges.

SEATTLE, WASHINGTON RECEIVED JANUARY 15, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF COLUMBIA UNIVERSITY]

The Energy and Entropy of Activation of the Hydrolysis of Ethyl Orthoformate in Deuterium Oxide

BY FRANK BRESCIA* AND VICTOR K. LAMER

Introduction

Current theory of chemical kinetics recognizes the energy of activation and the entropy of activation as the important factors governing the specific rate of a reaction in the presence or absence of a catalyst. LaMer[1] derived the equation

$$k = e^{-\Delta H^*/RT}\, e^{\Delta S_{act}/R}\, Z^\circ \qquad (1)$$

or

$$\log k = -(\Delta H^*/2{\cdot}3RT) + B \qquad (2)$$

where

$$\Delta H^* = RT^2 \frac{\mathrm{d} \ln k}{\mathrm{d}T} \qquad (3)$$

from Tolman's statistical treatment[2] and a collisional mechanism for formation of the intermediate complex. In Eyring's treatment[3]

$$k = \kappa e^{-\Delta H^*/RT}\, e^{\Delta S^*/R}\, RT/Nh \qquad (4)$$

Hence

$$B = \frac{\Delta S^*}{2{\cdot}3R} + \log \kappa \frac{T}{Nh} \qquad (5)$$

Classical theory ascribed the entropy contribution $\Delta S^*/2{\cdot}3R$, to a so-called "steric or probability factor" expressed by P in the equation

$$k = e^{-\Delta H^*/RT}\, PZ^\circ \qquad (6)$$

The symbols have been defined in the literature cited.

Many previous investigators[4] have shown that the deuterium ion is a more effective catalyst than the hydrogen ion in many reactions. A noteworthy exception is the mutarotation of glucose.[5]

This increase in reactivity has been ascribed[6] to an increase in the equilibrium constant for the process Substrate + H^+ = SH^+ on passing from H^+ to D^+. The ratio of the equilibrium constants would be equal to the measured ratio for the specific rates. This is apparent when the theoretical equations for the rate constant are expressed in the form

$$k = \nu K^* \qquad (7)$$

where ν is a frequency term. Several investigators[7] have expressed the view that the increase in the concentration of the deutero complex can be accounted for by the lower zero point energy of the d-complex or, hence, by an observable difference in the activation energies, $\delta\Delta H^*$, of the two systems. ($\delta\Delta H^* = \Delta H^*_H - \Delta H^*_D$.) This is equivalent to the assumption that the ΔH^* factor

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(1) LaMer, *J. Chem. Phys.*, **1**, 289 (1933); LaMer and Kamner, THIS JOURNAL, **57**, 2662, 2669 (1935); Liotta and LaMer, *ibid.*, **60**, 1972 (1938).

(2) Tolman, "Statistical Mechanics," Chemical Catalog Co., New York, 1927, Chaper 21.

(3) Eyring, *J. Chem. Phys.*, **3**, 107 (1935); Wynne-Jones and Eyring, *ibid.*, **3**, 492 (1935).

(4) Moelwyn-Hughes and Bonhoeffer, *Naturwissenschaften*, **22**, 174 (1934); Gross, Suess and Steiner, *ibid.*, **22**, 662 (1934); Schwartz, *Akad. Anzeiger*, 26 April, 1934, Wien; Gross, Steiner and Suess, *Trans. Faraday Soc.*, **32**, 883 (1936); Hornel and Butler, *J. Chem. Soc.* (London), 1361 (1936); Gross, Steiner and Krauss, *Trans. Faraday Soc.*, **32**, 877 (1936); Reitz, *Naturwissenschaften*, **24** 814 (1936); *Z. physik. Chem.*, **179A**, 119 (1937); Brescia and LaMer, THIS JOURNAL, **60**, 1962 (1938); Nelson and Butler, *J. Chem. Soc.*, 957 (1938); Reitz, *Z. physik. Chem.*, **A183**, 371 (1939).

(5) Hammill and LaMer, *J. Chem. Phys.*, **2**, 891 (1934); **4**, 395 (1936).

(6) Moelwyn-Hughes, *Z. physik. Chem.*, **B26**, 272 (1934). LaMer, *Chem. Revs.*, **19**, 363 (1936); Bonhoeffer and Reitz, *Z. physik. Chem.*, **A179**, 135 (1937); Bonhoeffer, *Trans. Faraday Soc.*, **34**, 252 (1938); Wynne-Jones, *ibid.*, **34**, 245 (1938); *J. Chem. Phys.*, **2**, 381 (1934); Brescia and LaMer, THIS JOURNAL, **60**, 1962 (1938).

(7) Wynne-Jones, *J. Chem. Phys.*, **2**, 381 (1394); *Chem. Revs.*, **17**, 115 (1935); Halpern, *J. Chem. Phys.*, **3**, 456 (1935).

is solely responsible for the change in K^* and that the entropy of formation for the two complexes is identical. A test of this hypothesis by Gross, Steiner and Krauss,[8] who investigated the decomposition of diazoacetic ester catalyzed by protons and deutons, shows that the difference in the energies of activation ($\delta\Delta H^*$) is indeed largely responsible for the three-fold increase in the decomposition by deuterium ions. The marked decrease in the rate of reactions involving deuterium in the gas phase may also be explained satisfactorily in many cases on the basis of the lower zero point energy of the deuterium molecule, E_D^0.

However, $\delta E^0 = E_H^0 - E_D^0$, does not account for the reaction rate ratios observed in other gas phase reactions.[9] The resultant $\delta\Delta H^*$ based on δE^0 of the hydrogen and deuterium molecules may be augmented or partially compensated by a δE^0 for the light and heavy complexes or by a difference in the entropy of activation ($\delta\Delta S^* = \Delta S_H^* - \Delta S_D^*$) in forming the two complexes. Similarly, the difference in the ΔH^* factor ($\delta\Delta H^*$) in a liquid phase reaction involving a light and heavy complex may be augmented or compensated by a difference in the ΔS^* factor ($\delta\Delta S^*$).

The hypothesis that the entropy factor may often be of primary importance in determining the rate ratio on passing to D_2O is subjected to test with a study of the rate of hydrolysis of ethyl orthoformate at different temperatures.

Experiment and Calculations.—The rate constants, k, at constant buffer strength, 0.001 M Ac_2O/0.1 M NaAc, measured, in ordinary water and in a deuterium oxide mixture at 14.977 and 35.008°, by the dilatometric method previously used[10] to study the rate at 25°, are converted to specific rate constants by dividing k by the total hydrogen ion concentration. Hydrogen ion concentrations in ordinary water are obtained from the dissociation constants of protoacetic acid[11] at an ionic strength of 0.1; 2.85×10^{-5} at 35° and 2.81×10^{-5} at 15°.

The specific rate constant in the H_2O–D_2O mixture, k_m, is obtained from the concentrations of protons and deuterons calculated from the equations

$$K = \frac{1}{C_{D^+}}\left[\frac{2C_{Ac_2O}}{C_{Ac^-}}(K_H - K_M) + C_{D^+}\right] \quad (8)$$

and

$$K_M = \frac{(C_{H^+} + C_{D^+})C_{Ac^-}}{2C_{Ac_2O}} \quad (9)$$

Equation (8) is derivable from equations 2, 3, 4 of our previous work[10] and equation (9), this paper. $K = K_H/K_D$, where K_H is the dissociation constant of protoacetic acid and K_D is the dissociation constant of the deuteroacetic acid. K_M is the dissociation constant in the mixed waters. K is 3.39 at 15°, 3.26 at 35°; K_M is obtained from the ratios $K_H/K_M = 3.02$ at 15° and $= 2.91$ at 35°.[12]

The specific rate constant in pure deuterium oxide, k_{D^+}, is then obtainable from the equation

$$k = k_{H^+}\,C_{H^+} + k_{D^+}\,C_{D^+} \quad (10)$$

where k_{H^+} is the specific rate constant in ordinary water.

The energy of activation is obtained from equation (3), B from (2), and ΔS^* from (5) assuming, as usual, $\kappa = 1$. All results are summarized in Tables I and II. The value for the energy of activation in ordinary water is in substantial agreement with that of Harned and Samaras.[13]

TABLE I

Temp., °C.	$F_D = \Delta S/0.1079$	k	Specific rate constant	k_{D^+}/k_{H^+}
14.977	0.0	0.0129	2.30×10^4	
	0.925	.0107	5.75×10^4	
	1.00		6.22×10^4	2.70
35.008	0.0	.0782	1.37×10^5	
	0.917	.0564	2.88×10^5	
	1.00		3.16×10^5	2.31

TABLE II

	ΔH, kcal.	B	ΔS^*
H_2O	15.7 ± 0.2	16.3	7.83
D_2O	14.3 ± 0.2	15.7	4.90

Discussion

The observed difference in the energy of activation predicts a nine-fold increase in the rate in passing from ordinary water to deuterium oxide, whereas the observed increase is about threefold. The large decrease in ΔH_D^* is partially compensated by a decrease in the ΔS^* on deuterium substitution. Both factors are, therefore, important in explaining the observed increase in the rate of the hydrolysis of ethyl orthoformate in D_2O. The importance of an entropy of activation has already been emphasized for several ionic reactions,[14] and for the base catalyzed[15] decomposi-

(8) Gross, Steiner and Krauss, *Trans. Faraday Soc.*, **34**, 351 (1938).

(9) Urey and Teal, *Rev. Modern Phys.*, **7**, 34 (1935).

(10) Brescia and LaMer, THIS JOURNAL, **60**, 1962 (1938).

(11) Harned and Embree, *ibid.*, **56**, 1050 (1934); Harned and Hickey, *ibid.*, **59**, 1284 (1937).

(12) Brescia, LaMer and Nachod, *ibid.*, **62**, 614 (1940).

(13) Harned and Samaras, *ibid.*, **54**, 1 (1932).

(14) LaMer and Kamner, *ibid.*, **57**, 2662, 2669 (1935); LaMer and Miller, *ibid.*, **57**, 2674 (1935); Percival and LaMer, *ibid.*, **58**, 2413 (1936).

(15) Liotta and LaMer, *ibid.*, **60** 1967 (1938).

tion of nitramide in D_2O. The observed difference for the rate of mutarotation of glucose[16] in H_2O and D_2O is accounted for mainly by the change in the entropy term since $\delta \Delta H^*$ is zero within the experimental error.

Recently, Stern, Johnston and Clark[17] picture two general cases covering the effect of a catalyst on the reactant and the activated complex which may lead to positive or negative catalysis. A decrease in the energy of activation in passing from one solvent to another is taken to indicate that the catalyst has a greater tendency to combine with the activated complex than with the reactant and this effect is partly compensated by a decrease in ΔS^*. This mechanism corresponds to the explanation given previously that the increased rate in passing to D_2O is due to an equilibrium shift favoring the formation of the D-complex.

(16) Hammill and LaMer, *J. Chem. Phys.*, **4**, 395 (1936).
(17) Stern, Johnston and Clark, *J. Chem. Phys.*, **7**, 970 (1939).

Summary

1. The rate of hydrolysis of ethyl orthoformate has been measured at 14.977 and 35.008° in ordinary water and in deuterium water.

2. The observed difference in the energy of activation predicts a nine-fold increase in the rate; experimentally the increase is about threefold. The entropy of activation is, therefore, an important factor in determining the ratio of the two rates.

NEW YORK CITY RECEIVED DECEMBER 9, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF COLUMBIA UNIVERSITY]

The Temperature Dependence of the Dissociation Constant of Deuteroacetic Acid

BY FRANK BRESCIA,* VICTOR K. LAMER AND FREDERICK C. NACHOD*

Introduction

Current investigations of the activation energies for reactions involving deuteroacetic acid, for example, the hydrolysis of ethyl orthoformate[1] in ordinary water and deuterium oxide, require data for the dissociation constants of deuteroacetic acid which are comparable in precision with those available for the protoacetic acid. Some preliminary data for the dissociation constant of deuteroacetic acid obtained on severely limited quantities of solvent at 12.5°, 25° and 37.5° using the quinhydrone electrode[2] indicated a possible minimum, while the corresponding and well-established constants for protoacetic acid[3] exhibit a maximum. In general,[4] differences between the properties of the deutero and proto compounds tend to become less important at higher temperatures, since the differences in zero point energies ΔE^0 of the two hydrogens determine the properties as an exponential factor, exp. $[\Delta E^0/RT]$. Also, Rule and LaMer[5] have demonstrated that the temperature coefficient of the electromotive force of the cell $Pt/QQH_2\text{-}QQD$ HCl-DCl $(H_2O\text{-}D_2O)/AgCl\text{-}Ag$ involving the strong acid HCl–DCl is identical in pure H_2O and in pure D_2O. It is questionable, therefore, whether the temperature dependence of the two weak acids should be opposite in sign.

The determination of the dissociation constant of deuteroacetic acid at different temperatures has, therefore, been undertaken, using the conductance method.

Experimental

The equivalent conductances of sodium acetate, sodium chloride, hydrochloric acid and acetic acid solutions have been determined at 14.36, 25, 35 and 44.86°, for a solvent whose deuterium content, $F_D = S_g/0.1079$, where S_g is the difference in specific gravity of the solvent and of ordinary water, was approximately 0.925. A vacuum tube oscillator of the heat frequency type[6] and a Jones bridge[7] were employed. The constants, 0.4481 and 0.7017, of the two conductance cells, designed to be free from the Parker effect, were determined at 25° by the method of Kohlrausch. The temperatures were standardized with a Pt resistance thermometer, B. S. calibration.

The preparation of the salts, acetic anhydride,

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(1) Brescia and LaMer, THIS JOURNAL, **60**, 1962 (1938); *ibid.*, **62**, 612 (1940).
(2) Korman and LaMer, *ibid.*, **58**, 1396 (1936).
(3) Harned and Embree, *ibid.*, **56** 1050 (1934); Harned and Hickey, *ibid.*, **59**, 1284 (1937).
(4) Urey and Teal, *Rev. Modern Phys.*, **7**, 34 (1935).
(5) Rule and LaMer, THIS JOURNAL, **60**, 1974 (1938).
(6) Baker and LaMer, *J. Chem. Phys.*, **3**, 406 (1935).
(7) Dike, *Rev. Sci. Instruments*, **2**, 379 (1931).

constant boiling deuterochloric acid (DCl), purification of the water, and the details of the semi-micro technique have been described.[8]

Calculations.—The maximum equivalent conductances, Λ_0, for the strong electrolytes in H_2O–D_2O were calculated from the measured equivalent conductance, Λ_c, using the equation

$$\left(\frac{\Lambda_c}{\Lambda_0}\right)_{H_2O} = \left(\frac{\Lambda_c}{\Lambda_0}\right)_{D_2O} \qquad (1)$$

derivable from the Onsager equation and shown to be of satisfactory accuracy.[9] The ratios $(\Lambda_c/\Lambda_0)_{H_2O}$ were taken from the "Int. Crit. Tables."[10] The measured Λ_c values and the calculated Λ_0 values are shown for sodium chloride, deuterochloric acid, and sodium acetate in Tables I, II, III, respectively. The Λ_0 values for deuteroacetic acid are given in Table IV. The measured Λ_c values for the deuteroacetic acid and the dissociation constants, K_M, calculated by the equation

$$K_M = \frac{C_i^2}{C - C_i} \qquad (2)$$

are shown in Table V. $C_i = \kappa\,(1000)/\Lambda_0$, κ is the specific conductance of the solution, and C is the stoichiometric concentration of the acid.

TABLE I

SUMMARY OF VALUES OF Λ_C AND Λ_0 FOR NaCl IN H_2O AND D_2O AT DIFFERENT TEMPERATURES

Solution concentrations: B-15, 0.01088 *M*; B-16, 0.01887 *M*.

Temp., °C.	Solution	$\Lambda_0^{H_2O}$	$\Lambda_c^{H_2O}$	$\Lambda_c^{D_2O}$	$\Lambda_0^{D_2O}$	Av. $\Lambda_0^{D_2O}$	$\%_{av.\,dev.}$
44.86	B-15	174.54	168.83	144.8	149.7		
	B-16		165.21	141.4	149.4	149.6	0.1
35.00	B-15	150.26	143.79	121.1	126.5		
	B-16		140.86	118.1	126.0	126.3	.2
25.00	B-15	125.63	118.39	98.72	104.8		
	B-16		116.16	96.33	104.2	104.5	.3
14.36	B-15	99.44	92.75	76.29	81.79		
	B-16		91.05	74.36	81.21	81.50	.36

TABLE II

SUMMARY OF VALUES OF Λ_C AND Λ_0 FOR HCl AND DCl AT DIFFERENT TEMPERATURES

Solution concentration: B-17, 0.03707 *M*; B-18, 0.01860 *M*.

Temp., °C.	Solution	Λ^{HCl}	Λ_c^{HCl}	Λ_c^{DCl}	Λ_0^{DCl}	Av. Λ_0^{DCl}	$\%_{av.\,dev.}$
44.86	B-17	551.5	518.95	385.5	409.7		
	B-18		526.13	391.7	410.6	410.2	0.1
35.00	B-17	488.7	464.3	343.0	361.0		
	B-18		470.8	348.2	361.4	361.2	.06
25.00	B-17	425.0	401.97	296.2	313.2		
	B-18		407.37	300.3	313.3	313.3	.02
14.36	B-17	357.2	339.30	243.3	256.1		
	B-18		343.74	246.3	256.0	256.1	.02

TABLE III

SUMMARY OF VALUES OF Λ_C AND Λ_0 FOR SODIUM ACETATE IN H_2O AND D_2O AT DIFFERENT TEMPERATURES, 0.02026 *M*

Temp., °C.	$\Lambda_0^{H_2O}$	$\Lambda_c^{H_2O}$	$\Lambda_c^{D_2O}$	$\Lambda_0^{D_2O}$
44.86	128.83	115.80	100.5	111.8
35.00	110.22	98.64	83.20	93.0
25.00	91.36	81.24	66.99	75.3
14.36	71.30	62.73	50.98	57.9

	Chittum and LaMer[8] conductance
Λ_0^{NaCl}	
Λ_0^{NaCl}	104.8 at F_D = 0.937
Λ_0^{DOAc}	285.9 at F_D = .93
$K_M \times 10^5$	0.608 at F_D = .93

TABLE IV

SUMMARY OF VALUES OF Λ_0 FOR DAc AT DIFFERENT TEMPERATURES

Temp., °C.	Λ_0^{DAc}
44.86	372.4
35.00	327.9
25.00	284.1
14.36	232.5

TABLE V

SUMMARY OF K_M VALUES AT DIFFERENT TEMPERATURES, F_D = 0.925

Solution B-19, 0.03238 *M*; B-20, 0.12114 *M*; B-21, 0.04530 *M*; B-22, 0.07290 *M*.

Temp., °C.	Solution	$K_M \times 10^5$	Average $K_M \times 10^5$	% a.d.
44.86	B-19	0.610		
	B-20	.609		
	B-21	.605		
	B-22	.611	0.609	0.3
35.00	B-19	.622		
	B-20	.622		
	B-21	.617		
	B-22	.623	.621	.3
25.00	B-19	.613		
	B-20	.613		
	B-21	.609		
	B-22	.615	.613	.2
14.36	B-19	.605		
	B-20	.605		
	B-21	.603		
	B-22	.607	.605	.2

The accuracy of these measurements is indicated by the agreement of our Λ_0 values for sodium chloride, Λ_0 value for HOAc–DOAc, and our dissociation constant value at 25° with the corresponding values of previous work at the same temperature:

Korman and LaMer[2] e. m. f.	This paper conductance
.....	104.5 at F_D = 0.925
.....	284.1 at F_D = .925
0.612 at F_D = 0.917	0.613 at F_D = .925

(8) LaMer and Chittum, THIS JOURNAL, **58**, 1642 (1936); Chittum and LaMer, *ibid.*, **59**, 2425 (1937); references 1 and 6.

(9) LaMer and Chittum, *ibid.*, **58**, 1642 (1936).

(10) "Int. Crit. Tables," Vol. VI, pp. 230–248.

The excellent agreement between the conductance and e. m. f. data at 25° is not obtained at other temperatures. In the preliminary work on acetic acid,[2] the various precautions necessary to establish that the quinhydrone electrode had not deteriorated over the period of time that was required to obtain electrode equilibrium at a second (later) temperature were not realized as fully as in the later work on HCl.[5]

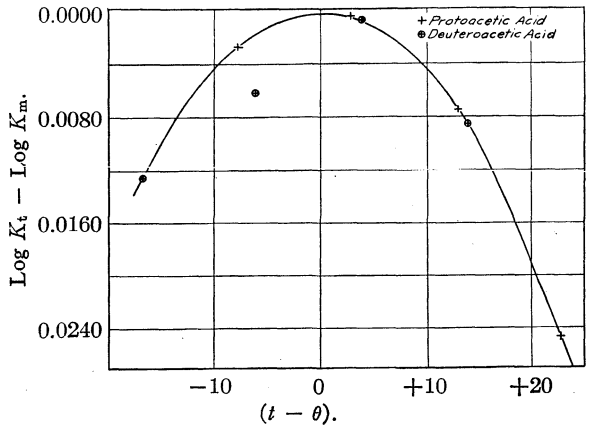

Fig. 1.—Protoacetic acid, +; deuteroacetic acid, ⊕.

K_D was determined by extrapolating the dissociation constant K_M observed in the mixed waters (H_2O–D_2O) to $F_D = 1$ with the equation[11]

$$K_M = K_D\left[1 + 3.76\,\frac{C_{H_2O}}{C_{HDO}}\Big/1 + 3.76\left(\frac{K_D}{K_M}\right)\frac{C_{H_2O}}{C_{HDO}}\right] \quad (3)$$

In equation (3), K_D is the dissociation constant of the deuteroacid; K_H, the dissociation constant of the protoacid. K_H values (converted to the classical dissociation constant) at the different centigrade temperatures t were calculated from the equation.

$$\log K_{H,t} - \log K_{H,m} = -p(t - \theta)^2 \quad (4)$$

$K_{H,m}$ is the maximum value of K_H which occurs at the characteristic temperature θ; p is a constant.

The K_H and K_D values and their ratios are given in Table VI.

TABLE VI

SUMMARY OF K_H, K_D, AND K_H/K_D AT DIFFERENT TEMPERATURES

Temp., °C.	$K_H \times 10^5$	$K_D \times 10^5$	K_H/K_D
44.86	1.74	0.545	3.19
35	1.81	.555	3.26
25	1.84	.548	3.36
14.36	1.83	.540	3.39

(11) Brescia, THIS JOURNAL, 60, 2811 (1938).

Discussion

As was expected, the temperature dependences of K_H and K_D follow the same general type of parabolic curve as shown in Fig. 1. K_D however, passes through the maximum at a higher temperature than K_H. Thus, the characteristic temperature θ is about 22° for protoacetic acid and about 31° for deuteroacetic acid. The ratio of K_H/K_D, Table VI, decreases with increasing temperature so that the two values probably approach each other at higher temperatures.

The data for K_D for the range of temperatures investigated may be represented by

$$\log K_{D,t} + 5.2550 = -4.5 \times 10^{-5}(t - 31.06)^2 \quad (5)$$

with an accuracy of 1%. The corresponding equation for protoacetic acid, over the same temperature range, is

$$\log K_{H,t} + 4.7348 = -4.5 \times 10^{-5}(t - 22.09)^2 \quad (5a)$$

A plot of equations (5) and (5a) is given in Fig. 1 in which it is seen that the resulting curves for each acid are superimposable. This behavior is quite general for weak protoacids,[3] and shows that p is the same for deutero- and protoacetic acids.

The differences of the heats, free energies and entropies of dissociation of the deutero- and protoacetic acids, corresponding to the exchange process

$$HOAc(H_2O) + D^+(D_2O) + OAc^-(D_2O) = DOAc(D_2O) + H^+(H_2O) + OAc^-(H_2O) \quad (6)$$

where the solvent involved[12] is inclosed in parentheses, have been calculated (Table VII). The

TABLE VII

DIFFERENCES OF HEATS, FREE ENERGIES, AND ENTROPIES OF DISSOCIATION, CORRESPONDING TO THE THERMODYNAMIC PROPERTIES OF THE EXCHANGE PROCESS (6)

Subscript D refers to deuteroacetic acid; subscript H to protoacetic acid.

Temp., °C.	$\Delta H_D - \Delta H_H$, cal.	$\Delta F_D - \Delta F_H$, cal.	$\Delta S_D - \Delta S_H$, cal./deg.	K_6
14.36	308.6	697.6	−1.3	0.530
25.00	329.2	717.7	−1.3	.526
35.00	349.2	724.0	−1.3	.513
44.86	368.9	733.6	−1.1	.504

chemical equation (6) is obtained by subtracting equation (6b) from equation (6a)

$$HOAc(H_2O) = H^+(H_2O) + OAc^-(H_2O) \quad (6a)$$
$$DOAc(D_2O) = D^+(D_2O) + OAc^-(D_2O) \quad (6b)$$

The ΔH for deuteroacetic acid decreases more slowly with increasing temperature than the corresponding function for protoacetic acid. Also,

(12) See reference 13 for the importance of including the solvent.

ΔF for the dissociation of DOAc increases more rapidly with the temperature than does ΔF for the dissociation of HOAc. On the other hand, the entropy differences are constant. Thus, the greater increase in K_D with increasing temperature is due to the greater increase in ΔH_D over ΔH_H. Since $\Delta F_D - \Delta F_H$ equals $-\Delta F$ for the exchange process (6), the reverse reaction, as expected, is favored on increasing temperature. The values for K_6, the equilibrium constant for the exchange process (6), calculated from $\Delta F_D - \Delta F_H$, are given in Table VII. Also

$$\left(\frac{\partial \Delta H_D}{\partial T}\right)_p - \left(\frac{\partial \Delta H_H}{\partial T}\right)_p = \Delta C_p$$

for process (6) is sensibly independent of temperature and equal to 2.0 cal. deg.$^{-1}$ mole^{-1}. Noonan and LaMer,[13] who made a careful study of the e. m. f. of the cell without transport

$$\begin{array}{c|c|c|c} D_2 & DCl & D_2O & \\ & & & \text{AgCl-Ag} \\ H_2 & HCl & H_2O & \end{array}$$

over a wide range of deuterium solvents, found that ΔC_p for the process

$$^1/_2H_2 + DCl(D_2O) = {}^1/_2D_2 + HCl(H_2O) \quad (7)$$

is also very small if not zero.

The almost zero value of ΔC_p in these exchange processes results from the fact that ions of the same valence type and almost identical chemical properties are involved in these equilibria. The partial molal heat capacity of an ionic species is determined primarily by its net charge and only secondarily by its internal constitution.[14]

(13) Noonan and LaMer, *J. Phys. Chem.*, **43**, 247 (1939); LaMer and Noonan, THIS JOURNAL, **61**, 1487 (1939).

Summary

1. The equivalent conductances of sodium chloride, sodium acetate, hydrochloric acid, and acetic acid have been measured at 14.36, 25, 35 and 44.86° in a solvent whose deuterium fraction is 0.925. From these data, the dissociation constant of deuteroacetic acid at $F_D = 1$ is calculated at corresponding temperatures.

2. The dissociation constant of deuteroacetic acid follows the Harned–Embree equation and passes through a maximum at 31°; protoacetic acid at 22°.

3. The ratio K_H/K_D decreases with increasing temperature.

4. The differences in the heats, free energies and entropies of ionization of the deutero and proto acids have been calculated. ΔC_p for the exchange process $HOAc(H_2O) + D^+(D_2O) + OAc^-(D_2O) = DOAc(D_2O) + H^+(H_2O) + OAc^-(H_2O)$ is sensibly zero; ΔS is sensibly constant and equal to -1.3 cal. deg.$^{-1}$ mole^{-1}.

(14) Rossini, *Bur. Standards J. Research*, **4**, 313 (1930); **7**, 47 (1931); LaMer and Cowperthwaite, THIS JOURNAL, **55**, 1004 (1933).

NEW YORK, N. Y. RECEIVED DECEMBER 9, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

Electrostatic Effects on Ionization Constants

BY VICTOR K. LAMER AND FRANK BRESCIA*

In a recent paper, E. C. Baughan[1] derived on the basis of theoretical suggestions of Gurney,[2] the equation

$$\Delta H_T = \Delta H_x + c\, 1/D_T \left[1 + T\frac{\partial \ln D}{\partial T}\right]_T \quad (1)$$

for the heat of ionization ΔH_T of a weak acid of the electric charge type $HA + H_2O \rightleftarrows H_3O^+ + A^-$, as a function of the temperature T, on the assumption that the electrical work involved in creating the electric field is adequately expressed by the well known formula of Born

$$c = \frac{\epsilon^2}{2}\left(\frac{1}{r_+} + \frac{1}{r_-}\right)$$

where ϵ is the elementary electric charge, r_+ and r_- are the radii of the cation and anion, and D is the dielectric constant of the solvent.

ΔH_x may be regarded either as the heat of ionization in a medium of infinite dielectric constant where no electrical work would be involved, or as the heat effect if there were no separation of electric charges in the dissociation process.

Since ΔH is zero at the characteristic temperature for which the dissociation constant is a maximum, equation (1) may also be expressed as

$$\Delta H_T = c\left[1/D_T\left(1 + T\frac{\partial \ln D}{\partial T}\right) - 1/D_\Theta\left(1 + \Theta\frac{\partial \ln \Theta}{\partial T}\right)\right] \quad (1a)$$

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(1) E. C. Baughan, *J. Chem. Phys.*, **7**, 951 (1939).

(2) Gurney, *ibid.*, **6**, 499 (1938).

Hence, ΔH_T is determined solely by the parameters Θ and r.

We have recently completed a series of accurate determinations of the dissociation constants of deuteroacetic acid by the conductance method,[3] which with the data of Harned and co-workers on protoacetic acid should serve as a particularly good test of these equations.

The dielectric behavior of both ordinary water and deuterium oxide has been carefully investigated by Wyman and his collaborators,[4] and is expressible in the form

$$D = ae^{-bT} \qquad (2)$$

When the experimental values of ΔH_T for a given acid are plotted against $X = \frac{1}{D_T}\left(1 + T\frac{\partial \ln D}{\partial T}\right)$ equation (1) requires a linear relationship. The mean radius r, defined by $\frac{2}{r} = \left(\frac{1}{r_+} + \frac{1}{r_-}\right)$, is calculable from the slope and ΔH_x from the intercept at $X = 0$. Both should be constants independent of temperature if equation (1) is valid. Baughan showed that equation (1) held for the best available data on weak acids in H_2O.

In Fig. 1 we plot our data for DOAc and for comparison the corresponding data for HOAc recalculated from Harned and Embree's equation and Wyman's dielectric data.

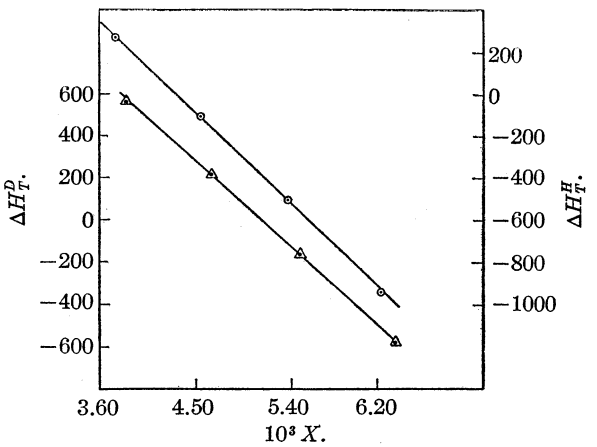


Fig. 1.—$X = \frac{1}{D_T}\left(1 + T\frac{\partial \ln D}{\partial T}\right)$: ⊙, HOAc; ▲, DOAc.

The values of the parameter c for the two acids have been obtained by simultaneous solution for two temperatures using the data[3,4] given in Table I and the equation:

$$\Delta H_T^D - \Delta H_T^H = c^D\left[1/D_\Theta^D\left(1 + T\frac{\partial \ln D^D}{\partial T}\right) - 1/D_\Theta^D\left(1 + \Theta^D\frac{\partial \ln D^D}{\partial T}\right)\right] + c^H\left[1/D_\Theta^H\left(1 + \Theta^H\frac{\partial \ln D^H}{\partial T}\right) - 1/D_T^H\left(1 + T\frac{\partial \ln D^H}{\partial T}\right)\right] \qquad (3)$$

The superscripts H and D refer to HOAc and DOAc, respectively.

(3) Brescia, LaMer and Nachod, THIS JOURNAL, **62**, 614 (1940).
(4) Wyman, *Phys. Rev.*, **35**, 623 (1930); Wyman and Ingalls, THIS JOURNAL, **60**, 1182 (1938).

TABLE I

t°C.	$\Delta H^D - \Delta H^H$	
14.36	308.6	$\log D^H = 1.9446 - 0.00198\,t$
25.00	329.1	$\log D^D = 1.9433 - 0.00199\,t$
35.00	348.9	$\Theta^H = 22.09$°C.
44.86	368.9	$\Theta^D = 31.06$°C.

TABLE II

Temperature, °C.	$c^H \times 10^{-5}$	$c^D \times 10^{-5}$
14.36–25.00	4.725	4.410
25.00–35.00	4.709	4.412
35.00–44.86	4.708	4.408
	Av. $c^H = 4.714 \times 10^5$	$c^D = 4.410 \times 10^5$
	a. d. = 0.15%	a. d. = 0.02%

The values of c (cal. mole^{-1}) are constant. Setting $\epsilon = 4.796 \times 10^{-10}$ e. s. u. and $N = 6.03 \times 10^{23}$ yields for the harmonic mean radius:

r^H (for protoacetic acid) = 0.704 Å.
r^D (for deuteroacetic acid) = 0.753 Å.

Using these values of r, we find as shown in Tables III and IV that $\Delta H_x^D = 2260$ cal. and $\Delta H_x^H = 2030$ cal. The difference, 230 cal., should be independent of electrostatic effects and hence should arise from the differences in fundamental vibration frequencies of the molecules involved in the dissociation process.

TABLE III

DEUTEROACETIC ACID

t,°C.	ΔH_x^D (calcd.)	ΔH^D (exptl.)	ΔH^D (calcd.)
14.36	226×10^1	570.9	569
25.00	227	222.6	210
35.00	226	−154.7	−158
44.86	223	−577.4	−547

TABLE IV

PROTOACETIC ACID

t,°C.	ΔH_x^H (calcd.)	ΔH^H (exptl.)	ΔH^H (calcd.)
14.36	203×10^1	262.3	265
25.00	204	−106.5	−114
35.00	203	−503.6	−502
44.86	200	−946.3	−912

Since r^H and r^D, D_T^H and D_T^D, and $\partial \ln D^H/\partial T$ and $\partial \ln D^D/\partial T$ are practically identical, equation (3) can be reduced to

$$\Delta H_T^D - \Delta H_T^H = c\left[1/D_{\Theta^H}\left(1 + \Theta^H\frac{\partial \ln D}{\partial T}\right) - 1/D_{\Theta^D}\left(1 + \Theta^D\frac{\partial \ln D}{\partial T}\right)\right] \qquad (4$$

According to this equation, the difference between the heats of ionization of the proto and deutero forms of an acid should be independent of temperature and, practically speaking, a function only of their respective characteristic temperatures, Θ. This requires that

$$\left(\frac{\partial \Delta H^D}{\partial T}\right)_p - \left(\frac{\partial \Delta H^H}{\partial T}\right)_p = \Delta C_p$$

should equal zero for the corresponding exchange reaction

$$\mathrm{HOAc} + \mathrm{D^+(D_2O)} + \mathrm{OAc^-(D_2O)} = \mathrm{DOAc(D_2O)} + \mathrm{H^+(H_2O)} + \mathrm{OAc^-(H_2O)} \quad (5)$$

Experimentally, ΔC_p for the exchange process where HOAc is acetic acid[3] is 2 cal. mole^{-1} deg.$^{-1}$; ΔC_p for the corresponding benzoic acid exchange process[5] is about 9.5 cal. mole^{-1} deg.$^{-1}$; but is exactly zero for the HCl–DCl exchange.[6] Presumably these very small ΔC_p values may be attributed to the small differences in the radii of $H^+(H_2O)$ and $D^+(D_2O)$, and of the anions in the respective waters, as well as in the dielectric properties of the two waters.

The validity of equation (1) is evidence that log K can be adequately expressed as

$$\frac{-\Delta F^\circ}{2.3RT} = \log K = A - B/T - \frac{C}{D}\frac{1}{T} \quad (6)$$

where A, $B = \Delta H_x/_{2.3R}$, and $C = c$ (eq. 1)$/2.3R$ are constants for each acid in a given solvent.

As a means of testing whether or not log K is a function of D and of T only, it may prove helpful to introduce a procedure which recently has found application in the analogous problem of interpreting the energies and entropies of activation in the kinetics of ionic reactions.[7]

The procedure consists in determining the temperature coefficients not only in media of constant composition but also in media of constant dielectric constant (isodielectric temperature coefficient). Thus the customary coefficient is composed of an isodielectric coefficient and a correction term involving $\partial D/\partial T$.

$$\left(\frac{\mathrm{d}\log K}{\mathrm{d}(1/T)}\right)_{\text{comp.}} = \left(\frac{\partial \log K}{\partial(1/T)}\right)_D + \left(\frac{\partial \log K}{\partial D}\right)_T \left(\frac{\partial D}{\partial T}\right)_{\text{comp.}} \left(\frac{\partial T}{\partial 1/T}\right) \quad (7)$$

where each term may be identified as

$$\left(\frac{-\Delta H}{2.3R}\right)_{\text{comp.}} = \left(\frac{-\Delta H}{2.3R}\right)_D - \frac{C}{D}\left[\frac{T}{D}\frac{\partial D}{\partial T}\right] \quad (8)$$

$$= -\left(B + \frac{C}{D}\right) - \frac{C}{D}\left[\frac{T}{D}\frac{\partial D}{\partial T}\right]$$

$$= -B - \frac{C}{D}\left[1 + \frac{T}{D}\frac{\partial D}{\partial T}\right] \quad (9)$$

Similarly for the entropy of dissociation in the standard state

$$\left(\frac{\Delta S^0}{2.3R}\right)_{\text{comp.}} = \left(\frac{\mathrm{d}(T\log K)}{\mathrm{d}T}\right)_{\text{comp.}} = A + \frac{C}{D}\left[\frac{T}{D}\frac{\partial D}{\partial T}\right] \quad (10)$$

From (9), which is identical with equation (1), it is evident that the slope of log K *vs.* $1/T$ should reduce to $-(B + C/D)$ in isodielectric solvents where $\partial D/\partial T = 0$. Similarly from equation (10), $\Delta S^0/2.3R$, obtained by plotting T log K against T, reduces to A for isodielectric solvents. $2.3RA$ is the increase in entropy in the standard state for the dissociation process corrected for all electrostatic contributions.

It is evident, therefore, that by determining isodielectric temperature coefficients by adjusting the composition of the medium to maintain D constant, one should determine directly the thermodynamic quantities for the process freed from electrostatic contributions; in other words, for a dissociation process which does not involve electrostatic work dependent upon the dielectric constant of the medium surrounding the molecules involved.

The neutral molecule quantities can of course be calculated from the temperature coefficient at constant composition by introducing the correction factors in $\partial D/\partial T$. This is the essence of equations (1) and (9), and their merit resides in the fact that the medium is not changed in composition with changing temperature.

Agreement between such calculated values of $(\partial \ln K/\partial(1/T))_D$ and those determined directly in isodielectric media will only be obtained if it is legitimate to express log K as function of D and T only (equation 6) and if r remains independent of temperature and of solvent. That $(\partial r/\partial T)$ is negligible now appears to be generally accepted. That r is indeed an adjustable parameter which takes into account undetermined specific solvent effects and only approximates the physical meaning ascribed to it is becoming more generally recognized.

The evidence[7] which is accumulating upon the kinetics of the bromoacetate–thiosulfate replacement and the ammonium cyanate → urea reactions demonstrate that when the isodielectric char-

(5) Rule and LaMer, THIS JOURNAL, **60**, 1974 (1938).

(6) Noonan and LaMer, *J. Phys. Chem.*, **43**, 247 (1939).

(7) LaMer, *J. Franklin Inst.*, **225**, 709 (1938); Amis and LaMer, THIS JOURNAL, **61**, 905 (1939); Svirbely and Warner, *ibid.*, **57**, 1883 (1935); Svirbely and collaborators, *ibid.*, **60**, 330, 1613 (1938); **61**, 3534, 3538 (1939).

acter of the medium is maintained by the addition of methanol and ethanol, the kinetic analog of A in equation (10) remains remarkably constant. On the other hand, when isopropanol, diethylene glycol, and particularly dioxane, are employed to produce media of very low dielectric constant, exact constancy of A is not obtained. This is to be expected since the addition of dioxane produces a greater change in specific solvent properties than does the addition of an alcohol most closely resembling water.

Differentiating equation (9) and evaluating coefficients from equation (2) yields

$$\Delta C_p = -b^2Tc/D \qquad (11)$$

The value of ΔC_p calculated for protoacetic acid (r = 0.70 Å.) is −39.9, whereas the experimental value is −41.3 cal. deg.$^{-1}$ mole^{-1}.

Treating in the same manner the empirical Harned–Embree[8] equation

$$\log K_T = \log K_M - p(T - \Theta)^2 \qquad (12)$$

$$[\Delta C_p/2.3R]_{T=\Theta} = -6pT^2 + 4pT\Theta = -2p\Theta^2 \qquad (13)$$

Equating (11) and (13)

$$p = \frac{\epsilon^2}{(2.3R)rD^3}\left(\frac{\partial D}{\partial T}\right)^2\frac{1}{2\Theta} \qquad (14)$$

Equation (14) can be shown to be correct by introducing numerical values for $T = \Theta$ and recovering the experimental value of $p \cong 4.5 \times 10^{-5}$.

Since D does not vary much for the values of $T = \Theta$ encountered for this group of acids and r proves to be almost a constant we have an explanation of why equation (12) represents the facts so well with an almost universal value of p.[8]

(8) Harned and Embree, THIS JOURNAL, **56**, 1050 (1934); Walde, *J. Phys. Chem.*, **39**, 478 (1935).

Summary and Conclusions

1. The equation

$$\Delta H_T = \Delta H_x + c\,1/D_T\left[1 + T\frac{\partial \ln D}{\partial T}\right]$$

represents with high precision ΔH, the heat of dissociation of deuteroacetic acid as a function of temperature, when ΔH_x = 2260, and c = 4.410 × 10^{+5}. The values for protoacetic acid are 2030 cal. and 4.714 × 10^{+5}, corresponding to (Born) r values of 0.75 and 0.70 Å., respectively.

2. ΔC_p for an acid–base exchange reaction involving deuterium and hydrogen in D_2O and in H_2O is practically zero since the radii of the ions and the dielectric properties of the two media are practically identical.

3. The difference in the heats of ionization of deutero and proto acids appears to be a function only of the characteristic temperature Θ at which the maximum value of the dissociation constants occurs.

4. The desirability of determining the temperature coefficients of dissociation constants of acids, not only in solvents of constant composition but also in solvents of constant dielectric constant, is pointed out.

5. The empirical constant $p \cong 4.5 \times 10^{-5}$ in the Harned–Embree equation is shown on theoretical grounds to be equal to

$$p = \frac{\epsilon^2}{(2.3R)rD^3}\cdot\left(\frac{\partial D}{\partial T}\right)^2\cdot\frac{1}{2\Theta}$$

NEW YORK, N. Y. RECEIVED FEBRUARY 1, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF YALE UNIVERSITY]

Thermodynamics of Concentrated Aqueous Solutions of Sodium Hydroxide[1,2]

BY GÖSTA ÅKERLÖF AND GERSON KEGELES

Introduction

The thermodynamic properties of strong electrolytes in highly concentrated solutions over a large temperature range may conceivably be obtained by a number of different methods. In most cases, however, the methods applicable narrow down to a single one, the determination of the vapor pressure of the solution. The alkali hydroxides and hydrochloric acid belong to the few electrolytes forming exceptions to this general rule since it would appear to be possible to study their solutions using an electromotive force method. The properties of hydrochloric acid already have been studied for a considerable temperature range by Åkerlöf and Teare,[3] who used solutions up to 16 molal. Solutions of the alkali hydroxides have been the subject of a series of studies by Harned

(1) This communication contains part of the material of a dissertation to be presented by Gerson Kegeles to the Graduate School of Yale University in partial fulfillment of the requirements of the degree of Doctor of Philosophy, June, 1940.

(2) The tables of this paper are published with the financial assistance of the authors and of Yale University.

(3) Åkerlöf and Teare, THIS JOURNAL, **59**, 1855 (1937).

and co-workers,[4] but the upper limit of the concentration range covered was only 4 molal. Since there is no particular reason to suspect that either the flowing amalgam or hydrogen electrodes employed would fail at still higher concentrations it was considered worth while to attempt to extend these measurements in the case of solutions of sodium hydroxide to cover as large a concentration range as possible. As a result we have succeeded in getting accurate measurements for the concentration range 0.1–17 molal over the temperature range 0 to 70°.

Experimental Procedure.—In older set-ups for measurements of cells with flowing amalgam electrodes as a general rule so-called "droppers" were used. During the introduction of this dropper in the cell it was unavoidable to expose the surface of the solutions at least momentarily to the air. Since the initial speed with which oxygen is absorbed by an air-free solution is very high and the flowing amalgam would tend to give a rapid mixing of the surface layers of the solutions with the underlying ones, the observed electromotive force would tend to vary slightly erratically on account of the high sensitivity of the amalgam electrodes toward oxygen. Furthermore, in the case of measurements extending over a larger temperature range elaborate precautions are necessary to keep droppers at the correct temperature. Some of our electromotive force measurements showed a temperature coefficient of over one millivolt per degree, which sufficiently illustrates the necessity of precise temperature control of the amalgam.

Another possible source of error in older amalgam cell measurements should also be pointed out. For every new measurement it was as a rule also necessary or customary to make up a new reference solution. A small error in the absolute concentration of this solution would apparently be less serious than individual fluctuations of the same magnitude for the different solutions employed as reference, since what is measured is a ratio of activities. In our case we made up about 60 liters of the reference solution, stored it in a closed stainless steel tank and piped it directly from the tank into the cell, thus avoiding any possibility of variations in its concentration.

A diagrammatical sketch of the apparatus is shown in Fig. 1. The thermostat was mounted inside an angle iron frame which on top carried the tank for the reference solution and a two-liter flask for the amalgam. Under the thermostat the frame carried a shelf for receivers of used amalgam and solutions, which were blown out as needed with compressed air. Each half of the cell was provided with an individual receiver in order to eliminate any possibility of internal electrical leakage during the measurements. To prevent freezing of the stopcocks by the hydroxide solutions when unused for some time a number of them were provided with plugs of stainless steel, bored obliquely. All tubing used was made of Pyrex glass, but

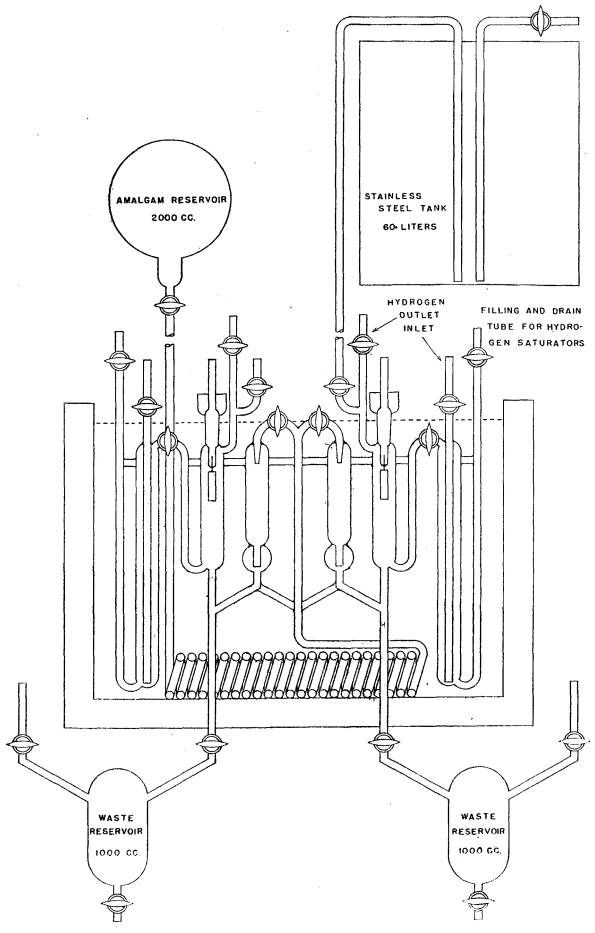


Fig. 1.—Diagrammatical sketch of apparatus used.

all parts of the cell had been left filled with concentrated sodium hydroxide solution for over a month and then carefully washed out with boiling hot solution and pure water before any of the final measurements were made. Errors due to subsequently dissolved silica should be negligible as already clearly shown by us in a previous paper.[5]

In setting up the cells all the usual precautions with regard to testing for leaks and pinholes were carefully observed and repeated several times during the course of the measurements due to the constant danger of cracks that might have developed, since it was impossible to relieve the cells entirely from small mechanical stresses. The design adopted proved, however, to be sufficiently strong and no cracks were found at any time. Due to the precautions taken and the absence of electrical leaks it was also found possible to extend our measurements up to 70°. A few measurements at 80° were, however, fairly erratic and the data for 70° have probably somewhat larger errors than those for lower temperatures.

The amalgam flowed from the reservoir through a heavy capillary down to the bottom of the thermostat, where it entered a long glass spiral to acquire the correct temperature. The exit tube from the glass spiral carried the amalgam upward and led it through two all-glass stopcocks

(4) Harned, THIS JOURNAL, **47**, 676 (1925); Harned and Swindells, *ibid.*, **48**, 126, (1926); Harned and Hecker, *ibid.*, **55**, 4838 (1933); Harned and Cook, *ibid.*, **59**, 496 (1937); see also Knobel, *ibid.*, **45**, 70 (1923).

(5) Åkerlöf and Kegeles, *ibid.*, **61** 1027 (1939).

into the two halves of the cell. The entrance tubes had a bore of about 0.5 mm. and their tips were properly drawn out and adjusted before the tubes were sealed in. The hydrogen electrodes were made as usual of platinum foil covered with platinum black deposited from a strongly acidified solution of platinum chloride using a current of about 0.5 ampere for two minutes.

As already mentioned the reference solution was stored in a stainless steel tank. The tank was first, after proper cleaning, filled with distilled water and then a steady stream of oxygen-free hydrogen was bubbled through the water continuously over a period of about one week. With the gas still streaming, the calculated amount of the standard concentrated sodium hydroxide solution, prepared as previously described,[5] was added so as to give a 0.1 molal solution. Since the tank could not be moved the hydrogen bubbling was continued for four to five days after the hydroxide had been added to ensure uniform concentration of the solution throughout the tank. The reference solution was afterward always kept under a small excess gas pressure to prevent any possibility of air contamination. At various times during the course of the measurements, samples were taken and analyzed gravimetrically by neutralizing with hydrochloric acid and weighing the residue after light ignition. The different analyses all agreed to about one part in 5000 and gave as a general average 0.10166 as the molality of the reference solution. The hydroxide solution to be measured was prepared by diluting in a nitrogen atmosphere the standard concentrated solution, which was available in sufficient quantity (18 liters) to last for all our measurements without change. The diluting apparatus was the same as the one previously employed by Åkerlöf and Teare for the study of the thermodynamics of hydrochloric acid. The finished solutions were analyzed in triplicate in the same manner as already indicated for the analysis of the reference solution.

The electromotive force of the cells was measured with a Leeds and Northrup type K potentiometer. The working standard cells were thermostated and at frequent intervals checked against the laboratory primary standard set certified by the Bureau of Standards and permanently kept immersed in oil at 30.00°. The temperature of the cell thermostat was controlled by a mercury thermoregulator having a sensitivity of about 0.02°. The solid stem thermometer employed had previously been calibrated against a Bureau of Standards certified platinum resistance thermometer using a Mueller resistance bridge.

The cells were filled with the reference and the measuring solutions after they had been cleaned with hot hydroxide solution, thoroughly rinsed with warm distilled water and finally dried while evacuated. In all cases the cells were allowed to come to equilibrium over a period of at least twelve to fourteen hours. At increasingly higher concentrations of the measuring solution it was found, however, that longer and longer time was needed for the hydrogen electrodes to come to equilibrium. Above 14–15 molal extremely rigid exclusion of air contamination shortened the time needed to attain equilibrium and get reproducible results very appreciably but for solutions with a hydroxide concentration above 18 molal even after over a week's time definite end-points could not be obtained although the solutions had been swept and saturated with hydrogen for several hours before they were introduced into the highly evacuated cells.

Preliminary Treatment of the Experimental Results.—Since it would have been very difficult and time consuming to adjust the thermoregulator for each new measurement to an exact temperature, the electromotive force values observed were first corrected linearly to round temperatures. The corrections needed were always very small and seldom exceeded 0.1 millivolt. Next in order to be considered are corrections due to changes in atmospheric pressure and the vapor pressure of the solutions. The cell measured has the following composition

$$\mathrm{Pt,H_2/NaOH}\ (m_1)/\mathrm{Na_xHg/NaOH}\ (m_2)/\mathrm{H_2,Pt}$$

where m_1 and m_2 represent the concentrations of the sodium hydroxide. The electromotive force E of the cell is given by the equation

$$E = \frac{RT}{F} \ln \frac{a_{\mathrm{NaOH}(m_1)} a_{\mathrm{H_2O}(m_2)} a_{\mathrm{H_2}(m_1)}^{\frac{1}{2}}}{a_{\mathrm{NaOH}(m_2)} a_{\mathrm{H_2O}(m_1)} a_{\mathrm{H_2}(m_2)}^{\frac{1}{2}}} \qquad (1a)$$

where a denotes the thermodynamic activity of the species indicated. R, T and F have their usual significance. Differentiating with respect to pressure we obtain

$$\frac{\partial E}{\partial P} = \frac{1}{F}\left[(\bar{v}_{2(m_1)} - \bar{v}_{2(m_2)}) - (\bar{v}_{1(m_1)} - \bar{v}_{1(m_2)})\right] + \frac{1}{2F}\left[(v_{\mathrm{H_2}(m_1)} - v_{\mathrm{H_2}(m_2)})\right] \qquad (2a)$$

where $\bar{v}_1$ and $\bar{v}_2$ represent the partial molal volumes of solvent and hydroxide, respectively. Since $v_{\mathrm{H_2}} = RT/p_{\mathrm{H_2}}$ and $p_{\mathrm{H_2}} = P - p$, where P is the atmospheric and p the vapor pressure of the solution, equation (2a) takes the form

$$\frac{\partial E}{\partial P} = \frac{1}{F}\left[(\bar{v}_{2(m_1)} - \bar{v}_{2(m_2)}) - (\bar{v}_{1(m_1)} - \bar{v}_{1(m_2)})\right] + \frac{RT}{2F}\left[\frac{1}{P - p_{(m_1)}} - \frac{1}{P - p_{(m_2)}}\right] \qquad (2b)$$

Neglecting compressibilities and integrating between P and $P + \Delta P$, the atmospheric pressure correction would thus be given by the equation

$$\Delta E_p = \frac{1}{F}\left[(\bar{v}_{2(m_1)} - \bar{v}_{2(m_2)}) - (\bar{v}_{1(m_1)} - \bar{v}_{1(m_2)})\right]\Delta P + \frac{RT}{2F} \ln \frac{(P - p_{(m_1)} + \Delta P)(P - p_{(m_2)})}{(P - p_{(m_2)} + \Delta P)(P - p_{(m_1)})} \qquad (2c)$$

Using the values for $\bar{v}_1$ and $\bar{v}_2$ calculated from the density measurements of Åkerlöf and Kegeles,[5] it has been found that equation (2c) gives values for ΔE_p which even for unusually large variations of the atmospheric pressure are negligible. For a pressure change of 10 millimeters the order of magnitude of the first term is 10^{-7} and of the second 10^{-5} volt.

As already indicated the next correction to be considered is due to the vapor pressure of the solutions. To evaluate this correction we may write equation (2a) in the form

$$dE = \frac{1}{F}\left[(\bar{v}_{2(m_1)} - \bar{v}_{1(m_1)} + {}^1/_2 v_{H_2(m_1)})\, dP_{(m_1)} - (\bar{v}_{2(m_2)} - \bar{v}_{1(m_2)} + {}^1/_2 v_{H_2(m_2)})\, dP_{(m_2)}\right] \quad (2a')$$

Neglecting the partial molal volume terms which in the worst case amount to 10^{-6} volt and using the ideal gas law for v_{H_2}, we may correct the electromotive forces measured to 760 mm. partial hydrogen pressure in each half cell by adding the following correction term

$$\Delta E_p = \frac{RT}{2F}\left[\int_{P=p}^{760+p_{(m_1)}} \frac{dP}{P - p_{(m_1)}} - \int_{P=p}^{760+p_{(m_2)}} \frac{dP}{P - p_{(m_2)}}\right] = \frac{RT}{2F} \ln \frac{P - p_{(m_2)}}{P - p_{(m_1)}} \approx \frac{RT}{2F} \ln \frac{760 - p_{(m_2)}}{760 - p_{(m_1)}} \quad (3)$$

To compute the value of this correction the measurements given in the literature[6] for the vapor pressure of sodium hydroxide solutions were plotted logarithmically and interpolated with respect to both temperature and concentration. Table I gives a summary of the values for log p thus obtained. As will be shown in the following, the data in Table I agree on the whole surprisingly well with the values calculated from our electromotive force measurements. The vapor pressure of the reference solution was computed using Raoult's law assuming that sodium hydroxide in 0.1 molal solution has an activity coefficient of 0.77 at all temperatures. The value of ΔE_p increases with temperature and concentration and reaches 4.0 millivolts at 70° and 17 molal. Table II gives a summary of the observed electromotive forces as corrected according to equation (3) and least squared at each concentration with respect to temperature using a second order equation.

TABLE I

VALUES FOR THE LOGARITHM OF THE VAPOR PRESSURE OF AQUEOUS SOLUTIONS OF SODIUM HYDROXIDE AS INTERPOLATED FROM DATA IN THE LITERATURE

m	0°	10°	20°	30°	40°	50°	60°	70°
0	0.661	0.964	1.244	1.503	1.743	1.966	2.174	2.369
1	.651	.953	1.233	1.491	1.731	1.953	2.160	2.354
2	.637	.938	1.218	1.475	1.715	1.936	2.143	2.337
3	.616	.918	1.198	1.456	1.696	1.918	2.125	2.319
4	.590	.893	1.174	1.433	1.674	1.897	2.104	2.299
5	.560	.864	1.146	1.406	1.648	1.872	2.079	2.275
6	.525	.830	1.113	1.374	1.617	1.842	2.050	2.247
7	.484	.791	1.076	1.339	1.581	1.810	2.019	2.217
8	.437	.746	1.033	1.298	1.537	1.764	1.983	2.182
9	.384	.696	0.986	1.250	1.489	1.716	1.944	2.144
10	.322	.638	0.937	1.200	1.439	1.667	1.899	2.104
11	.258	.579	0.886	1.148	1.389	1.618	1.849	2.062
12	.188	.520	0.834	1.096	1.339	1.569	1.796	2.020
13	.118	.461	0.781	1.044	1.290	1.521	1.750	1.978
14	+ .051	.403	0.727	0.992	1.241	1.474	1.706	1.935
15	− .016	.345	0.673	0.940	1.192	1.428	1.662	1.892
16	− .083	.287	0.619	0.888	1.143	1.382	1.618	1.849
17	− .150	.229	0.565	0.836	1.094	1.336	1.573	1.807

(6) Dieterici, *Ann. Physik*, **42** 513 (1891); *ibid.*, **50**, 47 (1893); *ibid.*, **62**, 616 (1897); *ibid.*, **67**, 859 (1899); Muralt, Diss. Zürich Techn. Hochsch.; Paranjpe, *J. Indian Inst. Sci.*, **2**, 59 (1918); Tammann, *St. Petersb., Ac. Sci. Mem.*, **35**, No. 9 (1887); Stock and Selig, *Ber.*, **52**, 678 (1919); Fricke, *Z. Elektrochem.*, **35**, 633 (1929); Baker and Waite, *Chem. Met. Eng.*, **25**, 1137 (1921); Hayward and Perman, *Trans. Faraday Soc.*, **27**, 59 and 66 (1931); Jänecke, *Z. anorg. Chem.*, **188**, 72 (1930); Shibata, *J. Sci. Hiroshima Univ.*, (A), **1**, 215 (1931); see also Monrad and Badger, *Ind. Eng. Chem.*, **21**, 42 (1929); Adams and Richards, *ibid.*, **20**, 470 (1928).

The Calculation of the Water Transfer Potential.—Using mean ion activities for the electrolyte the expression for the observed electromotive force corrected to 760 mm. partial hydrogen pressure in each half cell takes according to equation (1a) the form

$$E = \frac{2RT}{F} \ln \frac{a_{NaOH(m_1)}^{\frac{1}{2}} a_{H_2O(m_2)}^{\frac{1}{2}}}{a_{NaOH(m_2)}^{\frac{1}{2}} a_{H_2O(m_1)}^{\frac{1}{2}}} \quad (1b)$$

The activity of the solvent is related to the activity of the solute according to the Gibbs–Duhem equation

$$d \ln a_{NaOH} = -55.507/m \; d \ln a_{H_2O} \quad (4)$$

Differentiating (1b) at constant temperature and pressure regarding m_1 as a variable while keeping m_2 constant as reference concentration and introducing equation (4), gives

$$dE = -\frac{RT}{F}(55.507/m + 1)\, d \ln a_{H_2O} \quad (5)$$

Rearrangement and integration of equation (5) from $m = m_2$ to $m = m_1$ results then in the following expression for the water transfer potential E_{H_2O}

$$E_{H_2O} = -\frac{RT}{F} \ln \frac{a_{H_2O(m_1)}}{a_{H_2O(m_2)}} = \int_{m_2}^{m_1} \frac{m}{55.507 + m}\left(\frac{dE}{dm}\right) dm \quad (6a)$$

To obtain the coefficients dE/dm needed for the application of equation (6a), the data of Table II were plotted and least squared at each temperature with respect to m. It was found necessary, due to the shape of the E *vs.* m curves, to separate the least squaring into two ranges, one from 0.1 to 4 and the other from 4 to 17 molal. In the lower range it was found that E was adequately expressed by the formula

$$E = a \log m/0.10166 + b(m - 0.10166) + c(m - 0.10166)^2 \quad (6b)$$

where 0.10166 is the reference concentration. In the upper range E was computed from a somewhat simpler equation

$$E = A + Bm + Cm^2 \quad (6c)$$

TABLE II

CORRECTED ELECTROMOTIVE FORCE DATA, LEAST SQUARED WITH RESPECT TO TEMPERATURE

m	0°	10°	20°	30°	40°	50°	60°	70°
0.2505	0.03935	0.04065	0.04194	0.04324	0.04453	0.04583	0.04712	0.04842
.3523	.05310	.05543	.05754	.05945	.06113	.06258	.06382	.06485
.5058	.06928	.07194	.07449	.07693	.07926	.08148	.08359	.08560
.7562	.08757	.09120	.09465	.09792	.10102	.10394	.10669	.10926
1.0045	.10068	.10491	.10891	.11269	.11624	.11957	.12266	.12542
1.4191	.11689	.12230	.12729	.13186	.13600	.13973	.14304	.14592
1.8718	.13168	.13756	.14307	.14822	.15301	.15743	.16149	.16519
2.6601	.15239	.15925	.16559	.17139	.17666	.18140	.18562	.18930
3.3234	.16812	.17532	.18197	.18803	.19353	.19845	.20282	.20660
4.0484	.18396	.19166	.19882	.20545	.21154	.21708	.22210	.22657
5.0239	.20523	.21308	.22030	.22689	.23284	.23815	.24284	.24689
6.0351	.22729	.23484	.24183	.24825	.25411	.25941	.26415	.26833
7.0449	.24903	.25666	.26369	.27013	.27597	.28120	.28585	.28989
8.0963	.27075	.27846	.28544	.29169	.29722	.30202	.30610	.30945
9.3814	.30140	.30822	.31440	.31992	.32480	.32902	.33260	.33552
10.0434	.31362	.32131	.32800	.33367	.33832	.34197	.34460	.34623
11.0200	.33248	.34141	.34879	.35461	.35887	.36158	.36273	.36233
11.0524	.33335	.34195	.34911	.35484	.35913	.36197	.36339	.36336
12.1980	.35787	.36426	.36957	.37379	.37693	.37899	.37997	.37987
13.2982	.37659	.38445	.39089	.39590	.39949	.40166	.40241	.40174
13.9845	.38761	.39500	.40084	.40514	.40790	.40911	.40878	.40690
15.0087	.40695	.41344	.41831	.42156	.42319	.42320	.42159	.41836
16.4405	.43221	.43845	.44317	.44635	.44801	.44813	.44673	.44379
16.8395	.43885	.44583	.45117	.45488	.45695	.45737	.45617	.45332

TABLE III

WATER TRANSFER POTENTIALS

m	0°	10°	20°	30°	40°	50°	60°	70°
0.2505	0.00011	0.00011	0.00011	0.00011	0.00011	0.00011	0.00011	0.00011
.3523	.00019	.00019	.00019	.00019	.00019	.00018	.00018	.00018
.5058	.00030	.00030	.00030	.00029	.00029	.00029	.00028	.00028
.7562	.00050	.00050	.00050	.00049	.00048	.00047	.00046	.00044
1.0045	.00069	.00069	.00068	.00067	.00066	.00065	.00064	.00062
1.4191	.00103	.00103	.00102	.00101	.00099	.00097	.00094	.00091
1.8718	.00141	.00140	.00139	.00137	.00134	.00131	.00128	.00125
2.6601	.00212	.00211	.00209	.00206	.00203	.00199	.00192	.00188
3.3234	.00279	.00277	.00275	.00272	.00268	.00263	.00256	.00247
4.0484	.00364	.00362	.00359	.00355	.00349	.00342	.00333	.00321
5.0239	.00507	.00504	.00500	.00494	.00486	.00476	.00466	.00448
6.0351	.00720	.00715	.00709	.00700	.00689	.00675	.00658	.00634
7.0449	.00958	.00956	.00947	.00937	.00921	.00900	.00875	.00845
8.0963	.01231	.01227	.01216	.01203	.01182	.01155	.01121	.01082
9.3814	.01594	.01590	.01575	.01558	.01530	.01494	.01450	.01398
10.0434	.01795	.01790	.01772	.01754	.01722	.01681	.01630	.01572
11.0200	.02107	.02102	.02087	.02060	.02021	.01970	.01909	.01838
11.0524	.02118	.02113	.02098	.02071	.02031	.01982	.01922	.01851
12.1980	.02468	.02461	.02436	.02408	.02362	.02302	.02231	.02147
13.2982	.02885	.02877	.02847	.02815	.02761	.02691	.02607	.02507
13.9845	.03140	.03131	.03099	.03063	.03004	.02928	.02835	.02724
15.0087	.03515	.03305	.03469	.03428	.03360	.03274	.03167	.03041
16.4405	.04058	.04047	.04005	.03956	.03875	.03773	.03647	.03499
16.8395	.04215	.04203	.04158	.04107	.04024	.03916	.03784	.03630

The constants obtained for equations (6b) and (6c) were then least squared as a function of temperature. Introduction of (6b) and (6c) into (6a) and integration leads to the following expressions:

A. For the lower concentration range 0.1 to 4 molal

$$E_{H_2O} = [a - 2.303 \cdot 55.507b - 4.605 \cdot 55.507(55.507 + 0.10166)c] \log \frac{55.507 + m}{55.507 + 0.10166} + [b - 2(0.10166 +$$

$$2\cdot55.507)c](m - 0.10166) - c[(55.507 + m)^2 - (55.507 + 0.10166)^2] \quad (6d)$$

B. For the upper concentration range 4 to 17 molal

$$E_{H_2O} = 2.303\cdot55.507(-B + 2\cdot55.507C)\log\frac{55.507 + m}{55.507 + 0.10166} + (B - 4\cdot55.507C)(m - 0.10166) + C[(55.507 + m)^2 - (55.507 + 0.10166)^2] \quad (6e)$$

From equations (6d) and (6e) values of E_{H_2O} were calculated at the concentrations and temperatures given in Table II. These values were then cross-plotted with an accuracy of 0.01 millivolt. A summary of the interpolated values appears in Table III. Still better values could be obtained by a second approximation using smoothed values for the activity coefficient of the solute and the activity of the solvent. However, the experimental accuracy does not justify such a refinement. Subtraction of the data in Table III from the corresponding ones in Table II gives the sodium hydroxide transfer potential

$$E_{NaOH} = \frac{2RT}{F}\ln\frac{a_m}{a_{ref.}} = \frac{2RT}{F}\ln\frac{\gamma_m m}{\gamma_{ref.} m_{ref.}} \quad (7)$$

where γ represents the mean ion activity coefficient of sodium hydroxide.

Equations for the Activity Coefficient of Sodium Hydroxide.—The formal equation employed for this purpose was identical with the one used by Åkerlöf and Teare for hydrochloric acid solutions

$$\log\gamma = -\frac{u\sqrt{m}}{1 + \sqrt{2m}} + Bm + Cm^2 + Dm^3 + Em^4 \quad (8)$$

where u is the universal constant of the limiting law, B, C, D and E are empirical constants. In the case of the acid these constants were found to vary linearly with the temperature. In the case of sodium hydroxide, however, the data indicated a more complicated behavior. Therefore the observed values for $\log \gamma_m/\gamma_{ref.}$ in the concentration range 0.1 to 12.2 molal were least squared according to the equation

$$y = \log\frac{\gamma_m}{\gamma_{ref.}} + u\alpha = B(m - 0.10166) + C(m^2 - 0.10166^2) + D(m^3 - 0.10166^3) + E(m^4 - 0.10166^4) \quad (9a)$$

where α is given by the formula

$$\alpha = \frac{\sqrt{m}}{1 + \sqrt{2m}} - \frac{\sqrt{0.10166}}{1 + \sqrt{2\cdot0.10166}}$$

We thus obtain for the normal equations the expressions

$$\Sigma y(m - 0.10166) = B\Sigma(m - 0.10166)^2 + C\Sigma(m - 0.10166)(m^2 - 0.10166^2) + D\Sigma(m - 0.10166)(m^3 - 0.10166^3) + E\Sigma(m - 0.10166)(m^4 - 0.10166^4) \quad (9b)$$

..... (9c)

..... (9d)

$$\Sigma y(m^4 - 0.10166^4) = B\Sigma(m^4 - 0.10166^4)(m - 0.10166) + C\Sigma(m^4 - 0.10166^4)(m^2 - 0.10166^2) + D\Sigma(m^4 - 0.10166^4)(m^3 - 0.10166^3) + E\Sigma(m^4 - 0.10166^4)^2 \quad (9e)$$

The values for B, C, D and E calculated using equations (9b, c, d and e) were found to give curves very nearly having the form of symmetrical parabolas when plotted against the temperature. These constants were accordingly least squared assuming a second order equation in the following manner. The least squared values of B which were computed first were re-introduced in the normal equations and a new set of C values was obtained. The least squared new values for C changed the D values again a little and after they also had been treated the final values of E were calculated and least squared. A summary of the

TABLE IV

CONSTANTS USED FOR THE CALCULATION OF THE ACTIVITY COEFFICIENT OF THE SOLUTE IN AQUEOUS SOLUTIONS OF SODIUM HYDROXIDE

Part I. Constants for the concentration range 0 to 12 molal

$B = 0.006519 + 0.0015995\,t - 0.000018327\,t^2$

$C = 0.013713 - 0.00050071\,t + 0.0000056385\,t^2$

$D = 0.0005994 + 0.000050215\,t - 0.00000064754\,t^2$

$E = 0.00000596 - 0.0000018056\,t + 0.000000024073\,t^2$

Values of constants B, C, D and E at 10° intervals

Temp.	B	C	D	E
0°	0.006519	0.013713	−0.0005994	0.00000596
10	.021681	.009270	− .0001620	− .00000969
20	.031178	.005954	.0001459	− .00002052
30	.038010	.003767	.0003243	− .00002654
40	.041176	.002707	.0003731	− .00002774
50	.040676	.002773	.0002925	− .00002414
60	.036512	.003969	.0000824	− .00001572
70	.028682	.006292	− .0002573	− .00000247

Part II. Constants for the concentration range above 12 molal

$a = -0.32747 + 0.0030936\,t - 0.000032946\,t^2$

$b = 0.09880 - 0.000586\,t$

$c = -0.000002139 - 0.0000003927\,t + 0.000000005268\,t^2$

Values of constants a, b, c and u at 10° intervals

Temp.	a	b	c	u
0°	−0.32747	0.09880	−0.00000214	0.487
10	.29982	.09294	.00000554	.494
20	.27878	.08708	.00000789	.502
30	.26431	.08122	.00000918	.511
40	.25644	.07536	.00000942	.522
50	.25516	.06950	.00000861	.534
60	.26046	.06364	.00000674	.549
70	.27236	.05778	.00000382	.565

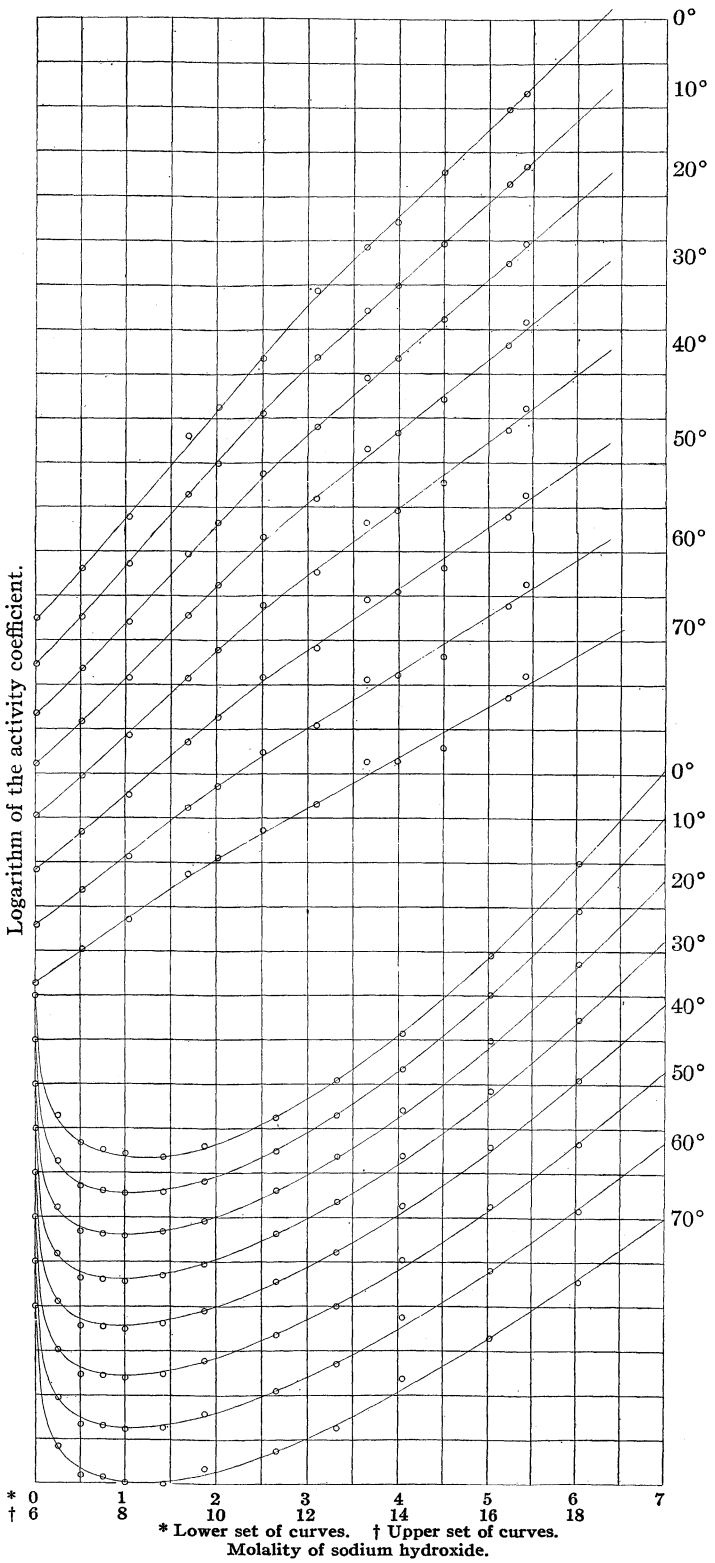


Fig. 2.—Isotherms for the logarithm of the activity coefficient of sodium hydroxide. The curves for the concentration range 6 to 17 molal are plotted on half the scale of those for the range 0 to 7 molal. Ordinates are shifted successively to avoid interference of the different curves.

constants obtained is given in Part I of Table IV. It is interesting to note that while the temperature variation of all the constants is given by parabolas, the corresponding values for B and C give when plotted against each other a practically straight line.

Equations for the activity coefficient of sodium hydroxide at concentrations above 12 molal were obtained by least squaring the observed values according to second order equations. Part II of Table IV summarizes the result. The purpose of dividing up our data in two groups, one for solutions with concentrations lower and the other one higher than 12 molal, was that this possibly would give us an indication whether the curves for the activity coefficient show a break at the concentrations where the corresponding curves for the apparent partial molal volume of the hydroxide appear to have one. As shown graphically in Fig. 2 the observed values for log γ do not have sufficient accuracy to give any definite indication of the presence of similar breaks. Due to thermodynamical reasons we know that breaks, if present, must be very faint and require an unusually high degree of accuracy in the experimental data for their detection.

Using the constants given in Table IV the value of the logarithm of the activity coefficient of sodium hydroxide has been calculated at a series of round concentrations. Table V contains the computed values. They agree quite well with those of Harned at 25° but differ particularly at higher concentrations appreciably from those of Harned and Hecker. On the other hand, our observed and calculated values agree very closely at concentrations up to 10 molal with an average difference of less than 0.2 millivolt in the corresponding electromotive force values.

Activity and Vapor Pressure of the Solvent.—The activity of the solvent may be computed most simply from the values of E_{H_2O} given in Table III but more accurate values for the concentration range 0.1 to 12 molal are ob-

TABLE V

CALCULATED VALUES FOR THE LOGARITHM OF THE ACTIVITY COEFFICIENT OF THE SOLUTE IN AQUEOUS SOLUTIONS OF SODIUM HYDROXIDE

m	0°	10°	20°	30°	40°	50°	60°	70°
0.1	−0.1056	−0.1056	−0.1065	−0.1079	−0.1100	−0.1126	−0.1163	−0.1205
.2	− .1316	− .1306	− .1311	− .1322	− .1347	− .1381	− .1429	− .1488
.4	− .1578	− .1547	− .1541	− .1548	− .1574	− .1616	− .1681	− .1762
.6	− .1713	− .1663	− .1648	− .1646	− .1672	− .1719	− .1797	− .1895
.8	− .1786	− .1720	− .1694	− .1688	− .1713	− .1765	− .1851	− .1963
1.0	− .1821	− .1738	− .1706	− .1696	− .1719	− .1774	− .1868	− .1993
1.5	− .1823	− .1684	− .1644	− .1626	− .1649	− .1713	− .1822	− .1970
2	− .1664	− .1539	− .1495	− .1475	− .1503	− .1573	− .1695	− .1858
3	− .1172	− .1048	− .1028	− .1020	− .1063	− .1152	− .1296	− .1482
4	− .0458	− .0360	− .0382	− .0406	− .0479	− .0594	− .0760	− .0969
5	+ .0426	+ .0484	+ .0405	+ .0337	+ .0225	+ .0073	− .0126	− .0365
6	+ .1438	+ .1451	+ .1309	+ .1189	+ .1028	+ .0828	+ .0582	+ .0298
7	.2545	.2514	.2305	.2131	.1909	.1649	.1344	.0996
8	.3718	.3646	.3372	.3134	.2847	.2517	.2133	.1708
9	.4929	.4816	.4475	.4171	.3812	.3399	.2930	.2407
10	.6153	.5994	.5578	.5204	.4765	.4266	.3699	.3075
11	.7367	.7148	.6646	.6191	.5667	.5076	.4413	.3688
12	.8547	.8242	.7633	.7085	.6469	.5786	.5036	.4226
13	.9565	.9075	.8519	.7900	.7216	.6469	.5657	.4781
14	1.0553	1.0003	.9388	.8710	.7967	.7161	.6292	.5358
15	1.1540	1.0930	1.0256	.9519	.8718	.7854	.6926	.5935
16	1.2528	1.1858	1.1125	1.0329	.9469	.8546	.7560	.6511
17	1.3515	1.2786	1.1993	1.1138	1.0220	.9238	.8195	.7088

tained by using the equation

$$\log a_1 = -\frac{2m}{2.303\cdot 55.51} + \frac{u}{55.51\sqrt{2}}\left[(1+\sqrt{2m}) - 2\ln(1+\sqrt{2m}) - \frac{1}{1+\sqrt{2m}}\right] - \frac{2}{55.51}(Bm^2/2 + 2Cm^3/3 + 3Dm^4/4 + 4Em^5/5) \quad (10)$$

At concentrations above 12 molal $\log a_1$ may be obtained in the following manner

$$\log a_1 = -\frac{2m}{2.303\cdot 55.51} - \frac{2}{55.51}\int_0^m m\,\mathrm{d}\log\gamma \quad (11)$$

Above 12 molal the value of $\log\gamma$ is given by a second order equation, which when introduced in (11) results in the expression

$$\log a_{1(m>12)} = \log a_{12} - \frac{2(m-12)}{2.303\cdot 55.51} - \frac{2}{55.51}\int_{12}^m m(b+2cm)\mathrm{d}m \quad (12)$$

where b and c are empirical constants given in Part II of Table IV. The last term of equation (12) when integrated gives the formula

$$-\frac{2}{55.51}\int_{12}^m m(b+2cm)\,\mathrm{d}m = -\frac{(m^2-144)b}{55.51} - \frac{4(m^3-1728)c}{3\cdot 55.51}$$

The vapor pressure of the solutions may finally be calculated from the simple relation

$$\log p_{m_1} = \log a_1 p_0$$

where p_0 is the vapor pressure of the pure solvent.

The result of the calculation of solvent activity and vapor pressure is summarized in Tables VI and VII. A comparison between the data in Tables I and VII shows the good agreement obtained between experimentally observed values and those computed from our electromotive force measurements. However, even though this is the case, the accuracy of the vapor pressure data is far too low to allow their use for the reverse procedure, the calculation of the thermodynamic properties of the solute. In Fig. 3 the variation of $\log a_1$ with the hydroxide concentration is shown graphically. The different isotherms are quite similar to the corresponding ones for hydrochloric acid but their curvature and dispersion is considerably larger. The direct measurements of Shibata and Murata[6a] of $\log a_1$ give values which agree very closely with ours at 20 and 30° over the entire concentration range.

Relative Partial Molal Free Energy of Solute and Solvent.—These quantities which we will need for the calculation of the entropy changes may be computed from the equations

$$\bar{F}_2 - \bar{F}_2^\circ = 2RT\,2.303\log\gamma m \quad (13)$$

$$\bar{F}_1 - \bar{F}_1^\circ = RT\,2.303\log a_1 \quad (14)$$

The calculated values are collected in Tables VIII and IX.

(6a) Shibata and Murata, *J. Chem. Soc. Japan*, **52**, 393 (1931).

TABLE VI

CALCULATED VALUES FOR THE LOGARITHM OF THE ACTIVITY OF THE SOLVENT IN AQUEOUS SOLUTIONS OF SODIUM HYDROXIDE. *All Values Negative*

m	0°	10°	20°	30°	40°	50°	60°	70°
0.1	0.0015	0.0015	0.0015	0.0015	0.0015	0.0015	0.0015	0.0015
.2	.0029	.0029	.0028	.0028	.0028	.0028	.0028	.0028
.4	.0057	.0058	.0058	.0058	.0058	.0058	.0058	.0058
.6	.0086	.0086	.0087	.0087	.0088	.0088	.0086	.0086
.8	.0116	.0116	.0118	.0117	.0117	.0117	.0116	.0115
1.0	.0145	.0147	.0148	.0149	.0148	.0148	.0147	.0146
1.5	.0226	.0230	.0230	.0230	.0231	.0229	.0228	.0226
2	.0312	.0316	.0317	.0317	.0319	.0316	.0314	.0311
3	.0514	.0516	.0517	.0516	.0515	.0511	.0507	.0502
4	.0762	.0761	.0756	.0751	.0746	.0739	.0731	.0723
5	.1061	.1055	.1040	.1027	.1015	.1002	.0990	.0978
6	.1419	.1403	.1375	.1355	.1332	.1310	.1289	.1265
7	.1834	.1809	.1766	.1730	.1695	.1659	.1622	.1585
8	.2309	.2272	.2210	.2158	.2106	.2050	.1993	.1935
9	.2834	.2786	.2705	.2633	.2556	.2478	.2392	.2306
10	.3411	.3347	.3238	.3143	.3039	.2929	.2814	.2691
11	.4026	.3939	.3799	.3672	.3537	.3392	.3240	.3078
12	.4672	.4548	.4365	.4199	.4026	.3844	.3655	.3458
13	.5273	.5122	.4912	.4720	.4520	.4312	.4097	.3874
14	.5910	.5731	.5492	.5271	.5043	.4806	.4562	.4311
15	.6582	.6371	.6102	.5849	.5591	.5324	.5050	.4768
16	.7290	.7046	.6744	.6459	.6168	.5867	.5561	.5248
17	.8033	.7754	.7416	.7096	.6770	.6435	.6094	.5746

TABLE VII

CALCULATED VALUES FOR THE LOGARITHM OF THE VAPOR PRESSURE OF AQUEOUS SOLUTIONS OF SODIUM HYDROXIDE

m	0°	10°	20°	30°	40°	50°	60°	70°
0.1	0.6593	0.9627	1.2424	1.5013	1.7414	1.9647	2.1728	2.3672
.2	.6579	.9613	1.2411	1.5000	1.7401	1.9634	2.1715	2.3659
.4	.6551	.9584	1.2381	1.4970	1.7371	1.9604	2.1685	2.3629
.6	.6522	.9555	1.2352	1.4941	1.7341	1.9574	2.1657	2.3601
.8	.6492	.9524	1.2321	1.4911	1.7312	1.9545	2.1627	2.3572
1.0	.6463	.9494	1.2291	1.4879	1.7281	1.9514	2.1596	2.3541
1.5	.6382	.9412	1.2209	1.4798	1.7198	1.9433	2.1515	2.3461
2	.6296	.9326	1.2122	1.4711	1.7110	1.9346	2.1429	2.3376
3	.6094	.9126	1.1922	1.4512	1.6914	1.9151	2.1236	2.3185
4	.5846	.8881	1.1683	1.4277	1.6683	1.8923	2.1012	2.2964
5	.5547	.8587	1.1399	1.4001	1.6414	1.8660	2.0753	2.2709
6	.5189	.8239	1.1064	1.3673	1.6097	1.8352	2.0454	2.2422
7	.4774	.7833	1.0673	1.3298	1.5734	1.8003	2.0121	2.2102
8	.4299	.7370	1.0229	1.2870	1.5323	1.7612	1.9750	2.1752
9	.3774	.6856	0.9734	1.2395	1.4873	1.7184	1.9351	2.1381
10	.3197	.6295	.9201	1.1885	1.4390	1.6733	1.8929	2.0996
11	.2582	.5703	.8640	1.1356	1.3892	1.6270	1.8503	2.0609
12	.1936	.5094	.8074	1.0829	1.3403	1.5818	1.8088	2.0229
13	.1335	.4520	.7527	1.0308	1.2909	1.5350	1.7646	1.9813
14	.0698	.3911	.6947	0.9757	1.2386	1.4856	1.7181	1.9376
15	.0026	.3271	.6337	.9179	1.1838	1.4338	1.6693	1.8919
16	− .0682	.2596	.5695	.8569	1.1261	1.3795	1.6182	1.8439
17	− .1425	.1888	.5023	.7932	1.0659	1.3227	1.5649	1.7941

Relative Partial Molal Heat Content of Solute and Solvent.—The former quantity is given in the case of sodium hydroxide concentrations below 12 molal by the formula

$$\bar{L}_2 = -6.9078RT\frac{u\sqrt{m}}{1+\sqrt{2m}}(1-\beta T) - 4.6052RT^2\left[m\frac{dB}{dT} + m^2\frac{dC}{dT} + m^3\frac{dD}{dT} + m^4\frac{dE}{dT}\right] \quad (15)$$

where β is the constant of Åkerlöf[7] for expressing the change of the dielectric constant of the solvent with temperature. For concentrations above 12

(7) Åkerlöf, THIS JOURNAL, 54, 4125 (1932).

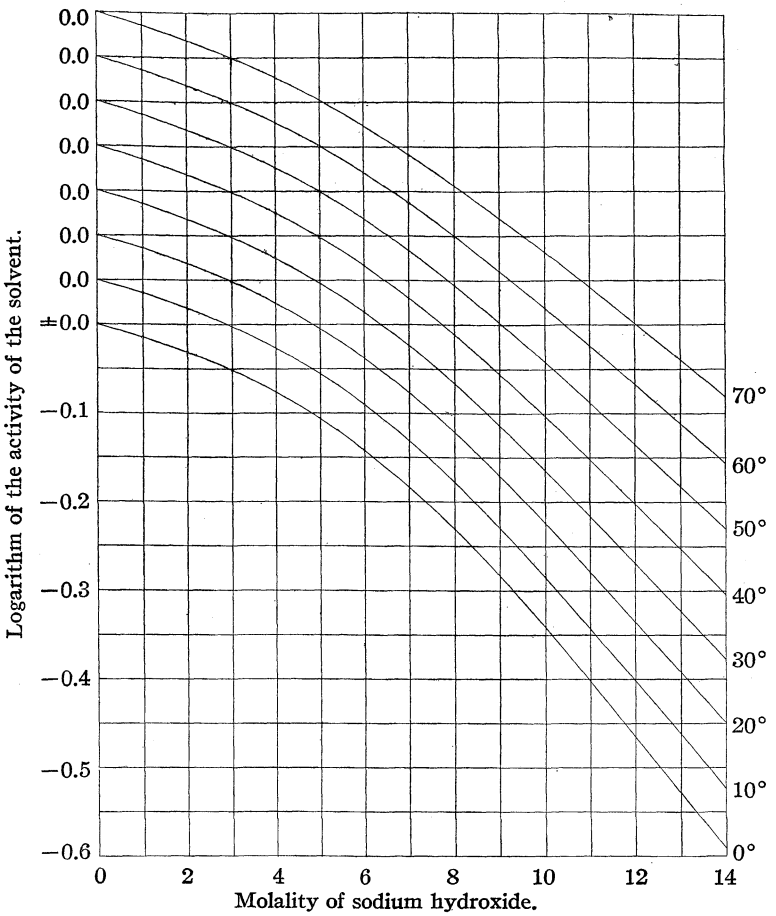


Fig. 3.—Isotherms for the logarithm of the activity of the solvent in aqueous solutions of sodium hydroxide. Ordinates are shifted successively for the different curves.

molal the following equation should be used

$$\bar{L}_2 = -2RT^2\, 2.303\ \mathrm{d}\log\gamma/\mathrm{d}T = -4.6052RT^2[\mathrm{d}a/\mathrm{d}t - m\,\mathrm{d}b/\mathrm{d}t - m^2\,\mathrm{d}c/\mathrm{d}t] \quad (16)$$

where a, b and c are the empirical constants given in Table IV for the equation

$$\log\gamma = a + bm + cm^2$$

The heat content of the solvent in solutions belonging to the lower concentration range may be computed from the formula

$$\bar{L}_1 = \frac{6.9078RTu(1-\beta T)}{2\cdot 55.51\cdot\sqrt{2}}\left[(1+\sqrt{2m}) - 4.6052\log(1+\sqrt{2m}) - \frac{1}{1+\sqrt{2m}}\right] + \frac{4.6052RT^2}{55.51}\left[\frac{m^2}{2}\frac{\mathrm{d}B}{\mathrm{d}T} + \frac{2m^3}{3}\frac{\mathrm{d}C}{\mathrm{d}T} + \frac{3m^4}{4}\frac{\mathrm{d}D}{\mathrm{d}T} + \frac{4m^5}{5}\frac{\mathrm{d}E}{\mathrm{d}T}\right] \quad (17)$$

where the constant β has the same meaning as in equation (15). For the higher concentration range we obtain the expression

$$\bar{L}_{1(m>12)} = -2.303RT^2\ \mathrm{d}\log a_1/\mathrm{d}T = \bar{L}_{1(12)} + \frac{2.303RT^2}{55.51}[(m^2-144)\mathrm{d}b/\mathrm{d}t + 4/3(m^3-1728)\mathrm{d}c/\mathrm{d}t] \quad (18)$$

Tables X and XI contain a summary of the values computed for $\bar{L}_1$ and $\bar{L}_2$. The values of the latter quantity calculated by Harned and Hecker from their data agree in dilute solutions quite well with ours but separate appreciably at higher concentrations. A graphical representation of our results is shown in Figs. 4 and 5. The former figure illustrates in particular the large deviations of the heat content of the hydroxide from the limiting law already in fairly dilute solutions.

Relative Partial Molal Entropy of Solute and Solvent.—As $F = H - TS$ the relative partial molal entropies may most simply be calculated from the free energies and heat contents

$$-(\bar{S}_2 - \bar{S}_2^\circ) = [(\bar{F}_2 - \bar{F}_2^\circ) - (\bar{H}_2 - \bar{H}_2^\circ)]/T \text{ and} \quad (19)$$

$$-(\bar{S}_1 - \bar{S}_1^\circ) = [(\bar{F}_1 - \bar{F}_1^\circ) - (\bar{H}_1 - \bar{H}_1^\circ)]/T \quad (20)$$

TABLE VIII

RELATIVE PARTIAL MOLAL FREE ENERGY OF THE SOLUTE IN AQUEOUS SOLUTIONS OF SODIUM HYDROXIDE

m	0°	10°	20°	30°	40°	50°	60°	70°
0.1	−2766	−2867	−2971	−3076	−3184	−3293	−3406	−3522
.2	−2078	−2151	−2229	−2308	−2391	−2477	−2569	−2664
.4	−1390	−1433	−1482	−1535	−1593	−1656	−1727	−1804
.6	− 983	−1006	−1038	−1073	−1116	−1165	−1225	−1293
.8	− 689	− 697	− 715	− 738	− 769	− 809	− 860	− 921
1.0	− 456	− 451	− 458	− 471	− 493	− 525	− 570	− 626
1.5	− 16	+ 20	+ 31	+ 37	+ 32	+ 14	− 19	− 66
2	+ 337	+ 381	+ 407	+ 426	+ 432	+ 425	+ 401	+ 362
3	900	965	1005	1041	1064	1071	1060	1034
4	1392	1468	1514	1559	1590	1606	1605	1588
5	1855	1938	1986	2034	2069	2090	2094	2082
6	2307	2394	2441	2491	2527	2548	2552	2539
7	2751	2843	2888	2938	2971	2989	2988	2969
8	3190	3287	3330	3377	3407	3418	3406	3375
9	3620	3723	3764	3807	3830	3830	3805	3755
10	4041	4148	4183	4221	4235	4222	4180	4109
11	4448	4554	4581	4610	4612	4584	4524	4432
12	4838	4936	4947	4963	4951	4906	4829	4720
13	5180	5242	5278	5286	5265	5211	5124	5003
14	5507	5566	5598	5600	5572	5511	5416	5286
15	5829	5884	5912	5908	5874	5805	5701	5561
16	6147	6197	6220	6211	6169	6093	5980	5831
17	6459	6506	6524	6508	6460	6376	6254	6095

TABLE IX

RELATIVE PARTIAL MOLAL FREE ENERGY OF THE SOLVENT IN AQUEOUS SOLUTIONS OF SODIUM HYDROXIDE. *All Values Negative*

m	0°	10°	20°	30°	40°	50°	60°	70°
0.1	1.9	1.9	2.0	2.1	2.2	2.2	2.3	2.4
.2	3.6	3.8	3.8	3.9	4.0	4.1	4.3	4.4
.4	7.1	7.5	7.8	8.1	8.3	8.6	8.8	9.1
.6	10.8	11.2	11.7	12.1	12.6	13.0	13.1	13.5
.8	14.5	15.0	15.8	16.2	16.8	17.3	17.7	18.1
1.0	18.1	19.1	19.9	20.7	21.2	21.9	22.4	22.9
1.5	28.3	29.8	30.9	31.9	33.1	33.9	34.8	35.5
2	39.0	41.0	42.6	44.0	45.7	46.8	47.9	48.9
3	64.3	66.9	69.4	71.6	73.9	75.6	77.3	78.9
4	95.3	98.7	101.5	104.3	107.0	109.4	111.5	113.6
5	132.7	136.8	139.6	142.6	145.6	148.3	151.0	153.7
6	177.5	181.9	184.6	188.1	191.0	193.9	196.6	198.8
7	229.4	234.5	237.1	240.2	243.1	245.5	247.4	249.1
8	288.8	294.6	296.7	299.6	302.0	303.4	304.0	304.1
9	354.5	361.2	363.1	365.5	366.6	366.7	364.9	362.4
10	426.7	434.0	434.7	436.3	435.8	433.4	429.3	422.9
11	503.6	510.7	510.0	509.7	507.2	501.9	494.3	483.7
12	584.4	589.7	586.0	582.9	577.4	568.8	557.6	543.4
13	659.6	664.1	659.4	655.2	648.2	638.1	625.0	608.8
14	739.3	743.1	737.3	731.7	723.2	711.2	695.9	677.4
15	823.3	826.1	819.2	812.0	801.8	787.8	770.4	749.2
16	911.9	913.6	905.4	896.6	884.6	868.2	848.3	824.7
17	1004.8	1005.4	995.6	985.1	970.9	952.3	929.6	902.9

The results of the calculations appear in Tables XII and XIII. A graphical representation is given in Figs. 6 and 7. The curves for the solute show an increasingly sharper minimum and large changes of form with increasing temperature. As a comparison the corresponding entropy curves for hydrochloric acid are all practically symmetrical parabolas.

TABLE X

RELATIVE PARTIAL MOLAL HEAT CONTENT OF THE SOLUTE IN AQUEOUS SOLUTIONS OF SODIUM HYDROXIDE

m	0°	10°	20°	30°	40°	50°	60°	70°
0.1	+ 9	+ 53	+103	+159	+223	+293	+373	+462
.2	− 60	+ 7	+ 85	172	272	384	509	648
.4	−208	−102	+ 20	159	317	496	697	921
.6	−345	−207	− 48	134	341	575	840	1132
.8	−463	−300	−110	107	358	638	956	1308
1.0	−565	−377	−162	86	371	692	1054	1456
1.5	−742	−511	−250	57	405	801	1245	1741
2	−823	−564	−275	67	454	893	1388	1939
3	−761	−477	−170	195	611	1079	1607	2193
4	−502	−207	+88	449	858	1319	1835	2409
5	−145	+162	445	800	1203	1652	2154	2711
6	+237	575	857	1228	1644	2104	2618	3184
7	602	996	1300	1712	2174	2684	3249	3868
8	938	1411	1763	2248	2789	3385	4043	4764
9	1260	1834	2251	2832	3479	4188	4973	5829
10	1616	2297	2783	3467	4227	5060	5978	6982
11	2080	2862	3398	4166	5019	5954	6979	8099
12	2756	3603	4144	4950	5839	6805	7865	9018
13	3136	3842	4621	5482	6426	7455	8575	9789
14	3544	4277	5086	5977	6952	8012	9164	10411
15	3952	4713	5552	6471	7477	8568	9752	11032
16	4361	5150	6018	6966	8002	9125	10341	11653
17	4769	5587	6483	7461	8527	9681	10928	12272

Relative Partial Molal Heat Capacity of the Solute.—According to definition $\bar{c}_{p_2} - \bar{c}_{p_2}^\circ = d\bar{L}_2/dT$ and we thus obtain for the lower concentration range the following expression for the calculation of the heat capacity of the solute

$$\bar{c}_{p_2} - \bar{c}_{p_2}^\circ = 3.4539R(1 - 2\beta T + 3\beta^2T^2)\frac{u\sqrt{m}}{1+\sqrt{2m}} - 9.2104RT\left[m\frac{dB}{dT} + m^2\frac{dC}{dT} + m^3\frac{dD}{dT} + m^4\frac{dE}{dT}\right] -$$

TABLE XI

RELATIVE PARTIAL MOLAL HEAT CONTENT OF THE SOLVENT IN AQUEOUS SOLUTIONS OF SODIUM HYDROXIDE

m	0°	10°	20°	30°	40°	50°	60°	70°
0.1	0.0	0.0	0.0	− 0.1	− 0.1	− 0.1	− 0.2	− 0.2
.2	+ 0.3	+ .2	+ .1	− .1	− .3	− 0.4	− 0.6	− 0.8
.4	1.0	.7	.3	.0	− .4	− 1.0	− 1.6	− 2.2
.6	2.2	1.6	.9	+ .2	− .6	− 1.5	− 2.8	− 4.2
.8	3.7	2.8	1.8	.6	− .9	− 2.5	− 4.3	− 6.3
1.0	5.4	4.2	2.4	1.0	− 1.0	− 3.4	− 6.0	− 8.8
1.5	9.2	7.1	4.4	1.6	− 2.0	− 5.8	− 10.3	− 15.1
2	11.7	8.6	5.3	1.3	− 3.5	− 8.6	− 14.6	− 21.2
3	8.6	4.3	0.3	− 4.7	− 10.6	− 17.1	− 24.4	− 32.6
4	− 8.0	− 12.8	− 16.1	− 20.1	− 26.4	− 32.3	− 38.9	− 46.1
5	− 37.0	− 43.0	− 45.2	− 49.7	− 54.3	− 59.5	− 65.0	− 70.9
6	− 74.8	− 83.8	− 86.1	− 92.1	− 98.2	− 104.6	− 111.0	− 118.0
7	− 117.7	− 133.0	− 138.1	− 149.0	− 160.7	− 172.5	− 185.3	− 198.5
8	− 162.9	− 189.2	− 200.6	− 221.4	− 243.8	− 267.6	− 292.8	− 319.7
9	− 212.6	− 253.8	− 275.3	− 310.6	− 349.4	− 390.6	− 435.3	− 483.1
10	− 273.3	− 333.4	− 366.4	− 419.4	− 477.7	− 539.9	− 607.5	− 680.4
11	− 361.3	− 440.0	− 482.8	− 552.0	− 627.6	− 708.8	− 796.7	− 891.6
12	− 502.1	− 594.2	− 637.9	− 714.2	− 797.3	− 885.2	− 980.0	−1081.5
13	− 593.8	− 692.3	− 742.6	− 825.7	− 915.7	−1010.7	−1112.7	−1221.7
14	− 692.9	− 798.3	− 855.7	− 946.0	−1043.5	−1146.1	−1256.0	−1373.0
15	− 799.5	− 912.3	− 977.2	−1075.3	−1180.8	−1291.6	−1409.7	−1535.2
16	− 913.6	−1034.2	−1107.3	−1213.5	−1327.5	−1446.9	−1573.9	−1708.4
17	−1035.4	−1164.2	−1245.8	−1360.7	−1483.7	−1612.1	−1748.6	−1892.6

TABLE XII

RELATIVE PARTIAL MOLAL ENTROPY OF THE SOLUTE IN AQUEOUS SOLUTIONS OF SODIUM HYDROXIDE. VALUES OF $-(\bar{S}_2 - \bar{S}_2^\circ)$

m	0°	10°	20°	30°	40°	50°	60°	70°
0.1	−10.016	−10.314	−10.488	−10.673	−10.882	−11.099	−11.345	−11.612
.2	− 7.389	− 7.623	− 7.895	− 8.182	− 8.505	− 8.855	− 9.240	− 9.653
.4	− 4.328	− 4.702	− 5.124	− 5.589	− 6.100	− 6.660	− 7.277	− 7.942
.6	− 2.336	− 2.822	− 3.378	− 3.982	− 4.653	− 5.385	− 6.199	− 7.068
.8	− 0.827	− 1.402	− 2.064	− 2.788	− 3.600	− 4.478	− 5.452	− 6.497
1.0	+ 0.399	− 0.262	− 1.010	− 1.838	− 2.760	− 3.768	− 4.875	− 6.068
1.5	2.658	+ 1.876	+ 0.959	− 0.066	− 1.231	− 2.436	− 3.795	− 5.267
2	4.248	+ 3.338	+ 2.327	+ 1.184	− 0.070	− 1.448	− 2.963	− 4.596
3	6.082	5.094	4.009	+ 2.791	+ 1.447	− 0.015	− 1.642	− 3.378
4	6.935	5.917	4.865	3.662	+ 2.340	+ 0.888	− 0.690	− 2.393
5	7.323	6.273	5.258	4.071	2.766	+ 1.356	− .180	− 1.833
6	7.580	6.425	5.404	4.167	2.820	1.374	− .198	− 1.880
7	7.867	6.524	5.418	4.045	2.547	0.944	− .784	− 2.620
8	8.246	6.627	5.346	3.725	1.974	0.102	− 1.912	− 4.048
9	8.641	6.673	5.162	3.217	1.121	− 1.108	− 3.506	− 6.045
10	8.880	6.538	4.776	2.448	0.003	− 2.594	− 5.398	− 8.374
11	8.671	5.977	4.036	1.465	− 1.300	− 4.240	− 7.370	−10.688
12	7.624	4.709	2.740	0.043	− 2.836	− 5.877	− 9.114	−12.527
13	7.484	4.945	2.242	− 0.647	− 3.708	− 6.945	−10.360	−13.949
14	7.188	4.553	1.747	− 1.244	− 4.408	− 7.741	−11.252	−14.935
15	6.873	4.136	1.228	− 1.857	− 5.120	− 8.552	−12.162	−15.946
16	6.540	3.698	0.689	− 2.491	− 5.854	− 9.384	−13.092	−16.969
17	6.188	3.246	0.140	− 3.144	− 6.602	−10.229	−14.032	−18.003

$$4.6052RT^2\left[m\frac{d^2B}{dT^2} + m^2\frac{d^2C}{dT^2} + m^3\frac{d^2D}{dT^2} + m^4\frac{d^2E}{dT^2}\right] \quad (21)$$

For the upper concentration range differentiation of equation (16) would give the desired quantity, but the accuracy of the measurements is too low to warrant a second differentiation. The values calculated from equation (21) are presented in Table XIV. In the first part of Table XV our values at 25° are compared with values obtained

TABLE XIII

RELATIVE PARTIAL MOLAL ENTROPY OF THE SOLVENT IN AQUEOUS SOLUTIONS OF SODIUM HYDROXIDE. VALUES OF $-(\bar{S}_1 - \bar{S}_1^\circ)$

m	0°	10°	20°	30°	40°	50°	60°	70°
0.1	−0.0070	−0.0069	−0.0068	−0.0067	−0.0066	−0.0065	−0.0065	−0.0065
.2	− .0143	− .0140	− .0133	− .0125	− .0118	− .0114	− .0111	− .0108
.4	− .0297	− .0289	− .0279	− .0267	− .0252	− .0235	− .0216	− .0201
.6	− .0476	− .0452	− .0430	− .0406	− .0383	− .0356	− .0309	− .0271
.8	− .0666	− .0629	− .0600	− .0554	− .0508	− .0458	− .0402	− .0344
1.0	− .0860	− .0823	− .0761	− .0714	− .0645	− .0572	− .0492	− .0411
1.5	− .137	− .130	− .120	− .110	− .0993	− .0869	− .0735	− .0594
2	− .186	− .175	− .163	− .149	− .135	− .118	− .100	− .0807
3	− .267	− .251	− .238	− .221	− .202	− .181	− .159	− .135
4	− .320	− .303	− .291	− .277	− .257	− .238	− .218	− .196
5	− .350	− .331	− .322	− .307	− .292	− .274	− .258	− .241
6	− .376	− .346	− .336	− .317	− .296	− .276	− .257	− .235
7	− .409	− .358	− .338	− .301	− .263	− .226	− .186	− .147
8	− .461	− .372	− .328	− .258	− .186	− .111	− .034	+ .045
9	− .520	− .379	− .300	− .181	− .055	+ .074	+ .211	.351
10	− .561	− .355	− .233	− .056	+ .134	.329	.534	.750
11	− .521	− .250	− .093	+ .140	.384	.640	.908	1.189
12	− .301	+ .016	+ .177	.433	.702	.979	1.268	1.568
13	− .241	.100	.284	.563	.854	1.153	1.464	1.786
14	− .170	.195	.404	.707	1.023	1.346	1.681	2.027
15	− .087	.304	.539	.869	1.211	1.559	1.919	2.290
16	+ .006	.426	.689	1.046	1.415	1.791	2.178	2.575
17	+ .112	.561	.854	1.239	1.638	2.042	2.459	2.884

TABLE XIV

RELATIVE PARTIAL MOLAL HEAT CAPACITY OF THE SOLUTE IN AQUEOUS SOLUTIONS OF SODIUM HYDROXIDE

m	0°	10°	20°	30°	40°	50°	60°	70°
0.1	4.9	5.2	5.7	6.3	6.8	7.4	8.1	8.8
.2	7.6	8.4	9.1	9.8	10.7	11.6	12.6	13.5
.4	12.4	13.9	14.6	15.8	17.2	18.5	20.0	21.5
.6	16.2	17.7	19.3	20.8	22.4	24.2	26.1	28.0
.8	19.6	21.2	23.0	24.9	27.0	29.0	31.3	33.6
1.0	22.3	24.3	26.4	28.5	30.7	33.1	35.6	38.4
1.5	27.5	29.8	32.4	34.9	37.7	40.6	43.7	46.8
2	30.4	33.1	35.8	38.7	41.7	44.4	48.2	51.8
3	32.0	34.8	37.7	40.6	44.0	48.2	50.7	54.5
4	30.5	33.1	35.9	38.7	41.7	45.0	48.5	52.0
5	28.5	31.0	33.5	36.0	39.1	42.0	45.2	48.6
6	27.6	30.0	32.4	35.0	37.8	40.6	43.7	46.9
7	28.9	31.4	34.0	36.6	39.5	42.5	45.7	49.1
8	32.6	35.3	38.1	41.1	44.3	47.7	51.2	54.9
9	37.7	41.0	44.2	47.7	51.3	55.3	59.3	63.6
10	43.4	47.1	50.7	54.7	58.9	63.3	67.9	72.6
11	47.3	51.4	55.3	59.7	64.1	68.8	73.8	79.0
12	46.4	50.3	54.2	58.3	62.8	67.4	72.2	77.2

from direct calorimetric measurements made by Rossini[8] and by Gucker and Schminke[9] through 2 molal solutions. The agreement is remarkably good, our values above 0.6 molal all falling between the two sets of calorimetric data. The values calculated by Harned and Hecker are also in good agreement with ours. A graphical representation of the changes of the heat capacity of the hydroxide is given in Fig. 8. All the curves show a maximum around 3, a minimum around 6, and a second maximum near 12 molal seems to be indicated. In contrast the corresponding curves for hydrochloric acid are practically straight lines.

(8) Rossini, *Bur. Standards J. Res.*, **6**, 791 (1931).
(9) Gucker and Schminke, THIS JOURNAL, **55**, 1013 (1933).

TABLE XV

COMPARISON OF THE HEAT CAPACITY DATA IN TABLES XIV AND XVI INTERPOLATED TO 25° WITH DATA IN THE LITERATURE, ALSO AT 25°

I. Relative partial molal heat capacity of the solute

m	$\sqrt{m}$	Rossini	Åkerlöf and Kegeles	Gucker and Schminke
0.1	0.3162	9.01	6.0	8.29
.2	.4472	12.75	9.5	11.73
.4	.6325	18.0	15.2	16.6
.6	.7746	22.1	20.1	20.3
.8	.8944	25.5	24.0	23.5
1.0	1.0000	28.5	27.5	26.2
1.5	1.2247	34.9	33.7	32.1
2.0	1.4142	40.3	37.3	37.1

II. Relative partial molal heat capacity of the solvent

m	$m^{3/2}$			
0.1	0.0316	−0.0054	−0.002	−0.0050
.2	.0894	.0152	.008	.0141
.4	.2530	.0433	.035	.0400
.6	.4648	.0794	.081	.0734
.8	.7155	.122	.139	.113
1.0	1.0000	.171	.205	.158
1.5	1.8372	.314	.386	.290
2.0	2.8284	.484	.572	.447

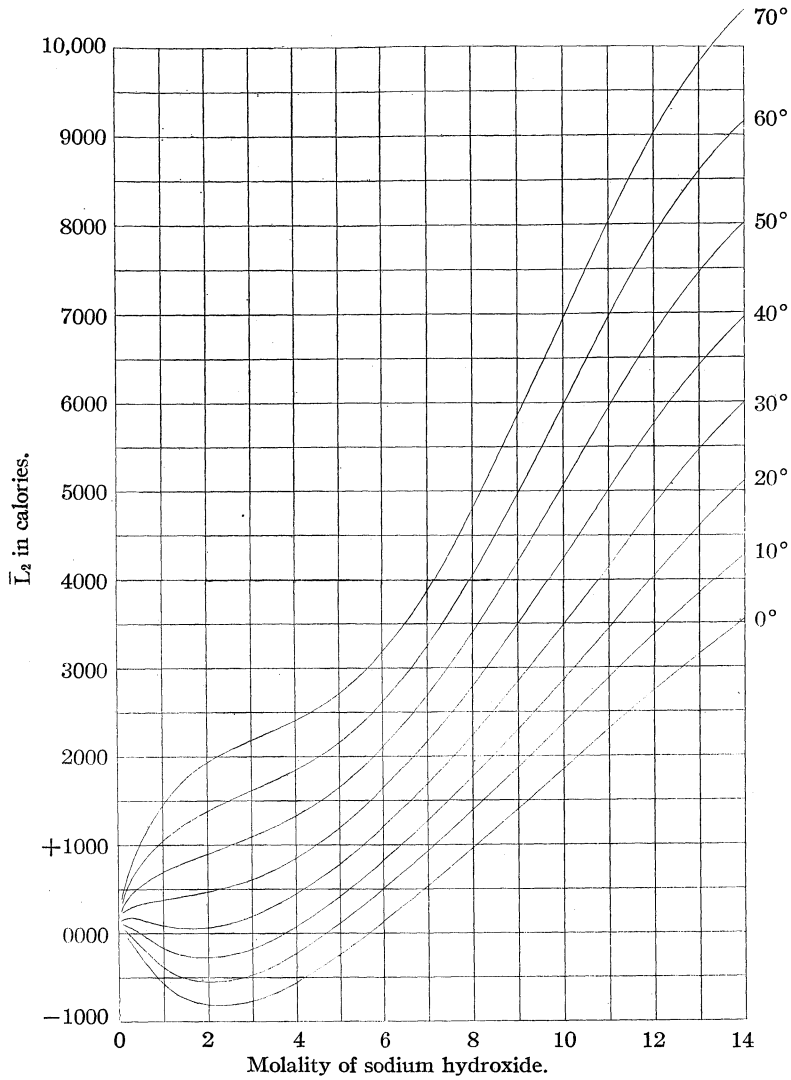


Fig. 4.—Isotherms for the relative partial molal heat content of the solute in aqueous solutions of sodium hydroxide.

Relative Partial Molal Heat Capacity of the Solvent.—For the lower concentration range differentiation of equation (17) gives directly

$$\bar{c}_{p_1} - \bar{c}_{p_1}^{\circ} = \frac{3.4539Ru}{2\cdot 55.51\sqrt{2}}(1 - 2\beta T + 3\beta^2T^2)\left[1 + \sqrt{2m} - 4.6052 \log (1 + \sqrt{2m}) - \frac{1}{1 + \sqrt{2m}}\right] + \frac{9.2104RT}{55.51}\left[\frac{m^2}{2}\frac{dB}{dT} + \frac{2m^3}{3}\frac{dC}{dT} + \frac{3m^4}{4}\frac{dD}{dT} + \frac{4m^5}{5}\frac{dE}{dT}\right] + \frac{4.6052RT^2}{55.51}\left[\frac{m^2}{2}\frac{d^2B}{dT^2} + \frac{2m^3}{3}\frac{d^2C}{dT^2} + \frac{3m^4}{4}\frac{d^2D}{dT^2} + \frac{4m^5}{5}\frac{d^2E}{dT^2}\right] \quad (22)$$

As in the case of the solute, values of the heat capacity of the solvent above 12 molal have not been calculated, although rough values could be obtained by differentiation of equation (18). Table XVI contains a summary of the values calculated from equation (22). In the second part of Table XV is again made a direct comparison with the result of the calorimetric measurements of Rossini and of Gucker and Schminke. As in the case of the solute the absolute agreement is quite good and only in one case, near the upper limit of the extrapolation function used by these authors, is the discrepancy between their values and ours greater than 0.1 calorie. Figure 9 gives a graphical representation of the changes of the heat capacity of the solvent. The curves have a very uniform appearance over the entire temperature range employed, but they are complicated in form. As a comparison the corresponding curves for hydrochloric acid solutions are practically

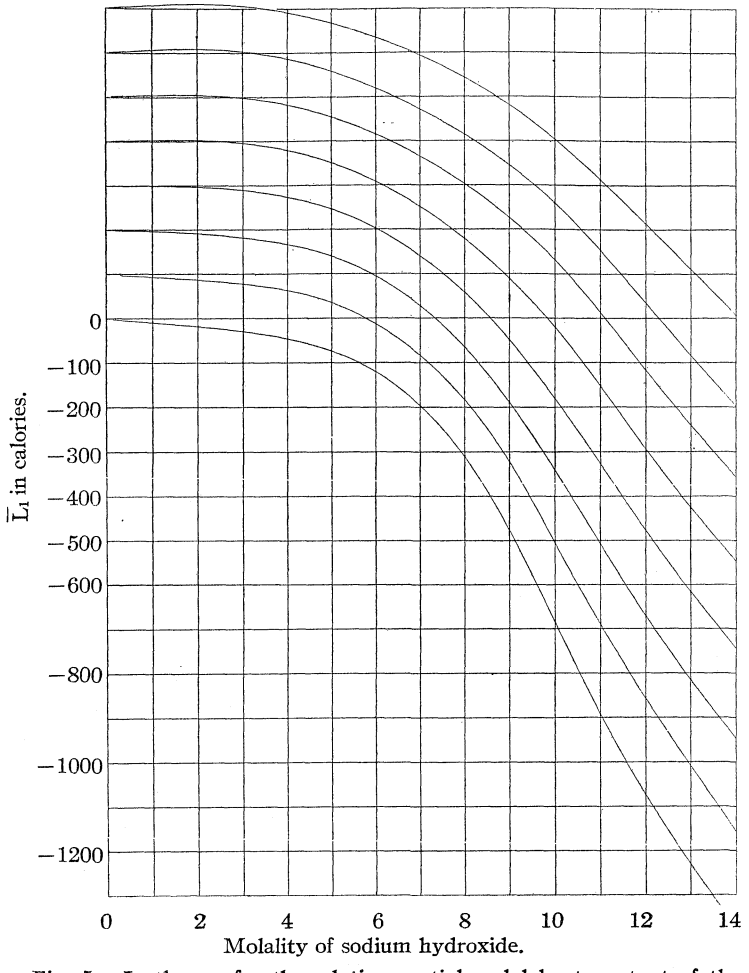


Fig. 5.—Isotherms for the relative partial molal heat content of the solvent in aqueous solutions of sodium hydroxide. Ordinates are shifted successively for the different curves.

TABLE XVI

RELATIVE PARTIAL MOLAL HEAT CAPACITY OF THE SOLVENT IN AQUEOUS SOLUTIONS OF SODIUM HYDROXIDE. *All Values Negative*

m	0°	10°	20°	30°	40°	50°	60°	70°
0.1	0.001	0.002	0.002	0.002	0.003	0.001	0.002	0.002
.2	.008	.008	.007	.008	.008	.009	.010	.010
.4	.029	.031	.034	.036	.040	.042	.044	.047
.6	.066	.072	.078	.083	.090	.095	.100	.107
.8	.115	.124	.134	.143	.152	.163	.174	.178
1.0	.168	.182	.198	.211	.213	.241	.255	.272
1.5	.319	.346	.372	.399	.426	.455	.484	.515
2	.475	.513	.552	.591	.634	.676	.719	.763
3	.733	.790	.847	.909	.972	1.035	1.099	1.167
4	.925	.994	1.066	1.145	1.214	1.292	1.371	1.451
5	1.137	1.221	1.305	1.392	1.482	1.574	1.667	1.765
6	1.526	1.637	1.748	1.866	1.982	2.105	2.229	2.356
7	2.240	2.405	2.568	2.741	2.918	3.100	3.286	3.477
8	3.381	3.637	3.889	4.154	4.427	4.707	4.995	5.293
9	4.939	5.316	5.690	6.084	6.491	6.910	7.340	7.784
10	6.737	7.255	7.772	8.314	8.877	9.455	10.049	10.663
11	8.387	9.033	9.675	10.351	11.054	11.774	12.517	13.281
12	9.220	9.928	10.623	11.359	12.122	12.905	13.712	14.543

linear when plotted against the square of the molality.

The Total Heat Capacity and the Specific Heat of the Solution.—These quantities are obtained from the relations: $C_p = 55.51\bar{c}_{p_1} + m\bar{c}_{p_2}$ per $1000 + Mm$ grams of solution and $s = C_p/(1000 + Mm)$ per gram of solution (M molecular weight of sodium hydroxide) respectively, in cases where it is possible to obtain values of $\bar{c}^\circ_{p_1}$ and $\bar{c}^\circ_{p_2}$. For sodium hydroxide solutions values of the latter quantity are given by Rossini at 18 and 21.5° and by Gucker and Schminke at 25°. Rossini also gives as a mean value for $d\bar{c}^\circ_{p_2}/dT = {}^2/_7$ cal. per degree. Using the value −26.6 of Gucker and Schminke, whose data are in better agreement with ours than those of Rossini, and the latter's value for $d\bar{c}^\circ_{p_2}/dT$ we get at 20° $\bar{c}^\circ_{p_2} = -28.0$ calories. This value combined with the values of $\bar{c}^\circ_{p_2} - \bar{c}^\circ_{p_2}$ in Table XIV for 20° would give values for $\bar{c}_{p_2}$ up to 12 molal.

The value of $\bar{c}^\circ_{p_1}$ is obtained by multiplying the specific heat of water by its molecular weight. The value used for the specific heat is 0.9988 cal. per degree, giving $\bar{c}^\circ_{p_1} = 18.014$. This value combined with the data in Table XVI for $\bar{c}^\circ_{p_1} - \bar{c}^\circ_{p_1}$ at 20° would give values for $\bar{c}_{p_1}$ up to 12 molal. With both $\bar{c}^\circ_{p_2}$ and $\bar{c}^\circ_{p_1}$ known, the total heat capacity and specific heat of the solutions may be calculated using the relations given above. A summary of the results is shown in Table XVII. An error analysis based on the data in Table XV indicates that the specific heats should have an accuracy of one unit in the third decimal place up to concentrations well above 2 molal. At higher concentrations the errors would be increasingly larger as found by a comparison with the calorimetric data of Bartetti and McCabe.[9a]

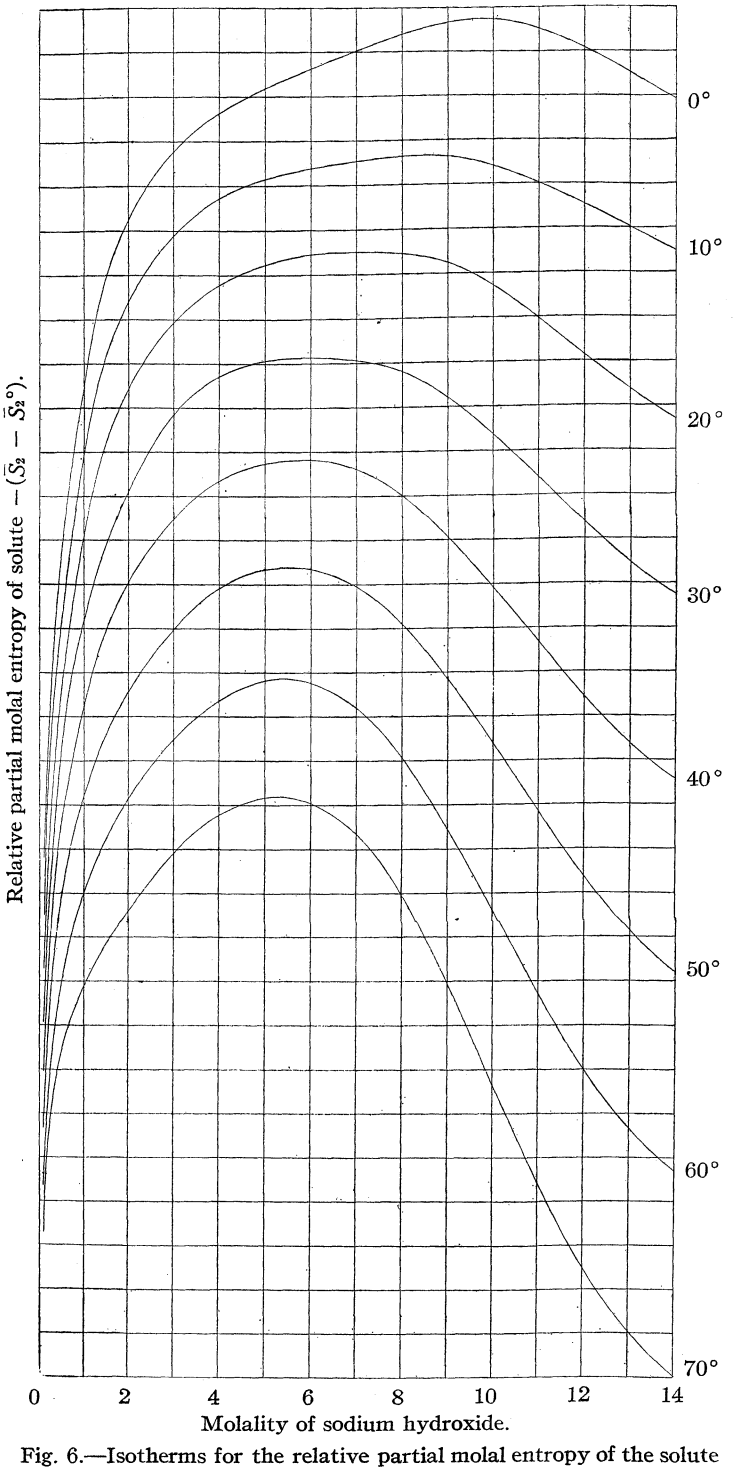


Fig. 6.—Isotherms for the relative partial molal entropy of the solute in aqueous solutions of sodium hydroxide. Ordinates are shifted successively for the different curves.

The Total Relative Heat Content of the Solutions.—This quantity which is equal to the heat evolved upon dilution to zero concentration is defined by the relation: $L_{(m)} = 55.51\ \bar{L}_1 + m\bar{L}_2$ per $1000 + Mm$ grams of solution. The molal value L/m, usually called the integral heat of dilution, also has considerable interest. Values

(9a) Bartetti and McCabe, *Ind. Eng. Chem.*, **28**, 375 (1936).

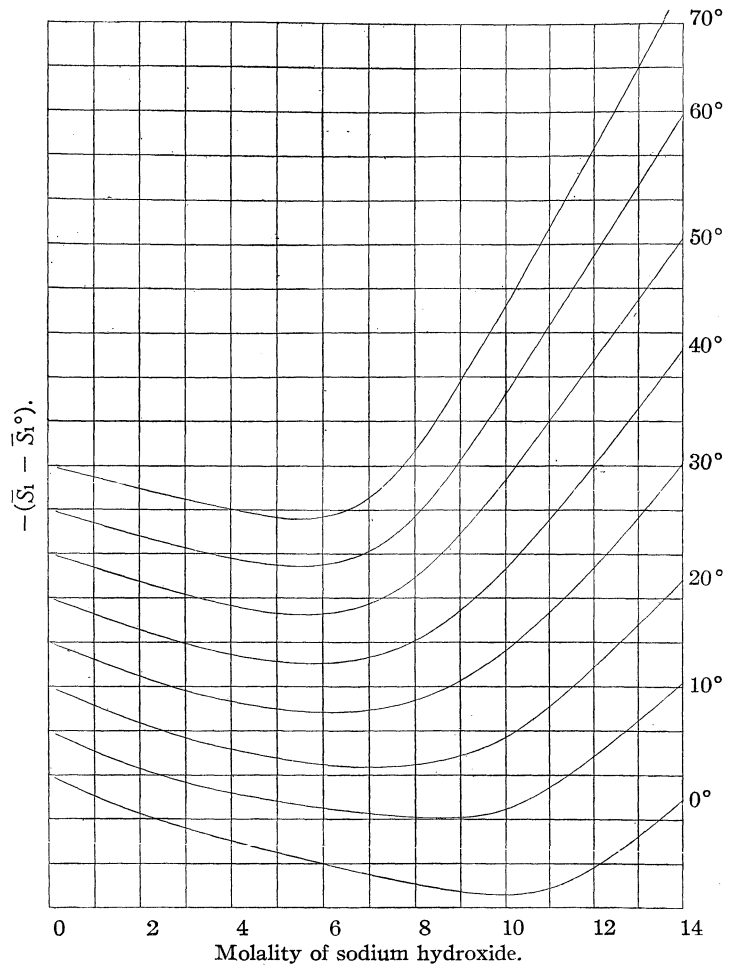


Fig. 7.—Isotherms for the relative partial molal entropy of the solvent in aqueous solutions of sodium hydroxide. Ordinates are shifted successively for the different curves.

of L and L/m are simply obtained by the use of the data in Tables X and XI for $\bar{L}_2$ and $\bar{L}_1$, respectively. Those calculated for 20° are collected in Table XVIII. They are needed for the computation of the following quantity which has a practical value.

TABLE XVII

TOTAL HEAT CAPACITY AND SPECIFIC HEAT OF AQUEOUS SOLUTIONS OF SODIUM HYDROXIDE AT 20°

m	C_p	s
0.1	997.58	0.9936
.2	995.75	.9878
.4	992.67	.9770
.6	990.37	.9672
.8	988.48	.9578
1.0	987.3	.9493
1.5	985.9	.9300
2.0	984.9	.9119
3.0	982.0	.8767

The Heat of Dilution between Two Finite Concentrations.—If n moles of water are used to dilute a solution of mass M and molality m to a molality m'

$$m' = \frac{55.51 \cdot M \cdot m}{55.51M + (1000 + 40m)n} \quad (23)$$

the isothermal heat absorbed by the system is given by the equation

$$\Delta H = \frac{M}{1000 + 40m}[L_{(m')} - L_{(m)}] + \frac{Mnm\bar{L}_{2(m')}}{55.51M + (1000 + 40m)n} + n\bar{L}_{1(m')} \quad (24)$$

The use of equation (24) permits the calculation of the heat of dilution of sodium hydroxide solutions at any temperature in the range 0 to 70° for any arbitrary amount of solution between any two molalities from 0.1 to 17 molal. Values of $\Delta H/m$ calculated from (24) agree remarkably well with the data of Richards and co-workers and Fricke.[9b]

The Differential Heat of Vaporization.—This quantity ΔH_v is defined as the amount of heat necessary to vaporize one mole of the solvent at constant temperature and pressure from a sufficiently large body of the solution so that no concentration change takes place. To calculate this quantity we will make use of the relationship

$$\bar{L}_1 = -RT^2\partial \ln p_1/\partial T + RT^2\partial \ln p_1°/\partial T \quad (25)$$

The second term of equation (25) is recognized immediately as the approximate Clausius–Clapey-

TABLE XVIII

TOTAL RELATIVE HEAT CONTENT OF AQUEOUS SOLUTIONS OF SODIUM HYDROXIDE AT 20°

(Heat of Infinite Dilution)

m	L	L/m	m	L	L/m
0.1	10	100	4	−542	−136
.2	23	115	5	−284	− 57
.4	25	63	6	363	61
.6	21	35	7	1434	205
.8	12	15	8	2969	371
1.0	− 29	− 29	9	4978	593
1.5	−131	− 87	10	7442	744
2.0	−256	−128	11	10579	962
3.0	−493	−164	12	23319	1943

(9b) Richards and Rowe, THIS JOURNAL, **43**, 770 (1921); Richards and Gucker, *ibid.*, **51**, 712 (1929); Richards and Hall, *ibid.*, **51**, 731 (1929); Fricke, *Z. Elektrochem.*, **35**, 631 (1929).

TABLE XIX

DIFFERENTIAL HEATS OF VAPORIZATION OF THE SOLVENT FROM AQUEOUS SOLUTIONS OF SODIUM HYDROXIDE

m	0°	10°	20°	30°	40°	50°	60°	70°
0.0	1091.4	1080.9	1070.5	1060.3	1049.9	1039.5	1029.1	1018.4
.1	1091.4	1080.9	1070.5	1060.4	1050.0	1039.6	1029.3	1018.2
.2	1091.1	1080.7	1070.4	1060.4	1050.2	1039.9	1029.7	1019.2
.4	1090.4	1080.2	1070.2	1060.3	1050.3	1040.5	1030.7	1020.6
.6	1089.2	1079.3	1069.6	1060.1	1050.5	1041.0	1031.9	1022.6
.8	1087.7	1078.1	1068.7	1059.7	1050.8	1042.0	1033.4	1024.7
1.0	1086.0	1076.7	1068.1	1059.3	1050.9	1042.9	1035.1	1027.2
1.5	1082.2	1073.8	1066.1	1058.7	1051.9	1045.3	1039.4	1033.5
2	1079.7	1072.3	1065.2	1059.0	1053.4	1048.1	1043.7	1039.6
3	1082.8	1076.6	1070.2	1065.0	1060.5	1056.6	1053.5	1051.0
4	1099.4	1093.7	1086.6	1080.4	1076.3	1071.8	1068.0	1064.5
5	1128.4	1123.9	1115.7	1110.0	1104.2	1099.0	1094.1	1089.3
6	1166.2	1164.7	1156.6	1152.4	1148.1	1144.1	1140.1	1136.4
7	1209.1	1213.9	1208.6	1209.3	1210.6	1212.0	1214.4	1216.9
8	1254.3	1270.1	1271.1	1281.7	1293.7	1307.1	1321.9	1338.1
9	1304.0	1334.7	1345.8	1370.9	1399.3	1430.1	1464.4	1501.5
10	1364.7	1414.3	1436.9	1479.7	1527.6	1579.4	1636.6	1698.8
11	1452.7	1520.9	1553.3	1612.3	1677.5	1748.3	1825.8	1910.0
12	1593.5	1675.1	1708.4	1774.5	1847.2	1924.7	2009.1	2099.9
13	1685.2	1773.2	1813.1	1886.0	1965.6	2050.2	2141.8	2240.1
14	1784.3	1879.2	1926.2	2006.3	2093.4	2185.6	2285.1	2391.4
15	1890.9	1993.2	2047.7	2135.6	2230.7	2331.1	2438.8	2553.6
16	2005.0	2115.1	2177.8	2273.8	2377.4	2486.4	2603.0	2726.8
17	2126.8	2245.1	2316.3	2421.0	2533.6	2651.6	2777.7	2911.0

ron expression for the heat of vaporization $\Delta H_v°$ of one mole of the pure solvent. By rigorous thermodynamic methods the first term is found to represent the analogous quantity for solvent in the solution, provided no concentration change takes place during the loss of one mole of solvent. This quantity is therefore the differential heat of vaporization as defined above.

Using the measurements of $\Delta H_v°$ for water by Keyes, Smith and Gerry[10] after conversion from cc. atm./g. to cal./mole and the values of $\bar{L}_1$ in Table XI, the values calculated for ΔH_v have been collected in Table XIX. These data are limiting values for the next quantity to be considered.

The Integral Heat of Vaporization.—This quantity is defined as the amount of heat necessary to vaporize one mole of solvent from a given finite amount of solution, the accompanying concentration change being determined by the original concentration and mass of the solution. If one mole of water is vaporized from a sodium hydroxide solution of original mass M and molality m, the isothermal heat absorbed by the system is thus given by the integral heat of vaporization

$$Q = \Delta H_v° + \frac{M}{1000 + 40m}[L_{(m')} - L_{(m)}] - \frac{MmL_{2(m')}}{55.51M - 1000 - 40m} - \bar{L}_{1(m')} \quad (26)$$

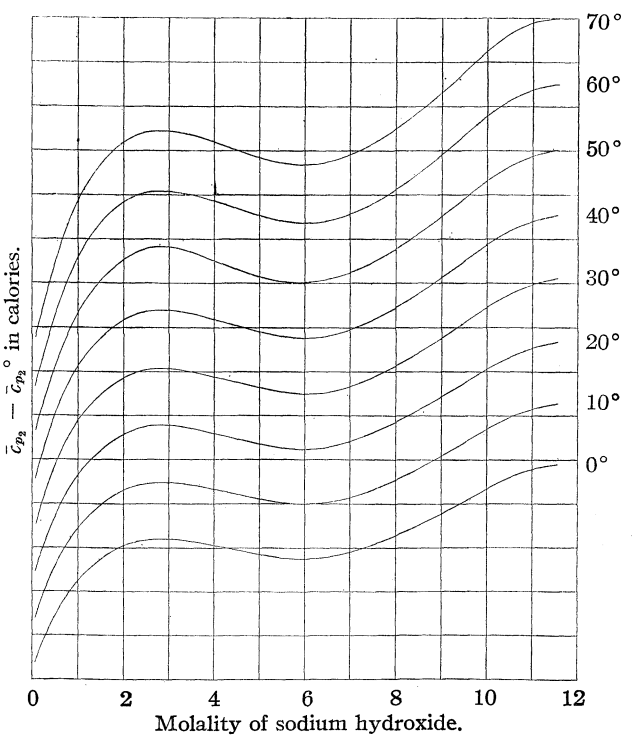


Fig. 8.—Isotherms for the relative partial molal heat capacity of the solute in aqueous solutions of sodium hydroxide. Ordinates are shifted successively for the different curves.

(10) Keyes, Smith and Gerry, *Proc. Amer. Acad. Arts and Sci.*, **70**, 318 (1936).

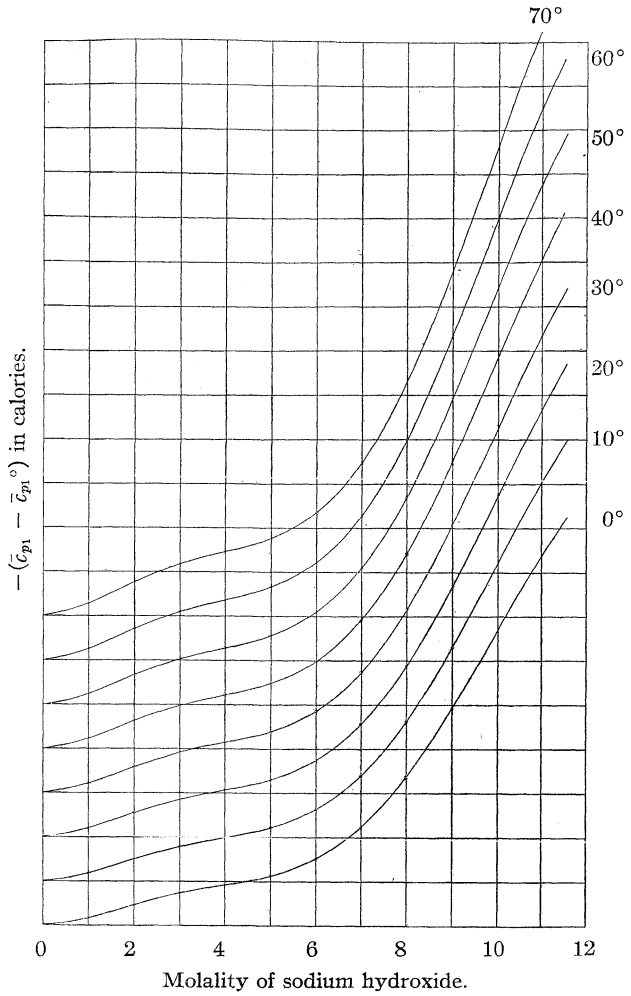


Fig. 9.—Isotherms for the relative partial molal heat capacity of the solvent in aqueous solutions of sodium hydroxide. Ordinates are shifted successively for the different curves.

where the resulting concentration m' should be computed from the following formula, analogous to equation (23)

$$m' = \frac{55.51Mm}{55.51M - 1000 - 40m}$$

For the vaporization of n moles of water from the same solution a similar equation is obtained

$$Q' = n\Delta H_v^{\circ} + \frac{M}{1000 + 40m}[L_{(m')} - L_{(m)}] - \frac{Mnm\bar{L}_{2(m')}}{55.51M - (1000 + 40m)n} - n\bar{L}_{1(m')} \quad (27)$$

$$\text{where } m' = \frac{55.51Mm}{55.51M - (1000 + 40m)n}$$

By use of the data in Tables X and XI and the values of ΔH_v° in Table XIX, equation (27) allows the calculation of the heat absorbed when an arbitrary amount of solvent is vaporized from a sodium hydroxide solution in the temperature range 0 to 70° at any concentrations between 0.1 to 17 molal. From Table XIX, $\Delta H_v^{\circ} = 1070.5$ cal., while ΔH_v for a ten molal solution is 1436.9 cal. This is to be compared with 1501.6 cal., the integral heat in going from 10 to 11 molal, computed from equation (26) with $M = 277.45$ g.

Pressure Variations of the Thermodynamic Properties of Solute and Solvent.—The rate of change of the chemical potentials of solute and solvent with pressure is given by the expressions

$$\left[\frac{\partial(\bar{F}_2 - \bar{F}_2^{\circ})}{\partial P}\right]_T = 2RT\left[\frac{\partial \ln \gamma}{\partial P}\right]_T = \bar{v}_2 - \bar{v}_2^{\circ} \quad (28)$$

$$\left[\frac{\partial(\bar{F}_1 - \bar{F}_1^{\circ})}{\partial P}\right]_T = RT\left[\frac{\partial \ln a_1}{\partial P}\right]_T = \bar{v}_1 - \bar{v}_1^{\circ} \quad (29)$$

The measurements of Smith and Keyes[11] show that the specific volume of pure liquid water changes by only 1 part in 1000 for a pressure change from 1 to 25 atmospheres. Since there is no reason to expect the compressibility of aqueous solutions to be much different from that of pure water, we may assume that in the pressure range mentioned the values of the partial molal volumes in equations (28) and (29) are constant within the experimental errors. This would give the following simple integrated equations

$$\log \gamma_P = \log \gamma + \frac{\bar{v}_2 - \bar{v}_2^{\circ}}{2 \cdot 2.303RT}(P - 1) \quad (30)$$

$$\log a_{1P} = \log a_1 + \frac{\bar{v}_1 - \bar{v}_1^{\circ}}{2.303RT}(P - 1) \quad (31)$$

where the pressure P is measured in atmospheres. The data for $\bar{v}_1$ and $\bar{v}_2$ needed for calculations using equations (30) and (31) are given in our previous study of the density of solutions of sodium hydroxide, which covers the temperature range 0 to 70° up to 27 molal.

Using the same fundamental thermodynamic relationships with $\log \gamma_P$ and $\log a_{1P}$ as those employed with $\log \gamma$ and $\log a_1$ in relation to other properties treated above, it is possible to calculate the values of the latter at higher pressures. It should be noted that in general the pressure correction term is so small that even if it has a large percentage error, this will not contribute any appreciable error to the final quantity obtained. Hence it would probably be quite feasible to apply equations (30) and (31) and all equations derived from them up to pressures of 100 atmospheres without introducing any serious errors. To obtain the derived equations it is necessary to know the temperature dependence of $\bar{v}_2$ and $\bar{v}_1$.

(11) Smith and Keyes, *Proc. Am. Acad. Arts Sci.*, **69** 285 (1934).

This may be calculated from the known variation of k with temperature according to the expressions

$$\bar{v}_2 - \bar{v}_2^\circ = k_1\sqrt{m} \quad \text{and} \quad \bar{v}_1 - \bar{v}_1^\circ = -\frac{18.016}{2000}k_1 m^{3/2}$$

where the concentration ranges from $m = 0$ to the density "break." The explicit temperature dependence of k_1 is obtained from third order equations given in our density paper.

The Chemical Significance of the Data.—Ions composed of single atoms like those of the alkali halides may probably without any large errors be considered to be non-deformable. The activity coefficients of strong electrolytes dissociating into ions of this type seem to follow with surprising accuracy, as has been tested for a large number of cases, the approximate rule of Åkerlöf and Thomas[12]

$$\log \gamma_1/\gamma_2 = km \qquad (32)$$

where the indices designate two electrolytes of the same valence type. The value of k is practically independent of the concentration except in very dilute solutions. The hydroxyl ion of the alkali hydroxides is composed of two atoms and should, in contrast to the behavior of single atom ions, be polarizable since it is unsymmetrical with respect to the electrical field of its associated positive ions. At infinite dilution the electrical strain and distortion must be at its minimum. With increasing concentration of the hydroxide the electrical distortion or induced polarization may be assumed as a first approximation to grow proportionally but the size of the effect would be unknown as there is no method available for the calculation of the "normal" thermodynamic properties of the alkali hydroxides. However, a saturation effect also should be present since the force needed to change the dimensions of an already stressed structure by a given amount would tend to increase with the hydroxide concentration or expressed in other words, the polarization per mole decreases with increasing concentration.

The presence of polarization of the hydroxyl ion is indicated already by the reversal of the behavior of the alkali hydroxides when compared to that of the corresponding alkali halides as previously pointed out by Harned and Åkerlöf.[13] A further support should according to the above be obtained by applying the rule of Åkerlöf and Thomas, which would indicate the presence of a saturation effect. The result is shown graphically in Fig. 10 where the value of k in equation (32) is plotted against the concentration. The data of Åkerlof and Teare for the activity coefficient of hydrochloric acid were used for the calculations since they were the only ones available in the literature covering the temperature and concentration ranges needed.

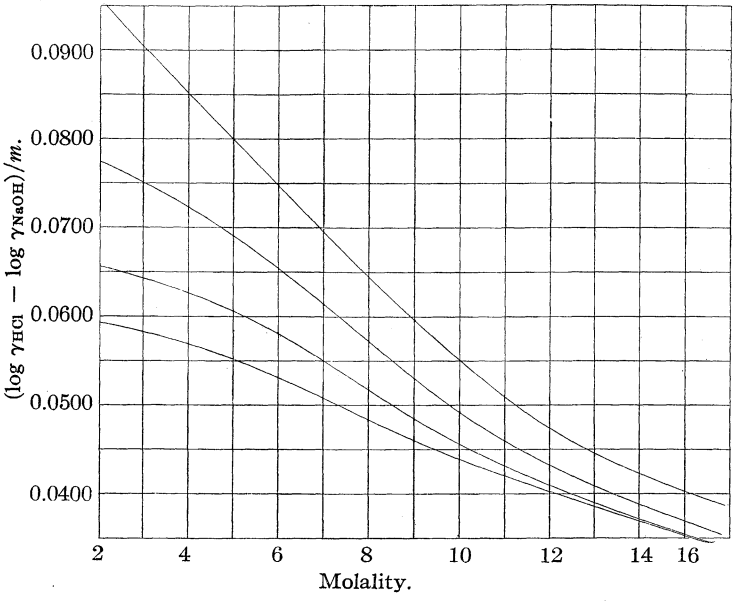


Fig. 10.—Isotherms at 0 (top curve), 20, 40 and 60° of the value for $(\log \gamma_{HCl} - \log \gamma_{NaOH})/m$.

The curves in Fig. 10 illustrate clearly the expected behavior of sodium hydroxide. Instead of a series of practically horizontal straight lines, they show a rapidly decreasing value of k with increasing concentration. The tendency of the curves to converge at higher concentrations and temperatures had also to be expected since when the ions of the hydroxide are brought closer and closer to each other the hydroxyl ion approaches its maximum polarization and the influence of the nature of the surrounding medium must decrease.

Summary

The electromotive force of the cell: $Pt,H_2/NaOH\ (m_1)/Na_xHg/NaOH\ (m_2)/H_2,Pt$ has been measured at a large number of hydroxide concentrations from 0.1 to 17 molal over the tempera-

(12) Åkerlöf and Thomas, THIS JOURNAL, 56, 593 (1934); Åkerlöf, *J. Phys. Chem.*, 41 1053 (1937).

(13) Harned and Åkerlöf, *Physik. Z.*, 27, 411 (1926).

ture range 0 to 70° using a considerably improved experimental procedure. The water transfer potential of the cell was calculated by a direct method eliminating tedious successive approximations.

The activity coefficient of the hydroxide for the concentration range 0.1 to 12 molal was found to be expressed adequately by the equation

$$\log \gamma = -\frac{u\sqrt{m}}{1+\sqrt{2m}} + Bm + Cm^2 + Dm^3 + Em^4$$

where u is the universal constant of the limiting law, m the molality of the hydroxide, B, C, D and E empirical constants varying according to second order equations with the temperature.

At higher concentrations a second order equation was used for the calculation of log γ. The curves for log γ do not within the experimental accuracy show any breaks at higher concentrations like those of the apparent partial molal volumes.

Using the formulas for log γ equations have been given for the calculation of the activity and vapor pressure of the solvent, the relative partial molal free energy, heat content, entropy, and heat capacity of both solute and solvent. Other properties that have been discussed are the total heat capacity, specific heat and relative heat content of the solutions, the heat of dilution between two finite concentrations, differential and integral heats of vaporization of the solvent and finally the effect of pressure upon the thermodynamic properties of sodium hydroxide. The computed values of most of the properties treated are given in a series of tables.

NEW HAVEN, CONN. RECEIVED OCTOBER 21, 1939

[CONTRIBUTION FROM THE MORLEY CHEMICAL LABORATORY, WESTERN RESERVE UNIVERSITY]

The Fluorination of Thionyl Chloride[1]

BY HAROLD SIMMONS BOOTH AND FRANCIS CARL MERICOLA

In 1896, M. Meslans[2] found that when thionyl chloride was treated with certain metallic fluorides such as zinc fluoride, a gaseous product, thionyl fluoride was formed. He reported this gas as being colorless and boiling in the neighborhood of −30° and added that the gas attacked the respiratory organs vigorously. Later Moissan and Lebeau[3] prepared this gas using free fluorine and also arsenic trifluoride as the fluorinating agents.

In 1905, Ruff and Thiel[4] prepared thionyl fluoride by heating N_4S_4 and hydrogen fluoride in the presence of water and cupric oxide in a sealed glass tube for two hours at 100°.

Since none of the previous investigators found any intermediate fluorination products, it seemed advisable to study the fluorination of thionyl chloride by means of antimony fluoride in the presence of a catalyst. This reaction has been successfully applied to the stepwise fluorination of various non-polar halides in this Laboratory.[5,6]

(1) From a portion of a thesis submitted by Francis Carl Mericola in partial fulfillment of the requirements for the Degree of Doctor of Philosophy in Chemistry, to the Graduate School of Western Reserve University, May, 1938.

(2) M. Meslans, *Bull. soc. chim.*, [3] **15**, 391 (1896).

(3) H. Moissan and P. Lebeau, *Compt. rend.*, **130**, 1436 (1900).

(4) O. Ruff and K. Thiel, *Ber.*, **38**, 549 (1905).

(5) H. S. Booth and C. F. Swinehart, THIS JOURNAL, **54**, 4751 (1932).

(6) H. S. Booth and A. R. Bozarth, *ibid.*, **61**, 2927 (1939).

Experimental

The generator was similar to that described by Booth and Bozarth.[6] The sublimed antimony trifluoride was slowly fed into the refluxing reaction mixture of 80% thionyl chloride and 20% antimony pentachloride (maintained at 50°, and at 200 mm. pressure) at such a rate that the automatic bleed-off valve would be continually in the open position but such that it would not allow the pressure to rise more than a few millimeters above this point. In this way as soon as any thionyl chlorofluoride was formed it was immediately removed from the reaction zone, thus ensuring the maximum yield. Reaction took place immediately.

The distillation analysis revealed the product to consist of 50% thionyl fluoride, 20% thionyl chlorofluoride, 5% sulfur dioxide and about 25% unreacted thionyl chloride. The yields were dependent upon the conditions of the reaction. Higher temperatures and pressures increased the percentage of thionyl fluoride and thus decreased the yield of the chlorofluoride. If the pressure were kept too low, thionyl chloride would distil out of the reaction zone.

The design and operation of the purification system was as already described[7] save that a glass spiral replaced the copper spiral in the fractionating column since copper was attacked. After the first rough separation two distillations in the column were sufficient to obtain pure gases for the determination of properties.

Analysis.—The samples were taken in small bulbs as liquids and absorbed in aqueous sodium hydroxide as usual.[8] Chlorine was determined gravimetrically as silver

(7) Booth and Bozarth, *Ind. Eng. Chem.*, **29**, 470 (1937).

(8) Booth and Dutton, THIS JOURNAL, **61**, 2937 (1939).

TABLE I

ANALYSES

	Sulfur, %			Oxygen, %			Chlorine, %		
	Theory	Found		Theory	Found		Theory	Found	
$SOCl_2$	26.74	26.70	26.63				59.97	59.84	59.90
SOClF	31.29	31.21	31.15	15.61	15.79	15.43	34.59	34.50	34.51
SOF_2	37.25	37.25	37.40	18.59	18.57	18.69			

chloride and sulfur as barium sulfate. In the latter case the solution was kept strongly acidic to avoid coprecipitation of barium fluoride. The oxygen was established indirectly by titration of the solution, alkaline with sodium bicarbonate, with excess iodine and back titration of the excess with sodium thiosulfate. The presence of fluorine was established qualitatively.

TABLE II[a,b]

VAPOR PRESSURE OF THIONYL FLUORIDE

$\log P_{mm.} = 30.333 - 1908.4/T - 8.1053 \log T$

Sample	Temp., °C.	P obsd. mm. (cor.)	P calcd. mm.	Deviation, mm.
B	−91.86	32.5	31.6	−0.9
A	−91.62	33.8	32.3	−1.5
B	−82.16	71.2	71.0	−0.2
A	−81.76	72.6	73.2	+ .6
B	−79.86	84.7	84.7	.0
B	−76.04	112.5	112.3	− .2
A	−71.04	158.3	159.2	+ .9
B	−68.46	187.4	188.4	+1.0
A	−64.44	244.4	244.2	−0.2
B	−61.65	286.8	286.6	−0.2
A	−57.60	365.4	366.7	+1.3
B	−57.59	366.9	366.9	0.0
B	−57.32	372.0	372.6	−0.6
B	−52.29	494.0	491.4	−2.6
B	−48.23	612.3	610.6	−1.7
A	−45.90	682.2	682.4	+0.2
B	−45.32	711.8	702.9	+8.9
A	−41.05	862.0	862.0	0.0

VAPOR PRESSURE OF THIONYL CHLOROFLUORIDE

$\log P_{mm.} = 7.0466 - 1278.2/T + 0.1268 \log T$

A	−73.62	8.5	8.4	−0.1
A	−69.52	11.5	11.5	.0
B	−64.90	15.9	15.9	.0
A	−53.44	34.5	33.6	− .9
B	−50.46	39.3	40.1	+ .8
B	−43.97	57.7	58.4	+ .7
A	−34.36	100.5	97.9	−2.6
B	−30.06	121.0	122.7	+1.7
A	−22.65	174.2	176.2	+2.0
A	−13.78	264.0	265.0	+1.0
B	− 9.15	323.6	323.6	0.0
A	− 5.39	380.2	379.8	−0.4
B	− 1.86	436.6	438.4	+1.8
A	+ 1.30	498.3	498.4	+0.1
B	+ 3.04	531.1	532.8	+1.7
B	+ 5.11	577.3	578.0	+0.7
B	+ 7.98	644.0	645.5	+1.5
A	+10.29	703.7	703.6	−0.1
A	+11.29	728.1	730.1	+2.0
B	+14.19	805.3	811.3	+6.0
A	+14.68	822.4	826.2	+3.8

[a] Samples A and B were from different distillations. [b] The calculated values were determined by use of the equations.

Physical Properties.—The liquid density was determined by means of a special pycnometer.[9] Freezing points, vapor pressures and gas densities were measured according to the standard practice in this Laboratory.[7] With thionyl chloride supercooling of from 10 to 15° occurred, but with thionyl fluoride none was observed. In the case of thionyl chlorofluoride much difficulty was encountered in measuring the freezing point. Upon cooling, the liquefied gas slowly solidified to a viscous transparent glassy solid which upon further cooling crystallized spontaneously with such force that on several occasions it burst the melting point tube. To obviate this difficulty the gas was first crystallized in the melting point tube and then allowed to melt slowly by placing a dewar flask, with a little liquid nitrogen in the bottom, around the jacketed melting point tube and the *melting point* of the thionyl chlorofluoride was obtained in this way.

Critical Constants.—The critical constants of thionyl chloride and thionyl chlorofluoride were not determined due to the fact that mercury reacts with both these compounds. The critical and vapor pressure data of thionyl fluoride at high pressures were obtained. The measurements were made in the apparatus and as described by Booth and Swinehart.[10]

TABLE III

CRITICAL DATA FOR SOF_2

Sample	Temp., °C.		Pressure, atm.	
1	25.1		11.2	
2	34.8		16.4	
1	40.2		19.3	
2	49.6		23.7	
1	52.3		25.3	
2	60.0		30.4	
1	61.4		30.8	
2	65.8		34.3	
1	71.1		37.7	
2	71.7		39.1	
1	81.4		46.3	
2	77.4		43.7	
2	85.1		51.3	
1	88.9	89.0°	55.3	Critical point 55.3 atm.
2	89.1		55.4	
3	89.0		55.3	

Table IV summarizes the physical properties of the three compounds as obtained in this Laboratory.

(9) Booth and Herrmann, THIS JOURNAL, **58**, 63 (1936).

(10) Booth and Swinehart, *ibid.*, **57**, 1337 (1935).

TABLE IV

PHYSICAL PROPERTIES OF THIONYL CHLORIDE, THIONYL FLUORIDE AND THIONYL CHLOROFLUORIDE

	$SOCl_2$		SOClF	SOF_2
Boiling point,[a] °C.	75.7[b]		12.2 ± 0.10	− 43.8 ± 0.1
Freezing point, °C.	−99.5	−104.5[c]		−129.5
				−110.0[d]
Melting point, °C.			−139.5	
Liquid density	1.675	1.676[13]	1.580	
Gas density (detd.)			102.0	86.8
(calcd.)			102.5	86.1
Critical temperature, °C.				89.0
Critical pressure, atm.				55.3
Heat of vaporization, cal.	7682		5937	5202
Trouton's constant	21.4		20.7	22.6

[a] Taken from the graph of the vapor pressure data. [b] K. Arii, *Bull. Inst. Phys. Chem. Res. Tokyo*, **8**, 719 (1929). [c] H. A. Mayes and J. R. Partington, *J. Chem. Soc.*, **128**, 2594 (1926). [d] Ruff and Thiel, *Ber.*, **38**, 549 (1905).

Chemical Properties.—Thionyl fluoride in the absence of moisture was found to be the most stable of the three compounds studied. It was found to be so stable that it would not decompose at red heat in an iron retort although in glass it reacted with the silica forming sulfur dioxide and silicon tetrafluoride. Water reacts with thionyl fluoride giving hydrogen fluoride and sulfur dioxide. It is very inert toward such elements as iron, nickel, copper, mercury, silicon, manganese, boron, magnesium, aluminum, zinc, etc., even at temperatures up to 125°.

An attempt to chlorinate thionyl fluoride by passing chlorine and thionyl fluoride over activated charcoal gave negative results, whereas this chlorination runs smoothly in the case of sulfur dioxide and chlorine, giving sulfuryl chloride.[11]

In contrast to thionyl fluoride, thionyl chloride is quite reactive with metals. Its reactions may be represented by the equations[12]

$$3M + 4SOCl_2 \longrightarrow 3MCl_2 + 2SO_2 + S_2Cl_2$$
$$3M + 2SOCl_2 \longrightarrow 2MCl_2 + MS + SO_2$$

With zinc, cadmium, magnesium, lead, chromium and nickel, no reaction was observed up to 200°.

In the case of metal sulfides, the reaction may be represented by

$$MS + SOCl_2 \longrightarrow MCl_2 + SO_2 + S_2Cl_2$$

These reactions were corroborated in this Laboratory.

Thionyl chlorofluoride reacts with very few metals at temperatures up to 150°. Tests with such metals and metalloids as boron, magnesium, silver, aluminum, silicon, zinc, phosphorus, manganese, arsenic and antimony were negative.

(11) "Inorganic Syntheses," Vol. I, McGraw-Hill Book Co., Inc., New York, N. Y., p. 114.

(12) H. B. North, THIS JOURNAL, **32**, 184 (1910); H. B. North and C. B. Conover, *ibid.*, **37**, 2486 (1915); H. B. North and A. M. Hageman, *ibid.*, **34**, 890 (1912).

With copper and mercury, reaction took place readily at room temperature. With iron reaction took place at about 70°. The products of the reaction were identified as SOF_2, SO_2, MS and MCl_2. In all cases some thionyl chloride was also found. This would indicate that a decomposition probably first occurs and that the speed of this reaction is greater than that of the reaction of the metals with thionyl chloride.

$$2SOClF + (Hg) \longrightarrow SOCl_2 + SOF_2 \text{ (fast)}$$
$$2SOCl_2 + 3Hg \longrightarrow 2HgCl_2 + HgS + SO_2 \text{ (slow)}$$

This is borne out by the fact that thionyl chlorofluoride on standing for some months in the gaseous state at room temperature decomposed to a considerable extent to $SOCl_2$ and SOF_2. In general, thionyl chlorofluoride behaves chemically like thionyl chloride.

An attempt to remove the chlorine by reaction with sodium amalgam in order to produce a condensation product of the formula $(SOF)_2$ was not successful. Instead, the reaction was one of oxidation–reduction. Reactions with Grignard reagents were analogous to those of thionyl chloride. No attempt was made to isolate the reaction products. When pure, all three substances are colorless in all states. They hydrolyze in moist air or water very readily.

Summary

The fluorination of thionyl chloride using antimony fluoride and antimony pentachloride, yields two gaseous products, thionyl fluoride, first described by Meslans, and a new compound, thionyl chlorofluoride. Physical and chemical properties of these two gases have been determined. The freezing point of thionyl chloride has also been redetermined.

CLEVELAND, OHIO RECEIVED OCTOBER 13, 1939

[CONTRIBUTION FROM THE BIOLOGICAL LABORATORY, COLD SPRING HARBOR, THE MEDICAL SERVICE OF DR. GEORGE BAEHR AND THE LABORATORIES OF THE MOUNT SINAI HOSPITAL, NEW YORK CITY, AND THE DEPARTMENT OF BOTANY, UNIVERSITY OF MINNESOTA]

The Effect of Phosphate Buffers on the Electrical Mobility of Hemoglobin

BY M. H. GORIN, H. A. ABRAMSON AND L. S. MOYER

This communication deals with part of the data in a recent article by Davis and Cohn[1] entitled, "The Influence of *p*H and Ionic Strength on Electrophoretic Mobility." It is clear that the influence of ionic strength on the electric mobility of proteins at a given *p*H must embody two important effects: (1) the direct effect of the ions on the charge of the particle, (2) the effect of the ionic atmosphere on the electric mobility of a molecule of given charge. It has been shown[2,3,4,5] previously that the second effect, the effect of the ion atmosphere on the motion of the particle, could be accounted for in certain simple systems by some form of the Debye equation

$$u = u_0/(1 + \kappa r) \qquad (1)$$

(where u is the electric mobility, u_0 the value of the mobility at infinite dilution, κ the well-known function of ionic strength) when suitable corrections for shifts in the isoelectric point due to specific ion effects (of the first type) were considered. Davis and Cohn[1] have stated that their data are not satisfied by equation (1). In doing so they reject the methods previously employed by us[2-5] as applied to their data. It will be shown in this communication that the methods previously employed by us are applicable to the more complicated systems studied by Davis and Cohn.

The method employed by Davis and Cohn[1] to apply equation (1), as far as we can judge from their paper, implies that at a given value of the *p*H the net charge of the protein molecule is the same for all ionic strengths. This obviously is impossible, for an inspection of their data discloses very large shifts in the isoelectric point. Since the net charge is zero only at the isoelectric point, the complete family of curves indicates protein molecules having net charges of zero and finite values at any given *p*H in the range investigated.

To use our previous approach[2,3,4,5] it is necessary to make some assumption regarding the change in net charge with ionic strength. For uni-univalent electrolytes it is generally agreed that the influence of ionic strength on the shape of the net charge–*p*H curve is not very great.[6] Indeed, the change in shape may be neglected for small shifts in ionic strength. To obtain a reference point where the net charge is zero at all ionic strengths, we have previously shifted all curves to the same isoelectric point, keeping the curves parallel along the mobility axis. That these assumptions also may apply to systems containing phosphate buffers is demonstrated by treatment of the data of Davis and Cohn which follows.

Without any assumptions, except those inherent in the theory itself, we may apply the Debye theory by multiplying all the mobilities by the expression $(2 + \kappa r)$, to calculate the value of the mobility at zero ionic strength for a molecule of the same net charge. The empirical function $(2 + \kappa r)$ is used here because it gives essentially the same results ($\mu = 0.02$ to 0.15) as the theoretical functions derived by Gorin,[5] in which the asymmetry of the protein and the finite size of the other ions in the solution are considered.[5,7] The value of $r = 27$ Å. was employed.

In Fig. 1 the data of Davis and Cohn[1] on the effect of phosphate buffers on the electric mobility of hemoglobin are plotted as smooth curves. The dashed lines passing through the same isoelectric points are corresponding values of the mobility multiplied by $(2 + \kappa r)$. It may be observed that all of the dashed curves are closely parallel to one another, any deviation being at the limit of experimental error. This is made more evident by an inspection of Fig. 2, in which all of the data have been plotted by shifting the parallel curves to the same isoelectric point. It therefore appears that the assumptions we have heretofore employed for proteins in solutions of uni-univalent electrolytes, contrary to the view of Davis and Cohn,[1] may be applied to their data in the case

(1) B. D. Davis and E. J. Cohn, THIS JOURNAL, **61**, 2092 (1939).

(2) H. A. Abramson, *J. Gen. Physiol.*, **15**, 575 (1932); **16**, 593 (1933).

(3) H. A. Abramson, "Electrokinetic Phenomena," The Chemical Catalog Co., Inc., New York, 1934.

(4) L. S. Moyer and J. C. Abels, *J. Biol. Chem.*, **121**, 331 (1937). L. S. Moyer and H. A. Abramson, *ibid.*, **123**, 391 (1938).

(5) H. A. Abramson, M. H. Gorin and L. S. Moyer, *Chem. Rev.*, **24**, 345 (1939).

(6) R. K. Cannan, "Symposia on Quantitative Biology," Cold Spring Harbor, 1938, p. 1.

(7) M. H. Gorin, *J. Chem. Phys.*, **7**, 405 (1939).

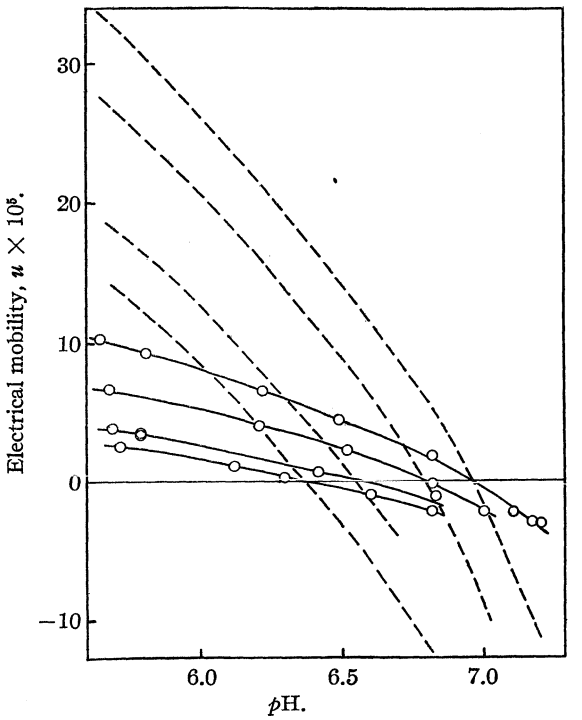


Fig. 1.—The data of Davis and Cohn at ionic strengths 0.02, 0.05, 0.10, 0.15, respectively, from top to bottom, are represented by the solid curves. The dashed lines represent their data multiplied by the function (κr + 2).

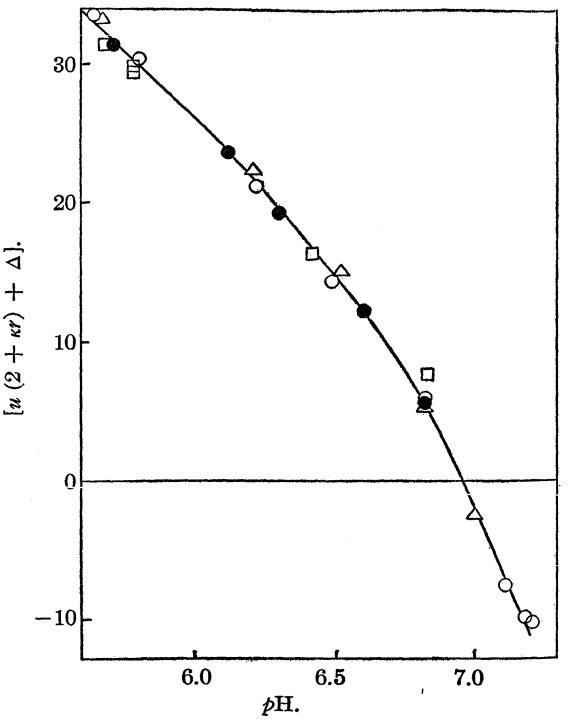


Fig. 2.—The recalculated data of Davis and Cohn have been brought to the same isoelectric point (that for ionic strength 0.02). The following symbols ○, △, □, ●, are for the data at ionic strengths 0.02, 0.05, 0.10 and 0.15, respectively. The values of △ are 0, 6.4, 13.0, 17.7, respectively.

under discussion. If the incomplete function, $(1 + \kappa r)$, is employed the agreement is not quite as good. This confirms similar observations made for proteins in simpler buffer solutions.[2,3,4,5]

In conclusion, with a view to avoiding confusion, it should be pointed out that the equation finally adopted by Davis and Cohn[1] (employing shifts in the isoelectric point)

$$u = u_0 - \beta\sqrt{\mu}/(1 + \sqrt{\mu}r/3) \qquad (2)$$

was in reality used as an empirical form of the equation[8]

$$u = u_0/(1 + \kappa r) \qquad (1)$$

(8) Compare D. A. MacInnes, "The Principles of Electrochemistry," Reinhold Publishing Corp., New York, 1939, page 325, with Abramson,[2] p. 104.

Summary

Variations of the ionic strength of a buffer at constant *p*H can affect the electric mobility of a protein in two ways: (1) a change in ion atmosphere will occur, (2) a change in the charge of the protein might occur due to specific interaction with the ions of the buffer. It is shown that when both effects are taken into consideration in a way that has previously been applied to proteins in buffer systems containing only uni-univalent ions the recent data of Davis and Cohn on the electric mobility of hemoglobin in phosphate buffers are reasonably explained.

RECEIVED OCTOBER 16, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. XCI. Oxidation of the Diacetate of Cholestanediol-3,6

BY RUSSELL E. MARKER, JOHN KRUEGER, JOHN R. ADAMS, JR., AND ELDON M. JONES

Windaus and Hossfeld[1] were unable to obtain *allo*-hyodesoxycholic acid by oxidation of the diacetate of cholestanediol-3,6. The oxidative opening of ring A occurred before the side chain was attacked and the product obtained was a lactone carboxylic acid. Recently we reported[2] the preparation of cholestanediol-3,6 of m. p. 190° which was epimeric with the cholestanediol-3,6 of m. p. 216° reported by Windaus.[3]

We have investigated the oxidation of the diacetate of cholestanediol (m. p. of the diol, 190°) and have obtained both *allo*-hyodesoxycholic acid and 6-hydroxyisoandrosterone from the reaction. *allo*-Hyodesoxycholic acid prepared in this way was characterized by direct comparison with a sample of *allo*-hyodesoxycholic acid and its methyl ester prepared from hyodesoxycholic acid by the method of Windaus.[4]

We have also degraded *allo*-hyodesoxycholic acid to *nor-allo*-hyodesoxycholic acid. *bis-nor-allo*-Hyodesoxycholic acid was prepared from *bis-nor*-hyodesoxycholic acid by the method of Windaus.[4]

We wish to thank Parke, Davis and Company for their generous help and assistance in the various phases of this work.

Experimental Part

Reduction of 6-Hydroxycholestanone.—6-Hydroxycholestanone (2.2 g.) in 125 cc. of 95% ethanol and 0.2 g. of Adams catalyst was shaken under 3 atmospheres of hydrogen for two hours. The catalyst was filtered off and the filtrate was concentrated by evaporation. The cholestanediol-3,6 which separated on cooling was recrystallized from ethanol. The substance melted at 191° and showed no depression in melting point when mixed with cholestanediol-3,6[2] prepared by reduction of 6-ketocholestanol; yield 2 g.

Oxidation of the Diacetate of Cholestanediol-3,6.—The cholestanediol used was prepared by reduction of 6-ketocholestanol in acetic acid rather than in ethanol as previously reported.[2] The diacetyl derivative (200 g.) was mixed with 8 liters of acetic acid and was heated to 90° on a steam-bath. The solution was stirred mechanically and 440 g. of chromic anhydride in 250 cc. of water and 1300 cc. of acetic acid was added dropwise during five hours. The reaction mixture was heated four hours longer. After cooling, excess chromic anhydride was destroyed by cautious addition of 200 cc. of ethanol. The reaction mixture was evaporated *in vacuo* to 25% of its volume. Water and ether were added and the layers separated. The ethereal layer water washed with and was then extracted with 10% sodium hydroxide. The insoluble sodium salt was filtered off and saponified. The free acid was crystallized by extraction from a Soxhlet thimble with boiling ethyl acetate. The *allo*-hyodesoxycholic acid so obtained melted at 280° and gave no depression upon mixing with *allo*-hyodesoxycholic acid prepared from hyodesoxycholic acid.

Anal. Calcd. for $C_{24}H_{40}O_4$: C, 73.4; H, 10.3. Found: C, 73.4; H, 10.2.

The methyl ester prepared with diazomethane melted at 179°. The mixed melting point with the methyl ester of *allo*-hyodesoxycholic acid (m. p. 181°) prepared from hyodesoxycholic acid was 180°.

Anal. Calcd. for $C_{25}H_{42}O_4$: C, 73.8; H, 10.4 Found: C, 73.7; H, 10.3.

The ethereal solution from which *allo*-hyodesoxycholic acid had been extracted was washed with water, and then evaporated. The oily residue was dissolved in 500 cc. of ethanol, chilled in ice, and the crystalline unchanged diacetate of cholestanediol was filtered off. The filtrate was evaporated to dryness *in vacuo* and was then steam distilled to remove volatile ketones. The oily suspension was extracted with ether and the ethereal layer was evaporated to dryness. The residue was dissolved in 600 cc. of ethanol, and to this solution was added 15 g. of semicarbazide hydrochloride and 18 g. of sodium acetate. The mixture was refluxed two hours on a steam-bath, then the alcohol was evaporated to half its volume. Addition of 1500 cc. of ether caused a precipitate of sodium chloride which was dissolved in water. The ether layer was washed repeatedly with water in order to remove alcohol. The semicarbazone of the diacetate of 6-hydroxyisoandrosterone was precipitated from the ether layer with pentane. After one recrystallization from methanol–ether–pentane and two recrystallizations from methanol it was obtained as small white needles melting at 222°; yield 3.1 g.

Anal. Calcd. for $C_{24}H_{37}O_5N_3$: C, 64.4; H, 8.3. Found: C, 64.4; H, 8.3.

One gram of this semicarbazone in 50 cc. of ethanol was refluxed one-half hour with 5 cc. of sulfuric acid in 10 cc. of water. The mixture was poured into water and was extracted with ether. The ether was evaporated and the residue was refluxed one hour with 30 cc. of 2% methanolic potassium hydroxide. The solution was poured into water and was extracted with ether. The ether layer was washed well with water and then pentane was added to precipitate the diol. 6-Hydroxyisoandrosterone, crystallized from methanol–ether–pentane, melted at 205°.

Anal. Calcd. for $C_{19}H_{30}O_3$: C, 74.4; H, 9.9. Found: C, 74.4; H, 9.9.

(1) Windaus and Hossfeld, *Z. physiol. Chem.*, **145**, 177 (1925).
(2) Marker and Krueger, THIS JOURNAL, **62**, 79 (1940).
(3) Windaus, *Ber.*, **50**, 133 (1917).
(4) Windaus, *Ann.*, **447**, 233 (1926).

nor-allo-**Hyodesoxycholic Acid.**—Fifty grams of *allo*-hyodesoxycholic acid was refluxed for two hours with 1 l. of 1% methanolic hydrogen chloride. The solution was concentrated by evaporation *in vacuo*. On cooling, the methyl ester which crystallized out was filtered, dried and dissolved in hot toluene. The toluene solution was added to 16 moles of ethereal phenylmagnesium bromide. The suspension was refluxed for two hours, then the ether was distilled off and was replaced with dry toluene. The mixture was heated overnight on a steam-bath. The carbinol was isolated, acetylated and dehydrated in the usual way. The ethylenic compound so obtained was oxidized with chromic oxide and *nor-allo*-hyodesoxycholic acid was thus obtained.[2] The acid, recrystallized from methanol melted at 225°.

Anal. Calcd. for $C_{23}H_{38}O_4$: C, 73.0; H, 10.1. Found: C, 73.2; H, 10.1.

3,6-Diketo-*bis-nor*-cholanic Acid.—Fifteen grams of *bis-nor*-hyodesoxycholic acid[2] dissolved in 300 cc. of acetic acid was treated at 12–15° during fifteen minutes with 15 g. of chromic oxide dissolved in 15 cc. of water and 35 cc. of acetic acid. The mixture was stirred a further ten minutes and then was diluted with water. The suspension was extracted with ether and the ethereal layer after washing with water was evaporated to dryness. The residue was crystallized from ether–pentane. 3,6-Diketo-*bis-nor*-cholanic acid melted at 185°; yield 12 g.

Anal. Calcd. for $C_{22}H_{32}O_4$: C, 73.3; H, 8.9. Found: C, 72.7; H, 8.9.

The methyl ester of 3,6-diketo-*bis-nor*-cholanic acid was prepared with ethereal diazomethane. It melted at 170° after crystallization from ether–pentane. The mixed melting point with the acid (m. p. 185°) was 160°.

Anal. Calcd. for $C_{23}H_{34}O_4$: C, 73.7; H, 9.1. Found: C, 73.9; H, 8.9.

3,6-Diketo-*bis-nor-allo*-cholanic Acid.—The diketo acid of m. p. 185° prepared above was refluxed for forty-five minutes with 150 cc. of acetic acid containing 1.5 cc. of C. P. hydrochloric acid. The mixture was concentrated to incipient crystallization by evaporation *in vacuo*. Ether was added and the gray precipitate was filtered off. The acid crystallized from ethanol as leaflets of m. p. 244°.

Anal. Calcd. for $C_{22}H_{32}O_4$: C, 73.3; H, 8.9. Found: C, 73.0; H, 8.9.

The methyl ester prepared with ethereal diazomethane after recrystallization from ether–pentane melted at 211°. The mixed melting point with acid of m. p. 244° was 200°.

Anal. Calcd. for $C_{23}H_{34}O_4$: C, 73.7; H, 9.1. Found: C, 73.8; H, 9.3.

bis-nor-allo-**Hyodesoxycholic Acid.**—Five and one-half grams of 3,6-diketo-*bis-nor-allo*-cholanic acid in 100 cc. of acetic acid was shaken with Adams catalyst under 3 atm. of hydrogen for three hours. The catalyst was filtered off and the filtrate was concentrated by evaporation *in vacuo*. The acid crystallized from methanol as white needles, of m. p. 259°; yield 5 g.

Anal. Calcd. for $C_{22}H_{36}O_4$: C, 72.5; H, 10.0. Found: C, 72.1; H, 9.9.

The methyl ester was prepared with ethereal diazomethane. It crystallized from ether–pentane as white leaflets of m. p. 233°. The mixed melting point with acid of m. p. 256° was 233°.

Anal. Calcd. for $C_{23}H_{38}O_4$: C, 72.9; H, 10.1. Found: C, 73.0; H, 10.1.

Diacetate of *bis-nor-allo*-hyodesoxycholic Acid.—One-half a gram of *bis-nor-allo*-hyodesoxycholic acid was refluxed for ten minutes with 20 cc. of acetic anhydride. The solvent was evaporated *in vacuo* and the residue was dissolved in methyl alcohol. The crystals obtained melted at 115°.

Anal. Calcd. for $C_{26}H_{40}O_6 \cdot 0.5CH_3OH$: C, 68.5; H, 9.1. Found: C, 68.2; H, 9.0.

The methyl ester was prepared with ethereal diazomethane. The substance crystallized by rubbing with pentane melted at 135°. The mixed melting point with acid (m. p. 115°) was 111°.

Anal. Calcd. for $C_{27}H_{42}O_6$: C, 70.1; H, 9.2. Found: C, 70.1; H, 9.0.

Summary

allo-Hyodesoxycholic acid and 6-hydroxyisoandrosterone have been prepared by oxidation of the diacetate of cholestanediol-3,6. The preparation of *nor-allo*-hyodesoxycholic acid and of *bis-nor-allo*-hyodesoxycholic acid has been described.

STATE COLLEGE, PENNA. RECEIVED JANUARY 10, 1940

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. XCII. The Preparation of Neotigogenin from Sarsasapogenin

BY RUSSELL E. MARKER AND EWALD ROHRMANN

The fact that tigogenin,[1,2,3] chlorogenin,[4] gitogenin[3,5] and digitogenin[3,5] show no noticeable tendency to react with boiling aqueous ethanolic hydrochloric acid indicates that the side chains of these sapogenins differ in configuration from that of sarsasapogenin which by similar treatment is isomerized to isosarsasapogenin[6] (smilagenin[7]).

We have now obtained substantiating evidence which conclusively shows that tigogenin differs from sarsasapogenin not only in its configuration at C-5 but also in the configuration of the side chain. Sarsasapogenone upon bromination with two moles of bromine yields dibromosarsasapogenone, a substance which has a bromine in the C-4 position as well as one in the side chain.[8] Dibromosarsasapogenone upon treatment with boiling pyridine yields bromo-$\Delta^{4,5}$-dehydro-sarsasapogenone. Reduction of this product with sodium and ethanol and separation of the isomers with digitonin yields a digitonin precipitable product, m. p. 198–200°, which is different from tigogenin and sarsasapogenin but which appears to be identical with neotigogenin, a substance recently obtained by Goodson and Noller[1] from the sapogenins of *Chlorogalum pomeridianum*. Inasmuch as tigogenin, chlorogenin and diosgenin[9] have been converted to the same desoxy compound it follows that these substances all have the same side chain configuration.

These results definitely indicate that the side chain of neotigogenin is of the "sarsasapogenin configuration." It seems most probable that the side chain of tigogenin, chlorogenin and diosgenin is of the "isosarsasapogenin configuration," although it is evident that final proof of this supposition is dependent upon the conversion of isosarsasapogenin to tigogenin. The stability of gitogenin and digitogenin to aqueous ethanolic hydrochloric acid suggests that these substances likewise have the isosarsasapogenin side chain configuration.

(1) Goodson and Noller, THIS JOURNAL, **61**, 2420 (1939).
(2) Marker and Rohrmann, *ibid.*, **61**, 1516 (1939).
(3) Unpublished experiments from this Laboratory.
(4) Marker and Rohrmann, THIS JOURNAL, **61**, 3479 (1939).
(5) Marker and Rohrmann, *ibid.*, **61**, 2724 (1939).
(6) Marker and Rohrmann, *ibid.*, **61**, 846 (1939).
(7) Kon, Soper and Woolman, *J. Chem. Soc.*, 1201 (1939).
(8) Marker and Rohrmann, THIS JOURNAL, **61**, 1921 (1939).
(9) Tsukamoto, Neno and Ohta, *J. Pharm. Soc., Japan*, **57**, 9 (1937).

We wish to thank Parke, Davis and Company for their generous help and assistance in the various phases of this work.

Experimental Part

Treatment of Dibromosarsasapogenone with Pyridine.—A solution of 5 g. of dibromosarsasapogenone[8] in 50 cc. of dry pyridine was refluxed for eight hours. Some crystalline material had separated at the end of this time. This was filtered, washed with water and dried to give small white crystals, m. p. 235° dec. The product is probably a pyridinium salt.

Anal. Calcd. for $C_{32}H_{45}O_3NBr_2$: C, 59.0; H, 7.0. Found: C, 58.6; H, 7.3.

The filtrate from the above was diluted with aqueous sulfuric acid and the precipitated solid taken up in ether, treated with Norite and crystallized from acetone to give small compact white crystals, m. p. 185–188° dec. This is bromo-$\Delta^{4,5}$-dehydrosarsasapogenone, yield 2.2 g.

Anal. Calcd. for $C_{27}H_{39}O_3Br$: C, 66.0; H, 8.0. Found: C, 66.2; H, 8.1.

Reduction of Bromo-$\Delta^{4,5}$-dehydrosarsasapogenone with Sodium and Ethanol.—To a boiling solution of 2 g. of bromo-$\Delta^{4,5}$-dehydrosarsasapogenone in 400 cc. of absolute ethanol was added 17 g. of sodium over a period of one hour. Water was added and the precipitated solid taken up in ether, washed well with water and the ether evaporated. A precipitate formed when a solution of the residual sirup was treated with digitonin in 80% ethanol. The insoluble digitonide was decomposed with pyridine in the usual manner. The product was dissolved in methanol and treated with norite. It crystallized from methanol as small white crystals, m. p. 198–200°; yield, 600 mg. A mixture with tigogenin, m. p. 204–206°, melted at 179–192° and a mixture with a sarsasapogenin, m. p. 199–201°, melted at 160–170°. It gave no depression with a sample of neotigogenin, m. p. 199–201°, isolated from *Chlorogalum pomeridianum*.

Anal. Calcd. for $C_{27}H_{44}O_3$: C, 77.8; H, 10.6. Found: C, 77.7; H, 10.6.

With boiling acetic anhydride the product gave an acetate which crystallized from methanol as white plates, m. p. 173–175°. This gave no depression with a sample of neotigogenin acetate, m. p. 173–175°.

Anal. Calcd. for $C_{29}H_{46}O_4$: C, 75.9; H, 10.1. Found: C, 75.9; H, 10.0.

Neotigogenone.—When oxidized with chromic anhydride at room temperature in acetic acid solution for thirty minutes, the neotigogenin yielded a product which crystallized from acetone as white plates, m. p. 207–210°. A mixture with tigogenone, m. p. 202–205°, melted at 198–204°. The mixture with neotigogenone, m. p. 208–211°, melted at 207–210°.

Anal. Calcd. for $C_{27}H_{42}O_3$: C, 78.2; H, 10.2. Found: C, 78.5; H, 10.2.

Summary

The preparation of $\Delta^{4,5}$-bromosarsasapogenone is described.

$\Delta^{4,5}$-Bromosarsasapogenone upon reduction with sodium and ethanol yields neotigogenin, indicating that tigogenin, chlorogenin and diosgenin differ from sarsasapogenin in the side chain configurations.

STATE COLLEGE, PENNA. RECEIVED JANUARY 10, 1940

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. XCIII. *epi*-Pseudosarsasapogenin, Pseudosarsasapogenone and Pseudochlorogenin

BY RUSSELL E. MARKER, EWALD ROHRMANN AND ELDON M. JONES

In continuation of our study of the pseudosapogenins[1,2,3,4] we have extended the acetic anhydride isomerization to *epi*-sarsasapogenin, sarsasapogenone, isosarsasapogenin and chlorogenin. All of these substances are thus isomerized to give pseudo compounds.

As in the case with pseudosarsasapogenin[3] both *epi*-pseudosarsasapogenin and pseudochlorogenin take up a mole of hydrogen in the presence of Adams catalyst to yield dihydropseudosapogenins. Dihydropseudochlorogenin forms a triacetate and *epi*-dihydropseudosarsasapogenin a di-*p*-nitrobenzoate. Pseudosarsasapogenone forms a monosemicarbazone.

As would be expected from the previous results with pseudosarsasapogenin[1,2,3] both *epi*-pseudosarsasapogenin and pseudosarsasapogenone yield $\Delta^{16,17}$-pregnenedione-3,20 on mild oxidation with chromic anhydride.

From the suggested structures of sarsasapogenin[5] and isosarsasapogenin[5] one might expect these substances to yield the same pseudo compound, which was found to be the case. It is a significant fact that dihydrosarsasapogenin[5] was unaffected by treatment with acetic anhydride.

We wish to thank Parke, Davis and Company for their generous help and assistance in the various phases of this work.

Experimental Part[6]

Reduction of Sarsasapogenone with Sodium and Ethanol.—To a boiling solution of 6 g. of sarsasapogenone in 800 cc. of absolute ethanol was added 25 g. of sodium over a period of two hours. Water was added and the precipitated solid taken up in ether, washed with water and crystallized from acetone as white needles, m. p. 205–207°, yield 5.1 g. This gave no depression with a sample of *epi*-sarsasapogenin, m. p. 205–207°.

With hot acetic anhydride the product gave an **acetate** which crystallized from acetone as white plates, m. p. 191–193°.

Anal. Calcd. for $C_{29}H_{46}O_4$: C, 75.9; H, 10.1. Found: C, 75.8; H, 10.0.

***epi*-Pseudosarsasapogenin.**—A mixture of 2 g. of *epi*-sarsasapogenin acetate and 20 cc. of acetic anhydride was heated at 200° for ten hours in a sealed tube. The acetic anhydride was evaporated *in vacuo* and the residue hydrolyzed with hot ethanolic potassium hydroxide. The neutral fraction was crystallized from acetone as white needles, m. p. 211–213°. This gave a large depression with both *epi*-sarsasapogenin, m. p. 205–207°, and sarsasapogenin, m. p. 199–201°.

Anal. Calcd. for $C_{27}H_{44}O_3$: C, 77.8; H, 10.6. Found: C, 77.6; H, 10.6.

***epi*-Dihydropseudosarsasapogenin.**—A mixture of 1.5 g. of *epi*-pseudosarsasapogenin, 1 g. of Adams catalyst and 150 cc. of acetic acid was shaken with hydrogen at 3 atm. pressure at room temperature for seventeen hours. After removal of the catalyst, concentration *in vacuo* gave a residue which was saponified for five minutes with ethanolic potassium hydroxide. The product was crystallized from acetone to give white needles, m. p. 135–137°.

Anal. Calcd. for $C_{27}H_{46}O_3$: C, 77.4; H, 11.1. Found: C, 77.3; H, 11.0.

With *p*-nitrobenzoyl chloride in pyridine at 60° the product gave a **di-*p*-nitrobenzoate** which crystallized from acetone as white needles, m. p. 207–209°.

Anal. Calcd. for $C_{41}H_{52}O_9N_2$: C, 68.7; H, 7.3. Found: C, 68.6; H, 7.3.

$\Delta^{16,17}$-Pregnenedione-3,20 from *epi*-Pseudosarsasapogenin.—To a solution of 100 mg. of *epi*-pseudosarsasapogenin in 10 cc. of acetic acid was added a solution of 300 mg. of chromic anhydride in 8 cc. of 80% acetic acid. After standing at room temperature for one hour, water was added and the precipitate taken up in ether and washed free from acids with a solution of sodium hydroxide. The neutral fraction crystallized from acetone as white

(1) Marker and Rohrmann, THIS JOURNAL, **61**, 3592 (1939).
(2) Marker and Rohrmann, *ibid.*, **62**, 518 (1940).
(3) Marker and Rohrmann, *ibid.*, **62**, 521 (1940).
(4) Marker and Rohrmann, *ibid.*, **62**, 647 (1940).
(5) Marker and Rohrmann, *ibid.*, **61**, 846 (1939).
(6) Microanalyses by Dr. John R. Adams, Jr., of this Laboratory.

plates, m. p. 199–201°. This gave no depression with a sample of $\Delta^{16,17}$-pregnenedione-3,20, m. p. 200–202°.

Anal. Calcd. for $C_{21}H_{30}O_2$: C, 80.2; H, 9.6. Found: C, 79.9; H, 9.5.

Pseudosarsasapogenone.—A mixture of 4 g. of sarsasapogenone and 30 cc. of acetic anhydride was heated in a sealed tube at 200° for ten hours. The product was worked up as described for *epi*-pseudosarsasapogenin. The neutral fraction after treatment with Norite in methanol was crystallized from aqueous acetone to give white needles, m. p. 165–166°.

Anal. Calcd. for $C_{27}H_{42}O_3$: C, 78.2; H, 10.2. Found: C, 78.2; H, 10.3.

With semicarbazide acetate under the usual conditions the product gave a **semicarbazone** which was crystallized from aqueous ethanol, m. p. 215–216°, dec.

Anal. Calcd. for $C_{28}H_{45}O_3N_3$: C, 71.3; H, 9.6. Found: C, 71.1; H, 9.5.

$\Delta^{16,17}$-Pregnenedione-3,20 from Pseudosarsasapogenone.—To a solution of 1.5 g. of pseudosarsasapogenin in 50 cc. of acetic acid was added a solution of 1.5 g. of chromic anhydride in 25 cc. of 80% acetic acid. After standing at room temperature for ninety minutes water was added and the precipitated solids taken up in ether and freed from acids with 5% sodium hydroxide. The neutral fraction was crystallized from acetone to give white plates, m. p. 199–201°. This gave no depression with a sample of $\Delta^{16,17}$-pregnenedione-3,20, m. p. 200–202°.

Reaction of Isosarsasapogenin with Acetic Anhydride.—A mixture of 3.3 g. of isosarsasapogenin acetate, m. p. 149–151°, and 25 cc. of acetic anhydride was heated at 195° for nine hours and worked up as described in previous reactions. The neutral fraction was crystallized from acetone to give 1.7 g. of fine white needles, m. p. 169–172°. This gave no depression with a sample of pseudosarsasapogenin.

Dihydrosarsasapogenin when treated with acetic anhydride as in previous experiments was recovered unchanged.

Pseudochlorogenin.—A mixture of 2.5 g. of chlorogenin and 30 cc. of acetic anhydride was heated at 200° for ten hours. The acetic anhydride was evaporated *in vacuo* and the non-crystalline residue hydrolyzed with hot ethanolic potassium hydroxide. Small crystals which separated from the saponification mixture were collected and washed well with ethanol. The product was recrystallized from methanol in a Soxhlet extractor to give a product of m. p. 268–270°, yield 1.4 g. This gave a depression of 30° with a sample of chlorogenin, m. p. 265–268°. The substance is very sparingly soluble in nearly all solvents.

Anal. Calcd. for $C_{27}H_{44}O_4$: C, 74.9; H, 10.2. Found: C, 74.5; H, 10.2.

Dihydropseudochlorogenin.—A mixture of 1 g. of pseudochlorogenin, 300 cc. of absolute ethanol, 50 cc. of acetic acid and 800 mg. of Adams catalyst was shaken at 3 atm. pressure of hydrogen at room temperature for twenty hours. Crystalline material had separated at the end of this time. This was dissolved by the addition of 75 cc. of hot acetic acid and the catalyst filtered. The filtrate was evaporated to a volume of 125 cc., diluted with water and the precipitated solid taken up in chloroform and crystallized from methanol as fine white needles, m. p. 269–272°. This gave a 20° depression with the starting material. It also gave a large depression with chlorogenin.

Anal. Calcd. for $C_{27}H_{46}O_4$: C, 74.6; H, 10.7. Found: C, 74.8; H, 10.7.

With boiling acetic anhydride this yielded a **triacetate** which crystallized from aqueous acetone as fine white needles, m. p. 149–152°, and gave a 20° depression with a sample of chlorogenin diacetate, m. p. 149–151°.

Anal. Calcd. for $C_{33}H_{52}O_7$: C, 70.7; H, 9.35. Found: C, 70.3; H, 9.2.

Summary

epi-Pseudosarsasapogenin and pseudosarsasapogenone have been prepared. Oxidation of these products with chromic anhydride yields $\Delta^{16,17}$-pregenedione-3,20.

Isosarsasapogenin reacts with acetic anhydride to give pseudosarsasapogenin.

Pseudochlorogenin has been prepared.

STATE COLLEGE, PENNA. RECEIVED JANUARY 12, 1940

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. XCIV. Persulfate Oxidation of *allo*-Pregnane Derivatives

BY RUSSELL E. MARKER, EWALD ROHRMANN, EUGENE L. WITTLE, HARRY M. CROOKS, JR., AND ELDON M. JONES

Although potassium persulfate has been used rather extensively to oxidize ketones of the terpene group[1,2,3] it has not been used to any appreciable extent in the oxidation of sterol ketones. In this Laboratory it was recently used in the oxidation of sarsasapogenin to pregnanetriol-3,16,20.[4]

The fact that persulfate oxidations bring about a cleavage of a carbon–carbon linkage adjacent to a carbonyl group suggested its possible use in the oxidation of C-20 keto *allo*-pregnane compounds to androstane derivatives. The oxidation of *allo*-preganone-20 with potassium persulfate yielded a neutral carbinol mixture which we were unable to separate. The acidic fraction from this oxidation gave an acid of the composition $C_{20}H_{32}O_2$, m. p. 228–230°. This formed a methyl ester, m. p. 141–143°. This acid is undoubtedly *etio-allo*-cholanic acid which was prepared by Tschesche.[5] His acid melted at 228–230° and the methyl ester at 140–142°.

The oxidation of *allo*-pregnanol-3(β)-one-20 yielded an acidic fraction which consisted of 3(β)-hydroxy-*etio-allo*-cholanic acid.[6,7] The neutral fraction which appeared to be a mixture was oxidized with chromic anhydride to yield androstanedione.

We wish to thank Parke, Davis and Company for their generous help and assistance in the various phases of this work.

Experimental Part[8]

Treatment of *allo*-Pregnanone-20 with Persulfuric Acid.—A mixture of 5 g. of *allo*-pregnanone-20, 500 cc. of 90% acetic acid, 5 cc. of concentrated sulfuric acid and 25 g. of potassium persulfate was refluxed for four hours, cooled, diluted with water and extracted with ether. The acids were removed from the ether by washing with water and sodium carbonate solution. The ether was evaporated and the residue was hydrolyzed with boiling ethanolic potassium hydroxide. Water was added and the neutral product extracted with ether. The carbinols were separated from the neutral fraction by means of their half-succinates. This apparently gave a mixture of epimeric carbinols which melted over a range of 110–142°, and could not be separated.

Anal. Calcd. for $C_{19}H_{32}O$: C, 82.8; H, 11.7. Found: C, 82.6; H, 11.5.

The water layer from the alkaline hydrolysis above was acidified and the precipitated acids taken up with ether. The solvent was removed and the product was recrystallized from ethyl acetate to give white crystals, m. p. 228–230°. This product is *etio-allo*-cholanic acid.

Anal. Calcd. for $C_{20}H_{32}O_2$: C, 78.9; H, 10.6. Found: C, 78.5; H, 10.6.

Upon treatment with diazomethane the acid gave a **methyl ester** which crystallized from dilute acetone as white crystals, m. p. 141–143°.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.2; H, 10.8. Found: C, 79.2; H, 10.6.

Treatment of *allo*-Pregnanol-3(β)-one-20 with Persulfuric Acid.—A mixture of 2.3 g. of *allo*-pregnanol-3(β)-one-20 acetate, 250 cc. of 90% acetic acid, 2.5 cc. of concentrated sulfuric acid and 10 g. of potassium persulfate was refluxed for four hours. The products were separated and hydrolyzed as in the preceding experiment. The neutral fraction was freed from some unchanged ketones by means of Girard's reagent in ethanol. The non-ketonic fraction upon crystallization from dilute methanol and dilute acetone gave crystalline material melting at 170–185°, which apparently consisted of a mixture of epimeric carbinols. The solvent was removed and the total product was dissolved in 25 cc. of acetic acid and 1 g. of chromic anhydride in 5 cc. of 80% acetic acid added. After standing one hour at 25° water was added and the precipitated solid extracted with ether and the acids removed by washing with water and sodium carbonate solution. The residue remaining after evaporation of the ether was crystallized from ether–pentane and from dilute acetone to give a product m. p. 128–130°. This gave no depression in melting point when mixed with androstanedione, m. p. 130°.

Anal. Calcd. for $C_{19}H_{28}O_2$: C, 79.1; H, 9.8. Found: C, 78.9; H, 9.8.

The water layer from the above alkaline hydrolysis was acidified and the precipitated acids taken up with ether. After removal of the ether, the residue was crystallized from dilute methanol to give a product, m. p. 249–252°. It gave no depression in melting point when mixed with an authentic sample of 3(β)-hydroxy-*etio-allo*-cholanic acid, m. p. 250–252°.[7]

Anal. Calcd. for $C_{20}H_{32}O_3$: C, 74.9; H, 10.1. Found: C, 74.8; H, 10.1.

(1) Baeyer and Villiger, *Ber.*, **32**, 3630 (1899).
(2) Ruzicka and Stoll, *Helv. Chim. Acta*, **11**, 1159 (1928).
(3) Rollett and Bratke, *Monatsh.*, **43**, 685 (1922).
(4) Marker, Rohrmann, Crooks, Wittle, Jones and Turner, THIS JOURNAL, **62**, 525 (1940).
(5) Tschesche, *Ber.*, **68**, 7 (1935).
(6) Steiger and Reichstein, *Helv. Chim. Acta*, **20**, 949 (1937).
(7) Marker and Wittle, THIS JOURNAL, **61**, 1329 (1939).
(8) Microanalyses by Dr. John R. Adams, Jr., of this Laboratory.

Summary

The persulfate oxidation of 20-keto-*allo*-pregnane compounds gave a mixture of androstanols-17 and *etio-allo*-cholanic acid.

STATE COLLEGE, PENNA. RECEIVED JANUARY 15, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

Osage Orange Pigments. III. Fractionation and Oxidation

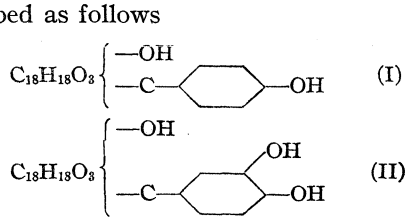
BY M. L. WOLFROM AND A. S. GREGORY

In continuation of our studies[1] on the pigments of the fruit of the osage orange tree (*Maclura pomifera* Raf.) we have made a rather exhaustive fractionation of the naturally occurring mixture of the two pigments, the results of which indicate that the two are probably present in about equal amounts.

The melting point–composition diagram obtained from mixtures of the two pure substances is shown in Fig. 1. The melting point behavior obtained on mixing the pure compounds is probably slightly different from the behavior of mixtures of equal composition which have been formed by co-crystallization.

The trimethyl ether of pomiferin has been reported previously.[1b] We have now obtained the corresponding dimethyl ether of osajin. When the former is subjected to oxidation, in acetone solution, with alkaline hydrogen peroxide, veratric (3,4-dimethoxybenzoic) acid is produced. Under the same conditions, osajin dimethyl ether yields anisic (*p*-methoxybenzoic) acid. These two acids were identified by analysis, by preparation of the anilide and amide of each, and by comparison with authentic specimens in all cases. The two acids have practically identical melting points. This is also true for their amides and anilides. Mixed melting points, however, give definite depressions.

The formulas of osajin (I) and pomiferin (II), both of which are methoxyl-free, may now be developed as follows



Further work on the structure of these two substances is in progress in this Laboratory.

(1) (a) E. D. Walter, M. L. Wolfrom and W. W. Hess, THIS JOURNAL, **60**, 574 (1938); (b) M. L. Wolfrom, F. L. Benton, A. S. Gregory, W. W. Hess, J. E. Mahan and P. W. Morgan, *ibid.*, **61**, 2832 (1939).

Experimental

Fractionation.—The whole fruit of the osage orange tree (*Maclura pomifera* Raf.) was cut, dried and crushed to a coarse meal. The meal (1500 g.) was extracted successively with petroleum ether and ether. From the latter extract was obtained a yellow solid; yield 47.8 g., m. p. 180–182°. This material was recrystallized from ten parts of hot xylene, the crop being removed by filtration when the temperature of the solution had reached approximately 40°. On repeated recrystallization in this manner pure pomiferin was obtained; yield 10.0 g., m. p. 200.5°. The combined mother liquors were concentrated to give a product melting at 173–175° and after repeated recrystallization from 95% ethanol pure osajin was obtained; yield 5.6 g., m. p. 189°. By employing a method of crystallizing the xylene mother liquor material from 95% alcohol, and then the alcohol mother liquor material from xylene again, and continuing this cycle, a total of 14.1 g. of high purity osajin and 15.8 g. of high purity pomiferin was obtained.

Although not all the material was accounted for, the above results would seem to indicate that the two substances are present in the crude extract in very nearly equal amounts. The total yield of crude extract in this lot of material was not as high as in the crops of previous seasons. The melting point–composition diagram obtained from mixtures of the two pure substances is shown in Fig. 1. The melting point behavior obtained on mixing the two pure substances is probably slightly different from the behavior of mixtures of equal composition which have been formed by co-crystallization.

Osajin Dimethyl Ether.—To a boiling solution of osajin (2 g., m. p. 189°) in acetone (130 cc.) were added under reflux the following portions of reagents over a period of forty minutes: 24 cc. of dimethyl sulfate, 14 cc. of 50% aqueous potassium hydroxide, then six alternate portions of 6 cc. each of dimethyl sulfate and 8 cc. each of 50% aqueous potassium hydroxide. The refluxing was continued for two hours longer and then the reaction mixture was poured on 1.5 l. of crushed ice and allowed to stand until the ice had melted before filtration of the precipitated solid; yield 2.16 g., m. p. 109°. Pure material was obtained on several recrystallizations from ethanol (95%); m. p. 118.5° unchanged on recrystallization from methanol, propanol-1 and benzene–petroleum ether. The substance crystallized in long, colorless needles and gave a negative ferric chloride–alcohol phenol test.

Anal. Calcd. for $C_{25}H_{22}O_3(OCH_3)_2$: C, 74.98; H, 6.53; OCH_3, 14.35. Found: C, 74.91; H, 6.53; OCH_3, 14.3.

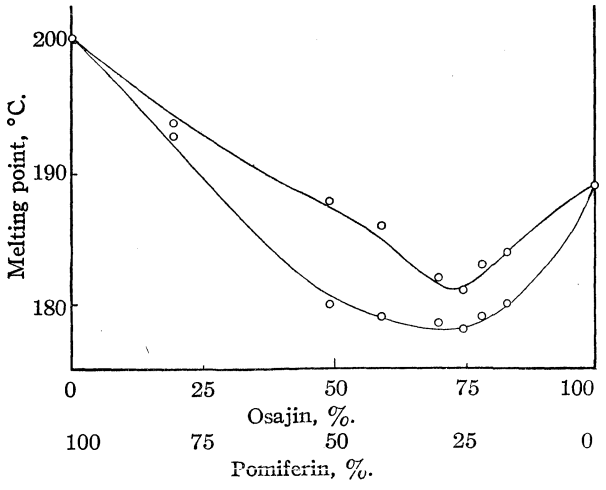


Fig. 1.—Melting point–composition diagram for mixtures of osajin and pomiferin. Lower curve represents beginning of melting and upper curve represents complete fusion.

Isolation of Anisic Acid from the Oxidation of Osajin Dimethyl Ether with Alkaline Peroxide.—Osajin dimethyl ether (1.7 g., m. p. 118°) dissolved in acetone (150 cc.) was treated under mechanical stirring with 1.5 cc. of 50% aqueous potassium hydroxide, followed by the dropwise addition of 20 cc. of 30% aqueous hydrogen peroxide. The oxidation was continued for forty-eight hours at room temperature, whereupon the solution tested only faintly oxidizing to potassium iodide paper. Saturated aqueous sodium bisulfite solution (5 cc.) was added slowly with cooling and the mixture then was neutral to potassium iodide paper and basic to litmus. The acetone was removed under reduced pressure, 50 cc. of 1% hydrochloric acid added and the solution extracted with ether. The concentrated ethereal extract (75 cc.) was extracted with several portions of 5% ammonium carbonate solution. This carbonate solution was concentrated to 50 cc., some tarry material removed by filtration, and the white precipitate that formed on acidification with hydrochloric acid was recrystallized from hot water; yield 0.10 g., m. p. 178°. After two further recrystallizations from water (decolorizing charcoal) the product appeared as fine white needles melting at 180°, which formed an anilide of melting point 167–168° and an amide of melting point 163–164°. Authentic specimens of anisic acid (m. p. 180°), anisic acid anilide (m. p. 167–168°) and anisic acid amide (m. p. 163–164°) were prepared and showed no depression in melting point with the corresponding products obtained from the oxidation.

Anal. Calcd. for $C_8H_8O_3$ (anisic acid): OCH_3, 20.4; neutral equivalent, 152. Found: OCH_3, 21.0; neutral equivalent, 157. Calcd. for $C_8H_9O_2N$ (anisic acid amide): OCH_3, 20.5. Found: OCH_3, 20.3.

Isolation of Veratric Acid from the Oxidation of Pomiferin Trimethyl Ether with Alkaline Peroxide.—In the description of the synthesis of pomiferin trimethyl ether[1b] previously described from this Laboratory, the addition of 14 cc. of 50% aqueous potassium hydroxide should follow the addition of the first amount of dimethyl sulfate. Pomiferin trimethyl ether (1.7 g.) was oxidized with alkaline peroxide exactly as described for osajin dimethyl ether. On the addition of the alkali and hydrogen peroxide a turbidity appeared which cleared slowly on continued stirring. The acid fraction of the oxidation mixture was isolated as described for the osajin dimethyl ether and yielded a crystalline product; yield 0.24 g., m. p. 173–175°. Pure material was obtained on several recrystallizations from hot water (decolorizing charcoal); m. p. 179.5°. The substance was identified as veratric acid by preparation of its anilide (m. p. 166.5–167°) and amide (m. p. 164°). The substance and its two derivatives showed no depression in melting point on admixture with authentic specimens of veratric acid, veratric acid anilide and veratric acid amide. Mixed melting points of (1) veratric acid (179.5°) with anisic acid (180°), (2) veratric anilide (166.5°) with anisic anilide (167–168°) and (3) veratric amide (164°) with anisic amide (163–164°) were, respectively: (1) 146–162°, (2) 138–142° and (3) 132–140°. The isolated substance also showed the sublimation characteristic of veratric acid.

Anal. Calcd. for $C_9H_{10}O_4$ (veratric acid): OCH_3, 34.1; neutral equivalent, 182. Found: OCH_3, 33.5; neutral equivalent, 182.

We are indebted to Mr. John Walker (W. P. A. Project 18062) for assistance rendered in the analytical determinations and to Mr. Joseph Tracht (N. Y. A. Project O. S. U. 181) for assistance in preparing the plant material.

Summary

1. It is shown that the two pigments of the fruit of the osage orange (*Maclura pomifera* Raf.) are present in approximately equal amounts.

2. Osajin dimethyl ether has been prepared.

3. Anisic (*p*-methoxybenzoic) acid has been obtained from the oxidation of osajin dimethyl ether with alkaline hydrogen peroxide.

4. Veratric (3,4-dimethoxybenzoic) acid has been obtained from the oxidation of pomiferin trimethyl ether with alkaline hydrogen peroxide.

COLUMBUS, OHIO RECEIVED JANUARY 18, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF NOTRE DAME]

Addition of Oxy Compounds to Acetylenic Alcohols[1]

BY J. F. FRONING AND G. F. HENNION

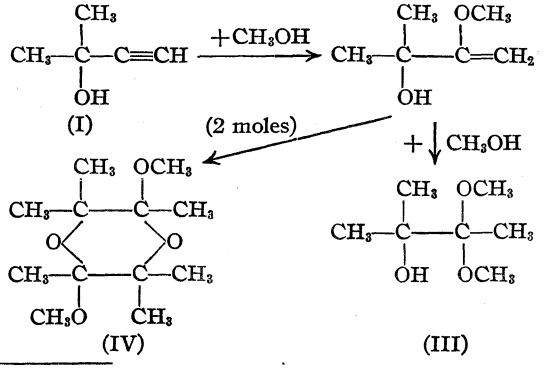
Introduction

Numerous examples of catalytic addition reactions of alcohols and carboxylic acids to acetylenic hydrocarbons have been reported from this Laboratory.[2] It was thought of interest to continue these investigations, particularly with acetylenes containing a reactive group in addition to the triple bond. The products found by the reaction of dimethylethynylcarbinol (I) and of the corresponding glycol, 2,5-dimethyl-3-hexyne-2,5-diol (II) with methanol and with acetic acid have now been investigated.

(I) and (II) were selected because they can be obtained readily by the reaction of acetone with sodium acetylide in liquid ammonia.[3,4] The carbinol (I) was obtained in yields up to 88%. High yields are favored by conducting the reaction at about −50° in the presence of excess acetylene. The glycol (II) was obtained as a by-product of the synthesis, in yields from 0–45%, depending on conditions. When excess acetylene is avoided in the reaction and the product aged for several days before hydrolysis, the yield of carbinol (I) is decreased and the yield of glycol (II) markedly increased.

As anticipated, certain anomalies in the behavior of these compounds toward methanol and acetic acid were noted.

In the presence of small amounts of mercuric oxide and boron trifluoride, methanol reacted smoothly with dimethylethynylcarbinol (I) to form principally 3,3-dimethoxy-2-methyl-2-butanol (III). A small amount of 2,5-dimethoxy-2,3,3,5,6,6-hexamethyl-1,4-dioxane (IV) was obtained as a by-product. The reactions are indicated by the equations just given.



When heated with dilute acid both (III) and (IV) hydrolyze to 2-hydroxy-2-methyl-3-butanone, $(CH_3)_2C(OH)COCH_3$ (V), previously reported[5] by direct hydration of the carbinol (I). When boiled with methanol containing a trace of acid (IV) reacts to form (III).

The reaction of the carbinol (I) with glacial acetic acid is particularly unique; the hydroxyl group is acetylated and the triple bond hydrated.

$$(CH_3)_2C(OH)-C\equiv CH + CH_3COOH \xrightarrow[BF_3]{Hg^{++}} (CH_3)_2C(OCOCH_3)-COCH_3$$

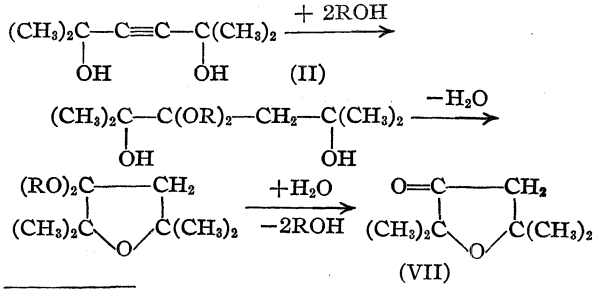
(VI)

The mechanism for this reaction is a matter of speculation. The product is identical with that obtained by Scheibler and Fischer[5] who acetylated the hydroxy ketone (V) with acetic anhydride.

$$(CH_3)_2C(OH)-COCH_3 \xrightarrow{(CH_3CO)_2O} (CH_3)_2C(OCOCH_3)-COCH_3$$

(V) (VI)

When either methanol or acetic acid reacted with the glycol (II) the triple bond was hydrated and the compound cyclized to form 2,2,5,5-tetramethyltetrahydro-3-furanone (VII). It is necessary for the triple bond to be saturated, at least partially, before cyclization can occur. The following mechanism is offered based on this fact (R is CH_3- or CH_3CO-).



(1) Paper XXXVII on the chemistry of substituted acetylenes and their derivatives; previous paper, THIS JOURNAL, **62**, 449 (1940).

(2) Hennion, Nieuwland, *et al.*, *ibid.*, **56**, 1130, 1384, 1802 (1934); **57**, 2006 (1935); **58**, 80 (1936).

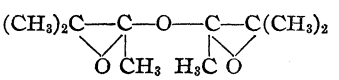
(3) Kreimeier, U. S. Patent 2,106,180 (1938).

(4) Campbell, Campbell and Eby, THIS JOURNAL, **60**, 2882 (1938).

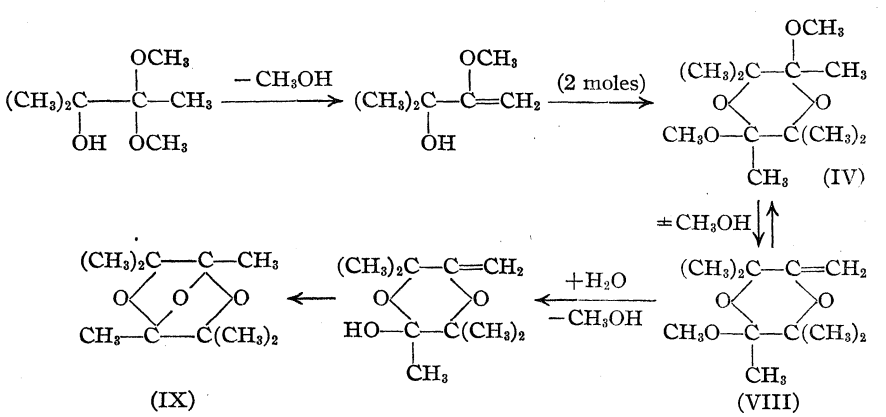
(5) Scheibler and Fischer, *Ber.*, **55**, 2903 (1922).

The product (VII) has been prepared previously[6] from the glycol (II) by heating with water in the presence of mercuric sulfate.

Since ketals are known to desaturate to vinyl ethers when heated with toluenesulfonic acid,[7] this reaction was applied to 3,3-dimethoxy-2-methyl-2-butanol (III). Methanol was eliminated upon heating with acid but the residue boiled over a wide temperature range. Two products were isolated, however, and their structures determined. The first of these was found to have the molecular formula $C_{10}H_{18}O_3$ as the structure 1,3,3,4,6,6-hexamethyl-2,5,7-trioxabicyclo[2-2-1]heptane (IX). This same compound was obtained by Scheibler and Fischer[5] upon treatment of the ketone (V) with phosphorus pentoxide. However, these investigators erroneously ascribed to this compound the structure



Distinction between these formulas was made by parachor measurement. Also the compound is unaffected by prolonged boiling with methanol containing toluenesulfonic acid, a fact which argues against the ethylene oxide structure. The second desaturation product was found to have a dioxane structure (VIII). These compounds are related in the following equations.



In the conversion of (VIII) to (IX) water is required. Presumably this is supplied by dehydration of (III) as a secondary reaction. In the presence of acid (VIII) adds methanol to its methylene group and reverts to (IV). When heated with a trace of acid (IV) loses methanol and yields (VIII) and (IX). These transformations confirm the mechanism cited above.

Experimental

Preparation of Dimethylethynylcarbinol (I).—Using the procedure[8] previously described, 7.35 moles of sodium acetylide was prepared as a solution in 3–4 liters of liquid ammonia. This was cooled to $-50 \pm 5°$ by immersion of the flask in a carbice bath. Acetylene was passed in for ten minutes. Acetone (465 g., 8 moles) was then added during a period of thirty minutes. Meanwhile the admission of acetylene was continued. The ammonia was then allowed to evaporate (usually overnight), 1 liter of ether added, followed by sufficient iced 35% sulfuric acid to dissolve the solid. The water layer was separated and extracted with ether. The extract was combined with the original ether layer, the whole dried over anhydrous potassium carbonate and fractionally distilled. Fractions boiling between 60 and 102° were redried and redistilled. The yield of dimethylethynylcarbinol, b. p. 102–104°, was 545 g. (88%). Constants for a pure specimen were b. p. 103.8° at 757 mm.; $n^{20}D$ 1.4211; d^{20} 0.8623.

Preparation of 2,5-Dimethyl-3-hexyne-2,5-diol (II).—The above procedure was followed except that the reaction product was aged for one week after evaporation of the ammonia. The residue after distillation of the dimethylethynylcarbinol was crystallized several times from carbon tetrachloride. Yields varied, usually between 20 and 45%. Large white needles were obtained, m. p. 95°. The compound may be prepared in better yields by heating the sodium salt of the carbinol (I) for several hours in an atmosphere of ammonia.[9]

Preparation of 3,3-Dimethoxy-2-methyl-2-butanol (III).—The catalyst was prepared by heating together 4–5 g. of red mercuric oxide, 5 ml. of ether–boron fluoride, 5 ml. of methanol and 1–3 g. of trichloroacetic acid in a 2-liter 3-necked flask. The flask was provided with a reflux condenser, mechanical stirrer and dropping funnel. Reagent grade methanol (100 g.) was poured over the catalyst, the stirrer started, and 300 g. (3.13 moles) of dimethylethynylcarbinol in 300 g. of methanol added dropwise. The temperature was held at 45–55° by occasional cooling. After three hours the mixture was cooled to room temperature and 10 g. of powdered anhydrous potassium carbonate added with vigorous stirring. The sludge was allowed to settle overnight, the supernatant liquid decanted, excess methanol distilled and the residue fractionated at 50 mm. The yield was 371 g. (80%); colorless liquid, b. p. 81° at 50 mm.; $n^{20}D$ 1.4248; d^{20} 0.974; *MR* (calcd.), 39.34; *MR* (obsd.), 38.9.

Anal. Calcd. for $C_7H_{16}O_3$: C, 56.76; H, 10.81; mol.

(6) Dupont, *Ann. chim.*, (8) **30**, 536 (1913).

(7) Killian, Hennion and Nieuwland, THIS JOURNAL, **57**, 544 (1935).

(8) Hennion, *Proc. Ind. Acad. Sci.*, **48**, 116 (1938).

(9) Macullum, U. S. Patent 2,162,676 (1939).

wt., 148.13. Found: C, 57.15; H, 10.89; mol. wt., cryoscopic in benzene,[10] 149.

Hydrolysis with dilute sulfuric acid gave 2-hydroxy-2-methyl-3-butanone (V); b. p. 139° at 750 mm., 65° at 50 mm.; $n^{20}D$ 1.4150; d^{20} 0.950; *MR* (calcd.), 26.83; *MR* (obsd.), 27.35.

Anal. Calcd. for $C_5H_{10}O_2$: C, 59.41; H, 9.78. Found: C, 58.82; H, 9.80.

Isolation of 2,5-Dimethoxy-2,3,3,5,6,6-hexamethyl-1,4-dioxane (IV).—A solid residue, partially organic, remained after the distillation of (III) described above. The solid was extracted with ether to yield an organic solid which was crystallized from methanol. The yield was 16 g. (4.4%), white rhombic crystals, m. p. 107°.

Anal. Calcd. for $C_{12}H_{24}O_4$: C, 62.02; H, 10.43; CH_3O, 26.72; mol. wt., 232.2. Found: C, 62.40; H, 10.50; CH_3O, 25.1; mol. wt., 235.

Preparation of 2-Acetoxy-2-methyl-3-butanone (VI).—Dimethylethynylcarbinol (126 g., 1.5 moles) was treated with glacial acetic acid (180 g., 3 moles) in the presence of mercuric oxide and boron fluoride as described above for the reaction with methanol. After completion of the reaction the product was neutralized with sodium carbonate solution and extracted with ether. The ether layer was dried over calcium chloride, the ether removed by distillation, and the residue fractionated *in vacuo*. There was obtained 105.5 g. (49% yield) of product, a colorless liquid with amyl acetate like odor: b. p. 93° at 50 mm.; $n^{20}D$ 1.4180; d^{20} 1.008; *MR* (calcd.), 36.2; *MR* (obsd.), 36.0.

Anal. Calcd. for $C_7H_{12}O_3$: C, 58.29; H, 8.39; mol. wt., 144.1. Found: C, 58.00; H, 8.65; mol. wt., 145.

This compound was prepared also according to the procedure of Scheibler and Fischer.[5] The yield was 69%.

Preparations of 2,2,5,5-Tetramethyltetrahydro-3-furanone (VII).—The glycol (II) (100 g., 0.7 mole) reacted with methanol (100 ml., 2.5 moles) with the catalyst and under the conditions described above. There was obtained 77 g. (77% yield) of product, a colorless, stable liquid of camphoraceous odor: b. p. 71° at 50 mm.; $n^{20}D$ 1.4197; d^{20} 0.9255; *MR* (calcd.), 38.60; *MR* (obsd.), 38.8; mol. wt. (calcd.), 142; mol. wt. (found), 143.

The melting point of the semicarbazone was 190°, in agreement with the value of Dupont.[6]

Similarly (II) with acetic acid gave (VII) in 78% yield.

(10) All molecular weights reported in this paper were determined in the same manner.

Thermal Desaturation of 3,3-Dimethoxy-2-methyl-2-butanol (III).—The ketal (351.5 g., 2.38 moles) was placed in a 1-liter round-bottomed flask, 0.1 g. of *p*-toluenesulfonic acid added, and the flask attached to a 1 × 30 cm. indented column with variable take-off. Distillation was begun by heating the flask in an oil-bath. Heating for eight hours at 150–180° gave 110 g. of distillate boiling at 64°. The residue was neutralized by shaking with powdered anhydrous potassium carbonate. Subsequent distillation gave several fractions: A, 115 g., b. p. 123–165° at 750 mm.; B, 67 g., b. p. 78–82° at 50 mm.; C, 5.5 g., b. p. 82–110° at 50 mm.; D, 33 g., b. p. 110–112° at 50 mm.; E, 10 g., residue.

Fraction A proved to be an intractable mixture which continued to boil over a wide temperature range, even after numerous distillations. However, redistillation with toluenesulfonic acid gave further quantities of methanol and fractions B and D.

Fraction B distilled at 165° at 750 mm. and at 81–82° at 50 mm.; $n^{20}D$ 1.4199; d^{20} 0.972. The compound is assigned the bicyclic structure (IX) based on analysis and parachor.[11]

Anal. Calcd. for $C_{10}H_{18}O_3$: C, 64.47; H, 9.68; mol. wt., 186.14; *MR*, 48.91; [P], 424.2. Found: C, 64.50; H, 9.75; mol. wt., 186; *MR*, 48.4; [P], 420.35. The parachor calculated for the structure of Scheibler and Fischer[5] is 449.2.

Fraction D redistilled at 110–112° at 50 mm.; $n^{20}D$ 1.4533; d^{20} 0.979. The compound is given structure (VIII) based on its reactions and the following.

Anal. Calcd. for $C_{11}H_{20}O_3$: C, 65.95; H, 10.08; CH_3O, 15.50; mol. wt., 200.16; *MR*, 55.26. Found: C, 65.85; H, 10.34; CH_3O, 14.67; mol. wt., 199.5; *MR*, 54.75.

Acknowledgment.—The junior author (J. F. F.) gratefully acknowledges assistance given by the Organic Chemicals Division of the du Pont Company.

Summary

The reactions of methanol and acetic acid with dimethylethynylcarbinol and 2,5-dimethyl-3-hexyne-2,5-diol are described. These reactions are more complex than the corresponding ones with acetylenic hydrocarbons.

NOTRE DAME, INDIANA RECEIVED JANUARY 8, 1940

(11) Ray, *J. Indian Chem. Soc.*, **12**, 764–767 (1935), gives the parachor constant for a bridged six-membered ring which was used. Other values are those of Sugden.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF McGILL UNIVERSITY AND FROM THE KODAK RESEARCH LABORATORIES]

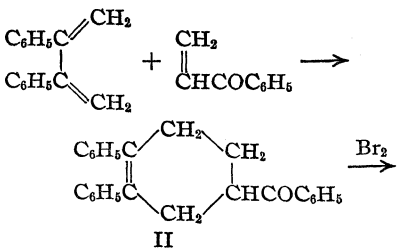
Addition Reactions of Vinyl Phenyl Ketone. VI. The Diene Synthesis

BY C. F. H. ALLEN, A. C. BELL, ALAN BELL AND JAMES VAN ALLAN

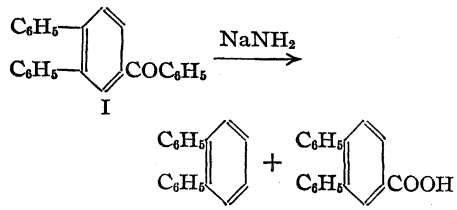
In a paper describing the reactions used in determining the structure of a dimeric diphenylcyclopentadienone,[1] one of the intermediate degradation products was the previously unknown 3,4-diphenylbenzophenone I, which was degraded stepwise to *o*-diphenylbenzene. This series of reactions demonstrated the presence of a benzene ring and two phenyl groups in the *ortho* position, but did not locate the benzoyl group. The original purpose of this work was to synthesize 3,4-diphenylbenzophenone by an unambiguous method, and show its identity with the ketone secured as mentioned. Not only has this been successfully accomplished, but its 6-carboxylic acid XXIV also has been synthetically prepared, proving conclusively the place of attachment of the indene ring in the bimolecular product. In addition, other products resulting from the use of vinyl phenyl ketone in the diene synthesis are described.

Vinyl phenyl ketone adds readily to many substances containing a conjugated system of double bonds, and, in general, the addition products have the expected properties. The reaction is most useful with unsaturated ketones; it is less satisfactory with hydrocarbons, and fails with furans.

2,3-Diphenylbutadiene-1,3[2] added vinyl phenyl ketone on long refluxing in xylene solution. The tetrahydroketone II was dehydrogenated by bromine to 3,4-diphenylbenzophenone I. As prepared in this way the latter proved to be identical with a specimen secured from the original degradation[1]; further, each gave the same oxime and 2,4-dinitrophenylhydrazone. In all instances, mixed melting points were not depressed. Finally, the ketone was cleaved by a sodium amide fusion to yield *o*-diphenylbenzene and 3,4-diphenylbenzoic acid.



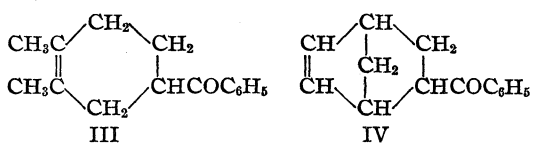
II



I

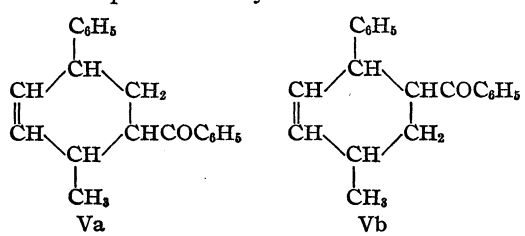
1,4-Diphenylbutadiene did not add vinyl phenyl ketone nearly as readily as the 2,3-isomer, and a crystalline addition product was not obtained. On treatment of the sirupy mixture with sulfur, 2,5-diphenylbenzophenone resulted. This was cleaved with sodium amide to terphenyl, thus showing that a six-membered ring had been formed in the addition.

The addition product from 2,3-dimethylbutadiene resembled the one from 2,3-diphenylbutadiene, except that it formed a dibromide instead of being dehydrogenated by bromine. The dimethyl tetrahydroketone III was dehydrogenated by sulfur to the known 3,4-dimethylbenzophenone.



III IV

Cyclopentadiene gave a homogeneous liquid that undoubtedly is represented by the structure IV. 1-Phenyl-4-methylbutadiene-1,3 gave a solid addition product that readily added bromine. The mode of addition was not determined; the tetrahydrobenzophenone may be either Va or Vb.

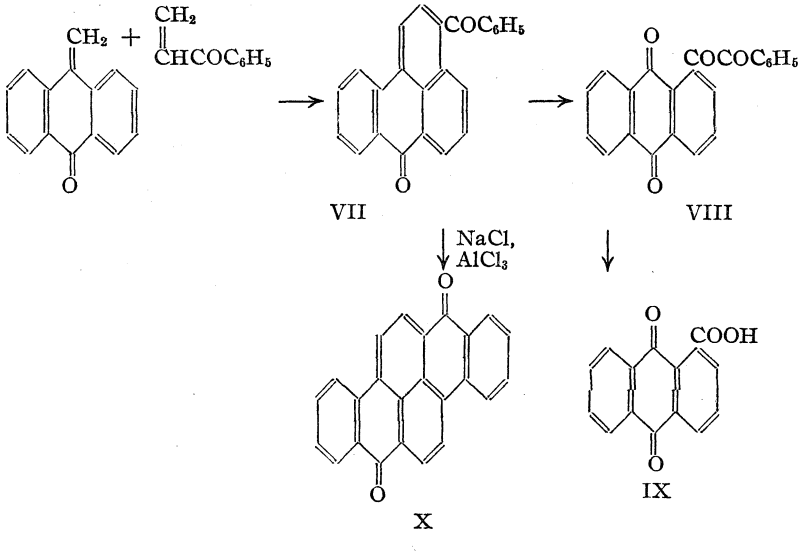


Va Vb

The liquid product from isoprene decomposed on distillation, but a ketonic derivative having the correct analysis was prepared from one fraction. Phellandrene gave a hopeless mixture, while with cyclohexadiene no product was obtained except β-ethoxypropiophenone, $C_2H_5OCH_2CH_2COC_6H_5$, VI, when alcohol was used as a solvent.

(1) Allen and Spanagel, THIS JOURNAL, **55**, 3773 (1933).
(2) Allen, Eliot and Bell, *Can. J. Research*, *B*, **17**, 75 (1939).

The use of methyleneanthrone furnished Bz-1-benzoylbenzanthrone VII directly. Although the product was identical with a specimen prepared as described in the patent literature,[3] its structure was independently shown by oxidation with chromic acid to α-benzoylformylanthraquinone VIII, which was then cleaved by sodium peroxide to anthraquinone-α-carboxylic acid IX.

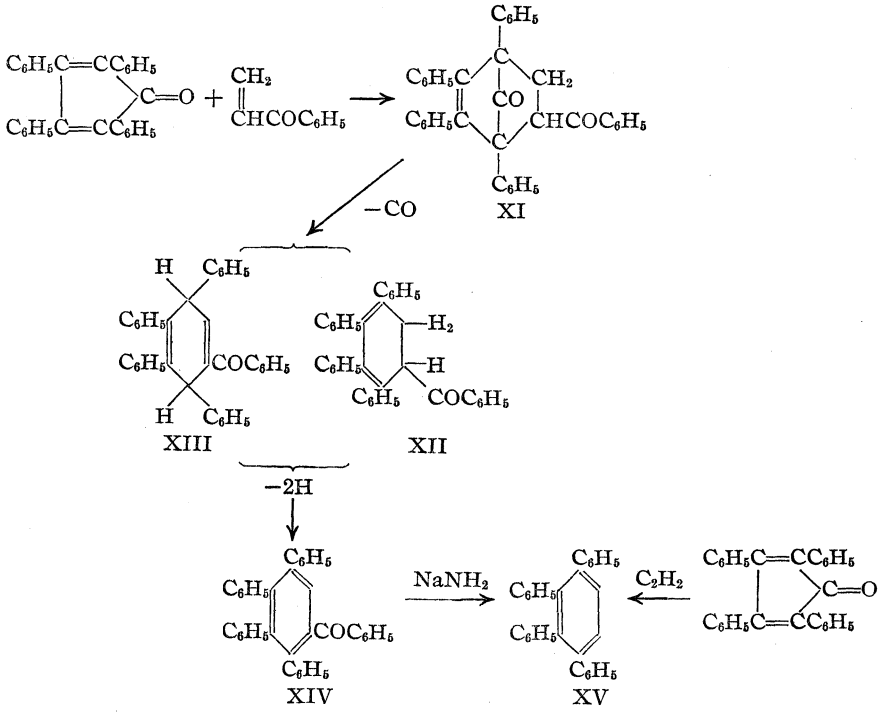


The formation of the benzanthrone VII shows that the direction of addition is that indicated by the formulas to the extent of at least 85%.

The Bz-1-benzoylbenzanthrone VII was also dehydrogenated in a sodium–aluminum chloride melt to 4,5,9,10-dibenzpyrene-3,8-quinone X identical in all respects with a specimen secured by the patent directions.[4]

Vinyl phenyl ketone added very easily to highly arylated cyclopentadienones; the primary addition products containing the carbonyl bridge could usually be isolated as would be expected.[1,5] Thus, tetraphenylcyclopentadienone gave the substance represented by formula XI. On moderate heating the bridge was lost as carbon monoxide, and two isomeric dihydrobenzophenones were formed. These may be geometrical isomers or some of the numerous possible forms differing only in the location of the double bonds, XII, XIII. When the addition reaction was carried out in a high-boiling solvent, these products resulted directly, the lower-melting form being the main product. The latter was also secured by heating the higher-melting modification at elevated temperatures for a short time.

Both the tetraphenyldihydrobenzophenones were easily dehydrogenated to yield tetraphenylbenzophenone XIV, and the latter was cleaved by sodium amide with the consequent formation of the known 1,2,3,4-tetraphenylbenzene XV.[6]



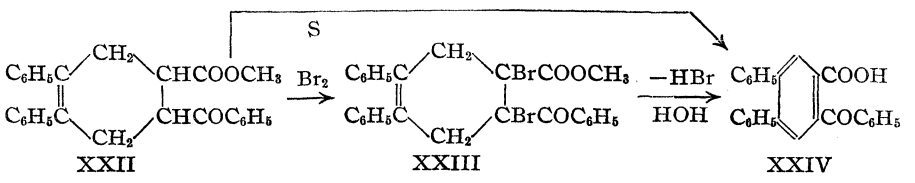
(3) German Patent 420,412; *Frdl.*, **15**, 736 (1928).

(4) German Patent 412,053; *Frdl.*, **15**, 731 (1928). In the patent the color with concd. sulfuric acid is said to be a blue-violet. A specimen of the quinone prepared exactly by the patent directions, as well as the one obtained in this work, gave a red-violet color with concd. sulfuric acid.

(5) Allen and Sheps, *Can. J. Research*, **11**, 171 (1934).

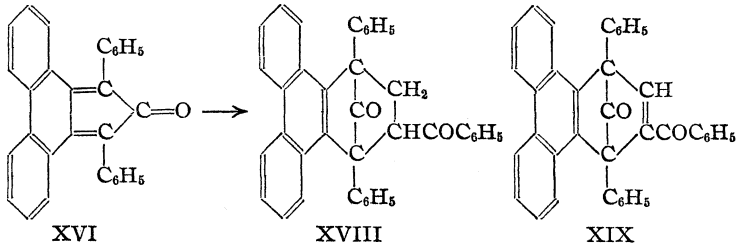
(6) Dilthey, U. S. Patent 2,097,854; *C. A.*, **32**, 367 (1938).

This sequence of reactions clearly demonstrates the presence of a benzene ring in the addition product.

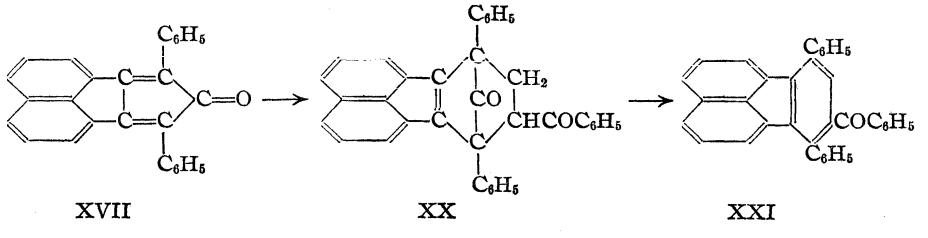


XXII XXIII XXIV

The cyclic ketones XVI and XVII also were used; the former gave an addition product XVIII only, but with the latter the tendency to lose the bridge and yield the aromatic form XXI was so great that the addition product XX was obtained analytically pure only with difficulty. When β-dimethylaminopropiophenone was substituted for β-chloropropiophenone, dimethylamine was eliminated; the resulting compound appeared to be the dihydro bridged ketone XIX or a reduction product.



XVI XVIII XIX

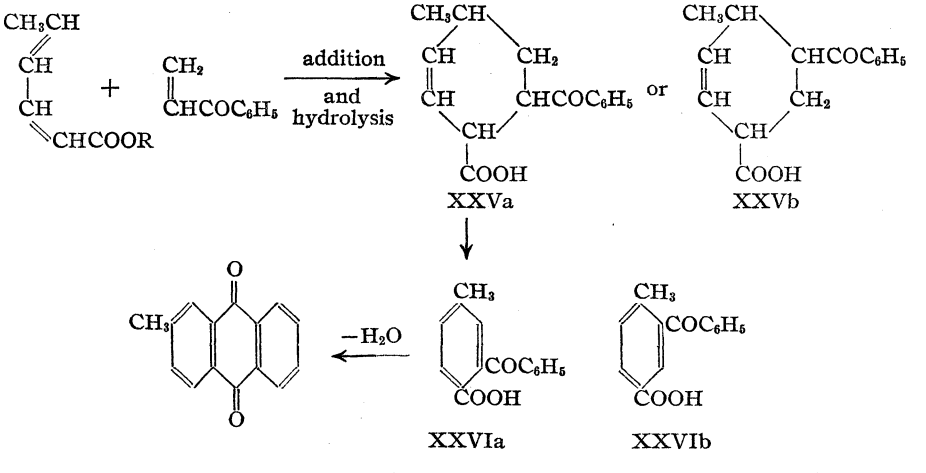


XVII XX XXI

Methyl β-benzoylacrylate and 2,3-diphenylbutadiene easily formed an addition product XXII. This did not decolorize bromine in a cold chloroform solution, but when the solution was heated, the halogen was completely used, hydrogen bromide was evolved, and a crystalline product resulted. Analysis showed the presence of two atoms of bromine. While the substance may be a dibromide, formed by addition of a molecule of bromine, it seems more probable that it is a substitution product XXIII, because (1) tetrahydrodiphenylbenzophenone II is dehydrogenated by bromine with no evidence of formation of a dibromide, and (2) this substance loses hydrogen bromide on heating, to give an oil that with alcoholic potash yields 6-carboxy-3,4-diphenylbenzophenone.

The ester XXII did not give a tractable product on sulfur dehydrogenation, but on treatment of the melt with alcoholic potash, followed by acidification, the aromatic acid XXIV precipitated. This was identical with the specimen secured previously.[1]

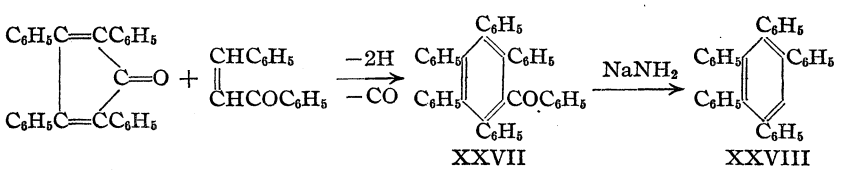
Vinyl phenyl ketone added readily to ethyl sorbate. Since there is a possibility of the formation of eight isomers, no attempt was made to separate the oily ester, but a part was hydrolyzed directly to the solid acids. Addition could have taken place so as to form either XXVa or XXVb. In order to distinguish, the remainder of the ester was dehydrogenated and hydrolyzed to the aromatic keto acids XXVIa or XXVIb, thus reducing the number of isomers to two. Treatment of these by concd. sulfuric acid would be expected to dehydrate XXVIa to β-methylanthraquinone but would have no effect on XXVIb. When this was done,



XXVa XXVb XXVIa XXVIb

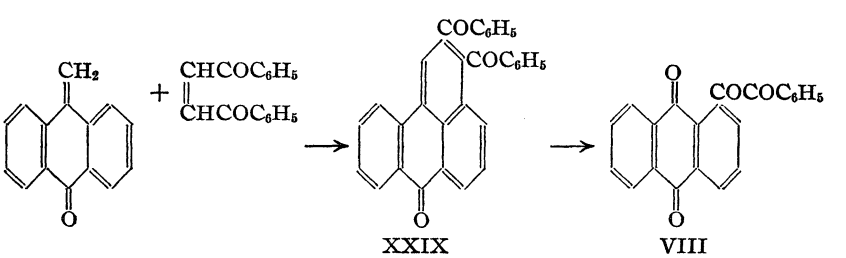
β-methylanthraquinone only was obtained, there being no acidic fraction recovered. Hence, the keto acid must have been almost exclusively XXVIa; the addition product acid must have been XXVa, and addition must have taken place nearly quantitatively in the direction indicated. No attempt was made to secure all the possible stereoisomeric forms of XXVa.

In an earlier paper[7] it was noted that the substituted vinyl phenyl ketone, benzalacetophenone, failed to react with tetraphenylcyclopentadienone. In the meantime, by operating in boiling trichlorobenzene, it has been found possible to force the addition, but the bridge and two hydrogen atoms are lost, so that the product is the aromatic pentaphenylbenzophenone XXVII. The latter was cleaved by the use of sodium amide, to give the known pentaphenylbenzene XXVIII.



XXVII XXVIII

trans-Dibenzoylethylene has been added to methyleneanthrone; the product is Bz-1-Bz-2-dibenzoylbenzanthrone XXIX. Its structure is evident from the production of α-benzoylformylanthraquinone VIII upon oxidation with chromium trioxide.



XXIX VIII

Furan, sylvan, and 2,5-dimethylfuran did not add to the pure ketone. In alcohol, β-ethoxypropiophenone VI was obtained.

Experimental

A. Reactions with Dienes. (a) 2,3-Diphenylbutadiene-1,3; 3,4-Diphenyltetrahydrobenzophenone.—The addition reactions were carried on in the same general manner as has been described in the earlier papers in this series, the main feature being the use of vinyl phenyl ketone in solution, as obtained from the interaction of potassium acetate and β-chloropropiophenone. This enables one to avoid the losses involved in its isolation. It also has been found that the β-dialkylaminoacetophenone hydrochloride can be substituted for the β-chloroketone, though the yields are not as good.[8]

A mixture of 11 g. of the hydrocarbon, 9.2 g. of β-chloropropiophenone, 5.4 g. of sodium acetate, and 75 cc. of xylene was refluxed for sixty hours and the solvent removed *in vacuo*. Most of the residual sirup dissolved in hot methanol, from which 8.5 g. of the ketone separated in fine prisms on cooling; recrystallization from ligroin (90–120°) gave a white product, m. p. 83°.

Anal. Calcd. for $C_{25}H_{22}O$: C, 88.8; H, 6.6. Found: C, 89.1; H, 6.6.

The 2,4-dinitrophenylhydrazone was obtained in the usual manner; it crystallized in orange rods from methanol–dioxane, m. p. 203°.

Anal. Calcd. for $C_{31}H_{26}O_4N_4$: N, 10.8. Found: N, 10.5.

For dehydrogenation 8 g. of bromine in 20 cc. of chloroform was added slowly to 7.8 g. of the addition product in 15 cc. of the same solvent; large amounts of hydrogen bromide were evolved. The sirup left on evaporation of the solvent solidified when treated with methanol; the yield of white solid was 7.5 g. (97%). On recrystallization from ethanol it separated in white prisms, m. p. 133°. A mixed melting point with a sample of the ketone[1] resulting from the degradation was not depressed. The oxime and 2,4-dinitrophenylhydrazone were prepared, compared, and found to be identical. The second derivative is new; it was secured by the usual procedure. It separated from dioxane–methanol in microscopic orange prisms, m. p. 248°.

Anal. Calcd. for $C_{31}H_{22}O_4N_4$: N, 10.9. Found: N, 10.6.

Sodium Amide Fusion.[9]—A mixture of 4 g. of 3,4-diphenylbenzophenone, 10 cc. of cymene, and 0.7 g. of powdered sodium amide was refluxed for six hours. The cooled solution was extracted with water and the alkaline layer separated. The cymene was then removed and the residue distilled with steam; 1.9 g. (70%) of *o*-diphenylbenzene was secured (mixed melting point not depressed). Acidification of the alkaline solution gave 0.2 g. (7%) of 3,4-diphenylbenzoic acid.[2]

(b) 1,4-Diphenylbutadiene; 2,5-Diphenylbenzophenone.—Exactly as described under the 2,3-isomer, a mixture of the same quantities of the components was refluxed for forty-eight hours and the solvent removed under reduced pressure. Upon extraction of the residue with methanol, 3.5 g. of diene remained undissolved. The methanol

(7) Allen and Sheps, *Can. J. Research*, **11**, 173 (1934).

(8) Mannich and Fourneau, *Ber.*, **71**, 2090 (1938).

(9) Haller and Bauer, *Ann. phys. chim.*, [8] **16**, 145 (1909); Lucas, *ibid.*, **17**, 127 (1909).

in the extract was replaced by chloroform and treated with bromine in the usual manner; 8 g. of a halogen-containing solid was obtained. This melted at 215° and analyzed for a dibromide of diphenylbutadiene. This and the unreacted hydrocarbon accounted for 70% of the diene, thus indicating not over 30% of addition.

In a later run, the methanol-soluble fraction was distilled *in vacuo*, and a sirupy distillate, b. p. 250–255° at 4–5 mm., secured; the analysis was about 1% low. It was not further purified, but at once dehydrogenated by heating 2.5 g. with 0.5 g. of sulfur at 200° for two hours; the residue was extracted with hot alcohol, from which 1.3 g. of the ketone separated. 2,5-Diphenylbenzophenone crystallizes in rods, m. p. 130°.

Anal. Calcd. for $C_{25}H_{18}O$: C, 89.8; H, 5.4. Found: C, 89.6; H, 5.4.

Sodium Amide Fusion.—In a similar manner, 0.20 g. of 2,5-diphenylbenzophenone gave 0.11 g. (80%) of *p*-diphenylbenzene; the melting point and mixed melting point with an authentic specimen were 211–212°.

(c) **2,3-Dimethylbutadiene; 3,4-Dimethyltetrahydrobenzophenone III.**—After refluxing a mixture of 8.4 g. of β-chloropropiophenone, 8 g. of potassium acetate and 30 cc. of 2,3-dimethylbutadiene for twenty-four hours, adding ether and filtering the inorganic salts, fractionation *in vacuo* gave the addition product, b. p. 184–188° at 12 mm. On redistillation it boiled from 163–165° at 6 mm.; the yield was 4 g.

Anal. Calcd. for $C_{15}H_{18}O$: C, 84.1; H, 8.4. Found: C, 84.1; H, 8.5.

The 2,4-dinitrophenylhydrazone, secured by the usual procedure, separated from methanol in orange-yellow leaflets, m. p. 152°.

Anal. Calcd. for $C_{21}H_{22}O_4N_4$: N, 14.2. Found: N, 14.1.

On treatment of the addition product with bromine there was no apparent action in the cold; on warming, hydrogen bromide was given off. The only substance isolated was a dibromide; this crystallized from ethanol in long white needles, m. p. 132°.

Anal. Calcd. for $C_{15}H_{18}OBr_2$: C, 48.1; H, 4.8; Br, 42.8. Found: C, 47.7; H, 4.8; Br, 42.8.

Dehydrogenation to the known 3,4-dimethylbenzophenone[10] was readily accomplished by heating 2.1 g. of the substance III with 0.8 g. of sulfur in a metal bath at 190–230°. When gas evolution had become negligible, the cooled melt was extracted with ethanol; 1 g. of ketone was obtained. The melting point (45°) was not depressed on admixture with a specimen secured by Elbs' method.

The 2,4-dinitrophenylhydrazone of this ketone was secured by the usual procedure. It separated from chloroform–methanol in microscopic prisms, m. p. 252°.

Anal. Calcd. for $C_{21}H_{18}O_4N_4$: N, 14.4. Found: N, 13.9.

(d) **Benzoylmethylphenylcyclohexene Va or Vb.**—A mixture of 7.2 g. of 1-phenyl-4-methylbutadiene-1,3,[11] 9.5 g. of β-chloropropiophenone, 6.3 g. of potassium acetate and 20 cc. of trichlorobenzene was refluxed for eight hours and distilled *in vacuo*. The portion of b. p. 150–167° at 1 mm. on redistillation boiled at 157–159° at 1 mm. On standing it crystallized, 5 g. of pure ketone being obtained; this separated from methanol in prisms, m. p. 61°.

Anal. Calcd. for $C_{20}H_{20}O$: C, 87.0; H, 7.1. Found: C, 86.4, 86.4; H, 7.3, 7.2.

The dibromide was obtained readily by treatment with bromine in chloroform, although there was some evolution of hydrogen bromide. It crystallized from methanol in plates or prisms, m. p. 125°.

Anal. Calcd. for $C_{20}H_{20}OBr_2$: Br, 36.7. Found: Br, 36.3.

(e) **1-Benzoyl-1,2,3,6-tetrahydro-3,6-methanobenzene IV.**—A mixture of 13 g. of cyclopentadiene, 25 g. of β-chloropropiophenone, 23 g. of potassium acetate and 50 cc. of toluene was heated in a sealed bottle at 95–100° for thirty hours. Inorganic salts were filtered after adding ether to facilitate manipulation and the solution fractionated *in vacuo*. The portion, b. p. 122–124° at 3 mm., was collected in a yield of 16 g.; $n^{26}D$ 1.5648.

Anal. Calcd. for $C_{14}H_{14}O$: C, 84.7; H, 7.1. Found: C, 84.3; H, 7.1.

The semicarbazone, obtained in the usual manner, separated from alcohol in shiny prisms, m. p. 178–180°.

Anal. Calcd. for $C_{15}H_{17}ON_3$: N, 16.4. Found: N, 16.1.

The addition product decolorizes permanganate and bromine in chloroform instantly.

(f) **Miscellaneous.**—A mixture of 10 g. of isoprene, 16.8 g. of β-chloropropiophenone, 15 g. of potassium acetate, and 15 cc. of toluene was heated in a steam-bath in a pressure bottle for twenty-four hours. After removal of the inorganic salt by precipitation with ether, the liquid was distilled *in vacuo*. The fraction, b. p. 120–122° at 2 mm., gave a 2,4-dinitrophenylhydrazone, m. p. 137°.

Anal. Calcd. for $C_{20}H_{20}O_4N_4$: N, 14.7. Found: N, 14.5.

From commercial phellandrene and the alcoholic solution of vinyl phenyl ketone an oil, b. p. 183–185° at 2 mm., was obtained in a 37% yield. It decolorized bromine instantly, with evolution of hydrogen bromide. The 2,4-dinitrophenylhydrazone was an oil, and a semicarbazone was not secured. The analysis was not satisfactory.

Anal. Calcd. for $C_{19}H_{24}O$: C, 85.1; H, 8.9. Found: C, 84.1; H, 8.6.

β-Ethoxypropiophenone VI was obtained when cyclohexadiene and an alcoholic solution of the unsaturated ketone were allowed to react (described under furan).

B. Reactions with Ketones. (a) **Bz-1-Benzoylbenzanthrone VII.**—A mixture of 5.2 g. of methyleneanthrone,[12] 6 g. of β-chloropropiophenone, 6 g. of potassium acetate, and 35 cc. of nitrobenzene was stirred and refluxed for two and a half hours at 180–190°; it became very dark and set to a mass of crystals on cooling. The solid was filtered after triturating with 125 cc. of methanol, washing with the same solvent until bright yellow, and then with water to remove soluble salts. It dissolved readily in hot acetic acid or chloroform. The analytical

(10) Elbs, *J. prakt. Chem.*, **33**, 180 (1886); **35**, 467 (1887).

(11) Klages, *Ber.*, **40**, 1769 (1907).

(12) Barnett and Matthews, *Ber.*, **59**, 767 (1926).

sample was recrystallized from chloroform–methanol, from which it separated in brownish-yellow needles, m. p. 192°. The yield was 6.5 g., 84%.

Anal. Calcd. for $C_{24}H_{14}O_2$: C, 86.2; H, 4.2. Found: C, 86.0; H, 4.2.

It was also synthesized from Bz-1-carboxybenzanthrone,[3] the requisite acid being secured through the diazo reaction from Bz-1-aminobenzanthrone, and also by the interaction of methyleneanthrone and β-chloropropionic acid.[13]

A mixture of 2 g. of the Bz-1-acid, 4 g. of phosphorus pentachloride, and 20 cc. of benzene was warmed on the steam-bath as long as hydrogen chloride was evolved, then cooled, and, after addition of 4 g. of anhydrous aluminum chloride, warmed for an hour at 70°. It was then poured upon ice, the benzene steam-distilled, and the residue boiled with hydrochloric acid, filtered, and washed. On recrystallization from 4 cc. of nitrobenzene, the Bz-1-benzoylbenzanthrone separated in brownish-yellow needles, m. p. 190–192°. A mixed melting point with the substance secured by the first procedure was 191–192°.

Oxidation by Chromium Trioxide.—To a solution of 1.9 g. of the ketone in 20 cc. of acetic acid, 5 g. of chromic acid in 36 cc. of 50% acetic acid was added slowly, the mixture was refluxed for five minutes, cooled, and 50 cc. of water added to precipitate the diketone VIII. The crystals so obtained were bright yellow, but the surface rapidly became greenish-colored, until after several recrystallizations from chloroform–methanol, from which it separated in rods, m. p. 174°.

Anal. Calcd. for $C_{22}H_{12}O_4$: C, 77.6; H, 3.6. Found: C, 77.6; H, 3.5.

This diketone gave a brown color with concd. sulfuric acid and a clear blue vat with alkaline hydrosulfite.

Cleavage.—To a suspension of 1.5 g. of the diketone in 30 cc. of cold water, 4 g. of sodium peroxide was added; after five hours' standing, the mixture was warmed to 70° and the unreacted solid filtered. Acidification of the filtrate precipitated anthraquinone-α-carboxylic acid. For identification this was converted into the methyl ester through the silver salt; a mixed melting point with an authentic sample was not depressed.

4,5,9,10-Dibenzpyrene-3,8-quinone X.—The sodium–aluminum chloride from 20 g. of anhydrous aluminum chloride and 4 g. of salt was mixed with 2 g. of Bz-1-benzoylbenzanthrone and the temperature raised to 180–200°, where it was held for eight hours. The melt was decomposed by iced hydrochloric acid and the dye filtered. It was then converted to a red vat by alkaline hydrosulfite, the solution was filtered and aerated. The orange-yellow dye was collected on a filter. After recrystallization from nitrobenzene it formed rods that melted at 385–388°. A mixed melting point with an authentic sample[4] (m. p. 386–388°) was 384–386°. Both samples gave the same red-violet color with concd. sulfuric acid.

(b) Tetraphenylbenzophenone and Related Compounds. (1) 3,4,5,6-Tetraphenyl-7-keto-1-benzoyl-1,2,3,-6-tetrahydro-3,6-methanobenzene XI.—A mixture of 134 g. of tetraphenylcyclopentadienone, 230 g. of β-chloropropiophenone, 200 g. of potassium acetate, and 520 cc. of toluene was refluxed for three hours, or until the red color had disappeared. After cooling, the pulverized solid was filtered, digested with warm (50°) water for one hour, filtered, and washed first with water and then with 400 cc. of acetone. Final purification was accomplished by recrystallization from toluene or mixtures of chloroform–methanol and ethyl acetate–methanol. The addition product XI forms prisms which melt at 210° to a red liquid with gas evolution. The yield was practically quantitative.

Anal. Calcd. for $C_{38}H_{28}O_2$: C, 88.4; H, 5.4. Found: C, 88.5; H, 5.4.

This addition product is insoluble in the alcohols and ether, slightly soluble in carbon tetrachloride, but dissolves easily in hot chloroform, ethyl acetate, benzene, toluene, and acetic acid. It was recovered unchanged after boiling with permanganate in acetone, glacial acetic acid, and selenium dioxide or hydrogen peroxide. Bromine in chloroform, and chromic acid in acetic acid slowly attacked it, but gave ill-defined products from which no individual substance could be isolated.

The addition product also resulted, less conveniently, when a benzene solution of vinyl phenyl ketone and tetraphenylcyclopentadienone was refluxed for two hours, or when the components were heated in the absence of a solvent at 130°. It was also obtained when one replaced the β-chloropropiophenone by an equivalent amount of β-dimethylaminopropiophenone hydrochloride; after twenty-four hours the yield was but 25%.

(2) Dihydro-3,4,5,6-tetraphenylbenzophenones XII or XIII.—The dihydroketone was easily secured by pyrolysis of the addition product or by carrying out the addition reactions in boiling trichlorobenzene or nitrobenzene, substituting β-dimethylaminopropiophenone for β-chloropropiophenone.

(i) Pyrolysis: High-Melting Form.—Ten grams of the addition product was heated for ten minutes in a metal bath at 215°; it formed a reddish liquid which evolved carbon monoxide; a few oily drops collected in the upper part of the flask, and the pungent odor of vinyl methyl ketone was evident. The cooled melt was taken up in chloroform and diluted with methanol. The dihydroketone crystallizes in pale yellow rods, m. p. 177°. It is sparingly soluble in the alcohols, acetone, and ether, but dissolves easily in ethyl acetate, chloroform, carbon tetrachloride, acetic acid, and benzene.

Anal. Calcd. for $C_{37}H_{28}O$: C, 91.0; H, 5.7. Found: C, 90.8; H, 5.7.

(ii) Low-Melting Form.—A mixture of 7.6 g. of tetraphenylcyclopentadienone, 6 g. of β-dimethylaminopropiophenone hydrochloride (or an equivalent amount of β-chloropropiophenone), 6 g. of potassium acetate, and 35 cc. of trichlorobenzene was heated at 180–190° for three hours with stirring; dimethylamine was evolved and the mixture became colorless after two hours. The potassium salts were precipitated by the addition of 50 cc. of methanol, and, after filtering, the solvent was removed *in vacuo*. The hard residue was taken up in chloroform and recrystallized in the usual manner. It forms pale yellow very fine rods, m. p. 158–159°.

Anal. Calcd. for $C_{37}H_{28}O$: C, 91.0; H, 5.7. Found: C, 91.2, 91.2; H, 5.5, 5.6.

(13) German Patent 597,325; *Frdl.*, **21**, 1121 (1936).

When nitrobenzene was substituted for trichlorobenzene, the high-melting isomer was isolated; the reaction product was rather sticky and not easy to manipulate.

The high-melting isomer (1 g., m. p. 177°) was heated at 250–270° for fifteen minutes, cooled, taken up in chloroform, and methanol added to incipient crystallization. After filtration, the solid melted at 156–158°; when it was mixed with the analytical sample, the melting point was 157–158°.

Mixtures of the low and high-melting forms may soften as low as 138°, but usually do not form a clear liquid until about 173°. They are often obtained in the pyrolysis of large quantities of the addition product.

(3) 2,3,4,5-Tetraphenylbenzophenone XIV.—This ketone was obtained from both forms of the dihydro compound by the dehydrogenating action of bromine, permanganate, and sulfur. The yields were good by all procedures. In each instance the melting points of the products were the same, and there was no depression on admixture.

(i) **Action of Bromine.**—To a solution of 1.0 g. of the dihydroketone in 8 cc. of chloroform was added 0.4 g. of bromine in 2 cc. of the same solvent. Hydrogen bromide was evolved; after three minutes on the steam-bath, methanol was added to incipient crystallization. After standing several hours, 0.8 g. of the aromatic ketone had separated. It forms long rods, m. p. 190°. The solubilities are the same as those of the dihydro compound.

Anal. Calcd. for $C_{37}H_{26}O$: C, 91.1; H, 5.4. Found: C, 91.3; H, 5.4.

(ii) **Action of Permanganate.**—A solution of 2 g. of the dihydroketone in 30 cc. of acetone was warmed, and potassium permanganate in acetone added as long as it was decolorized. The oxides of manganese were filtered and the solvent evaporated; the residue was crystallized from chloroform–methanol; 1.3 g. of product was secured.

(iii) **Sulfur Fusion.**—A mixture of 2 g. of the dihydroketone and 0.4 g. of sulfur was heated in a metal bath at 240–250° for fifteen to twenty minutes, when the evolution of gas became negligible. The cooled melt was dissolved, filtered, and recrystallized; the yield was 1 g.

(4) 1,2,3,4-Tetraphenylbenzene, XV.—One gram each of the tetraphenylbenzophenone and pulverized sodium amide in 50 cc. of *p*-cymene was refluxed for eight hours. The cooled mixture was washed with water, and the hydrocarbon slowly crystallized in a yield of 50%. Recrystallization from acetic acid gave a product, m. p. 193°. The melting point was not depressed on admixture with a specimen secured by Dilthey's procedure.[6]

(c) **Polynuclear Series.**—A mixture of 2 g. of the green unsaturated ketone XVII, 2.5 g. of β-chloropropiophenone, 2 g. of potassium acetate, and 25 cc. of toluene was heated until the green color disappeared (two hours), cooled, the inorganic salts filtered, and the solution concentrated to about 15 cc. Methanol was added to precipitate the yellow reaction product, which was recrystallized from chloroform–methanol. The addition product XX separated in prisms, m. p. 189–190°.

Anal. Calcd. for $C_{36}H_{24}O_2$: C, 88.5; H, 4.9. Found: C, 88.1, 88.3; H, 5.1, 5.1.

It dissolved readily in hot acetic acid but the melting point of the crystalline product was lowered; subsequent purification from chloroform–methanol gave a yellow substance, m. p. 194–195°, with analytical figures approaching the bridgeless formula XXI.

Anal. Calcd. for $C_{35}H_{24}O$: C, 91.3; H, 5.2. Found: C, 90.2, 90.5; H, 5.1, 5.2.

In a similar manner from β-chloropropiophenone and 3.8 g. of diphenylenediphenylcyclopentadienone XVI there was obtained an addition product XVIII, which separated from chloroform–methanol in white needles, m. p. 273°. Above the melting point it dissociated appreciably into its components.

Anal. Calcd. for $C_{38}H_{26}O_2$: C, 88.7; H, 5.4. Found: C, 88.4; H, 5.1.

When β-dimethylaminovinyl phenyl ketone was substituted for the β-chloropropiophenone, the resulting substance appeared to be the dihydro-bridged ketone XIX or its reduction product; the latter, however, is not identical with XVIII, nor are the two interconvertible. This reaction is being studied further. The ketone XIX separated from chloroform in very fine white needles, m. p. 312–315°.

Anal. Calcd. for $C_{38}H_{24}O_2$: C, 89.1; H, 4.7; for $C_{38}H_{26}O_2$: C, 88.7; H, 5.4. Found: C, 88.8; H, 5.3.

C. Miscellaneous. (a) Methyl Benzoylacrylate; Methyl 2-Benzoyl-4,5-diphenyltetrahydrobenzoate XXII.—A solution of 0.6 g. of 2,3-diphenylbutadiene and 0.6 g. of methyl β-benzoylacrylate was heated for fifteen hours at 165°. The cooled residue was taken up in boiling methanol and treated with Norite; on cooling, the addition product separated in fine white prisms. The yield was 0.6 g., 52% of the theoretical amount. It could also be secured in a yield of 20% by refluxing a xylene solution of the components for sixty hours. The analytical sample was recrystallized from methanol; m. p. 147°.

Anal. Calcd. for $C_{27}H_{24}O_3$: C, 81.8; H, 6.1. Found: C, 82.0; H, 6.0.

The addition product did not react appreciably with bromine in a cold chloroform solution, but, on warming, hydrogen bromide was evolved in considerable amount. On evaporation of the solvent, followed by crystallization from methanol, a substance containing two bromine atoms was secured. It separates in rods, m. p. 183°, with decomposition.

Anal. Calcd. for $C_{27}H_{22}O_3Br_2$: C, 58.5; H, 4.0; Br, 28.9. Found: C, 58.7; H, 4.0; Br, 28.6.

Dehydrogenation was accomplished by heating 0.8 g. of the ester and 0.2 g. of sulfur for several hours at 230°. The untractable melt was warmed with alcoholic potash, evaporated to dryness and extracted with water. Acidification of the filtered solution precipitated the 6-carboxy-3,4-diphenylbenzophenone XXIV, which was recrystallized from dilute methanol. The melting point was 240–241° and was not depressed when mixed with a specimen of the original ketoacid.[1]

(b) From a mixture of 16.8 g. of β-chloropropiophenone, 12.8 g. of ethyl sorbate, 9.8 g. of potassium acetate and 50 cc. of xylene, refluxed eighteen hours and treated in the usual manner, was obtained 13.4 g. of the addition

product (mixed esters), m. p. 165–170° at 3 mm. It was hydrolyzed by refluxing with 3 g. of potassium hydroxide in 50 cc. of ethanol for two and a half hours; the solution was then poured into water, filtered and the oily acid that separated on acidification allowed to crystallize slowly from methanol. In this way, 8 g. of mixed stereoisomers XXVa, m. p. 128–133°, was secured on recrystallization from ethanol; one form was easily isolated in a yield of 75%; it separates in tiny rods, m. p. 162–163°.

Anal. Calcd. for $C_{15}H_{16}O_3$: C, 73.8; H, 6.6. Found: C, 73.7; H, 6.5.

The crude ester (5.2 g.) was also dehydrogenated by heating with 0.7 g. of sulfur at 200–240° for ten minutes; the cooled melt was extracted with alcohol, and the filtered solution refluxed for two hours after the addition of 1.4 g. of potassium hydroxide. After dilution it was treated with Norite, filtered, and acidified, the oily acid being dehydrated directly, as follows: a mixture of 1 g. of this and 4.6 cc. of 20% fuming sulfuric acid was warmed on the steam-bath for two hours, and, after cooling, poured into water. The precipitate was insoluble in sodium hydroxide. After two crystallizations from alcohol it melted at 166° and did not depress the melting point of an authentic sample of β-methylanthraquinone.

(c) **2,3,4,5,6-Pentaphenylbenzophenone XXII.**—A mixture of 9.5 g. of tetraphenylcyclopentadienone, 6 g. of benzalacetophenone, and 30 cc. of trichlorobenzene was refluxed for twenty-four hours (210–213°); the red color gradually diminished but never entirely disappeared. On cooling, the product separated; it was filtered and recrystallized from chloroform–methanol. The melting point and mixed melting point with an authentic sample[7] were 338° (341° cor.). The ketone sublimes in long needles.

Anal. Calcd. for $C_{43}H_{30}O$: C, 91.8; H, 5.4. Found: C, 91.8; H, 5.5.

Pentaphenylbenzene XXIII.—The sodium amide cleavage was carried out as described under the tetraphenyl homolog, using 5 g. of ketone and 8 g. of amide; the yield of hydrocarbon was 1.8 g., m. p. 245–246°. A mixed melting point with a specimen secured by Dilthey's procedure[6] was not depressed.

(d) **Bz-1-Bz-2-Dibenzoylbenzanthrone, XXIX.**—This ketone appears to exist in polymorphic forms, one, melting at 208°, being formed when the components are refluxed in trichlorobenzene, and the other, m. p. 286°, when nitrobenzene is used as a solvent. Both forms separate from solutions as yellow rods, give the same scarlet color in concd. sulfuric acid, and show comparable solubilities in the same solvents, but the lower-melting form is changed into the higher by sulfuric acid.

A mixture of 2 g. of methyleneanthrone, 3 g. of *trans*-dibenzoylethylene, and 10 cc. of trichlorobenzene was refluxed for five hours, cooled, and 15 cc. of methanol added with stirring; the reddish crystals that separated were filtered and washed. This product was a mixture of uncertain composition that required repeated recrystallization before a substance having a constant melting point was obtained. The red color only slowly disappeared, although bromine removed it at once without greatly improving the melting point. The most suitable solvent was chloroform–methanol. When nitrobenzene was used, the high-melting form separated at once. Both forms are insoluble in the alcohols and ether, but dissolve readily in hot chloroform, acetic acid, and dioxane.

Anal. Calcd. for $C_{31}H_{18}O_3$: C, 84.9; H, 4.1. Found: (208°) C, 85.3; H, 4.0; (286°) C, 85.2; H, 4.1.

Oxidation.—A mixture of 2.5 g. of the ketone, 5 g. of chromium trioxide, and 86 cc. of acetic acid was refluxed for ten minutes, cooled, and diluted with 300 cc. of water. After two hours the precipitate was filtered and washed. The solid was extracted with dilute sodium carbonate solution, filtered, and acidified, the benzoic acid being extracted with ether and identified in the usual manner. The solid, insoluble in sodium carbonate, was crystallized from methanol and found to be identical with the α-benzoylformylanthraquinone VIII secured in another way as described above. The dibenzoylbenzanthrone XXIX was unaffected by melting with sodium–aluminum chloride at 170°.

(e) **Mixtures of vinyl phenyl ketone with furan, sylvan, and 2,5-dimethylfuran** did not react when allowed to stand at room temperature. When an alcoholic solution, prepared by the usual treatment of β-chloropropiophenone with potassium acetate, was heated with furan in a sealed tube, β-ethoxypropiophenone VI resulted. The latter was isolated, the 2,4-dinitrophenylhydrazone prepared, and both analyzed. The derivative separates from alcohol in orange prisms, m. p. 158°.

Anal. Calcd. for $C_{11}H_{14}O_2$ (VI): C, 74.2; H, 7.9; for the derivative, $C_{17}H_{18}O_5N_4$: N, 15.6. Found: (VI) C, 74.3; H, 7.8; (2,4-dinitrophenylhydrazone): N, 15.5.

(f) **Isolation of Vinyl Phenyl Ketone.**—In all the papers in this series, an alcoholic solution of β-chloropropiophenone containing an equivalent of potassium acetate has been used just as though it were vinyl phenyl ketone. That it actually does contain the unsaturated ketone, and is not β-acetoxypropiophenone, was shown by isolation of the free ketone. It was only necessary to extract the solution with chloroform (ether was avoided, as traces of peroxide caused polymerization to a tough, horn-like mass), wash out alcohol with water, and distil *in vacuo*. The yield of pale yellow oil was 71–78%, the lower quantity being obtained when 100 g. of chloroketone was employed; there was more loss by polymerization during the time of heating.

The distilled ketone keeps fairly well for several days at a low temperature (−9°), but at room temperature soon becomes solid. The effect of *p*-benzylaminophenol, hydroquinone, phenyl-β-naphthylamine, and copper acetate as stabilizers was examined; the last two were useless, but the others seemed to decrease the rate of polymerization. A specimen containing hydroquinone became quite viscous in six weeks but was not further changed after five years. This specimen was a dimeric form.

Calcd. Mol. wt., $(132)_x$. Found, in benzene: mol. wt., 257, 266, 259, whence $x = 2$.

The formation of the unsaturated ketone by the action of potassium acetate on β-chloropropiophenone would not of necessity be anticipated, for sodium cyanide gives β-cyanopropiophenone.[14]

(14) Allen and Young, *J. Org. Chem.*, **2**, 231 (1937).

Summary

1. Vinyl phenyl ketone adds readily to many substances containing a conjugated system of double bonds.

2. Addition products were obtained from this unsaturated ketone and 2,3- and 1,4-diphenylbutadienes, 1-phenyl-4-methylbutadiene, 2,3-dimethylbutadiene, cyclopentadiene, tetraphenylcyclopentadienone, and ethyl sorbate.

3. Secondary reaction products resulted from vinyl phenyl ketone and methyleneanthrone, *trans*-dibenzoylethylene and methyleneanthrone, and from benzalacetophenone and tetraphenylcyclopentadienone.

4. Methyl β-benzoylacrylate and 2,3-diphenylbutadiene also gave an addition product.

5. 3,4-Diphenylbenzophenone and its 6-carboxylic acid were synthesized and shown to be identical with specimens previously secured by degradation of a polynuclear indene derivative.

ROCHESTER, NEW YORK RECEIVED JANUARY 4, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, POLYTECHNIC INSTITUTE OF BROOKLYN]

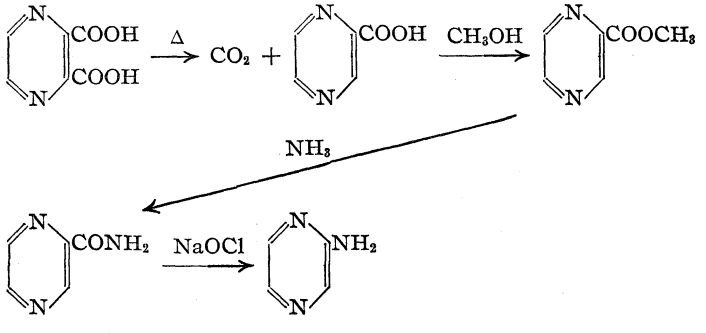
Syntheses in the Pyrazine Series. II. Preparation and Properties of Aminopyrazine

BY STANLEY A. HALL AND PAUL E. SPOERRI

Certain derivatives of diaminopyridine such as pyridium,[1] and its modifications,[2] exhibit valuable bacteriostatic properties.[3] However, little is known about the corresponding amino pyrazines.

Gabriel and Sonn[4] obtained aminopyrazine from pyrazine-2,3-dicarboxylic acid. However, their product was impure; m. p. 110–117°. Moreover, their synthesis is complicated by side reactions.

We have synthesized aminopyrazine by a modification of the method of Gabriel and Sonn



The Hofmann degradation of pyrazine-carboxylamide has not been described in the literature. An interesting intermediate compound was isolated which immediately decomposed with much effervescence in dilute acid (mineral or acetic) to give the desired aminopyrazine. This intermediate compound was identified as sodium pyrazine-carbamate.

(1) U. S. Patents 1,680,108-9-10-11 (1928).
(2) Bowie, *Brit. Med. J.*, **II**, 283–284 (1938).
(3) Ostromislensky, THIS JOURNAL, **56**, 1713–1714 (1934).
(4) Gabriel and Sonn, *Ber.*, **40**, 4851–4860 (1907).

Although Mohr,[5] in his study of the mechanism of the Hofmann reaction, isolated barium phenylcarbamate, this is the first time, as far as can be ascertained, that the Hofmann degradation of an amide has proceeded only to the stage of a stable sodium carbamate which must then be decomposed by acidification in order to obtain the amine. This adds confirmation to Mohr's theory of the mechanism of the Hofmann reaction and it also shows up the characteristic stabilizing effect of the pyrazine ring upon certain functional groups.

Aminopyrazine was obtained in pure white crystalline form, m. p. 117–118°. It is very soluble in water, giving a solution neutral to litmus. Aminopyrazine gives only a very faint isonitrile test, which differs from the observations of Gabriel and Sonn who reported a distinct isonitrile test.

Both aminopyrazine and acetaminopyrazine sublime without decomposition.

Experimental

Pyrazine-carboxylic Acid.—33.9 g. of pyrazine-2,3-dicarboxylic acid (m. p. 190°) was heated rapidly to 210° in a vacuum sublimation chamber. At 3 to 4 mm., simultaneous decarboxylation and sublimation took place. After resubliming *in vacuo* the product was recrystallized from hot water.

Fine white needles of pyrazine-carboxylic acid were obtained: m. p. 225° (decompn.); m. p. 225° (decompn.), Gabriel and Sonn; m. p. 229° (decompn.), Stoehr; yield 17.5 g. or 70.0%.

(5) Mohr, *J. prakt. Chem.*, (2) **73**, 117–191, 229 (1906).

Methyl Pyrazine-carboxylate.—10.5 g. of oven-dried pyrazine-carboxylic acid in 105 g. of absolute methyl alcohol saturated with dry hydrogen chloride was distilled at reduced pressure to remove excess hydrogen chloride. The residue was neutralized with saturated sodium carbonate solution and extracted with ethyl acetate. After evaporation of the ethyl acetate the solid reddish-yellow residue was sublimed at 4 mm. in an oil-bath at 100°. The pure white crystals melted at 59° unchanged after several recrystallizations from ether and other solvents (m. p. 62°; British Patent 451,304); yield 8.4 g. or 72%.

Pyrazine-carboxylamide.—8.4 g. of methylpyrazine-carboxylate in 8.4 g. of warm methyl alcohol was added to a saturated absolute methyl alcohol (17 g., 0°) solution of ammonia. The white crystals were filtered off the next day, washed with methanol, ether and dried: m. p. 189° (lit. m. p. 188°; British Patent 451,304); yield 6.9 g. or 92%.

Aminopyrazine.—After dissolving 4.2 g. of chlorine in 13.8 g. of sodium hydroxide and 150 g. of ice and water, 6.9 g. of finely powdered pyrazine-carboxylamide was added. The solution was warmed, with stirring for one hour.

The next day, the needle-like crystals were filtered off and dried; 3.5 g. of the product dissolved in water gave an alkaline solution which evolved carbon dioxide on acidification. The ethyl acetate extract of the neutralized solution was evaporated, leaving a solid yellowish residue which sublimed completely at 3 mm.; temp. of oil-bath 100°; yield, 1.5 g. of pure aminopyrazine.

The original filtrate was acidified and an alcoholic picric acid solution added. The picrate obtained and washed with alcohol, ether and dried had no definite m. p. but decomposed at 214 to 250°. The suspension of the picrate in cooled ether was saturated with hydrogen chloride. The hydrochloride filtered off and washed with ether was neutralized with saturated sodium carbonate solution and extracted with ethyl acetate. The residue remaining after the evaporation of the ethyl acetate was sublimed at 3 mm.; temp. of oil-bath 100°; yield of aminopyrazine, 0.9 g.; combined yields of aminopyrazine 2.9 g. or 55%: m. p. 117–118° (lit. m. p. 110–117°, Gabriel and Sonn).

Anal. Calculated for $C_4H_5N_3$: C, 50.5; H, 5.30; N, 44.2. Found: C, 50.4, 50.3; H, 5.16, 5.16; N, 44.1, 43.9.

Acetaminopyrazine.—M. p. 133°.

Anal. Calculated for $C_6H_7H_3O$: C, 52.54; H, 5.11; N, 30.66. Found: C, 52.50, 52.73; H, 6.25, 6.15; N, 28.99.

Intermediate Product in the Hofmann Reaction.—The properties of the needle-like crystals obtained were found to be as follows: no definite m. p.; began to turn brown at 257°; black at 275°; very soluble in water to give an alkaline solution; insoluble in organic solvents including absolute alcohol; contains sodium; halogen test negative; effervesces (CO_2 evolved) in dilute acid (mineral or acetic) to form aminopyrazine. The intermediate compound evidently is sodium pyrazine carbamate. *Anal.* Calculated for $C_5H_4N_3O_2Na$: N, 26.1; Na, 14.3. Found: N, 25.9; Na, 14.4.

Summary

1. The Hofmann degradation on pyrazine carboxylamide gave a 55% yield of aminopyrazine, m. p. 117–118°.

2. From the Hofmann reaction an intermediate compound was isolated and identified as sodium pyrazine-carbamate, which on acidification gave aminopyrazine and carbon dioxide.

BROOKLYN, N. Y. RECEIVED OCTOBER 25, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

The Conversion of Arylbismuth Halides to Triarylbismuth Compounds

BY HENRY GILMAN AND H. L. YABLUNKY

We have observed that one of the intermediate types formed in the recently described synthesis of triarylbismuth compounds by the diazonium reaction[1] is R_2BiX. This suggested an examination of procedures for the conversion of such compounds to the R_3Bi compounds. The best reagent, we now find, for this purpose is hydrazine hydrate. This reagent was first used to convert 2-furylmercuric chloride and phenylmercuric chloride to 2,2′-difurylmercury and diphenylmercury, respectively[2]; and it was shown subsequently that hydrazine is a reagent of choice for converting RHgX to R_2Hg compounds.[3]

If the equilibrium

$$3R_2BiX \rightleftharpoons 2R_3Bi + BiX_3$$

is valid, then one of the functions of the hydrazine may be to reduce the bismuth halide. The procedure was next extended successfully to the conversion of phenylbismuth dibromide to triphenylbismuth, and to the conversion of R_3BiX_2 compounds to the corresponding triarylbismuth compounds. Attention might be directed to two

(1) Gilman and Svigoon, THIS JOURNAL, **61**, 3586 (1939).

(2) Gilman and Wright, *ibid.*, **55**, 3302 (1933).

(3) Gilman and Barnett, *Rec. trav. chim.*, **55**, 563 (1936).

interesting cases of the conversion of triarylbismuth dihalides to the triarylbismuths. First, the very stable triphenylbismuth difluoride is converted rapidly and practically quantitatively to triphenylbismuth. Challenger and co-workers[4] have shown that triphenylbismuth difluoride is the most stable of a series of compounds like $(C_6H_5)_3BiX_2$ where X is halogen or a pseudo-halogen. Second, the almost quantitative yield of diphenyl-α-naphthylbismuth from diphenyl-α-naphthylbismuth dichloride is additional evidence[4a] for the stability of this unsymmetrical organobismuth compound.

The smooth and rapid reactions leading to excellent yields of R_3Bi compounds, suggest that the procedure might also be applicable to variously substituted organobismuth halides, as well as to analogous arsenicals and antimonials. By analogy with the related reaction with mercurials[3] it is altogether probable that reducing agents related to hydrazine also may be used effectively.

Other reagents have been used for the conversion of organobismuth halides to R_3Bi compounds: hydrogen sulfide,[5] ammonium sulfide,[6] moist silver oxide,[7a,b] alcoholic ammonia,[8] sodium hydrosulfite, formaldehyde, sodium and alcohol, and dimethyl sulfate and alkali.[9] Of these, the most successful one was sodium hydrosulfite which gave about 80% yields of triphenylbismuth and tri-*p*-tolylbismuth from the corresponding R_3BiCl_2 compounds. Unfortunately, secondary reactions took place with nitro-nuclear types.

Experimental Part

Two typical experimental procedures follow.

Conversion of Diphenylbismuth Chloride to Triphenylbismuth.—To a solution of 2.0 g. (0.04 mole) of hydrazine hydrate in 60 cc. of absolute alcohol contained in a 200-cc. three-necked flask equipped with mechanical stirring, was added 4.0 g. (0.01 mole) of diphenylbismuth chloride. Reaction occurred immediately. Stirring at room temperature was continued for an hour, after which the reaction mixture was heated to boiling and filtered. The insoluble material was once again extracted with hot alcohol. The alcoholic filtrate was then poured into 400 cc. of water and the precipitated triphenylbismuth extracted with ether. The ether extracts were dried over anhydrous sodium sulfate, and the ether distilled. The yield of triphenylbismuth was 2.75 g. (93.5%), m. p. 75–76°; mixed m. p. with an authentic sample, 75–76°.

Conversion of Triphenylbismuth Dichloride to Triphenylbismuth.—To a stirred suspension of 2.56 g. (0.005 mole) of triphenylbismuth dichloride in 60 cc. of 95% ethanol was added 2.0 g. of hydrazine hydrate. Reaction occurred immediately and the solution became yellow in color. After about a half-minute, the solution was decolorized and the triphenylbismuth precipitated out of solution. Stirring was continued for an hour, after which the mixture was poured into 300 cc. of water. The aqueous suspension was extracted with ether, the ether layer separated and dried, and the ether distilled. The yield was 2.1 g. (95.4%), m. p. 75–76°; mixed m. p. with triphenylbismuth, 75–76°.

The results are summarized in Table I. The method of mixed melting points was used to complete identity of each of the products.

TABLE I

CONVERSION OF $RBiX_2$, R_2BiX, AND R_3BiX_2 COMPOUNDS TO R_3Bi

Organobismuth halide	Product	Yield, %
$(C_6H_5)_2BiCl$	$(C_6H_5)_3Bi$	93.5
$C_6H_5BiBr_2$[a]	$(C_6H_5)_3Bi$	81.5
$(o\text{-}CH_3C_6H_4)_3BiCl_2$	$(o\text{-}CH_3C_6H_4)_3Bi$	99.0
$(o\text{-}CH_3C_6H_4)_3BiBr_2$	$(o\text{-}CH_3C_6H_4)_3Bi$	100
$(C_6H_5)_3BiCl_2$	$(C_6H_5)_3Bi$	95.4
$(C_6H_5)_3BiBr_2$	$(C_6H_5)_3Bi$	100
$(p\text{-}CH_3C_6H_4)_3BiCl_2$	$(p\text{-}CH_3C_6H_4)_3Bi$	100
$(p\text{-}ClC_6H_4)_3BiCl_2$[b]	$(p\text{-}ClC_6H_4)_3Bi$	78.0
$(C_6H_5)_3BiF_2$	$(C_6H_5)_3Bi$	97.8
$(C_6H_5)_2(C_{10}H_7(\alpha))BiCl_2$	$(C_6H_5)_2(C_{10}H_7(\alpha))Bi$	96.2

[a] In this experiment, dry ether was used as a solvent. [b] This was the only reaction where decomposition was apparent. The reaction mixture was red in color, and the red tint persisted in the final product.

Summary

Hydrazine effects a smooth and rapid conversion of arylbismuth halides of the general types $RBiX_2$, R_2BiX and R_3BiX_2 to R_3Bi compounds in excellent yields.

AMES, IOWA RECEIVED JANUARY 15, 1940

(4) (a) Challenger and Wilkinson, *J. Chem. Soc.*, **121**, 91 (1922); (b) Challenger and Richards, *ibid.*, 405 (1934).

(5) Michaelis and Polis, *Ber.*, **20**, 54 (1887).

(6) Michaelis and Marquardt, *Ann.*, **251**, 323 (1889).

(7) (a) Gillmeister, *Ber.*, **30**, 2843 (1897); (b) Challenger and Goddard, *J. Chem. Soc.*, **117**, 762 (1920).

(8) Challenger and Ridgway, *J. Chem. Soc.*, **121**, 104 (1922).

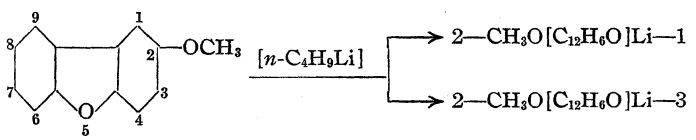
(9) Supniewski and Adams, THIS JOURNAL, **48**, 507 (1926).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Dibenzofuran. XVIII. Isomeric Metalation Products of Some Phenols and their Methyl Ethers[1]

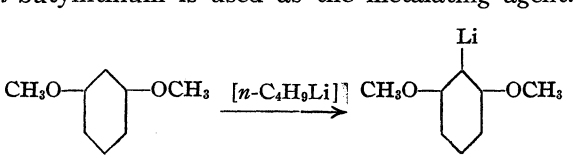
BY HENRY GILMAN, H. B. WILLIS, T. H. COOK, F. J. WEBB AND R. N. MEALS

Metalation in an ortho position is a general reaction not only of ethers but also of the corresponding phenols.[2] However, where isomeric metalation products are possible, the phenols of dibenzofuran appear to form a lesser number of isomers than do the corresponding methyl ethers. For example, metalation of 2-methoxydibenzofuran[3] takes place in the 1- and the 3-positions, whereas metalation of 2-hydroxydibenzofuran apparently involves the 1-position exclusively, for

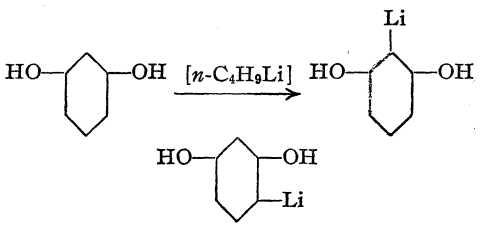


the only acid isolated subsequent to carbonation is 2 - hydroxy - 1 - dibenzofurancarboxylic acid. Similarly, metalation of 4-methoxydibenzofuran, followed by carbonation, gives both 4-methoxy-6-dibenzofurancarboxylic acid and 4-methoxy-3-dibenzofurancarboxylic acid; and metalation of 4-hydroxydibenzofuran gives, subsequent to carbonation, only 4-hydroxy-6-dibenzofurancarboxylic acid.

This more highly selective metalation of phenols is of particular interest in problems of orientation concerned with the dibenzofuran nucleus. However, because metalations of phenols and their ethers are of increasing diagnostic significance in establishing structures of compounds having nuclei other than dibenzofuran, it seemed of interest to examine some simple benzene types. Metalation of resorcinol dimethyl ether by phenyllithium gives 2,6-dimethoxyphenyllithium.[4] We have found that the same product is formed when *n*-butyllithium is used as the metalating agent.



However, metalation of resorcinol by *n*-butyllithium gives the two isomers: 2,6-dihydroxyphenyllithium and 2,4-dihydroxyphenyllithium.[5]



Accordingly there is a complete reversal here, the phenol giving more isomers than the ether. Inasmuch as the ratio of isomers that may result from particular phenols and their ethers might vary markedly, it becomes necessary to establish in each case the structure of the metalation product and not to carry over analogies from phenols to ethers or from ethers to phenols.

Carbonation of Organolithium Compounds.—In the first experiments[4] on the carbonation of 2,6-dimethoxyphenyllithium gaseous carbon dioxide was used, and there was obtained a 14% yield of 2,6-dimethoxybenzoic acid, accompanied by a 25% yield of 2,2′,6,6′-tetramethoxybenzophenone. However, we used solid carbon dioxide which gave a 55% yield of the acid and only traces of the ketone. Gaseous carbon dioxide also can be used under special conditions[6] to give improved yields of carboxylic acids from organolithium compounds, but solid carbon dioxide is more convenient, more rapid and more effective.[6]

Structure Determinations.—For convenience, the products of metalation were carbonated. The resulting acids obtained from resorcinol and its dimethyl ether were compared with previously described compounds. The structures of the dibenzofuran compounds were established by the following sequence of reactions.

The halogen–metal interconversion indicated by the transformation of [A] to [B] was reported

(1) Paper XVII, THIS JOURNAL, **62**, 348 (1940).

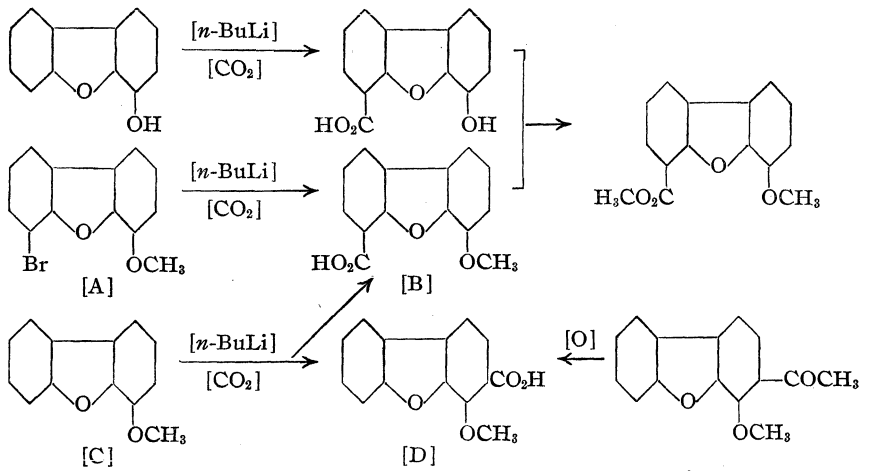
(2) Gilman, "Metalation and Related Interconversion Reactions," Eighth National Organic Chemistry Symposium, St. Louis, Dec. 30, 1939.

(3) Gilman and Bebb, THIS JOURNAL, **61**, 109 (1939).

(4) Wittig and Pockels, *Ber.*, **72**, 89 (1939).

(5) Actually, of course, the active hydrogens of the phenolic groups react first, and the true products are the —OLi salts of the organolithium compounds.

(6) Gilman and Van Ess, THIS JOURNAL, **55**, 1258 (1933).



recently[7a] starting with authentic 4-methoxy-6-bromodibenzofuran [A]. Such halogen–metal interconversions appear to be not only general, but also reliable when an equivalent or more of *n*-butyllithium is used.[7b] Additional supporting evidence for the formation of [B] and [D] from [C] is to be had in the preparation of 4-methoxy-6-hydroxydibenzofuran and 4-methoxy-3-hydroxydibenzofuran by oxidation of the metalation products of 4-methoxydibenzofuran.[7c]

Correlation with Bromination.—It is interesting to note that bromination of 2-hydroxydibenzofuran and of 2-methoxydibenzofuran parallels metalation of these compounds: 2-hydroxydibenzofuran yields 1-bromo-2-hydroxydibenzofuran, whereas 2-methoxydibenzofuran yields the isomeric 1- and 3-bromo-2-methoxydibenzofurans.[7d]

Experimental Part

Metalation of 2-Hydroxydibenzofuran.—A solution of approximately 0.034 mole of *n*-butyllithium in 75 cc. of ether was added slowly with constant stirring to 3.1 g. (0.0168 mole) of 2-hydroxydibenzofuran dissolved in 75 cc. of benzene. The reaction mixture was stirred and heated for four hours and then carbonated by pouring it upon crushed solid carbon dioxide. Following carbonation, the solvent was removed by distillation and the residue was extracted with hot, dilute alkali; then carbon dioxide was passed into the alkaline solution to precipitate the phenol. The bicarbonate solution was extracted three times with 100-cc. portions of ether to remove last traces of the phenol. The acid was precipitated by the addition of hydrochloric acid. The yield of 2-hydroxy-1-dibenzofurancarboxylic acid was 0.830 g. (21.5%); m. p. 209–214° (dec.).

Three-tenths gram of the acid was methylated with alkali and dimethyl sulfate, followed by treatment with diazomethane, to yield the known methyl 2-methoxy-1-dibenzofurancarboxylate, which melted at 98–99° after crystallization from methyl alcohol. A mixed m. p. with an authentic specimen[7d] showed no depression.

Metalation of 4-Hydroxydibenzofuran.—A solution of 0.031 mole of *n*-butyllithium in 35 cc. of ether was added slowly to a solution of 1.84 g. (0.01 mole) of 4-hydroxydibenzofuran dissolved in 35 cc. of dry benzene. During the addition there was a vigorous evolution of gas and a heavy white precipitate formed. The resulting mixture was refluxed with stirring for four hours, after which it was carbonated by pouring it upon crushed solid carbon dioxide. The carbonation mixture was extracted with dilute sodium hydroxide and then carbon dioxide was bubbled through the alkaline solution to precipitate the unchanged phenol, of which 1.22 g. (65%) was recovered. The bicarbonate solution after filtration was acidified to yield a precipitate which was recrystallized from a benzene–acetone solution (4:1). The resulting crystals of 4-hydroxy-6-dibenzofurancarboxylic acid (0.1 g. or 4.4% yield) melted at 251–253° (dec.).

Forty milligrams of the hydroxy acid was treated with diazomethane and the resulting product was recrystallized from alcohol to yield a compound melting at 122.5–124°. This same methyl 4-methoxy-6-dibenzofurancarboxylate (mixed m. p.) was prepared from authentic 6-bromo-4-methoxydibenzofuran by halogen–metal interconversion, followed by methylation.[7a]

Metalation of 4-Methoxydibenzofuran.—A solution of 0.06 mole of *n*-butyllithium in 40 cc. of ether was added to a solution of 10 g. (0.05 mole) of 4-methoxydibenzofuran dissolved in 40 cc. of dry ether and the resulting mixture was refluxed with stirring for four hours, after which it was carbonated in the usual manner. The ether was removed by distillation and the solid residue was extracted with hot dilute sodium hydroxide. Acidification of the hot alkaline solution yielded 3 g. of crude acidic product.

This crude product was dissolved in hot 10% potassium hydroxide solution, filtered, and cooled. The white silky needles were filtered off and the filtrate was acidified with dilute hydrochloric acid. The precipitate was recrystallized several times from glacial acetic acid to yield 0.65 g. (5.3%) of 4-methoxy-3-dibenzofurancarboxylic acid melting at 182–183°. The same 4-methoxy-3-dibenzofurancarboxylic acid (mixed m. p.) was prepared by permanganate oxidation of authentic 3-acetyl-4-methoxydibenzofuran.

Anal. Calcd. for $C_{14}H_{10}O_4$: neut. equiv., 242. Found: neut. equiv., 238, 240.

The white needles obtained from the alkaline solution were dissolved in hot water and the acid was precipitated by addition of hydrochloric acid. Recrystallization from

(7) (a) Gilman, Swislowsky and Brown, THIS JOURNAL, **62**, 348 (1940); (b) Gilman, Langham and Willis, *ibid.*, **62**, 346 (1940); (c) Gilman, Cheney and Willis, *ibid.*, **61**, 951 (1939); (d) Gilman and Van Ess, *ibid.*, **61**, 1365 (1939).

glacial acetic acid gave 1.12 g. or a 9.2% yield of 4-methoxy-6-dibenzofurancarboxylic acid melting at 240–242°.

Anal. Calcd. for $C_{14}H_{10}O_4$: neut. equiv., 242. Found: neut. equiv., 237.

The methyl 4-methoxy-6-dibenzofurancarboxylate prepared by means of diazomethane from the methoxy acid melting at 240–242° was proved identical with both the methoxy ester of the single acid obtained from metalation of 4-hydroxydibenzofuran and an authentic sample of methyl 4-methoxy-6-dibenzofurancarboxylate.

Anal. Calcd. for $C_{15}H_{12}O_4$: methoxyl, 24.20. Found: methoxyl, 24.25.

Metalation of Resorcinol.—To an ice-cold solution of approximately 0.3 mole *n*-butyllithium in 400 cc. of ether was added dropwise with stirring 11.0 g. (0.1 mole) of resorcinol in 75 cc. of ether. Gas was evolved but no precipitate formed during the ensuing twenty-one hour period of refluxing. Carbonation, in the usual manner, was followed by acidification with iced dilute hydrochloric acid and extraction with ether. The crude acid obtained from the ether layer[8] was recrystallized from water to give 3.3 g., m. p. 145–147°, and 0.8 g., m. p. 192–195°. An additional 0.7 g., m. p. 150°, was obtained from the filtrate; combined yield, 31.1%.

The 3.3-g. portion, melting at 150–152° after recrystallization from water, was treated with dimethyl sulfate and sodium hydroxide to form 2,6-dimethoxybenzoic acid,[9] m. p. 183–184°, identified by a mixed melting point determination with a reference sample.

The 0.8-g. portion, m. p. 206–207° after recrystallization from water, was converted with diazomethane to methyl 2-hydroxy-4-methoxybenzoate[10] melting at 49° alone or mixed with an authentic specimen. Hydrolysis of the ester with alcoholic potassium hydroxide gave 2-hydroxy-4-methoxybenzoic acid, m. p. 153–154°. The mixed melting point with a known sample showed no depression.

The third portion was not identified but was probably a mixture of the two acids contaminated with resorcinol.

Metalation of Resorcinol Dimethyl Ether.—A mixture of 0.1 mole of resorcinol dimethyl ether and 0.1 mole of *n*-butyllithium in ether was refluxed for twenty hours. Carbonation, by pouring the mixture jet-wise upon solid carbon dioxide, gave 10 g. (55% yield) of 2,6-dimethoxybenzoic acid melting at 186°. The methyl 2,6-dimethoxybenzoate, prepared by refluxing the silver salt of the dimethoxy acid with methyl iodide, melted at 87°.[9]

A small quantity (0.043 g.) of 2,2′,6,6′-tetramethoxybenzophenone,[4] melting at 204°, was also isolated.

(8) Nierenstein and Clibbens, *Org. Syntheses*, **10**, 95 (1930).
(9) Mauthner, *J. prakt. Chem.*, [2] **121**, 259 (1929).
(10) Herzig, Henzel and Batscha, *Monatsh.*, **24**, 888 (1903).

Summary

Metalation by *n*-butyllithium of 2-methoxydibenzofuran gives 2-methoxy-1-dibenzofuryllithium and 2-methoxy-3-dibenzofuryllithium; and metalation of 4-methoxydibenzofuran gives 4-methoxy-6-dibenzofuryllithium and 4-methoxy-3-dibenzofuryllithium. However, metalation of the corresponding phenols gives but one product in each case: 2-hydroxydibenzofuran yielding 2-hydroxy-1-dibenzofuryllithium (as a lithium salt of the phenol); and 4-hydroxydibenzofuran yielding 4-hydroxy-6-dibenzofuryllithium.

In contrast, metalation of resorcinol dimethyl ether gives apparently but one product (2,6-dimethoxyphenyllithium), whereas resorcinol gives the two isomers, 2,6-dihydroxyphenyllithium and 2,4-dihydroxyphenyllithium.

AMES, IOWA RECEIVED JANUARY 15, 1940

Tenth Report of the Committee on Atomic Weights of the International Union of Chemistry

BY G. P. BAXTER (*Chairman*), M. GUICHARD, O. HÖNIGSCHMID AND R. WHYTLAW-GRAY

The following report of the Committee covers the twelve-month period September 30, 1938 to September 30, 1939.[1] Three changes in the table of atomic weights have been adopted:

Hydrogen, from 1.0081 to 1.0080, iron, from 55.84 to 55.85, lutecium, from 175.0 to 174.99.

Hydrogen.—Several investigations of the H^1/H^2 ratio in certain natural waters during the last four years have given values higher than that used in computing the atomic weight of hydrogen for the Table, 5000 (see Eighth Report of this Committee).

Johnston, THIS JOURNAL, **57**, 484 (1935)	5900
Tronstad, Nordhagen and Brun, *Nature*, **136**, 515 (1935)	5840
Hall and Jones, THIS JOURNAL, **58**, 1915 (1936)	6550
Gabbard and Dole, *ibid.*, **59**, 181 (1937)	7020
Morita and Titani, *Bull. Chem. Soc. Japan*, **13**, 419 (1938)	6320
Tronstad and Brun, *Trans. Faraday Soc.*, **34**, 766 (1938)	5400
Voskuyl, Thesis, Harvard University (1938)	6700
Swartout and Dole, THIS JOURNAL, **61**, 2025 (1939)	6970
	6880

Since with $H^1 = 1.00785$ (chemical scale) and even with $H^1/H^2 = 6000$ the atomic weight of

(1) Authors of papers bearing on the subject are requested to send copies to each of the four members of the Committee at the earliest possible moment: Prof. G. P. Baxter, Coolidge Laboratory, Harvard University, Cambridge, Mass., U. S. A.; Prof. M. Guichard, Faculté des Sciences, Sorbonne, Paris, France; Prof. O. Hönigschmid, Sofienstrasse 9/2, Munich, Germany; Prof. R. Whytlaw-Gray, University of Leeds, Leeds, England.

hydrogen in natural waters becomes 1.0080 this value is adopted for the Table, although the nature of the hydrogen in any compound is bound to be subject to a slight uncertainty.

Chlorine.—Hönigschmid and Hirschbold-Wittner[2] have determined the atomic weight of chlorine in hydrogen chloride samples subjected to isotopic separation by the thermal diffusion method by Clausius and Dickel. Weighed amounts of silver were precipitated with excess acid and the silver chloride was collected and weighed. Vacuum weights are given.

Ag, g.	AgCl, g.	AgCl:Ag	At. wt., Cl
	Heavy fractions		
0.59164	0.78666	1.32963	35.560
.48005	.64450	1.34257	36.956
	Light fractions		
.73019	.96925	1.32739	35.310
.61237	.81188	1.32580	35.147
.58001	.76830	1.32463	35.021
.57969	.76765	1.32428	34.979

If the isotopic weights of the two chief isotopes of chlorine are 36.968 and 34.971 on the chemical scale the separation seems to have been nearly complete.

Iron.—Hönigschmid and Liang[3] have compared ferrous bromide with silver and silver bromide. A solution of Mohr's salt was freed from heavy metals with hydrogen sulfide. After oxidation ferric hydroxide was three times precipitated from acid solution, and the third precipitate was dissolved in sulfuric acid and electrolytically reduced to ferrous sulfate which was recovered by crystallization. Electrolytic precipitation of metallic iron from ammonium oxalate solution followed, and the metallic deposit was dissolved in nitric acid. Carbon was removed by filtration and the ferric nitrate solution evaporated to crystallization. Thermal decomposition to oxide and reduction in hydrogen yielded Sample I. Spectroscopic examination by Gerlach revealed no impurities. The remainder of the ferric nitrate was twice more recrystallized from nitric acid and converted to metal (Sample II).

Synthesis of the bromide was effected by heating the pure metal in a current of dry nitrogen and bromine. The sublimed product was resublimed in pure nitrogen and fused in nitrogen in a quartz weighing tube which could be bottled in dry air. After being weighed the salt was dissolved in very dilute sulfuric acid. The solution was clear and free from ferric salt. After careful oxidation with slightly less than the theoretical quantity of bichromate the solution was compared with silver in the conventional way with the help of a nephelometer. In many of the experiments the silver bromide was collected and weighed. Vacuum weights are given.

The average of all the experiments, 55.850, is slightly higher than that found by analysis of ferrous bromide by Baxter, Thorvaldson and Cobb,[4] 55.838, presumably because the material employed by the latter contained traces of carbon, silica and possibly ferric salt. By reduction of ferric oxide Baxter and Hoover[5] found 55.847, while Hönigschmid, Birckenbach and Zeiss[6] by analysis of ferric chloride obtained the value 55.853.

Recent determinations of abundance ratios with the mass spectrograph, when converted to the chemical scale with the packing fraction -7×10^{-4} (Dempster, *Phys. Rev.*, **53**, 869

THE ATOMIC WEIGHT OF IRON

Sample	$FeBr_2$, g.	Ag, g.	$FeBr_2$:2Ag	At. wt. Fe	AgBr, g.	$FeBr_2$:2AgBr	At. wt. Fe
I	1.85170	1.85236	0.999644	55.851			
I	3.30576	3.30690	.999655	55.854			
II	2.07499	2.07574	.999639	55.850			
II	3.28783	3.28900	.999644	55.851	5.72554	0.574239	55.848
I	2.92032	2.92137	.999641	55.850	5.08551	.574243	55.849
I	3.30851	3.30966	.999653	55.853	5.76158	.574237	55.847
I	2.32787	2.32870	.999644	55.851	4.05371	.574257	55.854
I	2.83665	2.83765	.999648	55.852	4.93977	.574247	55.851
II	2.80087	2.80188	.999640	55.850	4.87744	.574250	55.852
II	2.61260	2.61354	.999640	55.850	4.54968	.574238	55.847
II	2.85977	2.86078	.999647	55.852	4.98006	.574244	55.849
	Average		.999645	55.851		.574244	55.850

(2) Hönigschmid and Hirschbold-Wittner, *Z. anorg. allgem. Chem.*, **242**, 222 (1939).

(3) Hönigschmid and Liang, *Z. anorg. allgem. Chem.*, **241**, 361 (1939).

(4) Baxter, Thorvaldson and Cobb, THIS JOURNAL, **33**, 319 (1911).

(5) Baxter and Hoover, *ibid.*, **34**, 1657 (1912).

(6) Hönigschmid, Birckenbach and Zeiss, *Ber.*, **56**, 1473 (1923).

(1938)), and the conversion factor 1.000275 give the following values.

	Isotope 54	56	57	58	Mean mass number	At. wt.
de Gier and Zeeman[a]	6.5	90.2	2.8	0.5	55.908	55.853
Nier[b]	6.04	91.57	2.11	0.28	55.906	55.851

[a] *Proc. Roy. Soc. Amsterdam*, **38**, 959 (1935). [b] *Phys. Rev.*, **55**, 1143 (1939).

In view of the evidence the value 55.85 for iron seems more probable than the older one 55.84, and has been adopted for the Table, although the value 55.847 obtained by the most direct method, the reduction of the oxide, might well be looked upon as a maximum owing to the possibility of incomplete reduction.

Molybdenum.—Mattauch and Lichtblau[7] have redetermined the relative abundances of the molybdenum isotopes. In the following table their percentages are compared with those found earlier by Aston. The atomic weight is calculated with the packing fraction -6.0×10^{-4} (Dempster) and the conversion factor 1.000275.

	92	94	95	96	97
Aston	14.2	10.0	15.5	17.8	9.6
Mattauch and Lichtblau	15.5	8.7	16.3	16.8	8.7

	98	100	Mean mass number	At. wt. Mo
Aston	23.0	9.8	95.94[a]	95.86
Mattauch and Lichtblau	25.4	8.6	95.98	95.90

[a] Incorrectly calculated by Aston to be 96.03, *Proc. Roy. Soc.* (London), **A130**, 309 (1931).

Both these values are considerably lower than that obtained by Hönigschmid and Wittner by analysis of molybdenum pentachloride, 95.949, which was adopted for the Table two years ago. (See Eighth Report of this Committee.)

Europium.—Lichtblau[8] has determined the abundance ratio of the europium isotopes, Eu^{151}/Eu^{153}, to be 0.963 ± 0.012. With the packing fraction -2×10^{-4} (Dempster) and the conversion factor 1.000275 the atomic weight of europium is 151.95 ± 0.01. This value for europium agrees far better with that recently found by Baxter and Tuemmler by analysis of europous chloride, 151.96, than with Kapfenberger's recent value, 151.90 (see Ninth Report of this Committee).

Lutecium.—Hönigschmid and Wittner[9] have published details of their analyses of lutecium trichloride, already reported[10]; (see Eighth Report of this Committee). The starting material had been purified by von Welsbach and was identical with that used by him in his determination of the atomic weight. From examination of the X-ray spectrum Noddack estimates a content of 1.18% of ytterbium but no more than 0.04% of any other rare earth. Purification consisted in double precipitation of the hydroxide with solution in hydrochloric acid, double precipitation of the oxalate with subsequent ignition in each case, and double crystallization of the chloride from concentrated hydrochloric acid. The chloride was dehydrated in a stream of dry hydrogen chloride at gradually increasing temperatures finally at 450° and after being weighed was compared with silver in the conventional way. The silver chloride was determined in some cases. Vacuum weights are given.

The authors prefer the result of the former method of analysis, 174.966. Corrected for the ytterbium content this becomes 174.986.

Mattauch and Lichtblau,[11] with the mass spectrograph, find a new isotope of lutecium of mass number 176, to the extent of 2.52%. With the packing fraction $+1 \times 10^{-4}$ (Dempster) and the conversion factor 1.000275 the atomic weight of lutecium is 174.994, in close agreement with that found by Hönigschmid and Wittner.

The value 174.99 is adopted for the Table in place of the older value 175.0 which depends on von Welsbach's analysis of the sulfate.

Lead.—Nier[12] has determined the abundance ratios of the lead isotopes in twenty-one speci-

THE ATOMIC WEIGHT OF LUTECIUM

$LuCl_3$, g.	Ag, g.	$LuCl_3$:3Ag	At. wt. Lu	AgCl, g.	$LuCl_3$:3AgCl	At. wt. Lu
2.10076	2.41662	0.86930	174.968	3.21098	0.65424	174.961
2.94416	3.38688	.86928	174.964	4.50009	.65424	174.962
2.20514	2.53662	.86932	174.977			
2.63280	3.02874	.86927	174.960	4.02420	.65424	174.960
2.70083	3.10697	.86928	174.963			
	Average	.86929	174.966		.65424	174.961

(7) Mattauch and Lichtblau, *Z. physik. Chem.*, **B42**, 288 (1939).
(8) Lichtblau, *Naturwiss.*, **27**, 260 (1939).
(9) Hönigschmid and Wittner, *Z. anorg. allgem. Chem.*, **240**, 284 (1939).
(10) Hönigschmid and Wittner, *Naturwiss.*, **25**, 748 (1937).
(11) Mattauch and Lichtblau, *Z. Physik*, **111**, 514 (1939).
(12) Nier, *Phys. Rev.*, **55**, 153 (1939).

mens of radiogenic lead, and has computed the atomic weights of these specimens using the packing fraction $+1.55 \times 10^{-4}$ and the conversion factor 1.000275. While in most cases the agreement between the atomic weights found in this way and those which had been determined chemically is fair, in some cases considerable discrepancies appear. If Dempster's packing fraction for lead, $+2.3 \times 10^{-4}$, is used the agreement is far less satisfactory. The latter is also true for the results obtained by Nier with common lead (see Ninth Report of this Committee).

INTERNATIONAL ATOMIC WEIGHTS
1940

	Symbol	Atomic Number	Atomic Weight		Symbol	Atomic Number	Atomic Weight
Aluminum	Al	13	26.97	Molybdenum	Mo	42	95.95
Antimony	Sb	51	121.76	Neodymium	Nd	60	144.27
Argon	A	18	39.944	Neon	Ne	10	20.183
Arsenic	As	33	74.91	Nickel	Ni	28	58.69
Barium	Ba	56	137.36	Nitrogen	N	7	14.008
Beryllium	Be	4	9.02	Osmium	Os	76	190.2
Bismuth	Bi	83	209.00	Oxygen	O	8	16.0000
Boron	B	5	10.82	Palladium	Pd	46	106.7
Bromine	Br	35	79.916	Phosphorus	P	15	30.98
Cadmium	Cd	48	112.41	Platinum	Pt	78	195.23
Calcium	Ca	20	40.08	Potassium	K	19	39.096
Carbon	C	6	12.010	Praseodymium	Pr	59	140.92
Cerium	Ce	58	140.13	Protactinium	Pa	91	231
Cesium	Cs	55	132.91	Radium	Ra	88	226.05
Chlorine	Cl	17	35.457	Radon	Rn	86	222
Chromium	Cr	24	52.01	Rhenium	Re	75	186.31
Cobalt	Co	27	58.94	Rhodium	Rh	45	102.91
Columbium	Cb	41	92.91	Rubidium	Rb	37	85.48
Copper	Cu	29	63.57	Ruthenium	Ru	44	101.7
Dysprosium	Dy	66	162.46	Samarium	Sm	62	150.43
Erbium	Er	68	167.2	Scandium	Sc	21	45.10
Europium	Eu	63	152.0	Selenium	Se	34	78.96
Fluorine	F	9	19.00	Silicon	Si	14	28.06
Gadolinium	Gd	64	156.9	Silver	Ag	47	107.880
Gallium	Ga	31	69.72	Sodium	Na	11	22.997
Germanium	Ge	32	72.60	Strontium	Sr	38	87.63
Gold	Au	79	197.2	Sulfur	S	16	32.06
Hafnium	Hf	72	178.6	Tantalum	Ta	73	180.88
Helium	He	2	4.003	Tellurium	Te	52	127.61
Holmium	Ho	67	163.5	Terbium	Tb	65	159.2
Hydrogen	H	1	1.0080	Thallium	Tl	81	204.39
Indium	In	49	114.76	Thorium	Th	90	232.12
Iodine	I	53	126.92	Thulium	Tm	69	169.4
Iridium	Ir	77	193.1	Tin	Sn	50	118.70
Iron	Fe	26	55.85	Titanium	Ti	22	47.90
Krypton	Kr	36	83.7	Tungsten	W	74	183.92
Lanthanum	La	57	138.92	Uranium	U	92	238.07
Lead	Pb	82	207.21	Vanadium	V	23	50.95
Lithium	Li	3	6.940	Xenon	Xe	54	131.3
Lutecium	Lu	71	174.99	Ytterbium	Yb	70	173.04
Magnesium	Mg	12	24.32	Yttrium	Y	39	88.92
Manganese	Mn	25	54.93	Zinc	Zn	30	65.38
Mercury	Hg	80	200.61	Zirconium	Zr	40	91.22

NOTES

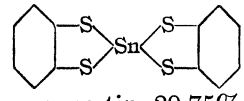
A Tin Derivative of Dithiocatechol

By Harold P. Brown and James A. Austin

In the preparation of dithiocatechol from *o*-benzenedisulfonyl chloride by reduction with tin and hydrochloric acid, Guha and Chackladar[1] obtained a red solid, which they supposed to be the lactone of benzene-1-thiol-2-sulfonic acid. Hurtley and Smiles[2] prepared dithiocatechol from the *o*-benzenedisulfonyl chloride by reduction with zinc dust and acid in the presence of alcohol and avoided the formation of the red solid. Repetition of the procedures described by both of these groups of workers verified the results which they had obtained. However, we cannot agree with the supposition of Guha and Chackladar with regard to the structure of the red solid which they obtained, but have found that it is a tin mercaptide.

The mercaptide can be obtained from the reaction of stannic chloride with dithiocatechol. Also, the same product is obtained when stannous chloride solutions in contact with air react with dithiocatechol. The completeness of the reaction suggests the possible application of dithiocatechol to qualitative and perhaps quantitative determination of tin and certain other elements. Among the other metallic ions which have been found to react with the dithiocatechol are antimony, zinc, ferric ion, lead and thallium. The analytical possibilities of the reagent are being investigated.

When *o*-benzenedisulfonyl chloride is added gradually to a boiling mixture of tin and excess concentrated hydrochloric acid, a red solid soon appears. If the reaction mixture be distilled during the process of reduction, the formation of this red solid is minimized and oily droplets of dithiocatechol distil from the reaction mixture. However, sufficient tin chloride often carries over with the distillate to cause the formation of red solid particles. The use of a large excess of concentrated hydrochloric acid in the reducing media promotes the decomposition of the red solid. Redistillation of distillate containing the red solid from concentrated hydrochloric acid yields pure dithiocatechol. The red mercaptide is insoluble in dilute mineral acid but soluble in alkali. When placed in concentrated hydrochloric acid, the color of the compound disappears and dithiocatechol separates. Addition of water or of alkali to the acid restores the color and precipitates the tin mercaptide. The solubility of the compound in alkali is similar to the solubility of stannic sulfide in alkali. The compound gradually darkens but does not melt below 250°. No traces of divalent tin could be detected in the compound. When stannous chloride reacts with dithiocatechol a yellow solid forms which may be a stannous mercaptide, but this is completely converted to the red stannic mercaptide by contact with air. A sample of the red complex obtained by the reduction of *o*-benzenedisulfonyl chloride with tin in concentrated hydrochloric acid was purified by dissolving in 4 *N* sodium hydroxide, filtering, reprecipitating with hydrochloric acid and drying at 110°. Analysis was accomplished by means of sodium peroxide fusion in a Parr bomb, the tin being precipitated from the alkali fusion mixture as stannic acid by means of nitric acid. The sulfur was precipitated from the filtrate as barium sulfate after elimination of the nitric acid. Analysis showed 29.44% tin and 31.88% sulfur. These values are in accord with the proposed structure



for which the calculated values are tin, 29.75% and sulfur, 32.14%.

University of Kansas City
Jensen-Salsbery Laboratories
Kansas City, Mo. Received December 4, 1939

(1) P. C. Guha and M. N. Chackladar, *Quart. J. Indian Chem. Soc.*, **2**, 318–335 (1925).

(2) Wm. R. H. Hurtley and S. Smiles, *J. Chem. Soc.*, 1821–1828 (1926).

Auto-Metalation with *m*-Tolylsodium

By Henry Gilman and H. A. Pacevitz

After carbonation of a reaction mixture of di-*p*-tolylmercury, sodium and benzene which had been allowed to stand for one month, Bachmann and Clarke[1] isolated benzoic acid (34%), *p*-toluic acid (30%) and phenylacetic acid (0.36%). The formation of phenylacetic acid establishes the migration of sodium from *p*-tolylsodium to benzyl-

(1) Bachmann and Clarke, This Journal, **49**, 2096 (1927); see also, Ziegler, *Angew. Chem.*, **49**, 455 (1936).

sodium, and is an interesting variation of the lateral metalation of toluene by ethylsodium which was first examined by Schorigin.[2]

Incidental to studies on interconversions by organometallic compounds, we have investigated procedures for the preparation of organoalkali compounds, particularly the benzylmetallic types.[3] One of the more interesting results is the conversion of *m*-tolylsodium to benzylsodium. *m*-Chlorotoluene and sodium in petroleum ether first give *m*-tolylsodium, as evidenced by the formation of *m*-toluic acid (free of phenylacetic acid) on carbonation. On refluxing the mixture, the *m*-tolylsodium is converted to benzylsodium. In the Bachmann–Clarke[1] migration with *p*-tolylsodium one may be dealing with an allylic rearrangement of the kind frequently observed with a variety of organometallic compounds. However, with *m*-tolylsodium it is difficult to account for the migration on the basis of an allylic rearrangement. Although mechanisms have not been proposed for the migrations cited, it is probable that the meta and para transformations proceed by different routes, if the relative rates of migration are criteria.

Experimental

A mixture of 12.7 g. (0.1 mole) of *m*-chlorotoluene, 5.7 g. (0.25 g. atom) of sodium sand and 100 cc. of petroleum ether (b. p., 85–100°) was heated to reflux temperature and then promptly cooled to room temperature. The reaction then proceeded spontaneously, and the temperature was kept between 35–40°. After two hours, the reaction mixture was black, and the evolution of heat ceased. Carbonation of an aliquot of the mixture by solid carbon dioxide yielded *m*-toluic acid as the only acid.[4] The remaining mixture was refluxed for six hours and then carbonated by pouring upon crushed solid carbon dioxide. From the resulting acids there was isolated a 5.3% yield of phenylacetic acid (mixed m. p.), but no *m*-toluic acid or phenylmalonic acid. A small quantity of clear, oily acidic material has not yet been identified.

With a twenty-hour period of refluxing, the yield of phenylacetic acid was 4.7%. However, with only a one-hour period of refluxing the yield of phenylacetic acid was 8.3%. It should be stated that carbonation after heating a mixture of *p*-chlorotoluene, sodium and petroleum ether yielded 65% of phenylacetic acid.[3]

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RECEIVED JANUARY 29, 1940

(2) Schorigin, *Ber.*, **41**, 2723 (1908).

(3) A detailed report on these studies by the authors together with Dr. Ogden Baine will be published shortly. An account of the reactions and their mechanisms was presented at the Eighth National Organic Symposium, St. Louis, Dec. 30, 1939.

(4) In a separate experiment where carbonation of the entire mixture was effected at this point, the yield of *m*-toluic acid was 84%.

Preparation of Borneol Glucuronide

BY HARVEY K. MURER AND LATHAN A. CRANDALL, JR.

We have had good success in the isolation of the zinc salt of borneol glucuronide by the method of Quick[1] and Pryde and Williams[2] from the urine of dogs fed borneol provided care is taken in the proper adjustment of acidity previous to the lead clarification of the urine.

In their preparation of the free glucuronide the zinc salt was dissolved in hot 3.4 *N* sulfuric acid, filtered and allowed to crystallize from the hot solution. The glucuronide was filtered off and washed with ice water and recrystallized from hot water for further purification. It is difficult to filter and wash this product in water, and several recrystallizations are necessary to obtain a pure product with subsequent loss in yield. Also uronic acids are destroyed by hot acid of this strength and some hydrolysis of the glucuronide takes place, giving rise to the difficulty of removing borneol from the product.

To avoid these difficulties the removal of the zinc was first attempted with hydrogen sulfide. The zinc salt was suspended in acetone. A slow but fairly good removal of zinc was accomplished but the product retained a strong odor of sulfide after several purifications from acetone.

The above use of acetone led to a simple method which has given good results in the preparation of large quantities of borneol glucuronide of good purity.

Two hundred grams of dry zinc borneol glucuronide is added with stirring to 800 ml. of warm acetone containing 14.7 ml. of concentrated sulfuric acid. The zinc sulfate and any unreacted zinc salt are easily centrifuged down and the clear acetone solution decanted. The centrifuge flasks and precipitate are washed once with 50 to 100 ml. of warm acetone, centrifuged and the clear solution added to the original. Fifty ml. of water is added to the acetone solution to allow for crystallization of the hydrate and to keep traces of zinc sulfate in solution. Crystals of fine needles will set the solution almost solid at room temperature. The product is filtered with suction, washed with cold acetone, and vacuum dried at 40°. The filtrate is easily concentrated and again cooled for crystallization without further addition of water, filtered and washed as before. A still

(1) A. M. Quick, *J. Biol. Chem.*, **74**, 331–341 (1927).

(2) J. Pryde and R. T. Williams, *Biochem. J.*, **27**, 1197–1204 (1933).

further small amount of pure product may be obtained by a third crystallization of the filtrate. Unreacted zinc salt and remaining glucuronide in the washings may be recovered by dissolving the sludge in hot acidified water, adding an excess of zinc acetate and recovering the insoluble salt by filtration.

Attempts to find some more suitable method for the hydrolysis of borneol glucuronide than the acid hydrolysis suggested by Quick for the preparation of glucuronic acid have not been successful. B-Emulsin will hydrolyze considerable quantities of glucuronide; however, the reaction rate is slow, the equilibrium poor for preparation purposes, and the high acidity produced by the free glucuronic acid destroys emulsin, necessitating continued addition of the enzyme. This last step therefore is the limiting one in the preparation of glucuronic acid by Quick's method.

DEPARTMENT OF PHYSIOLOGY
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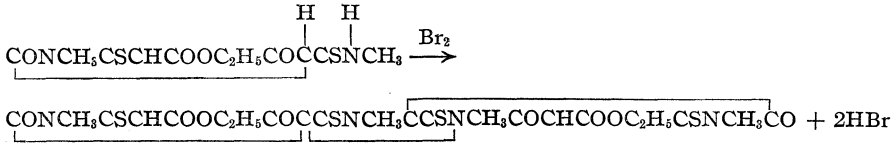
MEMPHIS, TENNESSEE RECEIVED JANUARY 29, 1940

The Action of Methyl Isothiocyanate on Ethyl Acetonedicarboxylate

BY DAVID E. WORRALL

The highly substituted derivatives of piperidine obtained ultimately by the action of aryl isothiocyanates on the sodium enolate of ethyl acetonedicarboxylate undergo further cyclization, in the presence of bromine, into piperidyl benzothiazoles.[1] An examination of similar reactions with an alkyl isothiocyanate has shown that a piperidine is formed which also loses a molecule of hydrogen. Thiazole formation is impossible, therefore the assumption has been made that a spiro piperazine is obtained as the result of a bimolecular condensation.



(1) Worrall, THIS JOURNAL, **61**, 2967 (1939).

Abenius[2] found that a reaction of this type occurs with the bromoacetyl derivative of aniline.

Experimental

1 - Methyl - 2,4 - dioxo - 5 - carbethoxy - 6 - sulfopiperidine-3-thioformomethylamide.—Using the customary technique, 0.1 g. mole of the ester was changed into the disodium derivative and mixed with two equivalents of methyl isothiocyanate. The mixture, after the spontaneous reaction subsided, was heated for an hour and decomposed in the usual manner. The pasty product was extracted with cold alcohol and the residue crystallized from alcohol. Bright yellow platelets resulted, m. p. 98°, yield 4–5 g.

Anal. Calcd. for $C_{11}H_{14}N_2O_4S_2$: C, 43.7; H, 4.6. Found: C, 43.6; H, 4.5.

The substance, soluble in sodium carbonate solution is reprecipitated unchanged by a strong acid. Hot acid changes it into an intractable tar, while boiling with alcoholic potash produces methylamine, hydrogen sulfide and other decomposition products. The original material contained an insoluble portion (0.3 g.) that separated from a large volume of alcohol in slender pale yellow needles, m. p. 235–236°. An analysis indicated the formula $C_{18}H_{14}N_4O_5S_4$, but it was not identified.

1 - Methyl - 2,4 - dioxo - 5 - carbethoxy - 6 - sulfomethoxypiperidine-3-thioformomethylamide.—The product, obtained by heating 1 g. of the amide with methyl iodide–ethyl alcohol mixture for thirty minutes, separated on cooling as slender colorless needles, m. p. 110°.

Anal. Calcd. for $C_{12}H_{16}N_2O_4S_2$: C, 45.6; H, 5.1. Found: C, 45.3; H, 5.0.

Di - spiro - 3,3' - di - (1 - methyl - 2,4 - dioxo - 5 - carbethoxy - 6 - sulfopiperidine) - 3'',3''' - (1,4 - dimethyl - 2,5-disulfopiperazine).—Bromination of 1 g. of the amide in glacial acetic acid formed a precipitate that, after heating on a water-bath for a short time, was crystallized from alcohol. Cream colored needles separated, m. p. 180°.

Anal. Calcd. for $C_{11}H_{12}N_2O_4S_2$: C, 44.0; H, 4.0. Found: C, 43.6; H, 3.9.

It is dissolved by cold concd. sulfuric acid, forms a gelatinous substance with hot alcoholic potash (probably the corresponding carboxy derivative) and is only slightly attacked by long heating with concd. hydrochloric acid.

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(2) Abenius, *J. prakt. Chem.*, (2) **40**, 431 (1889).

COMMUNICATIONS TO THE EDITOR

THE GELATION OF MAGNESIUM SILICATE SUSPENSIONS BY CARBON DIOXIDE AND OTHER AGENTS

Sir:

Several months ago, in the course of some experiments with precipitated and washed silicates of magnesium, we observed that the passage of carbon dioxide through fluid suspensions of these silicates in water soon caused the suspensions to "set up" or gel. The resulting gels were found to be thixotropic,[1] that is, capable of an isothermal, reversible sol-gel transformation, being liquefied on shaking and setting spontaneously.[2]

Thus, within one and one-half minutes following the treatment of 10 cc. of an 8.1% suspension of MgO, $1.6SiO_2$ (*p*H 9.3) with a rapid stream of carbon dioxide for one-half minute, the originally fluid suspension had "set up," so that the test-tube (16 by 150 mm.) containing it could be inverted without flow taking place. Vigorous shaking of the solidified material (*p*H 7.2) produced liquefaction; upon standing undisturbed, spontaneous reversion to the gel state occurred in less than a minute. The process could be repeated indefinitely.

Similar observations were made with suspensions of MgO, $1.1SiO_2$ (6.1%) and MgO, $3.6SiO_2$ (8.4%).

The magnesium silicates were prepared by slowly adding water solutions of various silicates of sodium to water solutions of magnesium sulfate,[3] with vigorous stirring. The resulting precipitates were collected and washed in a filter press,[4] and portions of the wet products[5] were ground with water for a few minutes in a mortar to yield the rather coarse suspensions which, after vigorous shaking, were employed in the above experiments.

More recently, we found that hydrochloric acid, sulfuric acid, or acetic acid, in small amounts, could be substituted for carbon dioxide in the above experiments, to give similar results. Thus, following the addition of 0.1 cc. of *N* hydrochloric acid (0.0004 mole) to 10 cc. of an 8.1% suspension of MgO, $1.6SiO_2$ (0.006 mole; *p*H 9.3), contained in a 16 by 150-mm. test-tube, gelation occurred in about half a minute. The setting time of the thixotropic product (*p*H 7.7) was less than fifteen seconds. Further work along these lines is in progress.

Aside from its scientific interest, the present phenomenon may find some application in the arts.[6]

(1) *Cf.* Freundlich and Gillings, *J. Chem. Soc.*, 546 (1938); MacArthur, U. S. Patent 2,168,228 (1939).

(2) For an excellent summary of our knowledge of the phenomenon of thixotropy, see Freundlich, "Thixotropy," No. 267 of "Actualités scientifiques et industrielles," Hermann et Cie, Paris, 1935.

(3) The proportions, concentrations, and composition of the reactants were:

$MgSO_4 \cdot 7H_2O$	Sodium silicate	Magnesium silicate[5]
3.22 moles (0.13 *M* soln.)	3.25 moles Na_2O, 1.00 SiO_2 (1.6 *M* soln.)	MgO, $1.1SiO_2$
3.44 moles (0.13 *M* soln.)	3.49 moles Na_2O, 1.48 SiO_2 (1.1 *M* soln.)	MgO, $1.6SiO_2$
2.71 moles (0.13 *M* soln.)	2.77 moles Na_2O, 3.27 SiO_2[a] (0.5 *M* soln.)	MgO, $3.6SiO_2$

[a] "E" Brand sodium silicate, of the Philadelphia Quartz Company from which the other sodium silicates were prepared by the addition of the requisite amounts of sodium hydroxide.

(4) Washing was continued at least until portions of the filtrates showed no tests (or only faint tests) for sodium (with uranyl zinc acetate) and sulfate (with $BaCl_2$, HCl).

(5) Complete analyses of the products, first dried (55°) and pulverized, were made, with the following results:

SiO_2, %	44.35	52.58	67.05
MgO, %	27.90	22.20	12.49
H_2O, %	27.14	24.05	18.67
R_2O_3, %	0.46	0.42	0.34
CaO, %	.26	.18	.12
Na_2O, %	.24	.35	1.21
SO_3, %	< .01	None	< 0.01
	100.35	99.78	99.88
Molecular ratio, MgO: SiO_2,	1:1.07	1:1.59	1:3.60

(6) *Cf.* Mutch, *Brit. Med. J.*, **1**, 143, 205, 254 (1936); Levin and co-workers, *Rev. Gastroenterol.*, **6**, 299 (1939); Hauser and Le Beau, *J. Phys. Chem.*, **42**, 961 (1938); **43**, 1037 (1939).

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RECEIVED JANUARY 9, 1940

REDUCTION OVER A RANEY CATALYST OF THE ESTERS OF α-AMINO ACIDS TO CORRESPONDING ALKAMINES

Sir:

P. L. de Benneville and Ralph Connor report [THIS JOURNAL, **62**, 283 (1940)] on the reduction of an ester to an alcoholic group by the aid of a nickel catalyst. This is regarded by the authors as the first instance of such a reaction.

We wish to report that within the last two years we have carried out the reduction over nickel catalyst (Raney) of the esters of α-aminoacids to the corresponding alkamines. The reaction was successfully carried out on the esters of leucine ethyl ester, of aminophenylacetic acid ethyl ester and of phenylalanine ethyl ester. In the case of the ester of *l*-leucine and of *levo*-phenylaminoacetic ethyl ester, the alkamines were obtained in active form. Depending on conditions of the reaction, it was possible to obtain from the ester of phenylaminoacetic acid either 2-phenyl-2-aminoethanol, or 2-cyclohexyl-2-aminoethanol. Under still other conditions it was possible to obtain from the esters corresponding secondary amines. Also, condensation to piperazine takes place over nickel (Raney) catalyst. The primary and the secondary amino groups may remain unsubstituted or alkylated, depending upon conditions of the reaction.

In the present note we report the analytical data of the alkamines only. The smallest yield of the active leucinol is 40% of the theoretical and the smallest yield of the phenylaminoethanol is 60%. The yields undoubtedly could be improved on working with larger quantities.

PROPERTIES AND ANALYSES

Ethyl ester		*d,l*-Leucine	*l*-Leucine	*levo*-Phenylaminoacetic acid	*d,l*-Phenylaminoacetic acid
$\alpha^{25}D$ (hom. 1 dm.)		..	+9.75°	−70.5°	..
t, °C.		135	70	40	40
p (initial), atm.		150	150	150	150
Duration, hours		24	9	9	18
Product		$C_8H_{15}ON\cdot HCl$	$C_8H_{15}ON$	$C_8H_{11}ON$	$C_8H_{17}ON$
$(\alpha)^{25}D$ (in CH_3OH)		..	+1.9°	− 5.61°	..
Carbon, %	Calcd.	46.87	61.47	70.02	67.07
	Found	47.19	61.59	69.86	67.30
Hydrogen, %	Calcd.	10.5	12.90	8.09	11.96
	Found	10.3	12.84	8.27	11.77

THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH
NEW YORK, N. Y.

G. OVAKIMIAN
MARTIN KUNA
P. A. LEVENE

RECEIVED FEBRUARY 16, 1940

NEW BOOKS

Ausführliches Lehrbuch der organischen Chemie. (Comprehensive Textbook of Organic Chemistry.) Vol. II. By WILH. SCHLENK. Verlag von Franz Deuticke, Helferstorferstrasse 4, Wien I, Germany, 1939. xvii + 896 pp. 11 figs. 17.5 × 26 cm. Price, RM. 30; bound, RM. 33. (Vol. I, now RM. 30; bound, RM. 33.)

This second volume of a contemplated three, the last of which according to the author will appear soon, covers the chemistry of the carbocyclic aromatic compounds. The first volume, published in 1932, was devoted to aliphatic chemistry and the third presumably will describe the heterocyclic compounds.

This publication when complete will be the most extensive modern textbook in organic chemistry available in any language. About 1600 pages have been consigned to aliphatic and aromatic chemistry. Since this work approaches more closely than any other the "Lehrbuch der organischen Chemie" by V. Meyer and P. Jacobson, a comparison is pertinent. Both works are presented in essentially the same style. Meyer and Jacobson, however, include a multitude of original references and devote much space to a description of the physical and chemical properties not only of the basic compounds but of their more important derivatives. Schlenk omits these and consequently is able to include in considerably less space the same amount of textual material. This publication, thus, becomes more literally a textbook from which a reader may acquire many of the important facts about any class of organic compounds, organic theories or mechanisms of reaction. It is not intended as a reference work for the investigator. In view of the ever-broadening scope of organic chemistry, Schlenk's plan appears to the reviewer to be the more feasible since the research man must of necessity search the original literature; such a text as this will supply him with general information about any class of compounds with which he happens to be less familiar.

Each class of aromatic compounds is systematically discussed. The theoretical considerations are correlated with the description of those substances which have been studied most in developing a theory or mechanism. Thus, the theories on the orientation of substituents introduced into the benzene nucleus are given in the chapter on benzene and its simple derivatives; the Fries rearrangement under the discussion of phenol esters and ethers; restricted rotation under biphenyls and the use of oxidation–reduction potentials under quinones, etc. The theoretical discussions are concise and give the reader sufficient information to understand the subjects.

These three volumes should serve admirably as an advanced text of organic chemistry for the student who is beyond the first year of study in this subject as well as for the research man who always requires general reading

in fields outside of his specialty if he is to retain his breadth of knowledge in organic chemistry. They should be a valuable addition to chemical libraries especially to those which are limited in scope. Beyond a text like this, the organic chemist must use monographs, advanced books on special topics or the original literature.

The material presented is entirely up-to-date. The book is well printed, readable and contains a minimum of typographical errors. It can be recommended highly to the organic chemist.

ROGER ADAMS

A Text-Book of Quantitative Inorganic Analysis. Theory and Practice. By ARTHUR I. VOGEL, D. Sc. (Lond.), D.I.C., F.I.C. Head of Chemistry Department, Woolwich Polytechnic: Lately Beit Scientific Research Fellow of the Imperial College. Longmans, Green and Company, 114 Fifth Avenue, New York, N. Y., 1939. 856 pp. Illustrated. 14.5 × 22.5 cm. Price, $5.00.

The author states, in his preface, that this book is designed as a text of quantitative inorganic analysis, theory and practice, to meet the needs of University and College students preparing for the various higher examinations in British universities and colleges.

Besides an appendix of data, the book consists of six chapters, on the theory of quantitative analysis, on experimental technique, and on volumetric, gravimetric, colorimetric and gas analysis. The chapter on theory appears to be adequately presented, the material including topics which are similarly treated in other modern texts on the subject. Emphasis is naturally on solutions. Chapter 2 on technique, has to do with apparatus, reagents and operations. The four chapters on analytical methods are unusually complete for a book of this type and really give it the character of a reference book. For instance, there are four methods given in detail for determining fluorides, and ten for antimony, to mention merely two cases taken at random. One more chapter, on quantitative calculations, particularly in volumetric analysis, would save much repetition in discussing volumetric methods.

References to the literature are not frequent and when given are by author and year without the journal reference, which is inconvenient for the reader. The very full cross-references in the book are to chapter, section and paragraph, with no page number given, which is so inconvenient as to be irritating. This system is an old one, but fortunately most writers have discarded it. There is the same tendency in this book as in many others to consider that the one consideration in analysis is accuracy and that time is not a factor. For instance, in igniting a precipitate with its filter paper, the student is told (p. 272) that it usually takes about twenty minutes to char the paper, and from thirty to sixty minutes to complete an ignition. Again in determining a sulfate as barium sulfate in a Gooch crucible, the student is told (p. 482) to ignite the precipitate for periods of fifteen minutes until constant weight is obtained. These, however, are all minor points. Taken as a whole, the author has produced a very good book indeed, and it will be useful both to beginners as well as to others who use it as a work of reference.

H. W. FOOTE

Physikalische Methoden der analytischen Chemie. Dritter Teil. (Physical Methods of Analytical Chemistry, Vol. III.) Edited by W. BÖTTGER. Akademische Verlagsgesellschaft m. b. H., Leipzig, Germany, 1939. xx + 836 pp. 42 figs. Price, RM. 63; bound, RM. 65.

In this third instalment of Volume III, Professor Böttger, the Editor, has brought the presentation of the whole subject up to date; first, by supplementary chapters covering the fields already discussed in Volumes I and II of this handbook which appeared in 1932 to 1936 and, second, by the addition of further chapters devoted to new physical methods of analysis which have arisen or have become important in the interim.

To the first group belong the chapters on Spectroscopic Analysis, Chemical Analysis by Means of X-Rays, Conductometric Titration, Applied Conductivity, Polarographic Analysis and Potentiometric Analysis. To the second group belong the chapters on chromatographic analysis, as applied both to organic and inorganic chemistry, the rapid analysis of inorganic compounds, particularly metals, by vaporization, analysis by means of Raman spectra and photometric methods of analysis.

The supplementary chapter on Polarographic Analysis consists of a complete bibliography of the new publications in this field between 1936 and 1938. The other supplementary chapters present unified and up-to-date discussions of their particular fields. The chapter on Potentiometric Analysis (282 pages) by Professor Böttger is especially thorough, illuminating and complete.

The chapters on the newer fields are, of course, particularly interesting. The striking results obtained by chromatographic analysis, the simple and rapid separation of metals from complicated alloys and minerals by evaporation, and the rapidity with which Raman rays have been utilized for analytical purposes are certainly impressive and inspiring.

The book will not only interest chemists in general but it will be very useful to those specializing in the fields which it discusses.

ARTHUR B. LAMB

Kurzes Lehrbuch der physikalischen Chemie. (Brief Textbook of Physical Chemistry.) By Prof. Dr. KARL JELLINEK, Emeritus Professor at the Technical Institute of Danzig. Heft 2 (Volume 2). N. V. Uitgevers-Maatschappij AE. E. Kluwer, Deventer, Holland, 1939. xii + 292 pp. 149 figs. 29 tables. 16 × 25 cm. Price, 7.50 Dutch fl.

Part 1 of Professor Karl Jellinek's 4-part brief, elementary textbook of physical chemistry already has been reviewed (THIS JOURNAL, **61**, 1298 (1939)). The present paper-bound section is Part 2 of the text; Parts 3 and 4 are promised for publication soon.

The same fine tone of clear explanation which characterized Part 1 is maintained here; and again the author presents a very extensive and helpful set of problems which are worked out in the body of the text as a part of the exposition. The subject matter is broken down in the different chapters and classified in a highly sub-divided, and quite logical, outline. An idea of the broader groupings of the discussion may be obtained from the following list:

Electrochemistry—A. General properties of solutions of electrolytes; B. Phenomena connected with reversible electrode potentials; C. Chemical equilibria in electrolytes; D. Chemical equilibria in fused salts; Phase Rule—A. Systems containing a single substance; B. Binary systems; Colloid Chemistry—A. Uncharged boundary surfaces; B. Electrically charged surfaces; C. Systems of abnormally large surface area; D. Formation of new phases; Chemical Kinetics—A. Homogeneous systems; B. Heterogeneous systems; C. Irreversible electrode potentials, and electrode reactions.

EDWARD MACK, JR.

A Textbook of Inorganic Chemistry for Colleges. Second edition. By JAMES F. NORRIS, Professor of Organic Chemistry, and RALPH C. YOUNG, Assistant Professor of Chemistry, Massachusetts Institute of Technology. McGraw-Hill Book Company, Inc., 330 West 42nd Street, New York, N. Y., 1938. x + 803 pp. 33 figs. 14.5 × 21 cm. Price, $3.75.

Inorganic Chemistry by Norris and Young is a well written and, for undergraduate work, a fundamental and comprehensive treatise of the subject. The tabulation of properties of the elements and compounds at the beginning of each chapter is a distinct improvement, in that it saves space and gives at a glance the information desired. The book, to my mind, is somewhat lacking in drawings and illustrations of commercial processes, which, I think, tends to increase interest.

J. P. SIMMONS

Physiological Chemistry. A Text-Book for Students. By ALBERT P. MATHEWS, Ph.D., Andrew Carnegie Professor of Biochemistry, The University of Cincinnati. Sixth edition. The Williams and Wilkins Co., Mount Royal and Guilford Avenues, Baltimore, Maryland, 1939. xvi + 1488 pp. 113 figs. 16 × 23.5 cm. Price, $8.00.

The sixth edition of Mathews' text-book has been extensively revised and enlarged. The section on practical methods has been omitted; there has been a rearrangement of some of the chapters, and the book has been set in a clearer type. The new typography accounts for an increase in number of pages of approximately 18% over the fifth edition of 1930. A rough calculation suggests that about 350 pages of new text have been added exclusive of the apparent increase due to the resetting.

The book is intended for the use of medical students and of graduate students and, as in earlier editions, the emphasis is placed on the functions of the organs of the animal body. These functions are discussed so far as possible in terms of chemical reaction. The fundamental chemistry of the carbohydrates, lipides, and proteins is described in the first eleven chapters (450 pages), the remaining two-thirds of the book being devoted to the consideration of the body as a mechanism. Blood is dealt with in seven chapters (177 pages), foods and digestion in four (218 pages), and metabolism in three (106 pages). In addition there are chapters on animal heat, brain and nerve tissue, muscle, connective and supporting tissues, skin, endocrine glands, excretions and vitamins.

The material in general is presented from a broad philosophical point of view; there is not too much insistence on details and the relationship of the separate functions to the whole organism is constantly kept before the reader. Nevertheless it is unfortunate that so much discussion from earlier editions, even from the first edition of 1915, has been retained unchanged. Statements that were at one time entirely proper are apt to lead to confusion in the mind of the student when they are placed in juxtaposition to more recently acquired knowledge, and phraseology that would indicate that many of these earlier conclusions have now only an historical significance is usually omitted. The teacher is faced with the task of pointing out to students what is authoritative and new and what has today been superseded.

The chapter on proteins (Chapter X, pp. 294–364) may be used to illustrate the worst features of this book. As a presentation of the present position of our knowledge of the proteins, this chapter is entirely inadequate. The section on nucleic acid and nucleoproteins, which formed a part of the chapter on proteins in earlier editions, now appears, with minor additions, as Chapter VI. Most of what remains in Chapter X has been transferred unchanged from the fourth edition of 1925, and much of this material was written for the first edition of 1915. A comparison page by page with the fourth edition shows that only about 8 pages of new material have been included. The advances in protein chemistry of the last 14 years are thus presumably dealt with in these 8 pages. Study of the text shows, however, that many of the additions consist merely of a sentence added to an older paragraph.

In the discussion of the molecular weight of proteins, Hüfner and Gansser's pioneering osmotic pressure studies of 1907 are fully described but no mention is made of Sörensen's and of Adair's demonstrations of the fundamental errors in this early work although these contributions appeared upward of 20 years ago. The work of Svedberg's laboratory which has appeared since 1926 is dismissed with four lines of text in which the ultracentrifuge is referred to as a super-centrifuge, and the page and a half of new text on molecular weights contains statements some of which contradict those made on preceding pages. No mention is made of modern diffusion methods nor of recent stoichiometric accomplishments and a student might well be left in a state of considerable misapprehension of what is now known of the molecular weights of proteins.

The list of "kinds of amino acids found in proteins" (pp. 310–312), newly prepared for the sixth edition, contains 31 entries. The inclusion in such a list of γ-hydroxy-α-aminobutyric acid (in canavalline), of citrulline, canavanine, prolysine and still more of the betaine ergothioneine is open to grave question. Some of these substances do in fact occur in plant tissues and one has been found in blood. They are related to the protein amino acids in a most interesting way and doubtless have metabolic significance which should be pointed out; but they have not yet been "found in proteins."

The best features of the book may be illustrated by the chapter on vitamins (Chapter XXXIV, pp. 1347–1428).

This has been entirely rewritten for the new edition and contains only about 4 pages of text from the fifth edition. It is complete, authoritative, and for the most part thoroughly accurate. One might question the failure to mention the share that Osborne and Mendel had in the discovery of vitamin A in 1914, particularly when a diagram from their paper is introduced to illustrate statements made about the work of McCollum and Davis that appeared only a few weeks earlier. But this is a minor omission. The chapter as a whole gives the present status of our knowledge of the vitamins clearly and succinctly.

Other chapters occupy an intermediate position. Some, like that on endocrine glands (Chapter XXIX, pp. 1055–1141), have been very extensively revised and enlarged; others, like that on animal heat (Chapter XII, pp. 462, 502), merely contain a few pages of additional material. On the whole, however, it may be said that the task of bringing this edition up to date has been taken seriously and has been performed with a considerable degree of success.

The bibliographies attached to each chapter are well-chosen but are in urgent need of revision. It is a serious defect that no consistent style of abbreviation of journal names is employed in spite of the inclusion of a list of abbreviations on p. xv; for example, seven different ways of expressing the name of THIS JOURNAL were noted. Furthermore, there is no consistency in the order in which volume number, page, and date are presented nor in the typographical style in which the references are classified. Several ambiguous references were found. This is not a good example to students who may one day be faced with the problem of preparing a bibliography in a style acceptable to the editor of a journal.

Mathews' text has long been held in high esteem by teachers and investigators alike as a source of stimulating ideas. It must, however, be read with careful discrimination since speculation on the meaning of various relationships is so frequently introduced. The distinguished author expressed the hope in the first edition that the book would raise more questions than it answered; there seems little doubt that this is still true of the latest edition.

H. B. VICKERY

BOOKS RECEIVED

January 10, 1940, to February 10, 1940

SYDNEY CHAPMAN AND T. G. COWLING. "The Mathematical Theory of Non-uniform Gases." The Macmillan Co., 60 Fifth Avenue, New York, N. Y. 404 pp. $7.50.

EARL C. H. DAVIES. "Fundamentals of Physical Chemistry." Second edition. P. Blakiston's Son and Co., 1012 Walnut Street, Philadelphia, Penna. 447 pp. $3.50.

A. EUCKEN AND M. JAKOB. "Der Chemie-Ingenieur." Band III. "Chemische Operationen." Dritter Teil. "Operationen bei normalem Druck und normaler Temperatur." Akademische Verlagsgesellschaft m. b. H., Sternwartenstrasse 8, Leipzig C 1, Germany. 332 pp. RM. 33; bound, RM. 35.

R. H. FOWLER AND E. A. GUGGENHEIM. "Statistical Thermodynamics." The Macmillan Co., 60 Fifth Avenue, New York, N. Y. 693 pp. $9.50.

ELWOOD D. HEISS, ELLSWORTH S. OBOURN AND C. WESLEY HOFFMAN. "Modern Methods and Materials for Teaching Science." The Macmillan Co., 60 Fifth Avenue, New York, N. Y. 351 pp. $2.50.

G. E. M. JAUNCEY AND A. S. LANGSDORF. "M. K. S. Units and Dimensions and a Proposed M. K. O. S. System." The Macmillan Co., 60 Fifth Avenue, New York, N. Y. 62 pp. $1.00.

OSCAR KNEFLER RICE. "Electronic Structure and Chemical Binding." McGraw-Hill Book Co., Inc., 330 West 42nd St., New York, N. Y. 511 pp. $5.00.

HENRY J. SAND. "Electrochemistry and Electrochemical Analysis." Volume I. "Electrochemical Theory." Blackie and Son Limited, 50 Old Bailey, London, England. Distributed in the United States by Chemical Publishing Co., Inc., 148 Lafayette St., New York, N. Y. 133 pp. $2.00.

WALTER A. SHEWHART. "Statistical Method from the Viewpoint of Quality Control." Edited by W. EDWARDS DEMING. The Graduate School, The United States Department of Agriculture, Washington, D. C. 155 pp.

ALBERT V. SZENT-GYÖRGYI. "On Oxidation, Fermentation, Vitamins, Health and Disease." The Williams and Wilkins Co., Mt. Royal and Guilford Aves., Baltimore, Maryland. 109 pp. $2.00.

F. WITTKA. "Moderne fettchemische Technologie." Heft 1. "Verderben der Seifen. Ursachen und Verhütung." Johann Ambrosius Barth, Salomonstrasse 18 B, Leipzig C 1, Germany. 148 pp. RM. 10.

"Gmelins Handbuch der anorganischen Chemie." Edited by E. PIETSCH. 1 Ergänzungsband, Teil 3. "Aluminum Legierungen Patentsammlung." By G. APEL. Verlag Chemie, G. m. b. H., Berlin W 35, Germany. 387 pp. RM. 31.50.

"Gmelins Handbuch der anorganischen Chemie." Edited by E. PIETSCH. "System-Nummer 68: Platin." Teil C, Lieferung 1. "Verbindungen bis Platin und Wismut." Verlag Chemie, G. m. b. H., Berlin W 35, Germany. 140 pp. RM. 16.50.

"Gmelins Handbuch der anorganischen Chemie." Edited by E. PIETSCH. "System-Nummer 68: Platin." Teil A, Lieferung 3. "Darstellung der Platinmetalle." Verlag Chemie, G. m. b. H., Berlin W 35, Germany. 119 pp. RM. 14.25.

"A List of the Books, Bulletins, Journal Contributions and Patents by Members of Mellon Institute, 1911–1938." The Mellon Institute, Pittsburgh, Penna. 242 pp.

JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

VOLUME 62 APRIL 5, 1940 NUMBER 4

[JOINT CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE JOHNS HOPKINS UNIVERSITY AND THE DEPARTMENT OF CHEMISTRY OF YALE UNIVERSITY]

Measurement of the Heat Capacity of a Small Volume of Liquid by the Piezo-thermometric Method.[1] I. Apparatus for Measuring $(\partial T/\partial P)_S$ and Results for Benzene and Toluene

BY JOHN S. BURLEW[2]

The Piezo-thermometric Method

Precise measurements of the heat capacity of pure organic liquids at frequent intervals over a wide range of temperature are of prime importance in the formulation and testing of a comprehensive theory of the liquid state. In order that compounds difficult and expensive to prepare may be highly purified before use in such an investigation, small samples are desirable. Adiabatic calorimetry, which heretofore has been the most precise method of measuring the heat capacity of liquids, requires a fairly large sample, especially if the heating interval is small, which it should be if the results are to be of any value whatever. The method described in the present series of papers was developed for the purpose of measuring precisely and conveniently the heat capacity of only 5 ml. of a liquid over a wide range of temperature using a cooling interval of 0.4°.

This method involves two independent sets of measurements for the evaluation of the two differential coefficients in equation (1)[3] at the same

$$c_p = T\frac{(\partial V/\partial T)_P}{(\partial T/\partial P)_S} \qquad (1)$$

absolute temperature T. For convenience in reference, I call it "the piezo-thermometric method" because the two principal measurements in the determination of the adiabatic temperature–pressure coefficient $(\partial T/\partial P)_S$ are those of pressure and temperature. Although this quantity is a derivative, it must be measured as the quotient of a finite change of temperature by a finite change of pressure. The coefficient of thermal expansion $(\partial V/\partial T)_P$ is obtained by differentiation of an empirical equation used to express measured values of the specific volume of the liquid as a function of temperature.

Joule[4] had used equation (1) as the basis of an experimental verification of the second law of thermodynamics. Although several later experimenters measured $(\partial T/\partial P)_S$ of various substances at relatively high pressures, only in recent years has it been measured in order to determine c_p of a liquid. Dixon and Rodebush[5] measured

(1) The application of this method to a small volume of liquid was described first in a dissertation accepted by The Johns Hopkins University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1934. The next year the apparatus was rebuilt at Yale University, and certain refinements were made in it. The apparatus and technique as herein described are those that were used at Yale University. They were described before the Division of Physical and Inorganic Chemistry at the New York Meeting of the American Chemical Society, April 26, 1935.

(2) Sterling Fellow in Chemistry, Yale University, 1934–1936; present address: Geophysical Laboratory, Washington, D. C.

(3) The units in equation (1) are: c_p (the heat capacity) in decijoules per degree per gram, $(\partial V/\partial T)_P$ in cubic centimeters per degree per gram, and $(\partial T/\partial P)_S$ in degrees per bar. For the derivation of this equation from the first and second laws of thermodynamics, see G. N. Lewis and M. Randall, "Thermodynamics," McGraw-Hill Book Co., Inc., New York, 1923, eq. 25, p. 137.

(4) J. P. Joule, *Phil. Mag.*, **17**, 364 (1859).

(5) A. L. Dixon and W. H. Rodebush, THIS JOURNAL, **49**, 1162 (1927).

$(\partial T/\partial P)_S$ of molten sodium, potassium, and lead; and Richards and Wallace[6] measured $(\partial T/\partial P)_S$ of five organic liquids. Then they computed c_p, using values of $(\partial V/\partial T)_P$ taken from the literature. In neither case was an effort made to use small samples.

An apparatus for the measurement of $(\partial T/\partial P)_S$ of 5 ml. of a liquid is described in the present paper; and a new type of weight dilatometer for the measurement of $(\partial V/\partial T)_P$ of this same quantity of liquid is described in the one[7] that follows. The values of the heat capacity resulting from a combination of the data obtained with these two pieces of apparatus in the case of benzene and of toluene are given in a third paper.[8]

Apparatus

Pressure System.—The manner of controlling and measuring the pressure is illustrated in Fig. 1. Compressed nitrogen was stored at convenient working pressures in a gas bottle (volume, 400 ml.), to which was connected a pressure distributor supported by cross-bars 7 cm. above the surface of the oil in a thermostat. The bomb (Fig. 2) that contained the piezo-thermometric cell was suspended in the thermostat by a short pipe by means of which it was connected to the under side of the pressure distributor. The release of pressure was very quick because the bore of this pipe was 6 mm. and the holes in the hollow-stem release valve were 3 mm. in diameter. A handle on the release valve enabled it to be opened by a single rapid motion of the operator's hand.

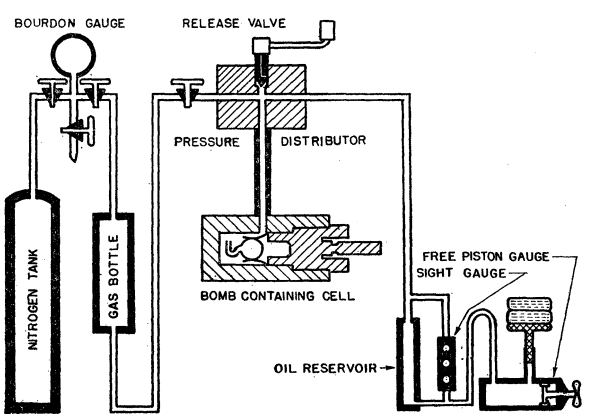

Fig. 1.—Pressure system of the piezo-thermometric apparatus (schematic).

A fourth connection from the pressure distributor led to a free piston gage[9] through an oil reservoir (volume, 50 ml.) and a U-trap. These accessories were needed in order to prevent nitrogen from blowing past the shallow layer of oil[10] in the cylinder of the gage. The level of oil in the reservoir could be adjusted by means of a screw, and the slight hydrostatic pressure from it could be measured to ±1 millibar by means of a sight gage.

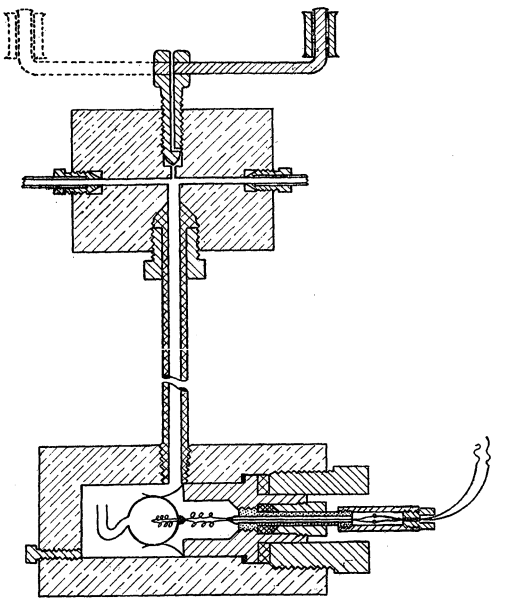

Fig. 2.—Piezo-thermometric cell in bomb attached to pressure distributor (scale, 1/4).

The nominal multiplier ratio of the free piston gage was 16:1. A measurement of the piston diameter with a micrometer agreed with this value within the manufacturer's tolerance limits of ±0.1%. The corresponding gage constant for local gravity in New Haven (980.28 cm./sec.²) was 2.431 bars per kilogram, and its probable error was assumed to be ±0.05%, half the tolerance limits. When the temperature of the gage changed 4.5°, the gage constant changed 0.01%. For the few measurements during which the temperature of the gage differed this much from ordinary room temperature (21°), a correction was applied to the observed pressure.

The masses of the weights were determined in terms of a 100-g. weight that had been calibrated at the Bureau of Standards. As a result of the calibration the mass of each weight was known with a maximum uncertainty of ±0.001%. The height at which the weights were rotated was kept the same in all experiments.

Thermostat.—The fluctuations of the temperature of the 65-liter oil-bath in which the piezo-thermometric bomb was immersed had to be less than ±0.005° in order not to interfere with the measurement of $(\partial T/\partial P)_S$. This degree of regulation was obtained by means of an intermittent bare nichrome heater that was controlled by a thermoregulator made of a long glass tube wound in a helix around a central U-tube and filled with xylene and mercury. Sticking in the capillary was prevented by having the electrical contact with the mercury made at a

(6) W. T. Richards and J. H. Wallace, THIS JOURNAL, **54**, 2705 (1932).

(7) J. S. Burlew, *ibid.*, **62**, 690 (1940).

(8) J. S. Burlew, *ibid.*, **62**, 696 (1940).

(9) A commercial "dead-weight gage tester" manufactured by the Consolidated Ashcroft-Hancock Co., Inc.

(10) The oil used was Wyrol, similar in properties to Nujol. It was colored red with an aniline dye (special oil-soluble cardinal dye No. A45035, distributed by National Aniline and Chemical Co.) to render it visible in the sight gage.

point of tangency[11] of a bent piece of No. 32 nichrome wire.

A heater wrapped on the bomb pipe just above the surface of the oil was used to block off heat leak. Without the heater the leak was so great that at 80° the bomb could remain indefinitely at a temperature 1° lower than that of the thermostat.

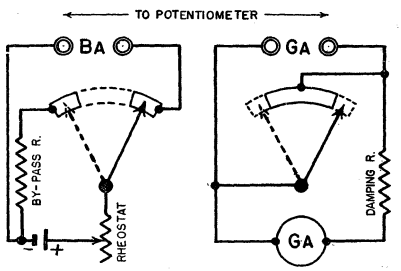

Fig. 3.—Short-circuiting switch for the thermel-galvanometer circuit. (The two contacts rotated simultaneously on a common shaft.)

The temperature of the thermostat up to 80° was measured with a mercury-in-glass thermometer graduated on the stem in 1/10° in accordance with the specifications of the Bureau of Standards. It was calibrated against a platinum resistance thermometer[12] used in conjunction with a Mueller resistance bridge[12] at 5° intervals in the oil thermostat under exactly the same conditions as later prevailed during use. In order to avoid large stem corrections, temperatures from 80 to 110° were measured with another platinum resistance thermometer. The resistance thermometers were calibrated at the ice and steam points. It is believed that the temperature observations had a probable error of ±0.02° up to 50°; ±0.03° from 50 to 80°; and ±0.02° from 80 to 110°.

Potentiometric System.—The potentiometer, a "thermo-free" instrument built to order by the Leeds and Northrup Company, had a range of 550 microvolts in steps of 5 microvolts. The circuit was similar to that in the lower decades of the White potentiometer made by the same company. The battery current was balanced against a self-contained standard cell by means of an auxiliary pointer galvanometer, the sensitivity of which was great enough to permit adjustment to ±0.03%, as determined by a test. The maker's calibration showed that the resistances had been adjusted to their nominal values with an uncertainty of less than 0.1%.

The galvanometer, a Leeds and Northrup narrow-coil, type HS instrument with a period of 6.1 sec., was packed in cotton wool in a wooden box and was mounted 3.15 meters from a ground-glass scale. It was used critically damped, and the working sensitivity then was 16 mm. per microvolt.

The potentiometer was housed in a dry air thermostat at 25°. A wooden cover protected the switches on top of the potentiometer from drafts. The storage battery was kept in a wooden enclosure. The electrical system was separated from its surroundings by a double equipotential shield.[13] The steel pressure bomb was made part of the outer grounded shield. Even in damp weather the parasitic electromotive force did not exceed 0.1 microvolt, and it showed no sudden changes.

A duplex short-circuiting switch (Fig. 3) obviated opening or closing the galvanometer circuit during the course of a measurement. The switch was constructed from two small radio rheostats by mounting them on a common shaft and replacing their resistance windings with copper contacts.

Piezo-thermometric Cell.—The piezo-thermometric cell shown inside the cylindrical steel pressure bomb in Fig. 2 consisted of a soft-glass sphere 20 mm. in outside diameter with a gooseneck opening. It was held in place by a set of phosphor-bronze fingers shaped like a glassblower's flask-holder that were screwed to the recessed face of a cylindrical steel holder. This holder was sealed into the bomb by means of a threaded plug and a lead gasket.

The soldered junction of a copper–constantan thermocouple was at the center of the glass sphere and the wires[14] leading from it were fused through the rear wall. In order to get them out of the pressure bomb, they were fused into the end of a soft-glass capillary tube that previously had been cemented into a steel sheath with glycerol–litharge cement.[15] This sheath was sealed into an axial hole in the cylindrical steel cell holder by means of a packing of asbestos, shredded lead, and graphite.

When the cell was first constructed, the free ends of the thermocouple wires coming out of the open end of the glass capillary tube were drawn through a U-shaped copper conduit that was screwed on the end of the steel sheath. The wires were soldered to copper wires, and these junctions were enclosed in a glass tube that was cemented into the end of the copper conduit, thus forming a closed U-shaped thermocouple.

Before this thermocouple was calibrated it was pressure-seasoned by placing the cell in the bomb under a pressure of 50 bars for twenty hours at a temperature of 70°. Then the cell was subjected to twenty sudden applications and instantaneous releases of pressure of about 50 bars each.

The thermocouple was calibrated in a duplex thermostat by a direct differential method[16] in terms of a copper–constantan reference thermel, the calibration of which is described elsewhere.[16a] After calibration, the thermocouple wires were cut off just beyond where they emerged from the glass capillary tube, and new junctions to copper wires were made[17] and imbedded in paraffin in a thin-walled

(11) S. Kambara and M. Matsui, *J. Soc. Chem. Ind., Japan*, **34** (Suppl. binding), 94 (1931).

(12) Made by the Leeds and Northrup Company.

(13) W. P. White, THIS JOURNAL, **36**, 2011 (1914).

(14) Both wires were no. 40, B. & S. gage. The constantan wire had been selected to have a maximum inhomogeneity equivalent to 0.2% of its thermoelectric power against copper, after a test of a large quantity of wire by the method of W. P. White, *Phys. Rev.*, **31**, 135 (1910), p. 142.

(15) Contrary to the findings of H. Stäger, H. Zschokke and J. P. Bohnenblust [*Kolloid-Z.*, **65**, 319 (1933)] oil (Wyrol) attacked this cement at a temperature as low as 70°. To prevent this the bottom of the recess in the steel holder was covered with a zinc oxide–water glass emulsion, which set to a hard glaze that was not affected by Wyrol even at 110°.

(16) J. S. Burlew and R. P. Smith, THIS JOURNAL, **62**, 701 (1940). (a) This was Thermel B, p. 703.

(17) This operation did not affect the thermoelectric power of the thermel any more than the inevitable shift in the temperature gradient from its position during calibration to its position during use. Because this gradient had been kept unidirectional during calibration by the use of the duplex thermostat, the greatest change in the thermoelectric power caused by the shift of the gradient would have been 0.2%, which was the maximum measured inhomogeneity of the constantan wire. If the gradient during calibration had not

metal cylinder that can be seen screwed to the right end of the steel sheath in Fig. 2.

Two separate cells were constructed. The calibration of Cell A was performed in duplicate at mean temperatures of 20, 30, and 40°, with first one limb cold and then the other; but no systematic difference was observed between the two sets of results. Cell B was calibrated at mean temperatures of 5, 35, 65, 95, and 135°. Inasmuch as the differences in the thermoelectric power did not vary regularly with the mean temperature, the thermoelectric power of the thermocouple in each cell was expressed by the same function of the mean temperature t' as had been derived for the reference thermel, but with the constant term changed by the mean observed difference in thermoelectric power. For convenience in use over the limited temperature range 20 to 30°, the quadratic equation for Cell A was transformed into a linear form. The systematic probable error of the calibration equations is estimated to be $\pm 0.1\%$, because of the uncertainty concerning the inhomogeneity of the constantan wire. The relative probable error of the equation for Cell A is $\pm 0.03\%$, and of that for Cell B is $\pm 0.15\%$, which combines the uncertainty of the original calibration of the reference thermel with the uncertainty of the comparison.

Technique

After the piezo-thermometric cell had been filled with the liquid to be studied, mercury was placed in the gooseneck until it came within 2 mm. of the entrance to the bulb. The bomb, containing the cell sealed in it, was filled with Wyrol[10] and the bomb-pipe was half-filled.[18] Pressure was applied to the cell by admitting nitrogen to the pressure distributor.[19] This always had to be done slowly in order to prevent mercury from being forced into the bulb of the cell. A preliminary measurement of $\Delta T/\Delta P$ was made, from which was computed the pressure drop needed to cause the thermocouple to develop a potential of between 15 and 16 μv. After this pressure had been applied, there was a wait of about an hour while the heat of compression leaked away.

When thermal equilibrium had been established within a few hundredths of a degree, the potentiometer dial was set at 15 μv., and the tapping key of the potentiometer was locked down. The release valve was opened suddenly, and at the same time the duplex switch (Fig. 3) was thrown from left to right. In the former position the battery had been connected to a by-pass resistance and the thermocouple had been connected to the galvanometer through the potentiometer coils and a damping resistance, so that the deflection of the galvanometer "spot" from its open-circuit position had been a measure of the temperature difference between the thermostat and the liquid in the cell. Turning the switch to the latter position applied the electromotive force of the potentiometer to the galvanometer. The thermocouple, however, had been cooled by the release of pressure; and since its potential opposed that of the potentiometer, the galvanometer, which first had moved toward its zero position while it was being short-circuited by the one moving arm of the duplex switch, finally was deflected a small amount. By a proper choice of the pressure drop this deflection was made to be always less than 2 cm. in the direction that indicated cooling of the liquid in the cell. The definiteness of the maximum of the galvanometer deflection was enhanced by the fact that the subsequent deflection, caused by the warming up of the cell to the temperature of the thermostat, was opposite the original deflection.

The position of the galvanometer spot before and after the release of pressure was estimated to the nearest 0.2 mm. The difference between the two positions measured[20] the amount by which the potential of the thermocouple exceeded the 15 μv. potential of the potentiometer. Thus the duplex switch not only obviated moving a contact in the galvanometer circuit at the time of a measurement, but also performed the same function as the eliminating switch[21] of a White potentiometer by furnishing a closed-circuit "zero."

As soon as the galvanometer spot began to drift, the duplex switch was placed in the short-circuiting position while pressure was reapplied. Thus the contents of the bomb were restored almost to thermal equilibrium with the thermostat. The potentiometer switch was thrown to the left, whereupon the galvanometer indicated that the cell was only about 0.1° warmer than the thermostat. This difference decreased in about five minutes to less than 0.02°. Ten minutes after the first release of pressure, a second measurement was made. This procedure was repeated for a total of five replicates. Then the temperature of the thermostat was raised, and the same routine was carried out at a new constant temperature.

The procedure of keeping the potentiometer setting the same for all measurements and varying the pressure, increased the precision considerably; for the pressure could be measured much more precisely than the electromotive force of the thermocouple. In effect the uncertainty of the adjustment of the potentiometer coils did not contribute to the observational error, but only to the systematic error. A similar increase in precision was obtained in connection with replicate measurements at a single temperature, by using the same pressure for all of them, so that the galvanometer deflection was the only quantity subject to significant observational variation. These two procedures had the important practical advantage that the mean temperatures for all observations of $(\Delta T/\Delta P)_S$ for a given liquid were a constant amount below the temperature of the thermostat, which simplified the mathematical reduction of the data.

been kept unidirectional, the possible change would have been much larger.

(18) The height of oil in the bomb-pipe increased from about 5 to 15 cm. during a series of experiments at different temperatures, because of the expansion of the oil in the bomb. The corresponding variation of the hydrostatic pressure on the cell, which amounted to ±5 millibars, was insignificant in view of the very small change of the temperature–pressure coefficient with pressure (*v. infra*).

(19) Although the application of pressure decreased the height of the oil column slightly, the decrease of the apparent pressure drop was less than 0.002%.

(20) During the course of a series of measurements the working sensitivity of the galvanometer, which varied gradually with change of room temperature, was measured at the beginning of each set of five measurements, by observing in duplicate the galvanometer deflection corresponding to a potential of 5 μv. Just prior to this observation the working current of the potentiometer was balanced against the standard cell.

(21) W. P. White, THIS JOURNAL, **36**, 1856 (1914), p. 1859.

TABLE I

VARIATION OF $(\partial T/\partial P)_S$ WITH PRESSURE

Toluene in Cell A — Thermostat temperature: 26.00 ± 0.01°

Mean temp., °C.	ΔP, bars	ΔT, °C.	$10^2 \times (\Delta T/\Delta P)$, deg./bar	Mean pr., bars	$10^2 \times (\Delta T/\Delta P)$ cor. to 25.70°	$10^5 \Delta$	$10^2 \times (\partial T/\partial P)_S$ at 1 bar, 25.70°
25.49	47.536	1.0289	2.1646	24.3	2.1666	−1.3	2.189
25.55	42.026	0.9104	2.1664	21.5	2.1678	+0.2	2.188
25.61	35.825	.7781	2.1720	18.4	2.1728	−1.8	2.190
25.67	30.313	.6579	2.1703	15.7	2.1706	+3.0	2.185
25.74[a]	24.114	.5246	2.1756	12.6	2.1754	+1.1	2.187
25.74[a]	24.114	.5247	2.1760				
25.80	17.912	.3920	2.1882[b]	9.5	2.1874	....	2.196
25.86	12.400	.2710	2.1852	6.7	2.1837	−1.5	2.189

[a] These two series of determinations were performed on two different days. Their mean was used as a single point in the least squares computation. [b] This value, which was in considerable disagreement with all the others, was neglected in the derivation of the equation.

Experimental Study of Method

Time between Successive Observations.—As the result of one hundred systematic observations of $(\Delta T/\Delta P)$ it was found that when the time between successive observations was six minutes or less the apparent cooling of the liquid was about 0.1% less than when a longer period elapsed, probably because of lack of thermal equilibrium in the cell. Hence it was concluded that the time between successive observations should be not less than ten minutes; and this rule was followed in all subsequent experiments.

Decrease of $(\partial T/\partial P)_S$ with Pressure.—The adiabatic temperature–pressure coefficient of a liquid decreases with increase of pressure, as was demonstrated by Pushin and Grebenshchikov[22] in the case of a number of organic liquids at pressures of 500 to 3000 bars. An extrapolation of their data for benzene at 90° to the relatively low pressure of 10 bars gives −0.059% per bar for the variation with pressure of $(\partial T/\partial P)_S$. Richards and Wallace[6] found no variation with pressure of $(\partial T/\partial P)_S$ over a range of mean pressures from 8 to 13 bars, probably because the error of an individual measurement was great enough to obscure the variation with pressure over such a small range of pressure.

In the present investigation the pressure variation of $(\partial T/\partial P)_S$ of toluene was measured. Eight sets of five observations each were made with the thermostat at 26.00°, using pressure differences of 12 to 47 bars, as shown in Table I. Not only was the range of mean pressures three times as great as that used by Richards and Wallace; but also the precision of the result was increased by making replicate observations at identically the same mean pressure, instead of using a different pressure for each observation, as they had done.

Because the amount of cooling of the liquid varied with the pressure difference, the mean temperature of the liquid varied by 0.4°. Before the results at different pressures could be compared, they had to be corrected to the same mean temperature, for which 25.70° was chosen, because it was in the middle of the range. The correction of $(\Delta T/\Delta P)$ to 25.70° was made in accordance with the linear temperature variation that was determined for this same sample in the same cell by measurements at 20, 22, 24, 26, 28 and 30°. These corrected values of $(\Delta T/\Delta P)$, which are listed in the sixth column of Table I, were fitted by the method of least squares to a linear equation in which the mean pressure was the independent variable, with this result:

$$(\Delta T/\Delta P) = 2.1877 \times 10^{-2} - 9.6 \times 10^{-6}(P - 1) \quad (2)$$

from which it follows that $(\partial T/\partial P)_S$ decreased 0.044 ± 0.005% per bar of mean pressure. The residuals with respect to this equation are given in the next to the last column of Table I. The probable error of a single observation of $(\Delta T/\Delta P)$ computed from these residuals is $\pm 1.4 \times 10^{-5}$. The last column of Table I lists the values of $(\partial T/\partial P)_S$ corrected to atmospheric pressure (1 bar) and the temperature 25.70°, from which it will be seen that the variation that had characterized the original values of $(\Delta T/\Delta P)$ in the fourth column has been reduced considerably by the correction to a uniform temperature and pressure.

Effect of Medium Surrounding the Cell.—The time required for the center of a sphere of liquid to begin to warm up following a sudden release of pressure will be shorter the smaller the radius of the sphere and the larger the thermal

(22) N. A. Pushin and E. V. Grebenshchikov, *J. Chem. Soc.*, **125**, 2043 (1924).

head between the liquid and the enveloping sphere. Although the glass wall of the thermometric cell furnished the maximum thermal head, because its temperature–pressure coefficient was only about 5% as large as that of the Wyrol that surrounded it, the Wyrol did act as a reservoir of heat after an expansion. When toluene was in the cell, for instance, the thermal head glass-to-toluene was 50% greater than the thermal head glass-to-Wyrol. Therefore it was considered possible that with a sphere as small as that used, the excess heat in the Wyrol might have been great enough so that the temperature at the center of the cell would have begun to change before it was measured.[23]

This possibility was investigated experimentally. Three series of measurements were made with portions of the same sample of toluene in Cell A at 2° intervals from 20 to 30°. Series I and II were performed a week apart with Wyrol in the bomb surrounding the cell. Series III was performed two days before Series II with toluene instead of Wyrol in the bomb. The following linear equation was derived by the method of least squares from the combined results of Series I and II:

$$(\partial T/\partial P)_S = 2.1835 \times 10^{-2} + 9.08 \times 10^{-5}(t' - 25) \quad (3)$$

The residuals with respect to this equation are shown in Fig. 4, from which it will be seen that the

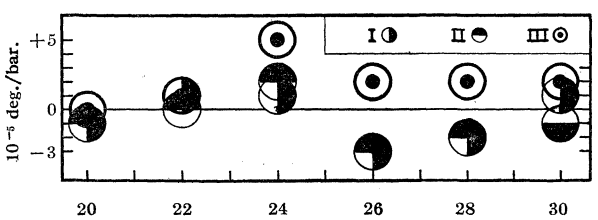

Fig. 4.—Residuals of $(\partial T/\partial P)_S$.

temperature decrease measured when toluene surrounded the cell was a trifle less than that measured when Wyrol surrounded the cell. This difference, which was just about the experimental uncertainty, was opposite that expected if the medium surrounding the cell had affected the measured temperature difference. Hence it was concluded that the use of Wyrol as the pressure-transmitting liquid introduced no error.

(23) Dr. William T. Richards has suggested in a private communication that the effect of radiation on the thermocouple was negligibly small. His opinion is supported by a calculation based on Kirchoff's law and the Stefan–Boltzmann law, which shows that the thermocouple would have been heated less than 0.0001°, if it is assumed that (a) the liquid in the cell transmitted only 0.1% of the black body radiation corresponding to temperatures below 110° and (b) the thermocouple junction absorbed 50% of the radiation incident upon it.

Contamination by Wyrol.—The data in Fig. 4 indicate that the mercury in the gooseneck of the cell acted as a complete barrier to the entrance of Wyrol. The measurements at 30° with Wyrol in the bomb gave results slightly higher than those with toluene in the bomb; whereas if a little Wyrol had slipped past the mercury during the previous twenty-five applications and releases of pressure, it would have lowered $(\partial T/\partial P)_S$.

Precision and Accuracy.—The *a priori* estimates of the probable errors involved in the measurement of the temperature–pressure coefficient of a liquid with the apparatus that has been described are summarized in Table II, which lists the effect on $(\partial T/\partial P)_S$ from each such error.

The data presented in Fig. 4 for $(\partial T/\partial P)_S$ of toluene measured on different days with the same cell illustrate the validity of these estimates of the total observational errors at a single temperature. The root mean square deviation of each value of $(\partial T/\partial P)_S$ from the mean of a pair of duplicates on different days was ±0.02%; the estimate given in Table II is ±0.06%.

TABLE II

ESTIMATED PROBABLE ERROR OF $(\partial T/\partial P)_S$

	Observed quantity	Errors, % Observational	Errors, % Systematic
1.	Pressure difference		
	a. Gage weights	±0.001	±0.001
	b. Piston area	.....	± .05
	c. Height of oil in gage	± .005	.....
	d. Temperature of gage	± .005	.....
2.	Electromotive force		
	a. Potentiometer coils	.....	± .07
	b. Battery current	± .01	.....
	c. Galvanometer deflection (for mean of five replicates)	± .05	.....
3.	Thermoelectric power of thermel	.....	± .18
4.	Temperature of thermostat	± .015	.....
5.	Pressure correction[a]	.....	± .05
	Total	±0.06	±0.21

[a] See p. 688 for a discussion of the uncertainty of the pressure correction at higher temperatures.

Confirmation of the estimates of the other errors, including some of the systematic ones, was sought by making measurements with the same sample of liquid in two different individually calibrated cells at 2° intervals from 20 to 30°. All the values of $(\partial T/\partial P)_S$ both of benzene and of toluene obtained with Cell A were less than those obtained with Cell B. The root mean square deviation of each individual value from the mean

of a pair of duplicates was ±0.10% for benzene and ±0.22% for toluene; whereas the combined value of the estimates of both the observational and systematic probable errors in Table II is ±0.22%.

Samples

Distillation Apparatus.—As the final step in its purification each sample was distilled in an all-glass apparatus that had interchangeable distilling flasks and interchangeable receivers. The round distilling flasks used were of different diameters, but each had a straight tube 3 cm. long and 1.5 cm. in diameter sealed on the bottom. An electric heater was wound on a copper tube that fitted snugly over this extension. Thus boiling took place in this small space, which had a volume of only 6 ml. An inverted cone of sheet copper resting on the upper surface of the distilling flask prevented excessive condensation there. The vacuum-jacketed column, 60 cm. high, which was packed with one-turn glass helices,[24] was surmounted by a reflux condenser. The progress of a distillation was followed by measurement of the refractive index of successive small fractions with an Abbé refractometer. The absolute accuracy of the refractive indices was not known, but the relative precision was ±0.0001.

Benzene.—Some Merck "reagent grade benzene, thiophene-free" was purified by treatment with the following reagents in succession: concentrated sulfuric acid, water, a dilute solution of sodium hydroxide, water, calcium chloride, hot mercury, and phosphorus pentoxide. Then it was fractionated. The refractive index was raised 0.0003 by the purification.

Toluene A.—Sample A, which was purified only slightly in order to give a basis of comparison for the highly purified Samples B and C, was obtained by distillation of 120 ml. of C. P. toluene from the General Chemical Company. After 50 ml. had passed over, a fraction of 6 ml. was preserved. Its refractive index was 0.0007 higher than that of the original material, but 0.0008 lower than that of Samples B and C.

Toluene B.—Some Baker C. P. toluene was purified by treatment with the following reagents in succession: hot mercury, concentrated sulfuric acid, water, a dilute solution of sodium hydroxide, water, calcium chloride, and phosphorus pentoxide. After fractionation, it was refluxed over sodium for two hours, and then fractionated from it. The refractive index was unchanged by this last distillation.

Toluene C.—Some Merck "reagent grade toluene" was purified principally by the preparation of toluenesulfonic acid,[25] from which the toluene was regenerated by distillation with superheated steam. It was treated further with concentrated sulfuric acid, water, a dilute solution of sodium hydroxide, water, and calcium chloride in turn. After having been refluxed over sodium for two hours, it was fractionated from the sodium. A forerun of 3 ml. was discarded, and the other fractions were mixed and refluxed over fresh sodium for an hour, after which the final sample was distilled off in several fractions, all of which had the same refractive index, which was only 0.0001 higher than that of the starting material. It was the same as the index of Sample B.

Effect of Impurities on $(\partial T/\partial P)_S$.—Six series of measurements, consisting of five replicates each, were made at 2° intervals from 20 to 30° with each sample of toluene in Cell A. The mean value for each sample, which was $(\partial T/\partial P)_S$ at 25°, was $(2.1808 \pm 0.0014) \times 10^{-2}$ deg./bar for Sample A, $(2.1827 \pm 0.0007) \times 10^{-2}$ for B, and $(2.1830 \pm 0.0004) \times 10^{-2}$ for C. In other words, Samples B and C were indistinguishable as far as $(\partial T/\partial P)_S$ was concerned although $(\partial T/\partial P)_S$ for the slightly impure sample was 0.1% lower than for the pure ones.

Experimental Data

Definitive measurements of $(\partial T/\partial P)_S$ of benzene and of toluene (Sample C) were made with Cell B at 3° intervals from 8° to the respective b. p., with the results shown in Tables III and IV: where t', the mean temperature of the liquid during an expansion, equals the thermostat temperature minus $\Delta T/2$; ΔP is the instantaneous pressure drop; and ΔT is the accompanying decrease of temperature.

TABLE III

MEASUREMENTS OF TEMPERATURE–PRESSURE COEFFICIENT OF BENZENE

t', °C.	ΔP, bars	ΔT, °C.	$10^2 \times (\Delta T/\Delta P)$, deg./bar	$10^2 \times (\partial T/\partial P)_S$, deg./bar	$10^5 \times \Delta$[a]
7.80	18.604	0.40927	2.1999	2.2080	+24
10.79	18.604	.41551	2.2334	2.2417	+ 9
13.79	18.604	.42209	2.2688	2.2773	−22
16.79	17.914	.41182	2.2989	2.3072	+ 5
19.79	17.912	.41726	2.3295	2.3379	+27
22.80	17.223	.40754	2.3663	2.3744	− 6
25.79	17.224	.41341	2.4002	2.4084	−11
28.80	16.534	.40216	2.4323	2.4402	+10
31.80	16.534	.40824	2.4691	2.4772	−17
34.80	15.845	.39683	2.5044	2.5122	−19
37.81	15.155	.38467	2.5382	2.5457	− 1
40.80	15.155	.39093	2.5795	2.5872	−57
43.80	15.155	.39579	2.6116	2.6194	−14
46.81	14.465	.38317	2.6489	2.6563	−11
49.81	14.465	.38838	2.6850	2.6925	+ 6
52.81	13.774	.37460	2.7196	2.7268	+49
55.81	13.774	.37999	2.7587	2.7660	+51
58.81	13.774	.38644	2.8056	2.8130	−17
61.81	13.087	.37268	2.8477	2.8548	−24
64.81	13.087	.37906	2.8965	2.9038	−93
67.84	12.399	.36224	2.9215	2.9281	+94
70.82	12.400	.36816	2.9690	2.9759	+56
73.81	12.400	.37405	3.0165	3.0236	+30
76.82	11.712	.35892	3.0645	3.0712	+16
79.82	11.712	.36562	3.1218	3.1286	−85

[a] Δ = *calcd.* minus *exptl.*

Each value of the apparent temperature–pressure coefficient $(\Delta T/\Delta P)$ was corrected to a mean

(24) C. D. Wilson, G. T. Parker and K. C. Laughlin, THIS JOURNAL, **55**, 2795 (1933); E. E. Roper, G. F. Wright, J. R. Ruhoff and W. R. Smith, *ibid.*, **57**, 954 (1935).

(25) A. F. Holleman and P. Caland, *Ber.*, **44**, 2504 (1911).

TABLE IV

MEASUREMENTS OF TEMPERATURE–PRESSURE COEFFICIENT OF TOLUENE

t', °C.	ΔP, bars	ΔT, °C.	$10^2 \times (\Delta T/\Delta P)$, deg./bar	$10^2 \times (\partial T/\partial P)_S$, deg./bar	$10^6 \times \Delta$[a]
7.79	20.668	0.41892	2.0269	2.0355	+ 9
10.79	19.980	.41002	2.0522	2.0605	+21
13.79	19.981	.41563	2.0801	2.0885	+ 5
16.80	19.291	.40616	2.1054	2.1135	+21
19.80	18.605	.39637	2.1304	2.1383	+41
22.80	18.604	.40183	2.1599	2.1679	+15
25.80	18.601	.40690	2.1875	2.1956	+11
28.80	17.911	.39749	2.2193	2.2272	−29
31.80	17.911	.40188	2.2438	2.2518	+ 4
34.80	17.224	.39151	2.2730	2.2807	− 2
37.80	17.224	.39706	2.3053	2.3131	−38
40.81	16.534	.38624	2.3360	2.3435	−50
43.80	16.534	.39109	2.3654	2.3731	−50
46.80	15.845	.38000	2.3982	2.4057	−73
49.81	15.844	.38348	2.4203	2.4278	+13
52.81	15.155	.37174	2.4529	2.4601	+ 4
55.81	15.155	.37718	2.4888	2.4961	−36
58.81	15.155	.38168	2.5185	2.5259	− 7
61.82	14.467	.36917	2.5518	2.5588	− 2
64.81	14.467	.37428	2.5871	2.5943	−16
67.81	14.467	.37838	2.6155	2.6228	+48
70.82	13.776	.36560	2.6539	2.6608	+26
73.82	13.776	.37090	2.6924	2.6994	+ 6
76.82	13.088	.35660	2.7246	2.7313	+61
79.80	13.087	.36193	2.7656	2.7726	+32
82.77	13.087	.36701	2.8044	2.8118	+34
85.76	12.400	.35303	2.8470	2.8542	+13
88.80	12.400	.35870	2.8927	2.8996	−27
91.81	12.400	.36334	2.9302	2.9371	+23
94.78	11.712	.34861	2.9765	2.9834	− 5
97.82	11.712	.35385	3.0213	3.0279	− 3
100.83	11.712	.35911	3.0662	3.0728	+ 7
103.83	11.023	.34342	3.1155	3.1217	−11
106.81	11.023	.34865	3.1629	3.1394	− 5
109.83	11.023	.35450	3.2160	3.2225	−40

[a] Δ = *calcd.* minus *exptl.*

pressure of 1 bar by means of the pressure coefficient −0.044% per bar that had been found[26] for toluene at 25.7°. This same coefficient was used to correct the measurements at all temperatures, for the pressure variation of $(\partial T/\partial P)_S$ was not measured at other temperatures because of lack of time. A change with temperature of ±50% in the pressure variation would cause an error of only ±0.2% in $(\partial T/\partial P)_S$. It is assumed[27] also that within these limits the same correction applies to benzene. When the mean temperature differed by a few hundredths of a degree from a value of 0.20° less than a whole degree, a correction amounting to 1×10^{-6} deg./bar for each hundredth of a degree was applied to $(\Delta T/\Delta P)$, so that the corrected values of $(\partial T/\partial P)_S$ in the fifth column refer to a mean pressure of 1 bar and a mean temperature 0.20° less than the whole degree next higher than that shown in the first column.

$(\partial T/\partial P)_S$ as a Function of Temperature.—Search for a suitable temperature function was made by analysis of the data for toluene by means of first, second, and third differences according to the plan outlined by Running.[28] Twelve three-parameter functions were tested by evaluating their parameters at the end and middle points and then computing two intermediate points. A cubic equation without a quadratic term and a double logarithmic equation involving the absolute temperature were the only ones that were very promising. These two together with the full cubic equation (four parameters) were investigated more carefully by evaluating their parameters by the method of least squares, using all the points. The probable error of an individual observation based on the residuals did not vary more than 10% for these three equations. The double logarithmic equation was discarded, however, because of a pronounced trend in the signs of the residuals. The data for benzene also were fitted to three- and four-parameter cubic equations by the method of least squares. The probable error of an individual observation was the same for both equations. Therefore, since the three-parameter cubic equation gave as good a general representation of the data for $(\partial T/\partial P)_S$ of both benzene and toluene as did the four-parameter cubic, it was preferred in the interest of simplicity.

computed by means of this equation

$$\left[\frac{d}{dP}\left(\frac{\partial T}{\partial P}\right)_S\right]_T = \frac{T}{(c_p)^2}\left\{c_p\left[\frac{d}{dP}\left(\frac{\partial V}{\partial T}\right)_P\right]_T - \left(\frac{\partial V}{\partial T}\right)_P\left(\frac{\partial c_p}{\partial P}\right)_T\right\} \quad (4)$$

using data from the present investigation for the other terms. At 25° $d(\partial T/\partial P)_S/dP$ is −0.054 ± 0.006% per bar. At higher temperatures the computed value increases numerically to −0.084% at 80°; but inasmuch as this temperature slope is due to a similar slope in $d(\partial V/\partial T)_P/dP$, and inasmuch as this slope was derived from a quadratic equation passed through four points based on measurements at a maximum temperature of 65°, the increase of $d(\partial T/\partial P)_S/dP$ may have been exaggerated.

(26) *Cf.* eq. (2).

(27) This assumption is substantiated partially by a calculation of $d(\partial T/\partial P)_S/dP$ that is made possible by the recently published data of R. E. Gibson and J. F. Kincaid [THIS JOURNAL, **60**, 511 (1938)] for the variation with pressure of the coefficient of thermal expansion of benzene. From the parameters in the equations for the coefficient of thermal expansion at five different pressures from 1 to 1000 bars, given in their Table V, the value of $d(\partial V/\partial T)_P/dP$ has been computed to be -8.6×10^{-7} (cc./g.-deg.)/bar at 25° and a mean pressure of 10 bars. The pressure variation of $(\partial T/\partial P)_S$ has been

(28) T. R. Running, "Empirical Formulas," John Wiley and Sons, Inc., New York, N. Y., 1917.

The equations evaluated by least squares were:

$$[C_6H_6]\quad (\partial T/\partial P)_S = 2.12695 \times 10^{-2} + 1.06806 \times 10^{-5}t + 2.7715 \times 10^{-9}t^3 \quad (5)$$

$$[C_7H_8]\quad (\partial T/\partial P)_S = 1.96840 \times 10^{-2} + 8.6990 \times 10^{-5}t + 2.2285 \times 10^{-9}t^3 \quad (6)$$

The residuals with respect to these equations are listed in the last column of Tables III and IV, respectively. The probable error of an individual observation based on the residuals was $\pm 2.9 \times 10^{-5}$ and $\pm 2.0 \times 10^{-5}$, respectively. These values are less than twice as great as the *a priori* estimates of the total observational probable error given in Table II. Values of $(\partial T/\partial P)_S$ for benzene and toluene computed at 5° intervals from equations (5) and (6) are listed in Table II of the paper[8] on the heat capacity of these liquids.

Comparison of Data.—A comparison of the present data with those of Richards and Wallace[6,29] is given in Table V. The differences between the two sets of data are actually larger than they appear at first, because the present values have been raised 7×10^{-5} on the average by the correction to 1 bar and also because the values of Richards and Wallace refer to the temperature of the thermostat rather than to the mean temperature of the liquid during the expansion. Inasmuch as the liquid cooled during the expansion, the value of $(\partial T/\partial P)_S$ that they reported for a particular temperature is a little too small. If we may judge from the data for benzene at 40° in their Table I, $(\partial T/\partial P)_S$ should be raised 3×10^{-5}. For the purpose of computing the deviations between the two sets of data, given in Table V, the values of Richards and Wallace have been increased by 1×10^{-4}. Except for the results at 20°, the agreement is fairly satisfactory.

(29) Their original values have been changed from the unit "deg./atm." to "deg./bar" by multiplication by the factor 0.98692 atm./bar.

TABLE V

COMPARISON OF DATA FOR $(\partial T/\partial P)_S$ WITH RESULTS OF RICHARDS AND WALLACE

$10^2 \times (\partial T/\partial P)_S$ in deg./bar

	Benzene			Toluene		
t, °C.	Burlew	R. & W.	Dev.,[a] %	Burlew	R. & W.	Dev.,[a] %
20	2.343	2.365	+1.4	2.144	2.162	+1.3
30	2.455	2.470	+1.0	2.235	2.242	+0.8
40	2.572	2.583	+0.8	2.331	2.334	+ .6
50	2.696	2.696	+ .4	2.431	2.438	+ .7

[a] Dev. = (*R. & W.* plus 1×10^{-4}) minus *Burlew* (see text).

Acknowledgments.—It is a pleasure to acknowledge the encouragement and advice given by Professor Donald H. Andrews during the course of this research. I thank Professor Herbert S. Harned and the other members of the staff of the Department of Chemistry at Yale University for their kindness in making available facilities for research. I am indebted to Mr. H. S. Bittner and Mr. Harry Johns of the Chemistry Shop, Johns Hopkins University, and to Mr. J. M. Berney, Mr. H. G. Cady, Mr. Wm. Duncan and Mr. F. P. Noble of the Chemistry Shop, Yale University, for the interest they took in the careful fabrication of the apparatus.

Summary

An apparatus has been described for the measurement of $(\partial T/\partial P)_S$ of 5 ml. of a liquid, the precision of the observations has been discussed, and the use of the apparatus has been illustrated by data for benzene and toluene at 3° intervals from 8° to the respective boiling points.

NEW HAVEN, CONN. RECEIVED SEPTEMBER 21, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

Measurement of the Heat Capacity of a Small Volume of Liquid by the Piezo-thermometric Method. II. Coefficient of Thermal Expansion of Benzene and of Toluene Measured with a New Type of Weight Dilatometer

BY JOHN S. BURLEW[1]

In the application of the piezo-thermometric method[2] to the measurement of the heat capacity of a sample of liquid as small as 5 cc., it is necessary to have a means of measuring the coefficient of thermal expansion of this quantity of liquid with a probable error of not more than $\pm 0.3\%$ over a wide range of temperature, without regard to the volatility of the liquid. The weight dilatometer (Fig. 1) devised for the purpose is similar in design to the Meyer–Neubeck pycnometer,[3a] except that in the present dilatometer a fixed weight of liquid is confined by mercury, so that the instrument may be used at any temperature up to the temperature of the boiling point.

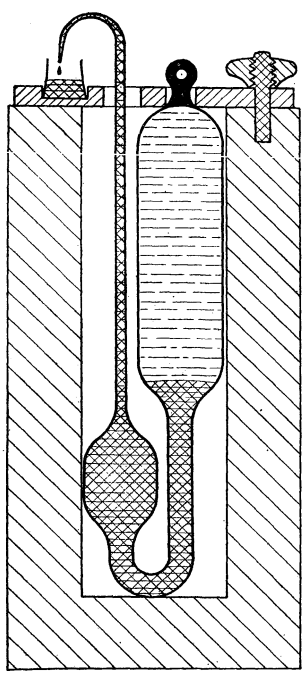

Fig. 1.—Weight dilatometer in steel holder (scale, 2/3).

The principle of this weight dilatometer is that the volume of liquid present at a given temperature can be computed from the weight of mercury contained at a reference temperature and the amount expelled when the dilatometer is heated to the given temperature, the volume of liquid present at the reference temperature being known. The total volume of the dilatometer at any temperature is equal to the sum of the volume of the liquid and the volume of mercury. Expansion of this fundamental relation in terms of the quantities actually measured gives the following equation[4] for the specific volume

$$v_t = \frac{1}{w}\left\{V_\Theta\,[1 + a(t - \Theta)] - \frac{w'_\Theta - w^*_t}{d'_t}\right\} \qquad (1)$$

Dilatometers employing this same principle have been described by Pesce and Hölemann[5] and by Jones and Jelen.[6] Each of them was larger and more elaborate, but furnished results no more precise. The present instrument recently has been adapted[7] to use with solutions.

Weight Dilatometer

Holder.—The dilatometer fitted into a circular hole drilled in a steel cylinder, as shown in Fig. 1. A circular cover plate screwed to the top of the cylinder kept the dilatometer submerged in the mercury with which the hole was filled. The glass ring at the rounded end of the dilatometer projected through a hole in the cover plate, and the capillary neck emerged through a notch cut in its side. The main portion of the dilatometer, which had been blown from 15-mm. pyrex glass tubing, had a volume of 3.5 cc.; the smaller tube and capillary 0.5 cc.; and the bulb 1 cc. The orifice at the end of the capillary neck was less than 0.1 mm. in diameter. A glass cup (6 by 7 mm.) that rested in a small recess cut in the cover plate,[8] caught the overflow of mercury from the capillary neck when the temperature was raised.

Thermostat.—A region of uniform temperature for the dilatometer was provided by an aneroid thermostat:

(1) Sterling Fellow, 1934–1936; present address: Geophysical Laboratory, Washington, D. C.

(2) See paper I of this series, THIS JOURNAL, **62**, 681 (1940).

(3) F. Neubeck, *Z. physik. Chem.*, **1**, 649 (1887); (a) p. 652; (b) pp. 654 and 656.

(4) The symbols used in this paper are as follows: v_t is the specific volume of the liquid under investigation; V_t is the total volume of the dilatometer; V'_t is the volume of mercury in the dilatometer; W_t is the total weight of the contents of the dilatometer; w is the constant weight of liquid in the dilatometer; w'_t is the weight of mercury in the dilatometer; w^*_t is the weight of mercury expelled between a temperature t and the next lower temperature at which an observation was made; d_t is the density of the liquid; d'_t is the density of mercury; and a is the coefficient of thermal expansion of the dilatometer. The subscript t refers to any temperature and the subscript Θ refers to an arbitrary reference temperature.

(5) G. Pesce and P. Hölemann, *Z. Elektrochem.*, **40**, 1 (1934).

(6) G. Jones and F. C. Jelen, THIS JOURNAL, **57**, 2532 (1935).

(7) R. E. Gibson and O. H. Loeffler, THIS JOURNAL, **61**, 2515 (1939).

(8) Figure 1 shows the dilatometer as if it had been rotated through an angle of 90° with respect to the diameter of the cover plate passing through the cup and the wing nut.

a brass cylinder that stood on three legs on the bottom of an oil thermostat. To the top of this cylinder, which was 7 cm. in diameter and 12 cm. high, was soldered a cylindrical extension about 20 cm. long, made from sheet copper, the upper end of which reached just above the surface of the oil. The steel holder for the dilatometer fitted snugly into an axial hole in the brass cylinder. It was raised and lowered by a stiff wire handle that was screwed into its top. The upper end of the aneroid thermostat was closed with a cork. In this way it was not necessary to make any correction for the small length of capillary that was not immersed in the mercury in the holder, for it was at substantially the same temperature as the immersed part.

Filling.—The dilatometer was filled by suction in a test-tube (4 by 18 cm.) provided with two side-arms carrying stopcocks. One was connected to an aspirator or vacuum pump and the other to a calcium chloride tube open to the air. First the dilatometer was hung by its capillary neck from a small cup filled with mercury. By evacuating the tube and then admitting dry air, mercury was forced into the dilatometer.

The dilatometer was turned upside down, and the mercury was shaken into the main portion of the instrument. A sample of the liquid to be studied, freshly boiled and then cooled to about 50° below its boiling point, was placed in a glass cup that rested on the bottom of the filling tube, and the capillary neck of the inverted dilatometer was submerged in it. The liquid was placed in the cup instead of directly in the filling tube in order to decrease the volume needed. The filling tube was evacuated until the liquid began to boil, when evacuation was stopped. Air was admitted slowly to the filling tube, whereupon the liquid rushed into the dilatometer. The lower end of the filling tube was cooled with ice water, so that when the tube was evacuated a second time the last traces of air were removed from the dilatometer by the boiling of the warm liquid in it, without boiling the liquid that remained in the filling cup. When air was readmitted to the filling tube, liquid completely filled the dilatometer, except for a tiny bubble at the top of the bend. This bubble was removed through the capillary stem by gently warming the instrument until a small quantity of mercury had been expelled. The capillary tube was dried on the inside by alternately cooling and heating the dilatometer half a dozen times.

Determination of w.—The dilatometer next was filled completely at a convenient reference temperature (t_Θ) near room temperature. It was placed in warm water until mercury began to be expelled, after which it was cooled to slightly below t_Θ while the nose of the capillary was held under the surface of mercury. Then it was placed in its steel holder in the aneroid thermostat at t_Θ for at least forty minutes; the steel holder previously had been in the thermostat at t_Θ. From the weight of the dilatometer after having been filled at t_Θ in this manner, the amounts of mercury and of liquid contained were computed by means of equations (3) below.

It is possible to measure w and w'_Θ directly at the time of filling the dilatometer (this was done during the calibration), but during routine measurements it is preferable to derive them from the total weight (W_Θ) of the contents of the dilatometer and the total volume (V_Θ). This procedure permits the use of a permanent table of volumes of the dilatometer, and also it does away with one tedious step in the filling of the instrument—namely, catching and weighing the mercury that is expelled when the final air bubble is being removed. The indirect determination of w and of w'_Θ is based on the simultaneous solution of two equations

$$W_\Theta = w + w'_\Theta = (V - V')_\Theta\, d_\Theta + (V'd')_\Theta \quad (2)$$

which gives

$$w = \left\{\left(\frac{d}{d' - d}\right)_\Theta\right\}\left\{(Vd')_\Theta - W_\Theta\right\} \quad (3a)$$

$$w'_\Theta = W_\Theta - w \quad (3b)$$

In one filling of the dilatometer with benzene, w was determined both directly and indirectly, with a difference of 0.4 mg. between the two values, which is good agreement, inasmuch as the direct determination involved four weighings for each of which the probable error was ±0.1 mg.

Measurements.—Although measurements at different temperatures could be made in any order desired, it was convenient to start a series of them with the weight dilatometer at 0° if possible. The dilatometer was filled at 0° by being packed in ice with its nose in a cup of mercury. Handling of the instrument during its transfer to the thermostat that had been set at the next higher temperature was facilitated by chilling it below 0° by pouring strong brine over the ice. After the dilatometer had been in the aneroid thermostat at a constant temperature for one hour, with a receiving cup under the end of the capillary tip, the cup was replaced by an empty one, and the temperature of the thermostat was raised to the next higher temperature; and so on.

Calibration.—The weight dilatometer was calibrated by means of a series of measurements with water at 10° intervals from 10 to 90°. The weight of mercury and water contained at 30° was determined separately, and then the mercury expelled during the successive heating periods was weighed. The specific volume of mercury was computed by the following formula given by Scheel and Blankenstein[9]

$$1/d'_t = 0.0735560(1 + 1.8182 \times 10^{-4}t + 7.8 \times 10^{-9}t^2)\ \text{cm.}^3/\text{g.} \quad (5)$$

The density of water in g./cc. was computed from the density in g./ml. listed in the "Int. Crit. Tables."[10] The values for the volume of the dilatometer at different temperatures, computed according to eq. (1), were fitted to a linear equation in t by the method of least squares, with this result

$$V_t(\text{cm.}^3) = 5.29379 + 5.625 \times 10^{-5}t \quad (6)$$

The relative probable error of V_t based on the residuals with respect to this equation was $\pm 2 \times 10^{-5}$ at the ends of the range, and only $\pm 0.8 \times 10^{-5}$ in the middle. The systematic probable error, however, was $\pm 3 \times 10^{-4}$, because of the uncertainty in the weight of water contained.

The coefficient of thermal expansion of the pyrex glass of the dilatometer as determined by this calibration was $1.063 \pm 0.005 \times 10^{-5}$. This value differs by 7.8% from that of 0.985×10^{-5} reported by Jones and Jelen[6] for their dilatometer; but the difference is not surprising

(9) K. Scheel and F. Blankenstein, *Z. Physik*, **31**, 202 (1925).
(10) "Int. Crit. Tables," Vol. III, pp. 25–26.

in view of the different heat treatments of the two instruments.

Precision and Accuracy

Systematic tests demonstrated that the dilatometer, if left in the thermostat for at least thirty minutes, could be filled at a particular temperature with an error not greater than the error of weighing, namely, ± 0.1 mg.

The question of whether the mercury used as a confining liquid had the same density and coefficient of expansion as that used by Scheel and Blankenstein did not affect the accuracy of the specific volume measurements made with the weight dilatometer, because about the same quantity of the same mercury was used during both the calibration and the volume measurements.

The systematic probable error for the present dilatometer (caused by the uncertainty in the weight of liquid contained compared with the weight of water contained during the calibration) was $\pm 0.01\%$. This uncertainty, which limits the accuracy of the measurements of specific volume, does not affect their relative precision; hence its effect on the accuracy of the coefficient of thermal expansion is negligible.

The maximum relative probable error of the total volume (caused by the uncertainty in the coefficient of expansion of the dilatometer) was $\pm 2 \times 10^{-5}$ cc., and that of the volume of mercury at any particular temperature (caused by the uncertainty[11] in the weight of mercury contained at different temperatures) was $\pm 4 \times 10^{-5}$ cc. Inasmuch as it is the difference of these two volumes that is proportional to the specific volume of liquid, the relative probable error of the latter was $\pm 6/w \times 10^{-5}$ cc./g., which became $\pm 0.0017\%$, when w, the weight of liquid contained, was 3.5 g.

The fourth source of error was the uncertainty in the temperature observations. Its contribution[12] to the total uncertainty in the specific volume is proportional both to the probable error of the temperature and to the coefficient of thermal expansion.

Combination of the errors from these four sources yields the following *a priori* estimates of the total probable error of the specific volume in the middle of the range: $\pm 3.5 \times 10^{-5}$ cc./g.-deg. for benzene and $\pm 4.4 \times 10^{-5}$ cc./g.-deg. for toluene.

The functional relation between the specific volume and the temperature should be derived by the method of least squares under the condition[13] that both these variables are subject to error. The labor of computation may be reduced considerably without violating this condition, if the observations are arranged to be made at equal intervals of temperature and with the probable errors approximately the same (say within a factor of two) for all points. Then the equation can be evaluated from the points distributed symmetrically on each side of the mid-point of temperature, each point being considered of unit weight.

Influence of Number of Observations

The relation of the probable error of the coefficient of thermal expansion to the probable error of the specific volume of a liquid depends considerably on the number of values of the specific volume at different temperatures and on their distribution. In order to find out how many observations with the weight dilatometer were needed to furnish a reliable value of the expansion, the proportional probable error of the coefficient of thermal expansion was computed[14] for different values of n, the number of observations, and of x, the independent variable. The results are given in Table I. Each curve of specific volume was assumed to have its points distributed symmetrically on either side of the mid-point ($x = 0$) from $x = -(n-1)/2$ to $+(n-1)/2$ and was assumed to be represented by a cubic equation.

From Table I it may be seen that over more than half the range of a cubic curve the probable error of the slope is not greater than it is at the mid-point, whereas at the ends of the range it is regularly nearly four times as large. Hence the probable error of the slope at the mid-point, which is very easy to compute, is a useful indicator of the reliability of the slope throughout the course of the curve.

(11) The errors of weighing the separate portions of mercury expelled, which are cumulative, can be minimized by weighing the dilatometer after it has been at the maximum temperature and then adjusting the individual values of w^*. When this is done the probable error in a single value of $(w'_\Theta - w^*_t)$ does not exceed ± 0.5 mg., which is equivalent to an uncertainty of $\pm 4 \times 10^{-5}$ cc. in the volume.

(12) For a liquid with an expansion of 0.001 cc./g.-deg. this contribution is 0.001% for a temperature uncertainty of 0.01°. Hence a weight dilatometer of the dimensions given above is sufficiently precise to make it worthwhile to employ a thermometer having a relative probable error of $\pm 0.005°$ for measurements with organic liquids having coefficients of thermal expansion about 0.0015. In that case the total uncertainty in the specific volume would be a little less than $\pm 2 \times 10^{-5}$ cc./g.-deg. In order to reduce it to one-half this amount, the dilatometer would have to be enlarged to three times its present volume.

(13) W. E. Deming, *Phil. Mag.*, **11**, 146 (1931).

(14) For the method of computation, suggested originally by Gauss see H. Schultz, *J. Am. Stat. Assoc.*, **25**, 139 (1930).

TABLE I

PROPORTIONAL PROBABLE ERROR OF COEFFICIENT OF THERMAL EXPANSION[a] (IN %)

x	$n = 15$	$n = 21$	$n = 25$	$n = 31$	$n = 35$	$n = 41$	$n = 45$
0	±0.38	±0.23	±0.18	±0.13	±0.11	±0.08	±0.07
2	.31	.21	.16	.12	.10	.08	.07
5	.62	.20	.14	.10	.09	.07	.06
7	1.33	.37	.19	.10	.08	.06	.06
10	....	.82	.42	.19	.12	.07	.06
12		....	.64	.28	.15	.10	.07
15			....	.47	.26	.16	.12
17				....	.40	.22	.15
20					....	.32	.22
22						....	.28

[a] Assumptions: (1) Coefficient of thermal expansion = 0.001 cc./g.-deg. (2) $v_t = a + bt + ct^2 + dt^3$. (3) Probable error of single observation of sp. vol. = $\pm 2.5 \times 10^{-5}$ cc./g.

Table I shows also that for any given value of x an increase in the number of observations causes a decrease in the probable error of the slope at a diminishing rate. Hence a table such as this helps one decide the number of observations demanded by a certain desired accuracy.

Experimental Data

Measurements of the coefficient of thermal expansion of benzene and of toluene (Sample C) were made with the weight dilatometer using the same samples that were used for the measurement[2] of $(\partial T/\partial P)_S$. The dilatometer was heated in the same oil thermostat used for the piezo-thermometric bomb, and so the temperature uncertainties were the same as previously listed,[2] namely: a probable error of ±0.02 up to 50°; ±0.03 from 50 to 80°; and ±0.02 from 80 to 110°. The weight[15] of liquid contained was computed from a weighing at 25° and the density of the liquid, for which the mean of a series of measurements with a 2-ml. Sprengel–Perkin pycnometer[16] at 1° intervals from 20 to 30° was used. Evidence that the liquids were air-free was furnished by the fact that successful measurements were made less than 1° below the normal b. p.

TABLE II

MEASUREMENTS WITH WEIGHT DILATOMETER CONTAINING BENZENE

W_{25} = 20.9496; d'_{25} = 13.5335; d_{25} = 0.87387. Therefore: w = 3.5006 g.; w'_{25} = 17.4490 g.

t, °C.	w^*, g.	v, cc./g.	$10^5 \times \Delta$[a]
8.00	.....	1.12132	− 9
11.00	0.1918	1.12520	+ 2
14.00	.1988	1.12923	+ 2
17.05	.2007	1.13329	+10
20.00	.2023	1.13740	+ 2
23.00	.2040	1.14155	+ 1
25.00	.....	**1.14434**	....
26.00	.2057	1.14574	± 0
29.00	.2075	1.14997	− 1
32.00	.2085	1.15422	+ 1
35.00	.2107	1.15854	− 2
38.00	.2135	1.16291	− 5
41.00	.2125	1.16727	− 2
44.00	.2143	1.17166	+ 2
47.00	.2187	1.17616	± 0
50.00	.2220	1.18073	− 4
53.00	.2185	1.18524	+ 2
56.00	.2222	1.18982	+ 6
59.00	.2298	1.19458	− 3
68.02	.6904	1.20889	+ 1
71.00	.2308	1.21369	+ 6
74.00	.2400	1.21868	± 0
77.00	.2386	1.22366	± 0
80.00	.2439	1.22875	− 4

[a] Δ = *calcd.* minus *exptl.*

TABLE III

MEASUREMENTS WITH WEIGHT DILATOMETER CONTAINING TOLUENE

W_{25} = 20.8059 g.; d'_{25} = 13.5335; d_{25} = 0.86220. Therefore: w = 3.4605 g.; w'_{25} = 17.3454 g.

t, °C.	w^*, g.	v, cc./g.	$10^5 \times \Delta$[a]
8.00	.....	1.13903	−4
11.00	0.1765	1.14262	−1
14.00	.1768	1.14623	+2
17.00	.1806	1.14992	±0
20.00	.1804	1.15361	+1
23.00	.1809	1.15731	+3
25.00	.....	**1.15983**	...
26.00	.1837	1.16108	+2
29.00	.1853	1.16489	−1
32.00	.1834	1.16866	+3
35.00	.1886	1.17247	+6
38.00	.1882	1.17643	−2
41.00	.1886	1.18033	−1
44.00	.1902	1.18426	+1
46.98	.1925	1.18825	−3
50.00	.1957	1.19231	−4
53.00	.1932	1.19632	±0
56.00	.1984	1.20045	−2
58.97	.1997	1.20461	−7
62.00	.2008	1.20880	−4
65.00	.2009	1.21299	±0
71.00	.4099	1.22157	+1
74.00	.2087	1.22594	+1
77.00	.2098	1.23035	+2
82.95	.4248	1.23929	±0
85.94	.2155	1.24383	+1
88.98	.2216	1.24851	±0
94.96	.4413	1.25785	+5
98.00	.2308	1.26274	±0
101.01	.2269	1.26755	+5
104.00	.2330	1.27251	−1
106.98	.2321	1.27745	−1
110.00	.2386	1.28254	−4

[a] Δ = *calcd.* minus *exptl.*

(15) All weights were corrected for air buoyancy.

(16) H. Sprengel, *J. Chem. Soc.*, **26**, 577 (1873); W. H. Perkin, *ibid.*, **45**, 421 (1884).

TABLE IV

NOTES ON PREVIOUS MEASUREMENTS OF THE COEFFICIENT OF THERMAL EXPANSION OF BENZENE AND OF TOLUENE

Observer	Method	Temp. control	No. obs.	Interval	Probable error $10^5 \times \Delta v$	Probable error $\Delta(\partial V/\partial T)_P$
		A. Benzene				
Biron[a]	Kopp dilatometer, 70 ml.	±0.01	11	*ca.* 17°	± 2.5	±0.4%
Tyrer[b]	Single-capillary pycn., 70 ml.	± .01	8	Very irreg.	?	±1%
Pesce[c]	Duplicate silica–glass dilatometer with Hg seal, 24 ml.	± .01	16	2°, 30 to 45°	± 2.2	±0.4%
			10	5°, 65 to 80°		
Goss[d]	Ostwald–Sprengel pycnometer	± .05	5	10°	± 5	±3%
Massart[e]	Thermometer-type dilatometers	?	7	15 or 20°	± 3	±1%
Cohen and Buij[f]	Dilatometer, 35 ml.	± .015	33	4°	± 3	±0.1%
		B. Toluene				
Tyrer[b]	Single-capillary pycn., 70 ml.	±0.01	11	Very irreg.	?	±1%
Jones and Jelen[g]	Weight dilatometer, Hg seal, 61 ml.	± .005	20	10°	± 1	±0.1%
Massart[e]	Thermometer-type dilatometers	?	14	10 to 20°	±12	±1.5%

[a] E. B. Biron, *J. Russ. Phys.-Chem. Soc.*, **42**, 135 (1910); *Chem. Zentr.*, **81**, I, 1912 (1910). [b] D. Tyrer, *J. Chem. Soc.*, **105**, 2534 (1914). [c] B. Pesce, *Gazz. chim. ital.*, **65**, 440 (1935). [d] F. R. Goss, *J. Chem. Soc.*, 727 (1935). [e] L. Massart, *Bull. soc. chim. Belg.*, **45**, 76 (1936). [f] E. Cohen and J. S. Buij, *Z. physik. Chem.*, **B35**, 270 (1937). [g] G. Jones and F. C. Jelen, THIS JOURNAL, **57**, 2532 (1935).

The specific volume was computed by equation (1) from the observed values of w^*, which are listed in Tables II and III. A cubic equation was fitted by the method of least squares to the values of the specific volume of each liquid. The results

$$[C_6H_6]\ v_t = v_0 + 1.29651 \times 10^{-3}t + 1.7516 \times 10^{-6}t^2 + 5.930 \times 10^{-9}t^3 \quad (7)$$

$$[C_7H_8]\ v_t = v_0 + 1.18497 \times 10^{-3}t + 1.0672 \times 10^{-6}t^2 + 7.366 \times 10^{-9}t^3 \quad (8)$$

are for benzene and toluene, respectively. The residuals with respect to these equations are listed in the last columns of Tables II and III. The probable error of an individual observation, based on the residuals, is $\pm 3.0 \times 10^{-5}$ cc./g. for benzene and $\pm 2.0 \times 10^{-5}$ cc./g. for toluene. Each of these values is somewhat less than the *a priori* estimate given on page 692.

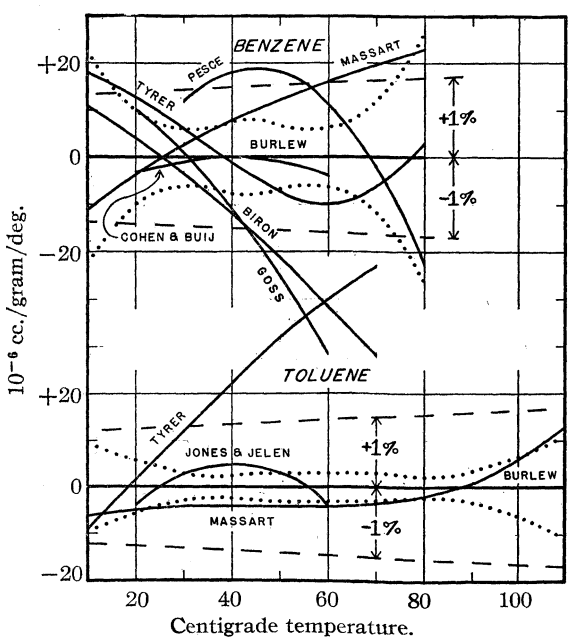

Fig. 2.—Deviations of expansion coefficients.

Differentiation of equations (7) and (8) yielded the following pair of equations for the coefficients of thermal expansion of benzene and of toluene, respectively

$$[C_6H_6]\ 1000\ (\partial V/\partial T)_P = 1.2965 + 3.503 \times 10^{-3}t + 1.779 \times 10^{-5}t^2 \quad (9)$$

$$[C_7H_8]\ 1000\ (\partial V/\partial T)_P = 1.1850 + 2.134 \times 10^{-3}t + 2.210 \times 10^{-5}t^2 \quad (10)$$

The values of the coefficients of thermal expansion, computed from these two equations at 5° intervals, are listed in Table II of the paper[17] on the heat capacity of these liquids.

Comparison of Data for $(\partial V/\partial T)_P$.—The deviations (*other observer* minus *Burlew*) of the results of other investigators from these values are shown in Fig. 2.[18] A summary of the accuracy[19] of their work is given in Table IV, in terms of an estimate of the probable error of $(\partial V/\partial T)_P$ that I have deduced from each author's stated or implied estimate of the probable error of his values of the specific volume. In only three of those investigations (Pesce, Cohen and Buij, and Jones and Jelen) was a sufficient number of observations of specific volume made at regular intervals to permit the

(17) J. S. Burlew, THIS JOURNAL, **62**, 696 (1940).

(18) In each graph of Fig. 2 three times the probable error of the present data is represented by a pair of dotted lines that are symmetrical with respect to the base lines.

(19) A measurement of the coefficient of thermal expansion of a liquid practically is unaffected by systematic errors in the specific volume. Hence its accuracy depends solely on the precision of the measurements of the specific volume.

computation of accurate values of the coefficient of thermal expansion. The deviations of the present data from each of those three are well within the limits of the sum of three times the probable error of each set of data. The results of Massart also agree well with mine, and those of the other four do not disagree by more than the experimental uncertainty except at the ends of the range.

In addition to the data on $(\partial V/\partial T)_P$ that are referred to in Fig. 2, there exist the results of density measurements over considerable ranges of temperature that have not been represented by equations. Although the corresponding coefficients of thermal expansion could not be evaluated accurately, a comparison of total expansions has been made, as shown in Table V. There is good agreement with all except the results of Perkin, whose extremely small expansions are inexplicable. Also the present value for the specific volume of benzene at the boiling point is in close agreement with that of Arbusov.[20] The values of Neubeck[3b] for both benzene and toluene were slightly larger than the present ones.

TABLE V

TOTAL EXPANSION OF BENZENE AND OF TOLUENE

Observer	Range	Expansion, cc./g.	$10^4 \times \Delta$
	A. Benzene		
Perkin[a]	10 to 70°	0.0612	−270
Young[b]	10 to 70°	.0882	± 0
	70 to 80°	.0154	− 12
Meyer and Mylius[c]	15.8 to 72.7°	.0847	− 1
Timmermans and	15 to 30°	.02052	+ 2.5
Martin[d]	30 to 60°	.04461	+ 1.4
	B. Toluene		
Perkin[a]	10 to 100°	0.0727	−519
Timmermans and	15 to 30°	.01859	− 0.8
Martin[d]	30 to 60°	.03964	− 1.8

[a] W. H. Perkin, *J. Chem. Soc.*, **69**, 1025 (1896). [b] S. Young, *Sci. Proc. Roy. Dublin Soc.*, **12**, 374 (1909). [c] J. Meyer and B. Mylius, *Z. physik. Chem.*, **95**, 349 (1920). [d] J. Timmermans and F. Martin, *J. chim. phys.*, **23**, 747 (1926).

Density of Toluene at 0 and 25°

An examination of the literature has revealed considerable variance among the values for the density of toluene, which does not seem to have been commented on previously. The several measurements of the density of toluene at 0 and 25° and the measured expansions between these two temperatures are summarized in Table V. The present value of the expansion agrees well with two of the others, inasmuch as the limit of accuracy is ±0.00001, imposed by the uncertainty of ±0.01° in the temperature scale. The several values of the density, however, are at considerable variance, so that a redetermination of the absolute density at both 0 and 25° of several samples of toluene differently prepared clearly is needed.

TABLE VI

DENSITY OF TOLUENE AT 0 AND 25°

Observer	d_0, g./ml.	d_{25}, g./ml.	$v_{25} - v_0$, ml./g.
Timmermans[a]	0.88448		
Tyrer[b]	.88412		0.03030
Timmermans and Martin[c]	.88545	0.86234	.03027
Kelley[d]	.88456		
Massart[e]	(.88545)		.03020
Smith and Wojciechowski[f]		.86174	
Burlew (this research)	.8854	.8622	.03031

[a] J. Timmermans, *Sci. Proc. Roy. Dublin Soc.*, **13**, 310, (1911–13), p. 354; *Bull. soc. chim. Belg.*, **26**, 205 (1912). This is the value listed in "Int. Crit. Tables," Vol. III, pp. 29 and 33. [b] D. Tyrer, *J. Chem. Soc.*, **105**, 2534 (1914), p. 2540. The expansion has been computed from his empirical equation. [c] J. Timmermans and F. Martin, *J. chim. phys.*, **23**, 747 (1926), p. 752. The density at 25° had been interpolated linearly by the authors from measurements at 15 and 30°. [d] K. K. Kelley, THIS JOURNAL, **51**, 2738 (1929). [e] L. Massart, *Bull. soc. chim. Belg.*, **45**, 76 (1936), p. 83. The density at 0° was an arbitrary base point and not a new determination. The expansion has been computed from his empirical equation. [f] E. R. Smith and M. Wojciechowski, *Bull. intern. acad. polon. sci.*, **1936A**, 123.

Summary

A weight dilatometer for the measurement of the coefficient of thermal expansion of 5 cc. of a volatile liquid over a wide range of temperature with a probable error of a few tenths of one per cent. has been described, and its manipulation has been outlined. An analysis has been given of the factors, including the number of observations, that affect the precision of the measurement of the coefficient of thermal expansion. Data for $(\partial V/\partial T)_P$ of benzene and of toluene from 8° to the respective boiling points have been presented and compared with the results of previous investigators. Discrepancies in the current values for the density of toluene at 0 and 25° have been pointed out.

NEW HAVEN, CONN. RECEIVED SEPTEMBER 21, 1939

(20) A. E. Arbusov, *Z. physik. Chem.*, **131**, 49 (1927), p. 59.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

Measurement of the Heat Capacity of a Small Volume of Liquid by the Piezo-Thermometric Method. III. Heat Capacity of Benzene and of Toluene from 8°C. to the Boiling Point

BY JOHN S. BURLEW[1]

As a first application of the piezo-thermometric method of measuring the heat capacity of a small volume of liquid, the heat capacity of benzene and of toluene was determined. Not only did these results furnish an opportunity for comparison with those obtained by other methods by other investigators, but also they extended the data concerning these two liquids.

Method.—The piezo-thermometric method[2] is based on the following thermodynamic equation

$$c_p = T(\partial V/\partial T)_P/(\partial T/\partial P)_S \qquad (1)$$

The heat capacity of each liquid was computed according to equation (1) at each temperature[3] at which a measurement of the adiabatic temperature–pressure coefficient, $(\partial T/\partial P)_S$, had been made, with the results given in Table I. The corrected experimental values of $(\partial T/\partial P)_S$ which are listed in the next to the last column of Tables III and IV of Ref. (2) were employed, in order that no spurious trend might be given to the values of c_p by the use of calculated values of $(\partial T/\partial P)_S$. The coefficients of thermal expansion, $(\partial V/\partial T)_P$, were computed from the equations[4a] that had been obtained by differentiation of the empirical equations used to express the results of measurements of the specific volumes of these two liquids made at 3° intervals from 8° to the respective boiling points. For the computation of the absolute temperature T in equation (1) the ice point was taken as 273.2° K.

Precision.—The uncertainty of a value of c_p determined according to equation (1) is a combination of the uncertainties that are contributed by each of the factors on the right-hand side of that equation. Those for $(\partial T/\partial P)_S$ have been summarized in Table II of Ref. 2. As explained elsewhere[5] the observational uncertainty in $(\partial V/\partial T)_P$ depends on the number of observations of specific volume and also varies over the temperature range. Combination of these several uncertainties gave for the estimated observational probable error of c_p of benzene and of toluene ± 0.25%

TABLE I

HEAT CAPACITY OF BENZENE AND OF TOLUENE

Temperature		Benzene			Toluene		
°C.	°K.	c_p, j./g.-deg.	p	$10^4 \times \Delta^a$	c_p, j./g.-deg.	p	$10^4 \times \Delta^a$
7.8	281	1.6861	1	−10	1.6606	1	+41
10.8	284	1.6931	2	− 4	1.6686	2	+16
13.8	287	1.6991	3	+17	1.6746	2	+21
16.8	290	1.7101	4	− 8	1.6837	2	− 4
19.8	293	1.7207	6	−26	1.6936	3	−29
22.8	296	1.7276	8	− 3	1.7002	4	−16
25.8	299	1.7367	10	0	1.7088	5	−17
28.8	302	1.7478	11	−15	1.7150	6	+10
31.8	305	1.7559	11	+ 3	1.7272	7	−19
34.8	308	1.7657	10	+ 6	1.7368	7	−17
37.8	311	1.7770	8	− 6	1.7442	8	+10
40.8	314	1.7834	7	+33	1.7537	8	+19
43.8	317	1.7964	7	+ 7	1.7645	8	+18
46.8	320	1.8068	7	+ 6	1.7735	8	+38
49.8	323	1.8182	8	− 4	1.7909	7	−25
52.8	326	1.8312	10	−31	1.8013	7	−15
55.8	329	1.8413	11	−29	1.8095	7	+18
58.8	332	1.8467	11	+18	1.8229	7	0
61.8	335	1.8561	10	+24	1.8346	7	0
64.8	338	1.8612	8	+71	1.8450	7	+13
67.8	341	1.8828	6	−49	1.8610	7	−30
70.8	344	1.8896	4	−23	1.8706	8	− 9
73.8	347	1.8971	3	− 8	1.8805	8	+ 8
76.8	350	1.9050	2	0	1.8955	8	−27
79.8	353	1.9075	1	+59	1.9047	8	− 5
82.8	356				1.9159	7	− 5
85.8	359				1.9254	7	+10
88.8	362				1.9336	6	+35
91.8	365				1.9475	5	0
94.8	368				1.9562	4	+15
97.8	371				1.9668	3	+ 6
100.8	374				1.9775	2	− 7
103.8	377				1.9861	2	− 3
106.8	380				1.9963	2	−21
109.8	383				2.0035	1	−13

[a] Δ = *calcd.* minus *exptl.*

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(2) For a discussion of this method see the first paper of this series, THIS JOURNAL, **62**, 681 (1940).

(3) These measurements had been made at 3° intervals; but the precision was so great over the whole range of temperature that now it is considered that measurements at ten to fifteen uniformly distributed temperatures would have been sufficient to yield results for $(\partial T/\partial P)_S$ comparable in precision to those obtained for $(\partial V/\partial T)_P$ by twice that number of measurements of the specific volume.

(4) J. S. Burlew, THIS JOURNAL, **62**, 690 (1940); (a) equations (9) and (10).

(5) Ref. (4), p. 692. Table I of Ref. (4) shows the extent of the variation of the probable error with temperature for a particular number of observations. The estimates of the probable error of $(\partial V/\partial T)_P$ for benzene and toluene are only 60 to 80% as large as the table indicates for n = 23 and 32, respectively, because $(\partial V/\partial T)_P$ of both liquids is greater than 0.001 cc./g.-deg.

at the middle of the range, somewhat less on either side of the middle, and about twice as much at the ends[6] of the range. The estimated systematic probable error of c_p was $\pm 0.20\%$ over the entire range.

c_p as a Function of Temperature.—The curves obtained by plotting as functions of the temperature the values of c_p listed in Table I are slightly S-shaped, the change of curvature being more pronounced for toluene than for benzene. It was proved by means of a calculation of the specific volume from computed values of the heat capacity that this change of curvature was greater than could be accounted for on the assumption that errors in the measurements of specific volume gave rise to false values of $(\partial V/\partial T)_P$.

Before equations were derived for these curves, it was necessary[7] to weight the individual values of c_p, because the probable error was not constant. The weights listed under p in Table I were taken in proportion to the reciprocal of the square of the estimated probable error of each point. The cubic equations based on the weighted points are

$$[C_6H_6]\ c_p = 1.6673 + 2.047 \times 10^{-3}t + 3.051 \times 10^{-5}t^2 - 2.196 \times 10^{-7}t^3 \quad (2)$$

$$[C_7H_8]\ c_p = 1.6534 + 1.119 \times 10^{-3}t + 4.294 \times 10^{-5}t^2 - 2.204 \times 10^{-7}t^3 \quad (3)$$

The residuals with respect to these equations are listed in Table I. The probable error of an individual observation in the middle of the range, computed from these residuals, is $\pm 0.08\%$ in the case of benzene and $\pm 0.05\%$ in the case of toluene. Both of these values are considerably smaller than the *a priori* estimate given above, which is to be expected, because the values of $(\partial V/\partial T)_P$ used in computing c_p had been smoothed by the process of differentiation. When the unit of c_p is changed from the joule to the defined 15°-calorie,[8] equations (2) and (3) become

$$[C_6H_6]\ c_p = 0.3984 + 4.89 \times 10^{-4}t + 7.29 \times 10^{-6}t^2 - 5.25 \times 10^{-8}t^3 \quad (4)$$

$$[C_7H_8]\ c_p = 0.3951 + 2.68 \times 10^{-4}t + 1.026 \times 10^{-5}t^2 - 5.27 \times 10^{-8}t^3 \quad (5)$$

Comparison of Data.—Values of c_p at 5°, intervals, computed from equations (4) and (5), are listed in Table II. They are compared with previous data[9] in Fig. 1, which shows the deviations (*other observer* minus *Burlew*) in millical. of those data that extend over any considerable temperature range. Table III summarizes the most pertinent information concerning the types of measurements that had been carried out in arriving at those values. In nearly all cases the estimated probable error listed in the last column is based on the original author's estimate of the accuracy of his measurements. In Fig. 1 the circles distributed along the two zero base lines indicate the individual values of c_p that are listed

TABLE II

COEFFICIENT OF THERMAL EXPANSION, TEMPERATURE-PRESSURE COEFFICIENT, AND HEAT CAPACITY OF BENZENE AND OF TOLUENE

t, °C.	$1000(\partial V/\partial T)_P$ cc./g.-deg. C_6H_6	C_7H_8	$100(\partial T/\partial P)_S$ deg./bar C_6H_6	C_7H_8	c_p cal./g.-deg. C_6H_6	C_7H_8
5	1.314	1.196	2.180	2.012	0.4010	0.3967
10	1.333	1.209	2.234	2.056	.4040	.3987
15	1.353	1.222	2.288	2.100	.4072	.4012
20	1.374	1.237	2.343	2.144	.4107	.4041
25	1.395	1.252	2.398	2.189	.4144	.4074
30	1.418	1.269	2.455	2.235	.4182	.4109
35	1.441	1.287	2.513	2.282	.4222	.4148
40	1.465	1.306	2.572	2.331	.4263	.4188
45	1.490	1.326	2.633	2.380	.4304	.4231
50	1.516	1.347	2.696	2.431	.4345	.4275
55	1.543	1.369	2.760	2.484	.4386	.4321
60	1.571	1.393	2.828	2.538	.4427	.4367
65	1.599	1.417	2.897	2.595	.4466	.4414
70	1.629	1.443	2.970	2.654	.4504	.4460
75	1.659	1.469	3.045	2.715	.4540	.4506
80	1.691	1.497	3.123	2.778	.4573	.4552
85		1.526		2.845		.4596
90		1.556		2.914		.4639
95		1.587		2.986		.4679
100		1.619		3.061		.4718
105		1.653		3.140		.4753
110		1.687		3.222		.4786

(6) Unless it is feasible to make measurements of specific volume over a wider range of temperature than it is desired to evaluate the coefficient of thermal expansion, one must be resigned to have the probable error of c_p determined by the piezo-thermometric method two to three times as great at the ends of the range as in the middle.

(7) W. E. Deming, *Phil. Mag.*, **11**, 146 (1931). When cubic equations for c_p are derived using equal weights, the individual parameters are somewhat different, but the interpolated values of c_p are not much different from those computed according to equations (2) and (3), respectively. The greatest differences occur at the ends. In the case of benzene, the value at 10° is lowered 0.2 millical. and that at 80° is raised 0.6 millical. by the weighting; whereas in the case of toluene the effect is opposite, the value at 10° being raised 0.3 millical. and that at 110° being lowered 0.3 millical.

(8) Calorie$_{15}$ = 4.1850 absolute joules. F. R. Bichowsky and F. D. Rossini, "The Thermochemistry of the Chemical Substances," Reinhold Publishing Corp., New York, N. Y., 1936, p. 9.

(9) Whenever necessary and possible the data have been corrected to the defined 15°-calorie. In addition it has been necessary to recompute the data of von Reis and of Mills and MacRae, because the equations they published had been derived without regard to all their data. The new equations, evaluated by the method of least squares from all the original data, are

$$[C_6H_6\text{—von Reis}]\ c_p = 0.3853 + 9.0 \times 10^{-4}t \quad (6)$$

$$[C_7H_8\text{—von Reis}]\ c_p = 0.3985 + 6.7 \times 10^{-4}t \quad (7)$$

$$[C_6H_6\text{—Mills and MacRae}]\ c_p = 0.39593 + 5.72 \times 10^{-4}t \quad (8)$$

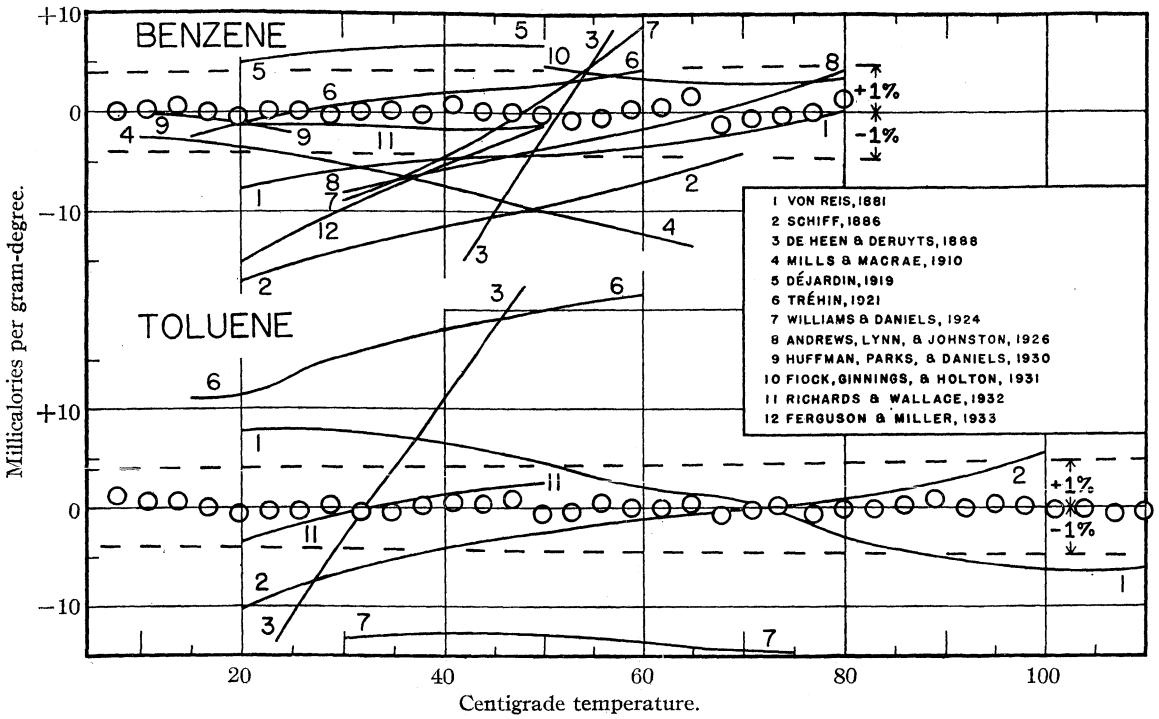


Fig. 1.—Deviations of heat capacities.

TABLE III

NOTES TO ACCOMPANY FIGURE 1

Curve[a]	Method	Sample, g.	Interval,[b] deg.	Detn.	Prob. error, %
1	Method of mixtures: 90 g. H_2O in calorimeter at 20°	5	23 to 96	7	±1.0
2	Method of mixtures: 500 g. H_2O in calor. at 6 to 15°	58	48 to 88	10	±1.0
3	Cooling method	?	5	12	±2
4	Unstirred, elec. heated, adiabatic calorimeter (500 ml. Dewar flask)	393	10	15	±0.2
5	Unstirred, elec. heated, adiabatic calorimeter (2 Dewar flasks)	100	5 to 10	16	± .4
6	Unstirred, elec. heated, adiabatic calorimeter	100	*ca.* 4	?	± .3
7	Stirred, elec. heated adiabatic calorimeter with controlled thermal head	140	6	12	± .1
8	Method of mixtures: kerosene calor. at 22° calibrated with a bar of silver	3	8 to 88	11	± .5
9	Nernst aneroid adiabatic calorimeter	35	1 to 5	6	± .4
10	Stirred, elec. heated, adiabatic, pressure calor. with controlled thermal head	?	10	36	± .5
11	Piezo-thermometric method	?	0.4 to 0.7	8	± .2
12	Method of balanced cooling	900	5 to 10	11	± .3

[a] The sources of data are (1) M. A. von Reis, *Ann. Physik*, **13**, 447 (1881); (2) R. Schiff, *Ann.*, **234**, 300 (1886); (3) P. deHeen and F. Deruyts, *Bull. classe sci. Acad. roy. Belg.*, **15**, 168 (1888); (4) J. E. Mills and D. MacRae, *J. Phys. Chem.*, **14**, 797 (1910); (5) G. Déjardin, *Ann. phys.*, [9] **11**, 253 (1919); (6) R. Tréhin, *ibid.*, **15**, 246 (1921); (7) J. W. Williams and F. Daniels, THIS JOURNAL, **46**, 903 (1924); (8) D. H. Andrews, G. Lynn and J. Johnston, *ibid.*, **48**, 1274 (1926); (9) H. M. Huffman, G. S. Parks and A. C. Daniels, *ibid.*, **52**, 1547 (1930); (10) E. F. Fiock, D. C. Ginnings and W. B. Holton, *Bur. Standards J. Research*, **6**, 881 (1931); (11) W. T. Richards and J. H. Wallace, THIS JOURNAL, **54**, 2705 (1932); (12) A. Ferguson and J. T. Miller, *Proc. Phys. Soc.* (London), **45**, 194 (1933).

[b] The temperature interval through which the liquid was heated or cooled during a single experiment.

in Table I. The radius of each circle is 1 millical., which is approximately the estimated probable error of a single observation in the middle two-thirds of the range.

The present data differ by less than 1% from the mean of all the previous measurements[10] shown in Fig. 1 (neglecting the results of deHeen and Deruyts); but there are great differences among the results of the various investigators, for which no reason is apparent. Although some samples may have been more pure than others, there probably was no gross impurity present in any, for all had been especially purified. What impurities did remain probably would have changed c_p by not more than 0.5%.

The comparison with the work of the early investigators von Reis, Schiff, and deHeen and Deruyts is important, because it furnishes an estimate of the worth of their values of the heat capacity of the many liquids that they alone investigated. The results of deHeen and Deruyts appear worth-

(10) The close agreement between the present results and those of Richards and Wallace is partly accidental, because some of the difference between their values of $(\partial T/\partial P)_S$ and the present ones happened to be balanced by an opposite difference between the present measurements of $(\partial V/\partial T)_P$ and the values that they had taken from the "Int. Crit. Tables."

less. Those of von Reis and of Schiff[11] are within ±2% or ±3% of the truth, if their results for benzene and toluene are fair samples of their work.

In addition to the measurements over a considerable range of temperature recorded in Fig. 1, there have been a considerable number of others. Some[12] of the early ones consisted of only a few measurements by the method of mixtures. Others[13] were just incidental to the investigation of c_p of solutions. Still other measurements[14] made at isolated temperatures involved either single experiments of unverified precision or samples of unknown purity. All these miscellaneous data have been compared with the present results; but the details are scarcely worth recording. Just as those different results show considerable variance among themselves, so the present ones agree with some of them and disagree with others.

Although equation (3) is not suitable for extrapolation to low temperatures, the present data for toluene are consistent with those of Battelli[15] and of Kelley[16] at low temperatures, as can be seen when the several sets of data are plotted on the same graph. Kelley's value at 11.3°, which was the upper limit of temperature in his measurements, is only 2 millical. (0.5%) lower than the present one.

Minimum in c_p of Benzene.—Williams and Daniels,[17] shortly after the publication of the data referred to in Fig. 1, published the results of further experiments with the same calorimeter. They found that the c_p *vs.* t curve of dry samples of benzene exhibited at about 20° a minimum with slight curvature, which they considered indicative of molecular changes in the liquid. A sample saturated with moisture at 6° (0.035% H_2O), however, showed only a marked decrease in slope in the vicinity of 20°. Unfortunately they were not able to trace the course of the curve very far on the low-temperature side of the minimum. The present results, which extend 12° below 20°, give no indication of a minimum. The curve is slightly S-shaped, as mentioned above, which means that the slope is a little less at the low-temperature end than in the middle; but the decrease is not nearly so marked as was found by Williams and Daniels for even a moist sample.

Le Blanc and Möbius,[18] using a heating interval of only 0.1° with a Nernst vacuum calorimeter, made measurements of c_p both above and below the m. p. of a highly purified sample of 75 g. of benzene. Their values at 30.15 and 25.15° (each the mean of two determinations) were 2 and 3 millical., respectively, less than those computed from equation (4). At 14.90° the mean of their twelve determinations was only 1 millical. (0.25%) greater than that computed from equation (4). This value they considered a minimum on the c_p *vs.* t curve, because the mean of five determinations at 6.95° was 6 millical. higher than it and the mean of eighteen determinations at 5.75° was 5 millical. higher. The presence of the minimum they ascribed to the persistence of a state of partial order above the m. p. According to the present data c_p continues to decrease regularly with decreasing temperature down to the limit of the measurements at 7.8°. The present value at this temperature is 11 millical. less than the value found by Le Blanc and Möbius at 6.95°.

Cohen and Buij[19] made triplicate measurements of c_p of carefully purified benzene at 4° intervals from 8 to 24°, in a search for irregularities in the c_p *vs.* t curve. Their conclusion that the curve is linear in this temperature interval is supported by the present data. Their values of c_p were not absolute ones, but were relative to the value 0.4078 cal./g. at 20°, given by Williams and Daniels,[17] which is 0.0028 cal. lower than that found in the present investigation. If the straight line used by Cohen and Buij to express their data is shifted so that it passes through the present value at 20°, their results at other temperatures between 8 and 24° differ from those computed

(11) Schiff's conclusion (*Ann.*, **234**, 300 (1886), p. 327), sometimes referred to as "Schiff's Law," that the specific heat of the different members of a homologous series can be represented by a single straight line or by a few parallel straight lines, is not valid for the two homologs benzene and toluene, as can be seen from Table I. In the "Int. Crit. Tables," nevertheless, twenty-five paraffin esters of the fatty acids are listed on the authority of Schiff as having a heat capacity at 20° of 1.921 j./g., with an uncertainty of only ±0.5%.

(12) (a) *Benzene:* H. V. Regnault, *Mém. acad. sci. inst. imp.* (France), **23**, 3 (1862), p. 283; S. U[J] Pickering, *Proc. Roy. Soc.* (London), **49**, 11 (1890). (b) *Toluene:* F. L. Perrot, *Arch. sci. phys. nat.*, **32**, 145, 254, 337 (1894); W. Siivola, *Översikt av Finiska vetenskaps-societeten förhandlingar*, **56A**, no. 8 (1913), 13 pp.

(13) J. H. Schüller, *Ann. Physik, Erg. Bd.*, **5**, 116, 192 (1871); C. Forch, *Ann. Physik*, [4] **12**, 202 (1903); A. Schulze, *Ber. deut. physik. Ges.*, **14**, 189 (1912).

(14) (a) *Benzene:* A. Schlamp, *Ann. Physik*, (n. f.) **58**, 759 (1896); W. G. Marley, *Proc. Phys. Soc.* (London), **45**, 591 (1933). (b) *Toluene:* T. Estreicher and M. Staniewski, *Bull. intern. acad. sci. Cracovie. Classe Sci., math., nat. A.*, 834 (1912). (c) *Benzene and toluene:* Timofeev, *Chem. Zentr.*, **76**, II, 429 (1905); R. W. B. Stephens, *Phil. Mag.*, **17**, 297 (1934).

(15) A. Battelli, *Physik. Z.*, **9**, 671 (1908).

(16) K. K. Kelley, THIS JOURNAL, **51**, 2738 (1929).

(17) J. W. Williams and F. Daniels, THIS JOURNAL, **46**, 1569 (1924).

(18) M. Le Blanc and E. Möbius, *Ber. Verhandl. sächs. Akad. Wiss. Leipzig. Math.-phys. Klasse*, **85**, 75 (1933).

(19) E. Cohen and J. S. Buij, *Z. physik. Chem.*, **B35**, 270 (1937).

from equation (4) by not more than 0.2 millical. (0.05%), which is excellent agreement with respect to the temperature coefficient of c_p.

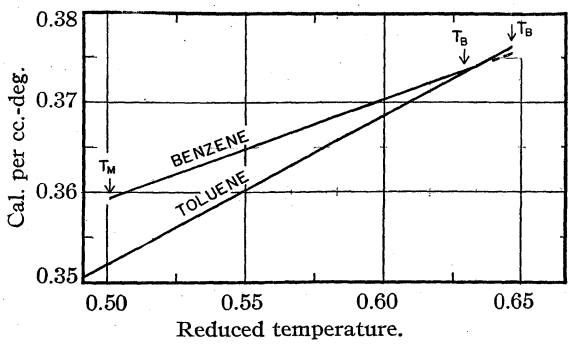


Fig. 2.—Heat capacity per unit volume.

Heat Capacity per Unit Volume

Williams and Daniels[20] suggested on the basis of their data that "the heat capacity per cubic centimeter of unassociated liquids is a constant, approximately 0.35 calorie per degree at room temperature and slightly more than this at higher temperatures." The present data are especially suitable for a test of this suggestion. The values[21] of c_p in cal. per cc., computed at each temperature at which a measurement of $(\partial T/\partial P)_S$ had been made, varied much less with the temperature than the corresponding values of c_p in cal. per gram; but they were by no means constant for either liquid over the whole temperature range nor were they the same for both liquids at the same temperatures. The variation with temperature was expressed by these two linear equations

$$[C_6H_6]\ c_p\ (\text{cal./cc.-deg.}) = 0.3579 + 1.97 \times 10^{-4}t \quad (9)$$

$$[C_7H_8]\ c_p\ (\text{cal./cc.-deg.}) = 0.3453 + 2.79 \times 10^{-4}t \quad (10)$$

The fit of these equations was better than that of linear equations for c_p in cal. per gram. Thus the probable error of an individual observation based on the residuals was 4% less for equation (9) than for the corresponding one for c_p in cal. per gram and 28% less for equation (10). The straight lines represented by equations (9) and (10) approach each other at higher temperatures, but they do not intersect within the normal liquid range.

When the temperature variable in equations (9) and (10) is changed to the reduced temperature (that is, the absolute temperature divided by the absolute temperature of the critical point), the relative slopes of the lines are scarcely changed, but the line for toluene is shifted to the left, so that the two lines intersect as shown in Fig. 2. The reduced temperature of the point of intersection (0.635) is in good agreement with the conclusion of Schiff[22] that at six-tenths of the critical temperature equal volumes of homologous liquids (in his case 27 esters of fatty acids) have equal heat capacities.

Alleged Allotropy of Benzene

It is desirable to emphasize that the data presented in this series of three papers contradict the several suggestions that have been made concerning irregularities in the variation of the physical properties of benzene with temperature. Not only was no minimum observed in the c_p *vs.* t curve, as discussed above, but also comparison of the observations of $(\partial T/\partial P)_S$ and of the specific volume of benzene with those of toluene show the former to vary just as regularly in the neighborhood of 40° as the latter. This conclusion, which is in opposition to the suggestion that Menzies and Lacoss[23] made after an examination of the data of others for several physical properties, agrees with the measurements by Pesce[24] of the specific volume and the refractive index and with those of the specific volume by Cohen and Buij,[19] all of which had been made for the purpose of testing the suggestion of Menzies and Lacoss.

Acknowledgment.—It is a pleasure to thank my wife, Grace Schaum Burlew, for assistance in the computation of these data and in the preparation of the manuscript.

Summary

Values of the heat capacity of benzene and of toluene, computed from $(\partial V/\partial T)_P$ and $(\partial T/\partial P)_S$ measured with 5-cc. samples at 3° intervals from 8° to the respective boiling points, have been shown to agree with results by other investigators. No evidence has been found to support the suggestion that benzene is allotropic.

NEW HAVEN, CONN. RECEIVED SEPTEMBER 21, 1939

(20) J. W. Williams and F. Daniels, THIS JOURNAL, **46**, 903 (1924).

(21) Each such value is the same as that which would have been obtained if $(1/V_t)(\partial V/\partial T)_P$ had been substituted for $(\partial V/\partial T)_P$ in equation (1).

(22) R. Schiff, *Ann.*, **234**, 300 (1886), p. 330.

(23) A. W. C. Menzies and D. A. Lacoss, *Proc. Nat. Acad. Sci. U. S.*, **18**, 145 (1932).

(24) B. Pesce, *Gazz. chim. ital.*, **65**, 440 (1935).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY]

A Direct Method of Calibration of a Copper–Constantan Thermel for Measurement of Temperature Differences at a Series of Temperatures

BY JOHN S. BURLEW[1] AND RODNEY P. SMITH

The suitability of a thermel for differential temperature measurements has long been recognized,[2a] but heretofore the advantage of a differential method of calibration has been neglected. Because of inhomogeneity, the accuracy of an actual thermel is not, like that of an "ideal" thermel, independent of the method of calibration. The requirement for the highest accuracy—namely, that the temperature gradients be of the same order of magnitude and occur at the same places during calibration as during use—is approached most closely by the direct differential method of calibration described in the present paper.

A thermel that is to be used for the measurement of individual temperatures is calibrated regularly according to any one of several procedures[3] that permits the expression of the total e. m. f. as a function $E(t)$ of the temperature of one junction, when the other junction is kept at a fixed reference temperature. Inhomogeneity of a thermel calibrated in this way (to which we shall refer as "the integral method of calibration") introduces an error[2b] that is approximately a fixed proportion of the total e. m. f., because both vary directly as the temperature. Usually it is possible, however, to increase[4] the accuracy of temperature measurements with such a thermel by having the temperature gradients during calibration occur at the same places along the wires as during use.

A thermel that is to be used for the measurement of temperature differences also may be calibrated by the integral method; but the error from inhomogeneity will be considerably greater than if the same thermel were used for single temperature measurements. The error is magnified because, first, the e. m. f. that corresponds to the difference in temperature is the difference between two large e. m. f.'s with each of which is associated an error due to inhomogeneity; and, second, the temperature gradients during calibration are much steeper and occur along different portions of the wires than those during subsequent use.

This magnification of the error from inhomogeneity is particularly important with a copper–constantan thermel, for even the best constantan wire, especially in the smaller sizes,[5] is not completely homogeneous. An effect of this sort interfered with the calibration of a thermel of No. 40 copper and constantan wires intended for use in the piezo-thermometric method[6] of measuring the heat capacity of a small volume of liquid. It was overcome by the direct method of calibration that we describe in this paper.

A thermel is arranged during calibration by this method in a manner similar to that during subsequent use, which not only diminishes the error from inhomogeneity, but also often simplifies the experimental set-up. A further advantage of this method is that the e. m. f.'s measured during calibration approach in magnitude those during the later use of the thermel. Consequently the electrical measurements may be performed with greater convenience and accuracy. It was for this reason that a 26-junction thermel used recently for the measurement[7] of boiling point elevations was calibrated by the differential method.

Differential Method

The Function μ.—The direct differential method of calibration that we have used involves the measurement of the e. m. f. (ΔE) of a thermel whose junctions are at two temperatures (t_1 and t_2) and the simultaneous measurement of the temperature difference ($\Delta t = t_2 - t_1$). The results of the calibration are expressed conveniently in terms of a function that we call μ, which is the quotient of these two measured quantities. Provided that the temperature differences remain approximately constant, a series of μ's obtained during calibration can be expressed as a quadratic function of the mean temperature of the junctions

$$\mu \equiv \frac{\Delta E}{t_2 - t_1} = \alpha + \beta t_m + \gamma t_m^2 \left[t_m = \frac{t_1 + t_2}{2} \right] \quad (1)$$

in which α, β and γ are empirical parameters.

(1) Sterling Fellow in Chemistry, Yale University, 1934–1936; present address: Geophysical Laboratory, Washington, D. C.

(2) W. P. White, *Phys. Rev.*, **31**, 135–158 (1910): (a) p. 152; (b) p. 135; (c) p. 142.

(3) White, Dickinson and Mueller, *Phys. Rev.*, **31**, 163 (1910); Roeser and Wensel, *J. Research Natl. Bur. Standards*, **14**, 247 (1935).

(4) Holborn and Day, *Am. J. Sci.*, **10**, 202 (1900).

(5) Giauque, Buffington and Schulze, THIS JOURNAL, **49**, 2343 (1927).

(6) John S. Burlew, THIS JOURNAL, **62**, 681 (1940).

(7) Rodney P. Smith, THIS JOURNAL, **61**, 497 (1939).

The function μ is the slope of a secant that cuts the curve representing the function $E(t)$. The thermoelectric power (dE/dt) is the tangent to this same curve; but because of the shape of the curve for a copper–constantan thermel, the tangent at a particular temperature t_m is not quite parallel to the secant whose mid-abscissa is t_m. This curve is represented accurately over fairly large ranges of t by

$$E = at + bt^2 + ct^3 \quad (2)$$

It can be shown algebraically by a combination of equations (1) and (2) that

$$\mu - \frac{dE}{dt} = c\left[\frac{t_2 - t_1}{2}\right]^2 = \frac{\gamma}{12}(\Delta t)^2 \quad (3)$$

Hence a value of μ that applies to one temperature difference Δ_1 may be transformed into one to apply to any other temperature difference Δ_k by this equation

$$\mu_{\Delta_k} - \mu_{\Delta_1} = \frac{\gamma}{12}[(\Delta_k)^2 - (\Delta_1)^2] \quad (4)$$

in which γ is the parameter in equation (1). For a copper–constantan thermel γ is about 1 (10^{-6}) (*cf.* equation (9)), and so this transformation term is not large. By the combination of equations (1) and (4), a temperature difference at any mean temperature within the range of the calibration may be computed directly from the measured e. m. f. of the differential thermel.

Relation of μ to the Integral Method.—Application of the function μ is not limited to a thermel calibrated by the differential method. If a homogeneous thermel that has been calibrated by the integral method is used for the measurement of a temperature difference, μ can be employed to compute that difference directly, which is simpler than the usual computation of the separate temperatures of the two junctions by a series of approximations. If the parameters in equation (2) have been evaluated as a result of the calibration by the integral method, it follows from equation (3) that the parameters in equation (1) can be derived from them as follows

$$\alpha = a + c\left[\frac{\Delta t}{2}\right]^2; \quad \beta = 2b; \quad \text{and } \gamma = 3c \quad (5)$$

If the total e. m. f. has been expressed by the exponential equation[8]

$$E = At + B(1 - e^{Ct}) \quad (6)$$

the parameters of equation (1) are given to a high degree of approximation by these relations

$$\alpha = (A - BC); \quad \beta = -BC^2; \quad \text{and } \gamma = -\frac{5}{6}BC^3 \quad (7)$$

(8) L. H. Adams, *J. Wash. Acad. Sci.*, **3**, 469 (1913).

Experimental Procedure

In the calibration of a thermel by the differential method, we used a duplex oil thermostat having two similar halves mounted in a wooden cabinet (60 × 110 × 55 cm., supported on legs 40 cm. high) with a wooden partition between them. Each half was a separate thermostat that could be heated and stirred independently. Each thermostat tank, which was a cylinder of galvanized iron (45 × 45 cm.), had an overflow pipe 4 cm. from the top in order to keep the level of the automobile "flushing oil" constant. A stirrer-propeller that rotated in a tube about 10 cm. in diameter was directly driven by a high-speed motor mounted on the cabinet. Tap water could be circulated through a cooling coil of copper tubing in the upper part of each propeller tube. The oil-baths were heated electrically by commercial resistance units of the type that are used in radiant heaters, screwed into porcelain sockets mounted on the underside of a wooden cover resting on top of the tanks. The main heaters were controlled by lamp-banks, and an intermittent heater in each tank was controlled through a magnetic relay by a conventional mercury-in-glass thermoregulator immersed in the oil-bath.

A region of constant temperature in each oil-bath was provided by a well containing mercury, the top of which was 9 cm. below the surface of the oil. The well was constructed from iron pipe fittings (inside dimensions, about 4 × 25 cm.), the bottom part being a flanged nipple filled with lead.

Above the wooden cover resting on the oil tanks, the thermostat cabinet had a separate cover with a removable center. The thermel to be calibrated straddled the partition between the oil tanks, its mid-section clamped to a copper plate and its limbs immersed in the two mercury wells. The mid-portion of the constantan wire was kept at nearly the mean temperature of the junctions, both by having the mid-section of the case of the thermel constructed from a metal tube[9] that dipped into the oil in both halves of the thermostat, and by having this part placed beneath the upper cover of the thermostat. Then, by observing similar precautions during the use of the thermel, it could be assured that the temperature gradients along the constantan wire would be of approximately the same magnitude and would occur at about the same places as during calibration. The wires from the thermel passed through a shielded slot in the upper cover to a shielded copper connection box mounted on top of the thermostat cabinet. From there an all-copper circuit led through a shielded conduit to the potentiometer.

The temperature of each half of the duplex thermostat was measured in turn with a platinum resistance thermometer,[10] that dipped into the mercury well through holes in the covers. The thermometer was kept in each

(9) *Cf.* W. P. White, THIS JOURNAL, **36**, 2303 (1914). We have found that the assembly of a thermel is facilitated by the use of copper pipe and the copper solder-joint fittings that have come into use recently for household plumbing. These fittings enable one to enclose the thermel wires by easy stages without making the case undesirably bulky. A copper straight-coupling makes an especially good socket in which to cement the glass tube that forms the lower end of a limb of the thermel.

(10) An alternative arrangement would be the use of a pair of resistance thermometers connected differentially, as described by Laby and Hercus, *Trans. Roy. Soc.* (*London*), **227**, 63 (1928).

side long enough to show that the temperature there was constant, after which it was returned to the first side to make certain that its temperature had not changed. During all three sets of observations the e. m. f. of the thermel was measured at regular intervals.

The temperature within either well of the thermostat in the temperature range 20 to 140° had a maximum variation of ±0.005° over a period of about one-half hour—although often the variation was only ±0.001°. The observed variation in the e. m. f. of the thermel gave a direct measure of the constancy of the temperature difference between the two halves of the thermostat. In a series of measurements during the calibration of a particular thermel at five mean temperatures from 20 to 65°, the average maximum fluctuation in the temperature difference of 10° was ±0.002°. At higher temperatures (up to 125°) the maximum fluctuation was about twice this amount. The latter variation represented an uncertainty of ±0.05% in the measured e. m. f., which was about the same magnitude as the uncertainty in the temperature difference as measured with the resistance thermometer.

The quotient of the e. m. f. divided by the temperature difference was a value of μ at a particular mean temperature t_m. A series of eight or ten such measurements was made, using a temperature difference between the junctions of approximately 10° at different mean temperatures. From the resulting μ's and t_m's the parameters in equation (1) were evaluated by the method of least squares.

Experimental Comparison of Methods

The differential and integral methods of calibration were compared by direct experiment using two copper–constantan thermels that had been constructed from No. 30 constantan and No. 36 copper wires. The maximum inhomogeneity of the constantan was less than 0.05% of its thermoelectric power against copper, as determined by the method described by White.[2c]

Calibration of Thermel A.—Thermel A was calibrated according to the integral method by measurement of the e. m. f. produced when one junction was kept at 0° and the other was heated to different temperatures between 40 and 130°. Temperatures were measured with a platinum resistance thermometer (Leeds and Northrup), the fundamental interval of which we redetermined prior to the calibration, measuring the resistance with the same Mueller-type bridge (Leeds and Northrup) that we used during the temperature measurements. The calibration measurements were made at 10° intervals with first one junction at 0° and then the other. Each value of the e. m. f. was divided by the corresponding temperature; and then the two sets of values of E/t were fitted to separate quadratic equations in t by the method of least squares,[11] with equal weight assigned to each variable. Residuals were computed for each set of data with respect to the equation derived from it and also with respect to the equation obtained by taking the mean values of the respective parameters of the two equations. The probable error (P. E.) of a single observation corresponding to the residuals of the mean equation was only slightly larger than that corresponding to the residuals of each individual equation—4% larger in one case and 16% in the other. For as few as ten observations these differences are without practical significance; and so the mean equation is used to represent the e. m. f. of the thermel

$$E = 38.3162\,t + 4.56212\,(10^{-2})t^2 - 3.3208\,(10^{-5})\,t^3 \quad (8)$$

The P. E. of this function,[12] based on the residuals, is 0.003% or less in the range 40 to 130°. This low P. E. and the agreement between the reversed calibrations indicate that the inhomogeneity of this thermel was very small.

Calibration of Thermel B.—Thermel B was calibrated according to the differential method in the duplex thermostat already described by measuring the e. m. f. that was produced by at emperature difference of about 10° at different mean temperatures at 15° intervals from 5 to 125°. Each junction of the thermel was the cold junction during half the measurements. The temperature differences were measured with the same resistance thermometer used in the calibration of Thermel A. The separate values of μ were fitted to a quadratic equation in t_m by the method of least squares,[11] with infinite weight assigned to the values of the mean temperature. The resulting function

$$\mu_{10} = 42.6744 + 7.6183\,(10^{-2})\,(t_m - 65) - 9.745\,(10^{-5})\,(t_m - 65)^2 \quad (9)$$

has a P. E.[12] of 0.03% or less in the range 10 to 110°.

Mode of Comparison.—For the comparison of the two methods of calibration, both thermels were placed in the duplex thermostat at the same time. The temperatures of the two sides of the thermostat were maintained 10° apart at each of six mean temperatures from 30 to 105°. The temperature of the colder side was measured with the platinum resistance thermometer that had been used in the calibrations. The same ends of the thermels were always on this side. Two sets of observations at each temperature were made twenty minutes to an hour apart.

(11) W E. Deming, *Phil. Mag.*, **11**, 146 (1931).

(12) H. Schultz, *J. Am. Stat. Assoc.*, **25**, 139 (1930).

TABLE I

MEASUREMENT OF TEMPERATURE DIFFERENCES WITH THERMEL A

Nominal mean temp., °C.	t_1, °C.	E_A μv.	E_1 μv.	E_2 μv.	t_2, °C.	$(\Delta t)_A = (t_2 - t_1)$, °C.
30	25.009	405.62	986.26	1391.88	34.911	9.902
	25.011	405.66	986.35	1392.01	34.915	9.904
45	40.106	412.64	1607.95	2020.59	49.880	9.774
	40.102	413.37	1607.79	2021.16	49.893	9.791
60	55.100	435.30	2244.17	2679.47	65.121	10.021
	55.099	434.47	2244.13	2678.60	65.101	10.002
75	69.917	446.48	2890.61	3337.09	79.930	10.013
	69.919	446.48	2890.71	3337.19	79.932	10.013
90	85.292	462.41	3579.34	4041.75	95.400	10.108
	85.291	462.76	3579.30	4042.06	95.407	10.116
105	100.088	509.31	4258.71	4768.02	110.963	10.875
	100.078	509.51	4258.24	4767.75	110.957	10.879

Data.—In Table I under "t_1" is listed the cold temperature measured with the resistance thermometer, and under "E_A" is listed the e. m. f. of Thermel A. The temperature difference corresponding to this e. m. f. difference was found by computing the temperature (t_2) of the hot side of the thermel in the following manner. First the e. m. f. (E_1) corresponding to t_1 was computed from equation (8). To it was added E_A to give E_2. Then the temperature (t_2) corresponding to E_A was computed from equation (8) by successive approximations.

TABLE II

MEASUREMENT OF TEMPERATURE DIFFERENCES WITH THERMEL B

Nominal mean temp., °C.	t_1, °C.	E_B μv.	t_m, °C.	μ μv./°C.	$(\Delta t)_B = E_B/\mu$, °C.	Difference $(\Delta t)_A - (\Delta t)_B$, °C.
30	25.009	394.87	29.959	39.885	9.900	+0.002
	25.011	394.87	29.961	39.885	9.900	+ .004
45	40.106	401.76	44.993	41.111	9.773	+ .001
	40.102	402.50	44.998	41.112	9.791	± .000
60	55.100	423.85	60.110	42.300	10.020	+ .001
	55.099	423.07	60.100	42.299	10.002	± .000
75	69.917	434.81	74.924	43.421	10.014	− .001
	69.919	434.81	74.926	43.421	10.014	− .001
90	85.292	450.47	90.349	44.543	10.113	− .005
	85.291	450.74	90.351	44.543	10.119	− .003
105	100.088	496.03	105.527	45.602	10.877	− .002
	100.078	496.25	105.519	45.601	10.882	− .003

In Table II under "E_B" is listed the e. m. f. of Thermel B. The temperature difference was found by a series of approximations, usually three. First a value was assumed for the mean temperature, and the corresponding value of μ was computed from equation (9). The first approximation to the temperature difference was found by dividing E_B by μ. Half of this difference was added to the measured cold temperature to obtain a second approximation for the mean temperature. The cycle was repeated until the same value of the mean temperature was obtained twice in succession. It is this final value of "t_m" together with the corresponding "μ" that is listed in Table II.

Conclusion.—The agreement between the values of Δt that were obtained with the two thermels is excellent, inasmuch as the estimated relative probable error of a single measurement of the temperature difference with either thermel was ±0.008°. The maximum difference between the two sets of values, as shown in the last column of Table II, is 0.005°, and the average difference without regard to sign is 0.002°.

Summary

The computations involved in the measurement with a thermel of temperature differences at a series of mean temperatures (t_m) are simplified by the introduction of the function

$$\mu \equiv \Delta E/(t_2 - t_1) = \alpha + \beta t_m + \gamma t_m^2$$

A direct differential method of calibration, whereby the parameters of this equation are evaluated, minimizes the error from inhomogeneity. For the demonstration of the experimental validity of this method, a copper–constantan thermel that had been calibrated by it was compared with one that had been calibrated by the ordinary integral method: in a series of temperature differences measured with the two thermels the maximum divergence was 0.005°, which was less than the experimental uncertainty.

NEW HAVEN, CONN. RECEIVED AUGUST 5, 1938

[CONTRIBUTION FROM THE LABORATORIES OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH]

The Interpretation of Simple Electrophoretic Patterns

BY L. G. LONGSWORTH AND D. A. MACINNES

Introduction.—An electrophoresis experiment with a single protein may be represented diagrammatically as follows. Initially boundaries are formed at the level a′-a, of Fig. 1, in the two sides of the cell, between the protein solution P and the buffer solution B. After displacement of the boundaries from behind the horizontal glass plates of the cell, passage of a current causes one of the boundaries, a, to descend through a volume V_d to a new position d, as in Fig. 2, and the other,

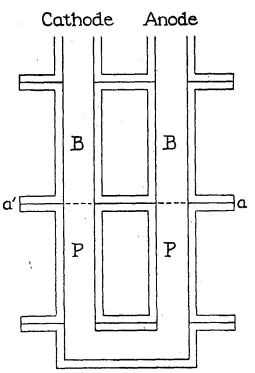


Fig. 1.

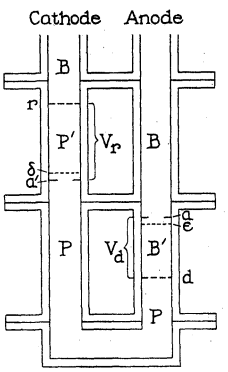


Fig. 2.

Figs. 1 and 2.—Diagrams of the electrophoresis cell illustrating the formation and relative position of the boundaries.

a′, to rise through a volume V_r to the position r of the same figure. Under ideal conditions, approximated with a dilute solution of a protein in a buffer of sufficient capacity, the volumes V_d and V_r are equal and a knowledge of their value permits a precise computation of the mobility of the protein. In general, however, the volume V_r is greater than V_d and an analysis of the concentration changes resulting from the electrolysis is necessary in order to obtain mobilities from the experimental results. It is the purpose of this paper to describe electrophoretic experiments on ovalbumin, at 0°, in which these concentration changes have been determined, and to outline an analysis of the data for the purpose of obtaining accurate mobilities.

Methods.—The recent development of methods for studying and recording refractive index gradients, initiated by Tiselius,[1] has made possible the precise study of electrophoretic boundaries. From "electrophoretic patterns" thus obtained concentration changes during electrophoresis may be computed. The available procedures are the scale method of Lamm,[2] the diagonal schlieren method of Philpot[3] and Svensson[4] and the schlieren scanning method developed in this Laboratory[5,6] and used in the present research.

In outline the schlieren scanning method is illustrated in Fig. 3. An image at P of the illuminated slit S-S is formed by the schlieren lens D. The camera lens O is focused on the electrophoresis cell E and forms an image (full sized in our apparatus) on the screen at G-G. Now if the fluid in the cell is homogeneous this image will be uniformly illuminated. On the other hand, if there is a boundary, B, between, for instance, a protein-bearing solution and a buffer, there will be a region in which the refractive index varies with the height in the cell, and light which would normally pass to P is deflected downward, since the solution with the greater refractive index is on the bottom. If the opaque schlieren diaphragm Q is raised to a point p where it intercepts the most deflected light, a dark band will

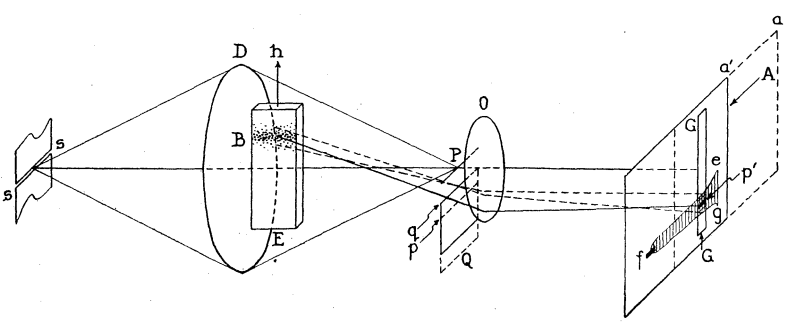


Fig. 3.—Diagram of the schlieren scanning method for the photographic recording of gradients of refractive index.

(1) Tiselius, *Trans. Faraday Soc.*, **33**, 524 (1937).
(2) Lamm, *Nova Acta Reg. Soc. Sci. Upsaliensis*, Series IV, **10**, No. 6 (1937).
(3) Philpot, *Nature*, **141**, 283 (1938).
(4) Svensson, *Kolloid-Z.*, **87**, 181 (1939).
(5) Longsworth, THIS JOURNAL, **61**, 529 (1939).
(6) Longsworth, Shedlovsky and MacInnes, *J. Exptl. Med.*, **70**, 399 (1939).

appear on the screen, conjugate to the region of steepest gradient in the boundary B. Such a band appears in the image G-G at p′.

However, a boundary between two solutions does not consist of a single geometric plane, but of a region in which the composition varies from that of one solution to that of the other. The refractive index, n, in such a region changes continuously with the height, h, of the liquid in the cell. The gradient, dn/dh, of refractive index, for each boundary, will thus, theoretically at least, vary from zero to a maximum, and back to zero. In Fig. 3 the variation of the gradient, dn/dh, of the boundary B in the cell E, is represented by the density of the shading. The pencil

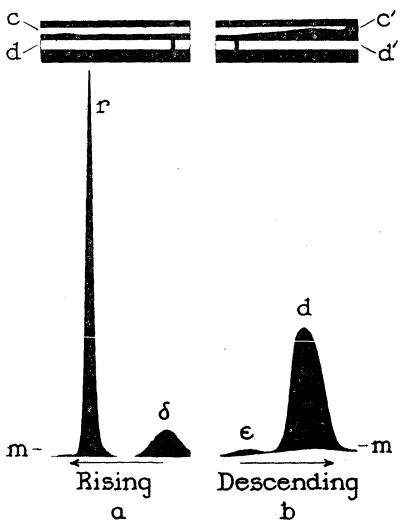


Fig. 4.—Electrophoretic patterns of a 1.36% solution of ovalbumin in a 0.1 N sodium acetate buffer at pH 3.92 and 0°. Scanning exposure made after electrolysis for 13,000 seconds at 5.39 volts per cm.

of light passing through the layer having the maximum value of the gradient will be most bent from the normal path and will be the first to be intercepted when the schlieren diaphragm Q is raised. On lifting this diaphragm still further, *i. e.*, to the level q, less refracted pencils of light will also be intercepted and the schlieren band in the image G-G will widen. This obviously can be continued until the whole field has been covered. In the schlieren scanning method this process is made continuous and is recorded photographically. The image of the cell at G-G is masked by a narrow vertical slit and a photographic plate A is moved in the direction of the arrow at a constant rate across this slit. Actuated by the same mechanism, the schlieren diaphragm Q is given a steady movement upward. The resulting (positive) photographic record for a typical single boundary is indicated by the area e-f-g. The displacement of the diaphragm Q from the position P is proportional to the gradient at levels in the cell E conjugate to the edges of the schlieren bands. Thus the contour of the area e-f-g indicates both the position and the magnitude, of the refractive index gradients existing in the boundary. Since the photographic plate A was in position a at the time the schlieren diaphragm was at p, a section of the band p′ appears at f when the plate has been moved to a′. It will be seen that the usual schlieren bands are narrow sections through the area e-f-g. By a system of gears the ratio of the rates of motion of the schlieren diaphragm Q to that of the plate A is given a constant value, such as one to three, and this ratio can be varied by changing the gears. For establishing the base line of the schlieren patterns the position of the diaphragm Q may be read accurately with a micrometer.

Experimental Results and Discussion.—The type of phenomenon to be discussed in this paper is illustrated in Fig. 4, which represents electrophoretic patterns of a 1.36% solution of ovalbumin at pH 3.92 in a 0.1 normal sodium acetate buffer.[7]

In order to interpret these patterns in terms of concentrations and mobilities, information must be available about (a) the base line of the diagram and (b) the starting position of the boundaries. The base line is obtained as shown at c-c′ of Fig. 4 by a scanning exposure of the cell immediately after the formation of the boundaries but before the latter have been shifted into view from behind the horizontal glass plates. The procedure consists in setting the schlieren diaphragm, Q of Fig. 3, just below P, the exact position of the diaphragm being given by the reading, m of a micrometer, and then scanning until the diaphragm is somewhat above P. The lower edges of the strips c and c′ of Fig. 4 are thus the schlieren patterns of the windows of the cell and thermostat, deviations of these edges from the horizontal indicating imperfections in the windows. The upper edges of the strips c and c′

(7) The ovalbumin used in this research was prepared from fresh hen's eggs. Although three times recrystallized, it was not electrophoretically homogeneous. At most pH values the main component is accompanied by a second component migrating somewhat more slowly, as shown in Fig. 2 of reference (5) and in Fig. 6 of this paper. Similar patterns have been obtained with samples of ovalbumin from four different laboratories. A study of egg white now in progress indicates that the slow component is present in the starting material. Ovalbumin appears homogeneous in the patterns reproduced in Fig. 4, because the pH-mobility curves of the two components apparently intersect in the neighborhood of the isoelectric point. At pH 3.92 the protein may be considered electrically homogeneous, thereby simplifying the interpretation of the patterns.

correspond to a reading, m, of the micrometer. The equivalent position on the patterns a and b, Fig. 4, is at m-m. Consequently when the upper edges of the strips c-c′ are brought into coincidence with the line m-m the lower edges of these strips constitute the base line for the patterns. In order to obtain the position of the freshly formed boundaries after they have been shifted into view, the schlieren bands shown at d-d′ in Fig. 4 are recorded on the photographic plate. As Guggenheim[8] has suggested, the diffusion process smooths out the slight irregularities in the distribution of concentrations resulting from the formation and shifting of the boundaries. As illustrated by the finite width of the bands in the strip d-d′, the boundaries are not infinitely sharp. However, the positions of the mid-points of these bands may be taken as the positions at zero time from which mobilities can be computed.

It will be seen in Fig. 4 that two peaks or maxima are evident in the patterns of both the rising and descending boundaries but that the patterns are far from being mirror images of each other. This may, possibly, be an extreme case but is all the more useful in illustrating deviations from ideal behavior and in testing the validity of the interpretation to be given below.

The deviations, or so-called "boundary anomalies," illustrated by these patterns are as follows. (1) The rising boundary r is much sharper than that, d, descending into the protein solution. (2) The boundary r has swept through a larger volume V_r, than that, V_d, of the boundary d. (3) The total shaded area of Fig. 4a is equal to that of Fig. 4b, but the partial area A_r under the rising boundary r is less than that, A_d, for the descending boundary d. Since these areas, as will be shown, are proportional to the concentration changes at the boundaries it is apparent that the change is less at the rising boundary than at the descending one. Also (4), the concentration distribution in a boundary is not, in general, symmetrical about the maximum as is shown by the shapes of the peaks d and r.

These deviations were explained qualitatively by the authors[9] as follows. In practice the protein solution is prepared by dialysis against a buffer solution. A difference, due to the Donnan equilibrium, of salt composition exists between the two solutions when dialysis is complete. Moreover, the protein solution contains conducting constituents, the protein ions, that are not present in the buffer solution. When passage of a current causes a boundary between two such solutions to move from a to d of Fig. 2, for example, there is found in the intervening volume V_d a buffer solution of composition [B′]. This composition has been adjusted, in general, to a value different from that of B.[10] The boundary ϵ, which moves very slowly, thus forms between two solutions of the same buffer, but at different concentrations,[11] and is quite evident in Fig. 4. With the boundary r moving upward into the buffer solution, there is a similar but more complicated adjustment of the composition of the protein solution which replaces the buffer as the boundary rises. The resulting concentration boundary δ, between the solutions P and P′, Fig. 2, also moves very slowly under the influence of the current. The δ boundary, also shown in Fig. 4, is much more visible than the ϵ boundary because the former involves a gradient of protein concentration whereas the latter does not.

Since the specific conductance, κ_P, of the protein solution P has been found experimentally to be less than that, κ_B', of the adjusted buffer solution, the electric field is greater in the protein solution than in the buffer and variations of this field thus exist at the descending boundary d. The protein ions in the dilute uppermost layers of the boundary d are therefore in weaker fields than are those in the concentrated layers and thus tend to lag behind, causing the boundary to become diffuse, as is shown in Fig. 4b. In the case of the boundary r rising into the buffer solution $\kappa_P' < \kappa_B$ so that the dilute, slowly moving protein ions tend to be overtaken by the faster concentrated ones, with the result that this boundary tends to remain sharp, as is illustrated by Fig. 4a. Due to these field gradients at the boundaries, and in some instances to *p*H gradients also, the distribution through a boundary may be unsymmetrical about the ordinate passing through the maximum of the refractive index gradient curve. This lack of symmetry, shown clearly by the boundary d of Fig. 4b, has been studied by Tiselius and Horsfall.[12] Assuming a proportionality between refractive index and protein concentration it is apparent that in such cases the position of the maximum gradient is not identical with that of the ordinate which divides the area under the

(8) Guggenheim, THIS JOURNAL, **52**, 1315 (1930).

(9) Longsworth and MacInnes, *Chem. Rev.*, **24**, 271 (1939).

(10) This adjustment is understood for some simple cases (Kohlrausch, *Ann. Physik*, **62**, 209 (1897); Weber, "Die partiellen Differential-Gleichungen der mathematischen Physik," 5te Aufl., Braunschweig, 1910, **1**, 195–203, 503–527; Longsworth, THIS JOURNAL, **52**, 1897 (1930); Henry and Brittain, *Trans. Faraday Soc.*, **29**, 798 (1933)) but the theory for the more complicated systems frequently encountered in practice has not been developed.

(11) See MacInnes and Longsworth, *Chem. Rev.*, **11**, 199 (1932).

(12) Tiselius and Horsfall, Jr., *J. Exptl. Med.*, **69**, 83 (1939).

curve into two equal parts. The position of the latter ordinate is the better value to use in mobility computations since it is approximately the position the boundary would have if it retained its original sharpness. The precise location of an unsymmetrical boundary requires an integration of the concentration–distance curve. Computations for the cases considered in this paper show that the position of the ordinate dividing the gradient curve into equal parts differs from the true value by at most 1%, whereas the position of the maximum ordinate may be in error by 19%.

It is important in this connection to be clear as to what is meant by the mobility, u, of a protein. It is the distance moved per second in a unit electric field by an average particle in the body of the protein solution. The movement of the particle through this distance corresponds to the transport of uA [P] grams of protein through a plane (to be discussed below) in the body of the protein solution, A being the cross-sectional area of the channel and [P] the concentration of protein in grams per milliliter. If the electric field, F, differs from unity and the transport continues for t seconds the total quantity, p, of protein transported through a reference plane is $p = uA[\mathrm{P}]Ft$, from which $u = p/FAt[\mathrm{P}]$. Since the field strength, F, in the body of the protein solution is $i/\kappa_{\mathrm{P}}A$ this expression becomes

$$u = p\kappa_{\mathrm{P}}/[\mathrm{P}]it \qquad (1)$$

in which i is the current. The quantity p is determined analytically in the Hittorf or "transport" method, whereas in the moving boundary method it is determined by following the motion of a boundary between the solution and the buffer. If the passage of electricity causes a boundary to descend from a to d, of Fig. 2, it sweeps through a volume $A(a - d) = V_{\mathrm{d}}$. Thus the amount of protein passing any plane in the unmodified solution is $A(a - d)[\mathrm{P}] = V_{\mathrm{d}}[\mathrm{P}]$. Equation 1 thus becomes

$$u_{\mathrm{d}} = \frac{A(a-d)[\mathrm{P}]}{[\mathrm{P}]}\frac{\kappa_{\mathrm{P}}}{it} = \frac{V_{\mathrm{d}}\kappa_{\mathrm{P}}}{it} \qquad (2)$$

in which u_{d} indicates the mobility computed from data on the descending boundary.

The computation of mobilities from data on the rising boundary is, however, complicated by the change of protein concentration at the δ boundary. Assuming, in essential agreement with experiment, that the latter remains stationary, the quantity, p, of protein migrating upward through a plane in the body of the solution on the passage of it coulombs is $(r - a')A$ [P′] $= V_{\mathrm{r}}$[P′] in which [P′] is the concentration of protein in the adjusted solution between the δ and r boundaries. Introducing this value of p into equation 1 we obtain

$$u_{\mathrm{r}} = \frac{[\mathrm{P}']}{[\mathrm{P}]}\frac{V_{\mathrm{r}}\kappa_{\mathrm{P}}}{it} \qquad (3)$$

which differs from equation 2 in that it contains the concentration ratio [P′]/[P]. Since it is one of the main conclusions of this paper that, correctly interpreted, the data on rising and descending boundaries yield the same value of the mobility, *i. e.*, $u_{\mathrm{d}} = u_{\mathrm{r}}$, it is important to establish values of the ratio [P′]/[P]. This requires an investigation, which is given below, of the changes of protein and salt concentrations in the channel of the apparatus during electrolysis.

Strictly, the reference plane from which mobilities are measured should be fixed with respect to the solvent. Since the observed boundary displacements refer to a plane fixed with respect to the apparatus they should be corrected for the displacement the solvent experiences as a result of electrolysis (see reference 11, page 203) otherwise the mobilities found will depend, among other things, upon the nature of the electrode reaction. This computation is greatly facilitated if one electrode chamber is closed since only the volume changes occurring on this side of the protein solution can affect the position of the boundaries. In the experiments reported in this paper the anode chamber was closed and the volume change, ΔV, was equal to

$$\Delta V = f(T_{-}\varphi_{\mathrm{NaAc}} - \varphi_{\mathrm{NaCl}} + V_{\mathrm{AgCl}} - V_{\mathrm{Ag}}) - [\mathrm{P}]V_{\mathrm{d}}\bar{\varphi}_{\mathrm{P}}$$

in which V_{d} is the volume swept through by the descending boundary, for example, on the passage of f Faradays, T_{-} the anion transference number of sodium acetate, φ and V are the apparent molal and molal volumes, respectively, of the materials indicated by the subscripts, and $\bar{\varphi}_{\mathrm{P}}$ is the apparent specific volume of the protein. On the basis of the available data

$$\Delta V = 19.03f - 0.749[\mathrm{P}]V_{\mathrm{d}}$$

A positive value for this volume change represents an expansion of the solution in the closed side and consequently the observed V_{d} is too large by an amount ΔV. The values of V_{d} and V_{r} recorded in Table I have been corrected for this volume change. The corrections for the descending boundary are 2.1, 1.5 and 0.5% at protein concentrations of 0.64, 1.36 and 2.74%,

respectively, and are thus by no means negligible. The validity of the correction is difficult to prove in the case of the electrophoresis of proteins but has been amply demonstrated for strong electrolytes.[11]

We have observed repeatedly, within a small experimental error, that (1) the total area of an electrophoretic pattern is independent of the time during the electrolysis at which a pattern may be obtained, *i. e.*, the area is independent of the mode of variation of the refractive index through the boundaries and (2) the total areas of the patterns for the two sides of the channel are identical. These observations are consistent with the fact that the total area of a pattern is given by the integral $\int_B^P (dn/dh)dh$, in which n is the refractive index at the level h in the cell, the limits of integration being the same for both sides of the channel and independent of the time of electrolysis. Thus the results of planimeter measurements on enlarged images of Figs. 4a and b, in arbitrary units, yielded $A_\epsilon = 18$, $A_d = 354$, $A_\delta = 72$ and $A_r = 302$, from which the sum of the areas for the descending boundaries, $A_\epsilon + A_d$, is 372, whereas the sum, $A_\delta + A_r$, for the rising boundaries has the closely agreeing value of 374.

From the discussion given above it is evident that the partial area A_ϵ of Fig. 4 is due to a gradient of buffer concentration. Since the solution P retains its original composition, in which the buffer electrolyte concentration differs but little from that of solution B, another variation of salt concentration, opposite in sign to that at the ϵ boundary, must exist in the boundary d. Consequently the area A_d must be increased by an amount A_ϵ in order to measure the change of protein concentration at the boundary d. Conductance measurements of the B′ and P′ solutions, to be described later in this paper, indicate that the δ boundary also contains a gradient of buffer salts. Since the same quantity of electrolyte enters the channel from the electrode vessel on one side as leaves the channel on the other side, it follows that the increment of buffer electrolytes in the B′ solution must be compensated by a corresponding decrement in the P′ solution. The concentrations of salts [B] and protein [P] as functions of the height can thus be represented schematically, as is shown in Fig. 5. The increment of buffer salts in the B′ solution is proportional to $A_\epsilon V_d$ while the corresponding and equal decrement in the P′ solution is proportional to $A'_\epsilon V_r$ in which A'_ϵ is that portion of the area A_δ due to the electrolyte gradient in the δ boundary. Therefore $A'_\epsilon = A_\epsilon V_d/V_r$. Moreover, since an electrolyte gradient, equal in magnitude but opposite in sign to that in the δ boundary, must also exist in the boundary r, the area A_r must be increased by an amount $A_\epsilon V_d/V_r$ in order to measure the change of protein concentration at this boundary. The ratio [P′]/[P] of equation 3 thus takes the value $(A_r + A_\epsilon V_d/V_r)/(A_d + A_\epsilon)$ and equation 3 becomes

$$u_r = \frac{V_r \kappa_P}{it} \times \frac{A_r + A_\epsilon V_d/V_r}{A_d + A_\epsilon} \qquad (3a)$$

A small error may arise from the use of equation 3a due to the fact that account has not been taken of slight pH changes at the boundaries.

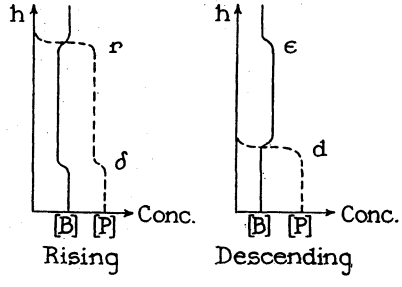


Fig. 5.—Schematic diagram of the changes of buffer electrolyte (———) and protein (– – –) concentrations at each of the electrophoretic boundaries.

The data necessary for the computation, and the resulting mobilities, at three concentrations of ovalbumin are recorded in Table I. The figures in the second column include data obtained from Fig. 4 and at the other concentrations

TABLE I

ELECTROPHORETIC MOBILITIES, u, OF OVALBUMIN IN A 0.1 NORMAL SODIUM ACETATE BUFFER AT pH 3.92 AND 0°

1	Protein concn., g. %	0.64	1.36	2.74
2	Conductance, κ_P, at 0°	0.003491	0.003434	0.003326
3	Coulombs, it	143.3	171.7	148.5
4	Volume, V_d, ml.	1.114	1.339	1.152
5	Volume, V_r, ml.	1.244	1.609	1.580
6	A_d, area	169	354	715
7	A_ϵ, area	7	18	36
8	A_r, area	151	302	533[a]
9	A_δ, area	23	72	218
10	Relative viscosity,[b] η, 0°	1.022	1.047	1.095
11	$u_r^* \times 10^5$	3.03	3.22	3.54
12	$u_r \times 10^5$ (Equation 3a)	2.71	2.74	2.63
13	$u_d \times 10^5$ (Equation 2)	2.71	2.68	2.59
14	$u_{d\eta}$	2.77	2.81	2.84

[a] By difference; the maximum refractive index gradient of this boundary was too great to be recorded. [b] Interpolated from measurements made in this Laboratory.

from similar electrophoretic patterns. The mobilities u_d given in line 13 have been computed with the aid of equation 2 whereas the values u_r in line 12 were obtained from equation 3a. It will be noted that they agree reasonably closely, as would be expected if our interpretation is correct. Line 11 contains values of u_r^* computed from the relation $\kappa_P V_r/it$, in which the change of protein concentration at the δ boundary, *i. e.*, [P']/[P], has been ignored. The large error which may arise from this procedure may be seen by comparing the figures of lines 11 and 12. The percentage deviations reach a maximum of 37% in our experiments.[13]

It will be observed that the mobilities of ovalbumin, computed as described above and recorded in lines 12 and 13 of Table I, change but slightly with the protein concentration and much of this change disappears if the mobilities are multiplied by the relative viscosity, η (line 10), the product $u_d\eta$ increasing but slightly with the protein concentration. This observation is important since it indicates that mobility measurements may aid in the identification of components in an electrophoretic pattern.

The Delta and Epsilon Boundaries.—Although the interpretation, given in the foregoing pages, of patterns of the type shown in Fig. 4, appears to be satisfactory, two questions may arise in the mind of the reader. Do gradients of buffer electrolyte really exist in the boundaries? And has the possibility that the δ and ϵ boundaries may be due, in part, to a slowly moving protein constituent been completely eliminated?

To answer the first of these questions the procedure was as follows. After the electrophoresis in which the patterns shown in Fig. 4 were obtained, the contents of each section of the cell were isolated and the specific conductances at 0° were measured. The results, before and after electrolysis, are given in Table II. In the lower cathode and upper anode sections of the cell, Fig. 2, no boundaries were present and no significant change of conductance occurred, showing, as would be expected, that the compositions of the solutions B and P are unchanged by the passage of current. In the upper cathode section, however, where the adjusted protein solution P' has partially replaced the buffer solution B originally present, the specific conductance had decreased 5.1%. A corresponding *increase* in the lower anode section accompanied the partial replacement of the protein solution P by the adjusted buffer solution B'. The conductance of the solution P', between the boundaries δ and r, can be readily estimated. The height of the upper cathode section is known, as well as the positions of the r and δ boundaries. In addition data are available, in Table II, on the conductances of the B and P solutions, and of the mixture of these with the P' solution. These, assuming simple proportionality, are sufficient data for computing the conductance of the latter solution, which is given as "P' solution, computed" in the table. A change of equivalent conductance from $\kappa_P = 0.00343$ to $\kappa_{P'} = 0.00322$ is therefore indicated at the δ boundary. Since the conductances of these solutions are due mainly to the buffer ions and are roughly proportional to their concentrations, this indicates that there is a decrease of concentration of buffer electrolyte in passing from solution P to solution P' across the δ boundary in accord with Fig. 5. It is of interest, however, that the ratio $\kappa_{P'}/\kappa_P (= 0.939)$ differs appreciably from that [P']/[P] (= 0.853) computed from refractive index measurements, showing that the P' solution is not obtained from the P solution simply by dilution with water as required by the theory of electrophoretic boundaries discussed by Henry and Brittain.[14] The theory, however, was developed for a ternary ionic system, *i. e.*, protein ions and the anions and cations of a binary buffer salt. At the *p*H of the experiments and with the buffer solution

TABLE II

CONDUCTANCE CHANGES ON ELECTROLYSIS OF A 1.36% OVALBUMIN SOLUTION IN A 0.1 NORMAL SODIUM ACETATE BUFFER, AT *p*H 3.92

Section	κ (before)	κ (after)	Diff. in %
Cathode, upper, B	0.00353	0.00336	−5.1
Cathode, lower, P	.00343	.00344	...
Anode, upper, B	.00353	.00353	...
Anode, lower, P	.00343	.00361	+5.3
P' solution, computed		.00322	

(13) This result indicates that mobility measurements involving observations of rising boundaries, without considering the δ effect, may be in error. Thus Landsteiner, Longsworth and van der Scheer (*Science*, **88**, 83 (1938)) used a mean value, $(u_d + u_r^*)/2$, which is about 2.5% higher, for the data of their Table I for example, than the correct value, u_d. It should be noted, however, that this correction does not affect the order of the mobilities, and consequently the conclusions of that paper remain unchanged. In a recent electrophoretic study of hemoglobin Davis and Cohn (THIS JOURNAL, **61**, 2092 (1939)) observed a mobility increase of 27% on increasing the protein concentration from 0.17 to 1.33%. They computed their results from observations on the rising boundary and it seems probable that most of this apparent mobility variation is due to neglect of the correction for the concentration change at the δ boundary.

(14) Henry and Brittain, *Trans. Faraday Soc.*, **29**, 798 (1933).

used (0.1 N NaAc + 0.5 N HAc) it is probable that the effects of the hydrogen ion constituent and of the undissociated acid cannot be neglected.

In this and other laboratories the δ and ϵ boundaries were first thought to be due to slowly migrating protein or carbohydrate constituents.[15] Attempts to isolate such materials were unsuccessful, however. Although the explanation, outlined in this paper, of the boundaries was soon evident[9] the possibility of a small concentration of electrophoretically inert material was not entirely eliminated. The work of Henry and Brittain, mentioned above, suggested a method by which the δ and ϵ boundaries might be suppressed under certain conditions if no inert material were present. In the case of the electrophoresis of ovalbumin in the neutral range, where the contribution of the hydrogen ion conductance to the system is negligible, the conductance ratio $\kappa_{P'}/\kappa_P$ is in fair agreement with the ratio [P']/[P] determined refractometrically. Thus in the electrophoresis experiment (the patterns for which are shown in Fig. 6) of a 1.36% solution of ovalbumin in a phosphate buffer at 6.80 the conductance, $\kappa_{P'}/\kappa_P$, and protein concentration, [P']/[P], ratios were found to have nearly the same value, *i. e.*, 0.935 and 0.923, respectively. Under these conditions the concentrations of the constituents of the P′ solution are such as would result from dilution of the P solution with water. Thus in this case if the boundaries were initially formed between the buffer and the solution P′, obtained by diluting solution P by the factor 1/0.935, there should be no δ and ϵ boundaries left behind when the protein boundaries migrate away from their original positions. This idea was tested experimentally with the result shown in Fig. 7. It will be seen that the δ and ϵ boundaries, quite evident in Fig. 6, have been eliminated. This would appear to be conclusive evidence of the nature of the δ and ϵ boundaries, as outlined above, and of the absence of inert constituents in the sample of ovalbumin.

(15) Tiselius, *Biochem. J.*, **31**, 1464 (1937).

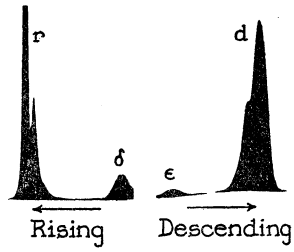


Fig. 6.—Electrophoretic patterns of a 1.36% solution of ovalbumin in a 0.1 μ sodium phosphate buffer at pH 6.80 and 0°. Scanning exposure made after electrolysis for 6000 seconds at 7.23 volts per cm.

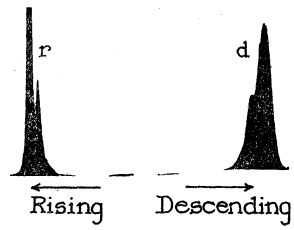


Fig. 7.—Same as for Fig. 6 except that the dialyzed ovalbumin solution was diluted in order to eliminate the δ and ϵ boundaries.

Summary

Electrophoretic studies of ovalbumin, at 0° and at pH 3.92, have been made by the moving boundary method. The research was undertaken in order to establish the conditions under which accurate values of protein mobilities may be found from moving boundary data. This involved investigation of the nature of the δ and ϵ boundaries, and of the concentration distributions in the rising and descending protein boundaries. The results indicate that, although in general more diffuse, the descending boundaries yield correct values of the mobility. The rising boundaries may give results that are greatly in error unless additional data are available from which corrections may be made, in which case the two types of boundary yield the same value of the mobility. Contrary to some recent conclusions, the mobilities have been found to vary but slightly with the protein concentration, if a small viscosity correction is made, within the composition limits studied. There is evidence that gradients of buffer concentration exist, in general, in all the boundaries. The correctness of the interpretation has been indicated by showing that, in certain cases, the δ and ϵ boundaries may be suppressed.

NEW YORK, N. Y. RECEIVED DECEMBER 22, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF PHYSICAL CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, NO. 443]

Vapor–Liquid Equilibrium. V. Carbon Tetrachloride–Benzene Mixtures[1]

BY GEORGE SCATCHARD, S. E. WOOD AND J. M. MOCHEL

These measurements on carbon tetrachloride–benzene mixtures complete the cycle of binary systems with the components: carbon tetrachloride, benzene and cyclohexane. They permit an interesting comparison of these three systems and a prediction of the behavior of ternary systems of these components.

The purification of materials was the same as in III and IV and the measurements were made as in IV, with nitrogen as the confining gas. The leakage through the stoppers was so reduced by moistening them with the liquid in the still and seating them very tightly that the temperature increase was only 0.0002–0.0004° per minute at 40° and not over 0.0001° per minute at 70°. The vapor pressures of the pure substances agreed with the equations given in IV as well as did the measurements from which the equations were obtained. Apparently no phosgene was formed during these measurements as not even its odor was detected.

The electrical heating permits a fairly precise measurement of the rate of boiling at atmospheric pressure and so makes possible an estimate of the difference in pressure necessary to keep the vapors streaming from the boiler and to the condenser, which is more accurate than the estimate made in I. Since the rate of heating is almost independent of the boiling temperature, the rate of boiling may be taken to be so, also. At atmospheric pressure 2–2.2 cc. of benzene distilled per minute. This corresponds to a pressure drop along a tube 9 cm. long and 0.5 cm. in diameter of 0.003 mm. at 760 mm. pressure, and of 0.013 mm. at 120 mm. pressure. These pressure drops are smaller than those estimated in I, because the rate of distillation is smaller than we estimated, and they are also much smaller than the errors in measuring the pressures.

The density measurements showed systematic errors of the same magnitude as those reported in IV, probably caused by the evaporation of the first component weighed out in the preparation of the standards. Since they correspond to less than 0.02% in the composition, the equation for the relation between density and composition was determined by applying an average correction to the measurements. Table I contains the uncorrected densities and their deviations from the equation

TABLE I

DENSITIES OF BENZENE–CARBON TETRACHLORIDE MIXTURES AT 25°

Wt. fract. CCl_4	Mole fract.	Density	Deviation	100 V^M/V^0
0.0000	0.0000	0.87370	.....	.....
.2189	.1246	0.96878	+0.00003	+0.004
.2488	.1440	0.98344	+ .00006	+ .002
.3838	.2402	1.05527	+ .00004	+ .008
.5383	.3719	1.15171	+ .00007	+ .009
.6572	.4932	1.23893	+ .00026	− .006
.6581	.4943	1.23963	+ .00023	− .003
.6593	.4956	1.24050	+ .00015	+ .003
.6601	.4965	1.24115	+ .00018	+ .001
.6642	.5011	1.24405	− .00020	+ .031
.6669	.5041	1.24614	− .00021	+ .032
.7780	.6403	1.34163	− .00020	+ .029
.8583	.7547	1.42024	− .00019	+ .024
.9302	.8712	1.49891	− .00013	+ .015
1.0000	1.0000	1.58426	.....	.....

$$d = (0.87370 + 0.71056z_1)/(1 + 0.00061)z_1z_2 \quad (1)$$

$$z_1 = 1 - z_2 = 1/(1 + w_2d_1/w_1d_2) \quad (2)$$

in which d is the density of the solution, d_1 and d_2 the densities of the components, w_1 and w_2 their weights in the solution, and z_1 and z_2 their volume fractions. The last column gives $100V^M/V^0 = 100(V - V^0)/V^0$, in which V^0 is the volume of the unmixed components, V is the volume of the solution, and V^M is the increase of volume on mixing. From equation 1 it follows that

$$V^M/V^0 = 0.00061\ z_1z_2 \quad (3)$$

Vapor–liquid equilibrium measurements were made at intervals of approximately one-eighth in the mole fraction of the liquid at 40 and 70° and for an approximately equimolal mixture at 30, 50 and 60°. The measurements at 40° are shown in Fig. 1, in which the curves are determined from equations 4 and 5 and the circles are the individual experimental points. The top curve with the plain circles gives the equilibrium pressure as ordinate and the liquid composition, expressed as mole fraction of carbon tetrachloride, as abscissa. The curve just below it with the

(1) Paper IV in this series appeared in THIS JOURNAL, **61**, 3206 (1939).

flagged circles gives the equilibrium pressure *versus* the vapor composition, and the two lower curves are the derived partial pressures. The broken lines represent the Raoult's law total and partial pressures *versus* the liquid composition. The measurements are reported in detail in Table II as mole

TABLE II

VAPOR PRESSURES OF BENZENE–CARBON TETRACHLORIDE MIXTURES

x_{CCl_4}	y_{CCl_4}	Dev. in y_1	P	Dev. in P	$F^E{}_x$	Dev. in $F^E{}_x$
			40°			
0.1398	0.1703	−0.0009	190.18	−0.06	9.11	−0.06
.2378	.2774	− .0018	194.70	− .06	13.85	+ .04
.3735	.4159	− .0012	200.07	− .05	17.78	− .01
.4919	.5295	− .0008	204.02	± .00	19.06	+ .08
.4986	.5359	− .0006	204.20	− .01	18.99	+ .02
.6201	.6475	− .0010	207.44	− .04	17.82	− .03
.7585	.7739	− .0005	210.37	± .00	13.86	+ .02
.8718	.8783	− .0002	211.97	− .13	8.06	− .37
			70°			
.1428	.1666	− .0003	568.89	+ .01	8.86	+ .05
.2394	.2702	− .0004	579.13	± .00	13.13	+ .04
.3791	.4105	− .0007	591.62	+ .02	16.98	+ .09
(.4930)	(.5204)	(− .0002)	(600.77)	(+ .85)	(18.92)	(+1.01)
.4939	.5215	± .0000	599.67	− .24	17.63	−0.27
.6224	.6411	− .0007	607.22	− .07	16.76	− .04
.7624	.7719	− .0002	613.08	+ .01	12.93	+ .01
.8750	.8780	− .0003	616.02	+ .01	7.80	+ .02
			30°			
.4865	.5298	+ .0002	134.40	+ .03	19.46	+ .14
			50°			
.4926	.5265	− .0005	300.20	+ .04	18.74	+ .12
			60°			
.4907	.5210	− .0007	429.52	+ .02	18.35	+ .09

fraction of carbon tetrachloride in the liquid, and in the vapor, equilibrium pressure, and the derived excess free energy of mixing. After each of the last three is given the deviation of the corresponding quantity from that calculated by the following equations together with these vapor pressures of the pure components at 30, 40, 50, 60 and 70° from IV: benzene—119.16, 182.70, 271.34, 391.66, 551.03; carbon tetrachloride—141.55, 213.34, 312.04, 444.28, 617.43.

$$\mu^E{}_1 = RT \ln Py_1/P_1x_1 + (\beta_1 - V_1)(P - P_1)$$
$$= (1.25141 - 0.0014837\,T)(1 + 0.14z_1)V_1z_2^2 \quad (4)$$
$$\mu^E{}_2 = RT \ln Py_2/P_2x_2 + (\beta_2 - V_2)(P - P_2)$$
$$= (1.25141 - 0.0014837T)(0.93 + 0.14z_1)V_2z_1^2 \quad (5)$$
$$F^E{}_x = (1.25141 - 0.0014837T)(1 + 0.07z_1)V^0{}_xz_1z_2 \quad (6)$$
$$H^M{}_x = 1.25141\,(1 + 0.07z_1)V^0{}_xz_1z_2 \quad (7)$$
$$S^E{}_x = 0.0014837\,(1 + 0.07z_1)V^0{}_xz_1z_2 \quad (8)$$

in which $V^0{}_x = x_1V_1 + x_2V_2 = V^0/(N_1 + N_2)$, x is the mole fraction in the liquid, y is that in the vapor, and the subscript $_1$ refers to carbon tetrachloride, V_1 and V_2 are the molal volumes at

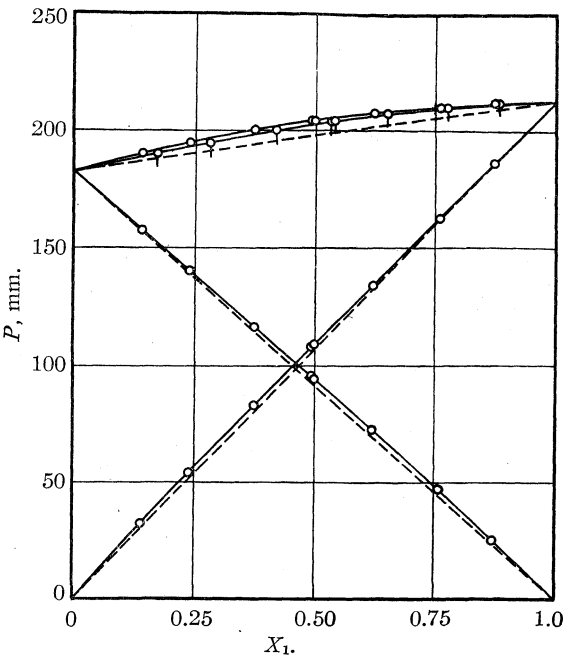


Fig. 1.—Vapor pressure *vs.* mole fraction for carbon tetrachloride–benzene at 40°.

25°, and β_1 and β_2 are the limits at zero pressure of the differences between the molal volumes of the vapors and those of perfect gases at the same temperature and pressure. The values of β used for benzene, carbon tetrachloride and cyclohexane, respectively, are −1839, −1864 and −2031 cc. per mole at 40° and −1287, −1310 and −1426 cc. per mole at 70°. The calculated results from which the curves in Fig. 1 and the deviations in Table II are calculated are from equation 6 for $F^E{}_x$ and from the combined equations 4 and 5 for P and y. The constants are chosen to give the average of $F^E{}_x$ at 40 and 70° and a linear variation of $F^E{}_x$ with temperature. The average deviation is 0.06% in y and 0.015% in P, which is about the same as for carbon tetrachloride–cyclohexane mixtures.

To calculate the thermodynamic functions for mixing at constant total volume, we have made use of the following expressions for the coefficients of thermal expansion and compressibility in reciprocal degrees centigrade or reciprocal atmospheres

$$\alpha_0 = 1.228 \times 10^{-3}(1 - 0.0024z_2)$$
$$\beta_0 = 1.10 \times 10^{-4}(1 - 0.1z_2)$$
$$\alpha_0/\beta_0 = 11.16(1 + 0.108z_2)$$
$$\mathrm{d} \ln \beta/\mathrm{d}T = 0.0076$$

and $V_0 = 97.104/(1 + 0.086z_2)$. Then

$$(A^E{}_v - F^E{}_p)_x = 4.05 \times 10^{-5}(97.104)z_1^2z_2^2/(1 - 0.1z_2)(1 + 0.086z_2) \quad (9)$$
$$(S^E{}_v - S^E{}_p)_x = -(16.40 \times 10^{-5})(97.104)(1 + 0.108z_2)z_1z_2/(1 + 0.086z_2) + 0.0076(A^E{}_v - F^E{}_p)_x \quad (10)$$
$$(E^M{}_v - H^M{}_p)_x = T(S^E{}_v - S^E{}_p)_x + (A^E{}_v - F^E{}_p)_x \quad (11)$$

In Fig. 2 are shown F^E_{px} at 25 and at 70° from equation 6, H^M_{px} from equation 7, and E^M_{vx} from H^M_{px} and equation 11. The value for A^E_{vx} at 25° is so near that of F^E_{px} that they could not be distinguished on a scale many times as large as this one. For the equimolal mixture at 25°, F^E_{px} (or A^E_{vx}) is 19.5, H^M_{px} is 30.2 and E^M_{vx} is 29.0 cal./mole. The correction to $(E^M_{vx} - A^E_{vx})$ caused by deviations from random distribution is calculated from Kirkwood's equation[1] as −0.18 cal./mole, which is very small relative to the measured +9.5 cal./mole. V^M_x/β is 3.27 cal./mole, which is scarcely more than a tenth of E^M_{vx}.

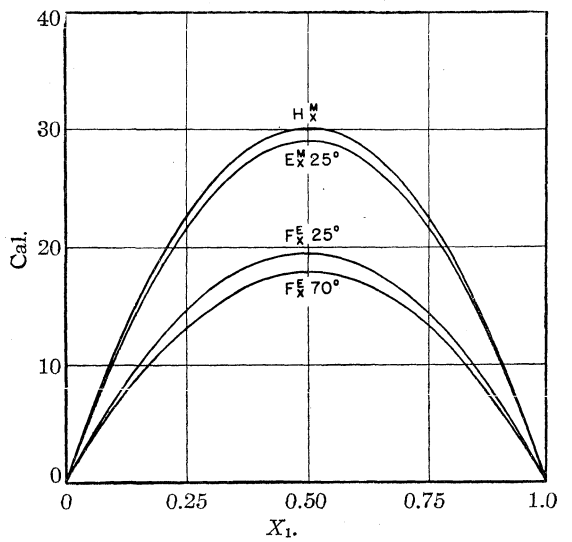


Fig. 2.—Various thermodynamic functions for carbon tetrachloride–benzene.

The results are made a little clearer if they are translated back to the measured pressure, for the effect on the vapor composition is very small. For equimolal solutions we find a pressure 2.75% greater than the average of the pressures of the components at 70°, and 3.15% greater at 40°. This decrease of 0.40% would be only 0.22% if the solutions were regular and 0.24% if the entropy of mixing at constant total volume were zero. A decrease of 0.16% in 30° is left unexplained. The deviations from random distribution, calculated by Kirkwood's equation, increase the unexplained deviations by 0.003%.

The cohesive energy densities at 25°, a_{11} and a_{22}, are calculated as −72.96 cal./mole for carbon tetrachloride and −84.11 for benzene. By quadratic combination they lead to 9.21 cal./mole for E^M_{vx}, or about one-third of the measured 29.0. However, the mutual energy per unit volume

$$a_{12} = \left(\frac{E^M/V^0}{z_1 z_2} + a_{11} + a_{22}\right)\Big/2$$

is −77.91, which is only 0.54% less than $\sqrt{a_{11}a_{22}}$. As in the other systems, the quadratic combination of constants leads to fairly good agreement in the calculation of a_{12}, but the percentage error in $(2a_{12} - a_{11} - a_{22})$ is very large.

This system has been studied by many observers, but we shall compare our measurements with only a few. Hubbard[2] found values of V^M/V^0 at 25° which correspond very closely to ours. At 50° he finds V^M/V^0 about four times as great as calculated by our equation for 25°, which indicates that the discrepancy between V^M/β and E^M decreases rapidly as the temperature increases. Hirobe's measurements[3] of the heat of mixing at 25° are about 15% smaller, and those of Vold[4] are about 30% smaller than those we calculate from our equilibrium measurements. Vold's measurements are also higher in benzene-rich solutions and lower in benzene-poor solutions than a symmetrical curve. The curvature in F^E *versus* T necessary to give agreement with either set of the heat measurements is probably within the error of our measurements, but we see no basis for a choice between the two sets. The measurements by Zawidski[5] of the vapor pressure at 49.99° are 2–5 mm. lower than those calculated from our equations. The vapor pressures of the pure components are also lower, and his ratio of pressure to ideal pressure agrees very well with ours in solutions rich in benzene, and is higher than ours for solutions poor in benzene. His vapor compositions differ from ours on the average by 0.2%, which is about the spread in his measurements, and his vapor is always richer in that component which is in excess in the liquid. The vapor pressure measurements at 50.15° by Tahvonen[6] are in excellent agreement with ours.

Table III contains various properties of equimolal mixtures of each of the three systems of this cycle. If the deviations from ideality are measured by the percentage increase in pressure, $100(P - P_I)/P_I$, the benzene–cyclohexane system shows much the largest deviation, and carbon tetrachloride mixtures with benzene deviate a little more than those with cyclohexane. The

(2) J. C. Hubbard, *Z. physik. Chem.*, **74**, 207 (1910).
(3) H. Hirobe, *J. Faculty Sci. Imp. Univ. Tokyo*, **1**, 155 (1925).
(4) R. D. Vold, THIS JOURNAL, **59**, 1515 (1937).
(5) J. von Zawidski, *Z. physik. Chem.*, **35**, 129 (1900).
(6) P. E. Tahvonen, *Finska-Vetenskaps Societeten, Comm. Phys. Mat.*, **10**, 1 (1938).

TABLE III

PROPERTIES OF EQUIMOLAL MIXTURES

	C_6H_6–C_6H_{12}	C_6H_{12}–CCl_4	C_6H_6–CCl_4
$100V^M/V^0$	0.65	0.16	0.003
$100(P - P_I)/P_I$ at 70°	9.73	2.17	2.75
$100(P - P_I)/P_I$ at 40°	12.32	2.63	3.15
Difference	2.59	0.46	0.40
Diff. from regular solution	1.77	0.28	0.18
Diff. from vol. regular solution	0.88	0.06	0.16
H^E_x (cal./mole)	175.8	34.2	30.2
F^E_x	74.4	16.7	19.5
TS^E_{xp}	101.4	17.5	10.7
E^E_x	120.0	20.7	29.0
TS^E_{xv}	50.0	4.0	9.5
E^E_x (calcd. quadratic combination)	26.0	3.8	9.2
$100(a_{12} - \sqrt{a_{11}a_{22}})/a_{12}$	2.5	0.5	0.5
TS^E_{xv} calculated Kirkwood	−3.6	−0.09	−0.18
Ratio to TS^E_{xv}	−0.07	−0.02	−0.02

thermodynamic functions show the same relations, except that the heat of mixing and the excess entropy at constant pressure interchange the last two systems. This indicates that that property which determines these deviations is intermediate for carbon tetrachloride between the values for the two hydrocarbons and nearer to that for cyclohexane. We also see that the value for benzene–cyclohexane is much greater than the sum of the other two. The square roots of these deviation measures are, however, approximately additive. This relation between the square roots is that predicted by quadratic combination, and the cohesive energy density of carbon tetrachloride does lie between those of the two hydrocarbons and nearer to that of cyclohexane than to that of benzene. The simple theory of non-polar mixtures states that it is the square of the difference between the square roots of the cohesive energy densities which determines the deviations from ideality rather than any difference in molecular structure or nature of the atoms. So it should be quite possible for substances which are very different chemically to give nearly ideal solutions. The quantitative calculations for the energy densities give, however, only about a fifth of the measured values.

The volume increase on mixing is greater than that calculated from the energy of mixing by simple theory for the mixtures containing cyclohexane, but it is very much smaller for carbon tetrachloride–benzene mixtures. However, the measurements of Hubbard indicate that the volume increase becomes rapidly larger as the temperature increases.

For the two systems with large increase of volume, the excess entropy of mixing at constant total volume is considerably smaller than that at constant pressure, but it is still important in all three cases. It was suggested in III[7] that the entropy increase in the benzene–cyclohexane system might be due to an abnormally small entropy in one of the liquids, probably caused by incomplete randomness of orientation which becomes complete in the mixtures. If this explanation were correct, the excess entropy of the first system should equal the sum of that for the other two if there were no lack of randomness in the more symmetrical carbon tetrachloride, and would in general be less than this sum by twice the effect for carbon tetrachloride. From Table III we see that the excess entropy for benzene–cyclohexane is almost four times as great as the sum for the other two systems. Barring the very improbable case of a large negative entropy in one of the mixtures giving compensation, the study of the two systems with carbon tetrachloride shows that most of the excess entropy cannot arise from an abnormally low entropy in either of the components.

To consider ternary mixtures we will assign the subscripts $_1$ to benzene, $_2$ to cyclohexane, and $_3$ to carbon tetrachloride. If the excess free energies of the binary mixtures are given by expressions of the type $F^E_{12} = V^0B_{12}z_1z_2$, the expression for the free energies of ternary systems should be the sum of those for the binary systems: $F^E = V^0(B_{12}z_1z_2 + B_{13}z_1z_3 + B_{23}z_2z_3)$. If the expression for binary systems contains a triple product of the type $C_{112}z_1^2z_2$, however, we may expect for ternary mixtures a term $C_{123}z_1z_2z_3$ which cannot be determined by measurements on binary mixtures. Of the three systems under discussion, benzene–cyclohexane mixtures deviate from the symmetrical expression only enough to give a maximum discrepancy of about 0.4% in the pressure; benzene–carbon tetrachloride mixtures give a maximum discrepancy of about 0.1%, and cyclohexane–carbon tetrachloride mixtures give none within the accuracy of our measurements. We may then expect an error of about the average, which is less than two parts per thousand, if we ignore the term in $z_1z_2z_3$ and adjust our expression to merge into each of those for a binary liquid as the third component

(7) G. Scatchard, S. E. Wood and J. M. Mochel, *J. Phys. Chem.*, **43**, 119 (1939).

disappears. Our expressions for the binary mixtures are

$$F_{12}/V^0 = z_1z_2(B_{12} + D_{12}z_2^2)$$
$$F_{23}/V^0 = z_1z_3(B_{13} + C_{13}z_3)$$
$$F_{23}/V^0 = z_2z_3B_{23}$$

For ternary mixtures we must eliminate the unsymmetrical method of writing the first two by replacing z_2 by its equivalent $(1 - z_1 + z_2)/2 = (2z_2 + z_3)/2$ and z_3 by $(z_2 + 2z_3)/2$. This gives the following expressions, in which the volume fraction of each component is eliminated in the expression for the potential of that component.

$$F^E/V^0 = B_{12}z_1z_2 + D_{12}(z_1z_2^3 + z_1z_2^2z_3 + z_1z_2z_3^2/4) + B_{13}z_1z_3 + C_{13}(z_1z_2z_3/2 + z_1z_3^2) + B_{23}z_2z_3$$

$$\mu^E_1/V_1 = B_{12}(z_2^2 + z_2z_3) + B_{13}(z_2z_3 + z_3^2) - B_{23}z_2z_3 + D_{12}(3z_2^4 - 2z_2^3 + 6z_2^3z_3 - 2z_2^2z_3 + 15z_2^2z_3^2/4 - z_2z_3^2/2 + 3z_2z_3^3/4) + C_{13}(z_2^2z_3 - z_2z_3/2 + 3z_2z_3^2 - z_3^2 + 2z_3^3)$$

$$\mu^E_2/V_2 = B_{12}(z_1^2 + z_1z_3) - B_{13}z_1z_3 + B_{23}(z_1z_3 + z_3^2) + D_{12}(3z_1^4 - 6z_1^3 + 6z_1^3z_3 + 3z_1^2 - 8z_1^2z_3 + 15z_1^2z_3^2/4 + 2z_1z_3 - 5z_1z_3^2/2 + 3z_1z_3^3/4) + C_{13}(z_1^2z_3 - z_1z_3/2 - z_1z_3^2)$$

$$\mu^E_3/V_3 = -B_{12}z_1z_2 + B_{13}(z_1^2 + z_1z_2) + B_{23}(z_1z_2 + z_2^2) + D_{12}(-3z_1^3z_2/4 + z_1^2z_2 + 3z_1^2z_2^2/2 - z_1z_2/4 - z_1z_2^2 - 3z_1z_2^3/4) + C_{13}(-2z_1^3 + 2z_1^2 - 3z_1^2z_2 + 3z_1z_2/2 - z_1z_2^2).$$

These equations readily may be extended to include the cases where any or all of the constants C_{12}, C_{13}, C_{23}, D_{12}, D_{13}, D_{23} are not zero by the appropriate interchange of coefficients, and to H^E or S^E instead of F^E. The values of the parameters for our system are: $V_1 = 89.400$, $V_2 = 108.754$, $V_3 = 97.104$, $B_{12} = (6.943 - 0.013233\ T)$, $B_{13} = (1.3335 - 0.0022916\ T)$, $B_{23} = (1.25141 - 0.0014837\ T)$, $D_{12} = 0.084\ B_{12}$, $C_{13} = 0.07\ B_{13}$. The units are cc./mole for the volumes and cal./cc. for the other parameters.

Applying these expressions to mixtures containing equal mole fractions of benzene and cyclohexane at 25° we find that, as the fraction of carbon tetrachloride increases from zero to unity, $\log Py_i/P_ix_i$ increases by 0.009 for benzene, decreases by 0.011 for cyclohexane and increases by 0.002 for carbon tetrachloride. As a result the total pressure is almost linear, and it varies only from 109.1 to 113.8 mm. The vapor pressures of benzene and cyclohexane are 94.98 and 97.45 mm., respectively, and the pressures of equimolal binary mixtures with carbon tetrachloride deviate 3.35 and 2.86% from Raoult's law. Therefore, the cross sections at constant mole fraction of carbon tetrachloride are nearly symmetrical and flatten out rapidly as the fraction of carbon tetrachloride increases. At one half mole fraction carbon tetrachloride, the excess over the average of the end-points has already decreased from 12.9 to 3.1 mm.

Summary

The vapor–liquid equilibrium pressure and compositions of benzene–carbon tetrachloride mixtures have been measured at 40 and 70° over the whole composition range, and at 30, 50 and 60° for approximately equimolal mixtures. The densities have been determined at 25°.

These measurements have been expressed analytically, and corresponding equations have been derived for the thermodynamic functions, including the energy and entropy of mixing at constant total volume.

These equations show a slight asymmetry, and a moderate deviation from regularity, which, on account of the nearly additive volumes, is almost the same at constant total volume as at constant pressure.

These results are compared with those obtained previously for mixtures of each of the components with cyclohexane, and approximate equations are derived for the ternary system: benzene–cyclohexane–carbon tetrachloride.

CAMBRIDGE, MASSACHUSETTS
RECEIVED JANUARY 15, 1940

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF INORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, NO. 77]

Preparation and Properties of Diborane Diphosphine

BY E. LEE GAMBLE AND PAUL GILMONT

Of the compounds formed by the hydrides of boron, diborane diammine $B_2H_6 \cdot 2NH_3$, has been investigated most extensively. This compound was first prepared by Stock,[1] and from its properties he concluded that it was a salt, $(NH_4)_2(B_2H_4)$, derived from the dibasic acid, $H_2(B_2H_4)$. Schlesinger and Burg[2] have reported that the low temperature reaction of metallic sodium on a solution of diborane diammine in liquid ammonia, gave results that could be explained only on the basis of a monobasic salt being formed. Therefore, they believed that the structure of diborane diammine is best represented by the formula, $NH_4(BH_3NH_2BH_3)$. When $B_2H_6 \cdot 2NH_3$ is heated rapidly to 200°, a volatile cyclic compound, $B_3N_3H_6$, is formed,[3] the six-membered ring having alternate boron and nitrogen atoms.

The similarities and differences between phosphine and ammonia led us to investigate the action of phosphine on diborane and the nature of the product so obtained.

Two volumes of phosphine react with one volume of diborane to form a white unstable compound of empirical composition $B_2H_6 \cdot 2PH_3$ or $BH_3 \cdot PH_3$.[4] The reaction takes place slowly in the gas phase at temperatures above −30°, and fairly rapidly in the liquid phase above −110°. The product, diborane diphosphine, dissociates above −30° into diborane and phosphine, the dissociation pressure at 0° being about 200 mm. No evidence for the corresponding dissociation of diborane diammine has ever been reported.

Diborane diphosphine is formed from the gas phase as long, white, crystalline needles, and from the liquid phase as a microcrystalline mass. It is spontaneously inflammable in air, and rapidly decomposed by water with the formation of hydrogen, phosphine and boric acid. On heating rapidly to 200°, large quantities of hydrogen and a non-volatile, unidentified residue are formed, but no volatile product corresponding to $B_3N_3H_6$, which is formed under comparable conditions, has been isolated.

The compound dissolves with difficulty in liquid ammonia at its melting point without apparent reaction. A true phosphonium salt, PH_4Br, slowly dissolves under the same conditions with complete evolution of the phosphine in the compound, and the formation of ammonium bromide. If the solution of diborane diphosphine in liquid ammonia or the solid compound in liquid ammonia is warmed to approximately −60°, phosphine is slowly evolved. The rate of evolution increases with increasing temperature, the maximum evolution at 0° taking place within twenty minutes. The maximum evolution of phosphine corresponds to between 52 and 58% of the total, an average of seven determinations being 55.5%. The resulting solution evolves no more phosphine even on standing for months dissolved in liquid ammonia at room temperature. When the solvent ammonia is pumped off, a white solid remains, whose composition is approximated by the formula $B_2H_6 \cdot PH_3 \cdot NH_3$.

Gaseous ammonia has been found to react slowly with diborane diphosphine with the displacement of 21 to 75% of the phosphine in the compound, depending chiefly on the temperature and the time of reaction. An interpretation of the above reaction may involve the fact that at temperatures much above −30°, the quantity of diborane formed by the dissociation of diborane diphosphine, $B_2H_6 \cdot 2PH_3 \rightleftarrows B_2H_6 + 2PH_3$, is sufficient to cause one to expect direct action between diborane and ammonia.[5]

(1) A. Stock and E. Kusz, *Ber.*, **56B**, 807 (1923); A. Stock and E. Pohland, *ibid.*, **59B**, 2213 (1926); A. Stock, E. Wiberg, H. Martini and A. Nicklas, *ibid.*, **65B**, 1711 (1932).

(2) H. I. Schlesinger and A. B. Burg, THIS JOURNAL, **60**, 290 (1938).

(3) A. Stock and E. Pohland, *Ber.*, **59B**, 2216 (1926); S. H. Bauer, THIS JOURNAL, **60**, 524 (1938); H. I. Schlesinger, D. M. Ritter and A. B. Burg, *ibid.*, **60**, 1296 (1938).

(4) While this work was in progress, Schlesinger and Burg[2] reported in a footnote the formation of this compound, but no details have been published. However, Professor Schlesinger has been kind enough to inform us of the results of his work with Dr. Burg. These results are given in the following footnote of this paper.

(5) Professor Schlesinger's private communication states that he and Dr. Burg have found that at −40°, gaseous ammonia reacts with diborane diphosphine with the displacement of 50% of the phosphine. They believe that two compounds containing diborane, phosphine and ammonia exist, namely, $B_2H_6 \cdot PH_3 \cdot NH_3$ and $B_2H_6 \cdot PH_3 \cdot 2NH_3$. The latter compound is quite unstable, losing one mole of ammonia at −30°. Trimethylamine displaces 100% of the phosphine from diborane diphosphine, with the formation of borine trimethylamine and phosphine. They have also noted that phosphine reacts with borine carbonyl with the formation of carbon monoxide and diborane diphosphine.

The product formed by the reaction of liquid ammonia on diborane diphosphine is a white pasty solid the stability of which is much greater than that of diborane diphosphine itself. It evolves hydrogen slowly over a period of time, either in the solid state or in solution in liquid ammonia, in which it is readily soluble. It burns with difficulty in air, and dissolves readily in water to form a clear solution. This solution evolves hydrogen, 10% of the hydrogen attached to boron being liberated in six hours, but no phosphine is liberated during this time. If the formula of diborane phosphine ammine is expressed as a phosphonium salt, $PH_4(BH_3NH_2BH_3)$, it would be expected that both liquid ammonia and water would liberate phosphine from the compound. Therefore, the ammonium salt, $NH_4(BH_3PH_2BH_3)$, seems more probable.

When diborane phosphine ammine was heated rapidly to 200°, $B_3N_3H_6$ was formed in yields of 30%, calculated on the nitrogen content. No volatile compounds containing phosphorus were detected.

Hydrogen chloride reacts with diborane diphosphine to form chlorinated derivatives, displacing hydrogen in volume equivalent to the hydrogen chloride introduced. Under controlled conditions, the following reaction takes place

$$B_2H_6\cdot 2PH_3 + 2HCl = B_2H_4Cl_2\cdot 2PH_3 + 2H_2$$

The product so formed is a clear, water-white, viscous, non-volatile liquid, which may further react with hydrogen chloride. The product with an empirical composition $B_2H_2Cl_4\cdot 2PH_3$ is usually formed as a white, crystalline solid, melting with decomposition near 68°. By the use of high pressures of hydrogen chloride above 0°, it can be converted to $BCl_3\cdot PH_3$.[6]

Four possible formulas have been considered for the compound formed by diborane and phosphine: [I], $(PH_4)_2B_2H_4$, corresponding to the formula $(NH_4)_2B_2H_4$ for the diammine suggested by Stock and Wiberg,[7] appears to be inadequate to account for the properties of the compound. [II], $BH_3\cdot PH_3$. If the simple monomer, borine phosphine, were capable of existence in the gas phase for a few minutes at room temperature, it could be detected easily by gas analysis. The results of numerous analyses have given no indication that borine phosphine exists as a stable gas; however, this does not preclude the possibility of its existence in the solid state. The monomeric form for the solid gives the simplest explanation for the reaction with hydrogen chloride, inasmuch as only when two, four and six moles of hydrogen chloride are introduced (for each mole of diborane in the compound) do the products appear to be homogeneous. The reactions with ammonia cannot be accounted for on the basis of the monomeric form, unless it is converted to the dimeric form by the ammonia, which is entirely possible. [III], $PH_4(BH_3PH_2BH_3)$, corresponding to $NH_4(BH_3NH_2BH_3)$ for the diammine, can be used to account for the reactions of the compound formed by diborane and phosphine. The salt-like nature of this compound is, however, not well defined, inasmuch as it will dissolve in liquid ammonia at −75° without the liberation of phosphine. [IV], $B_2H_6\cdot 2PH_3$ is unsatisfactory from many points of view, but it implies the mode of formation and decomposition of the compound and does not emphasize any salt-like character of the compound. It seems probable that without a more extended study of the other hydrides of boron, especially B_4H_{10} and B_5H_9, more definite conclusions may not be drawn concerning the salts or addition compounds formed from diborane.

Experimental

Description of Apparatus.—The apparatus was adapted from the type used by Stock and his co-workers[7] and Schlesinger and his co-workers.[8] The use of stopcocks instead of mercury valves was found to be permissible in situations where the grease was exposed to diborane at low pressures for short periods of time.

Analytical Methods.—The reactants were measured in a calibrated globe and distilled into the reaction tubes with liquid nitrogen. After the reaction had taken place the excess gases were pumped off from the reaction tube into a gas buret by means of a Toepler pump. Wherever possible, these gases were separated by fractional condensation before entering the buret. Diborane was determined by the increase in volume on hydrolysis or the volume of residual hydrogen. Phosphine was determined by the decrease in volume on treatment with 0.1 *N* silver nitrate solution.

Preparation of Diborane.—Diborane was prepared by the method of Schlesinger and Burg[9] as modified by Stock and Sütterlin.[10] Hydrogen saturated with boron tri-

(6) A. Besson, *Compt. rend.*, **110**, 516 (1890), originally prepared this compound by the reaction of equal volumes of gaseous boron trichloride and phosphine below 20°.

(7) A. Stock, "Hydrides of Boron and Silicon," Cornell University Press, 1933, p. 125; E. Wiberg, *Ber.*, **69**, 2816 (1936).

(8) H. I. Schlesinger and his co-workers, particularly A. B. Burg, have published twelve papers on the Hydrides of Boron in THIS JOURNAL, the last of which is **61**, 1078 (1939).

(9) H. I. Schlesinger and A. B. Burg, THIS JOURNAL, **53**, 4321 (1931).

(10) A. Stock and W. Sütterlin, *Ber.*, **67B**, 407 (1934).

bromide at 25° was passed through an electric arc 7 cm. in length at a pressure of 10 mm., and a rate of 500 cc. per minute.[11] The arc produced by a 10,000 volt, 500 volt-ampere transformer proved to be 50% more efficient for the ultimate yield of diborane than the arc produced by a 25,000 volt, 1000 volt-ampere transformer. Yields of 16 cc. of gaseous diborane per cc. of liquid boron bromide (measured at 0°) were obtained. About 85% of the BBr_3 used passed through the arc unchanged.

Preparation of Diborane Diphosphine.—When a mixture of diborane and phosphine was kept at a temperature of −20 to 0°, the pressure slowly decreased over a period of eight to fourteen hours, and long, white, crystalline needles were formed filling the void of the reaction tube. With the reaction tube cooled to −78°, the gases which did not take part in the reaction were pumped out and analyzed. The composition of the residue in the reaction tube, determined by fourteen experiments, is described by the formula $B_2H_6 \cdot (2.00 \pm 0.04)PH_3$. In a typical preparation, 15.0 cc. of diborane and 39.2 cc. of phosphine with an initial pressure of 1.8 atmospheres at 0° produced in six hours a yield of 92% of diborane diphosphine. Neglecting 1.3 cc. of hydrogen formed during this time, the composition of the product was $B_2H_6 \cdot 2.02PH_3$.

The degree to which the reaction takes place is influenced mostly by pressure, an increase from 0.6 to 6.0 atmospheres increasing the yield of product from 72 to 98%. The rate of reaction is also markedly influenced by pressure; at 0° after two to three hours the pressure in the reaction tube is quite independent of the original pressure of the reactants. High concentrations of phosphine and long time of reaction are favorable factors for high yields. The extent of secondary decomposition is increased by high temperatures and long periods of reaction.

Liquid diborane does not react with liquid phosphine at an appreciable rate much below −110°, but above that temperature liquid phosphine reacts within two or three hours with either gaseous or liquid diborane. When insufficient pressure of phosphine is left to maintain the liquid phase, the reaction apparently ceases. For this reason, the temperature should be kept as low as possible to reduce the vapor pressure of the phosphine, and the quantity of unreactive material in the gas phase without reducing the rate of reaction to too great a degree. Using a tube of 6 cc. volume, containing 25.9 cc. of diborane and 60.8 cc. of phosphine at −100°, a yield of 98% in three hours reaction time was obtained. The composition of the product is described by the formula $B_2H_6 \cdot 2.01PH_3$.

Of the two sets of conditions which have been used to prepare diborane diphosphine, the low temperature reaction is the more desirable, because of the increased rate and the elimination of any side reactions in which hydrogen is formed.

Diborane diphosphine dissociates to form one volume of diborane and two volumes of phosphine. An equilibrium exists which can be approached from either side.

$$B_2H_6 \cdot 2PH_3 \rightleftharpoons B_2H_6 + 2PH_3$$

At 0°, this pressure is about 200 mm. Other pressure measurements include: at +25°, 1400 mm.; at −11°, 71 mm.; and at −21°, 11 mm. Since the time required for equilibrium to be established is unusually long, and considerable quantities of hydrogen are formed by secondary decomposition during this time, the precision of the measurements of pressure is quite low.[12]

Pyrolysis of Diborane Diphosphine.—A mixture of 63.6 cc. of PH_3 and 33.9 cc. of B_2H_6 was stored overnight at 0° to form diborane diphosphine in equilibrium with its gaseous constituents. An electric sleeve furnace preheated to 200° and calibrated to maintain that temperature was placed around the reaction tube for fifteen minutes. The tube was cooled to −195°, and 76.7 cc. of hydrogen pumped out. Warming to −77°, 10.5 cc. of a mixture of diborane and phosphine was pumped off. On warming to room temperature, no more gas was evolved. The residue in the tube was a yellowish-white, greasy-looking solid covering the walls of the tube. Under comparable conditions, the pyrolysis of diborane diammine produces up to 40% of $B_3N_3H_6$.

Diborane Diphosphine and Ammonia.—While the solid diborane diphosphine dissolves with difficulty[13] in liquid ammonia at −75° with no apparent reaction, at higher temperatures the rate of solution is quite rapid, and phosphine is evolved. The evolution of phosphine was followed by cooling the tube to −78° and pumping off the phosphine together with some ammonia. At the end of the experiment, the solvent ammonia was pumped off completely. The results of the reaction are shown in Table I. The quantities of diborane diphosphine and ammonia used are expressed as cc. of gas. The fraction of the total phosphine given off in the reaction is expressed as per cent. evolved. The ratio of the sum of the ammonia introduced plus the phosphine calculated to be left in the compound, to the diborane in the compound, is shown in the eighth column. The last column shows the volume of hydrogen evolved; this is a measure of the secondary decomposition during the reaction.

The reaction of gaseous ammonia and diborane diphosphine is in all probability complicated by the decomposition of diborane diphosphine into diborane and phosphine, and thus by the possibility of direct reaction taking place between diborane and ammonia in the gas phase. It is also possible that the formation of phosphine in excess of 50% in the reaction with liquid ammonia is due to this reaction. Part B of Table I shows the results of the gas phase reaction.

Diborane Phosphine Ammine.—The product of the reaction of liquid ammonia on diborane diphosphine is best expressed as $B_2H_6 \cdot PH_3 \cdot NH_3$ although the analysis is not exact. The sum of the phosphine plus the ammonia bears the correct relation to the formula.

Pyrolysis of Diborane Phosphine Ammine.—A sample containing 24.1 cc. of diborane, 22.0 cc. of phosphine and

(11) All volumes referred to in this paper are at standard conditions of temperature and pressure.

(12) The slowness with which this equilibrium is established may very well be due to the reaction involving the borine molecule ($B_2H_6 \rightleftharpoons 2BH_3$) as has been suggested by Schlesinger and Burg[2] for the formation of diborane diammine.

(13) At a temperature just above the melting point of ammonia, 0.079 g. of diborane diphosphine (18.4 cc. B_2H_6 and 37.1 cc. PH_3 as gases) dissolve appreciably in 0.285 g. of liquid ammonia (375.8 cc. of gas) in twenty-nine hours. Solution is complete in forty-eight hours.

TABLE I

REACTION OF AMMONIA AND DIBORANE DIPHOSPHINE

Expt.	B_2H_6, cc.	PH_3, cc.	NH_3, cc.	Temp., °C.	Time	% PH_3 evolved	$\frac{NH_3 + PH_3}{B_2H_6}$	H_2 evolved, cc.
				A. Liquid Phase Reaction				
1	19.9	39.7	155.0	0	20 min.	56		0.1
				20	5 days	56	2.00	1.0
2	21.0	42.8	162.4	0	20 min.	52		0.2
				20	5 days	52	2.01	1.0
3	22.2	43.5	154.6	−25	40 min.	50		
				+25	1 hr.	54	2.07	0.6
4	23.3	43.8	162.2	−33	1 day	38		
					2 days	51		
					3 days	53		
				+25	3 days	58	2.12	2.0
				B. Gas Phase Reaction				
1	46.5	92.1	85.8	−33	3 days	21		
			27.6	+20	24 hrs.	73	2.04	41.3
2	45.4	87.9	163.4	0	40 hrs.	63	2.04	28.5
3	41.5	81.9	103.5	0	3 min.	31		
					24 hrs.	75	2.04	27.7
4	13.6	27.6	51.8	0	5 min.	60		0.1
				20	3 mo.	63	2.01	7.6

21.3 cc. of ammonia was heated in a sealed tube to 200° for fifteen minutes; 90.4 cc. of hydrogen and 2.1 cc. of $B_3N_3H_6$ were formed, while 1.5 cc. of phosphine, 0.2 cc. of B_2H_6 and 0.5 cc. of NH_3 were left unreacted. The vapor pressure of the $B_3N_3H_6$ was 79 mm. at 0° as compared with the reported value of 85 mm. at 0°. Thus, about 30% of the nitrogen in the diborane phosphine ammine was converted to the cyclic compound.

Reaction of Hydrogen Chloride on Diborane Diphosphine.—The results of the reaction of hydrogen chloride on solid diborane diphosphine are shown in Table II. The volume of the reactants is shown in the second, third and fourth columns, while the hydrogen produced and the hydrogen chloride introduced are shown in the last two columns.

Soon after one mole of hydrogen chloride is introduced into diborane diphosphine, the product begins to liquefy. When liquefaction is complete the product has the empirical composition $B_2H_4Cl_2 \cdot 2PH_3$. On addition of more hydrogen chloride, a mixture of solid and liquid is obtained, and when the composition is $B_2H_2Cl_4 \cdot 2PH_3$, it is completely solid. On further reaction with hydrogen chloride, the product can be converted completely into $BCl_3 \cdot PH_3$. When $BCl_3 \cdot PH_3$ is treated with diborane, a liquid containing boron, hydrogen, chlorine and phosphorus is obtained, but its composition could not be established definitely. When a tube containing $B_2H_2Cl_4 \cdot 2PH_3$ is heated rapidly the solid melts about 68° with decomposition. On warming the tube to 100° for an hour, a liquid is formed, and crystals of $BCl_3 \cdot PH_3$ sublime

TABLE II

REACTION OF HYDROGEN CHLORIDE ON DIBORANE DIPHOSPHINE

Expt.	B_2H_6, cc.	PH_3, cc.	HCl, cc.	Temp., °C.	Time, hr.	Press., atm.	$\frac{HCl}{B_2H_6}$	$\frac{H_2 \text{ evolved}}{B_2H_6}$
1	17.7	34.3	38.2	− 26	12	0.2	2.02	1.95
			89.7	− 20	6	0.3		2.92
				+ 25	1		4.00	3.68
2	22.2	44.4	50.8	− 77	24	4.5		1.07
				− 20	0.7	4.0	2.01	1.89
				0	12	0	2.01	2.33
3	10.2	20.2	73.0	− 20	10	3.0		2.93
				+ 25	1		4.05	3.96
4	18.8	37.6	74.9	− 77	2	4.0		0.85
				− 33	0.3	4.5		2.54
					17	1.7		3.30
				0	1	1.2		3.85
				100	1	0	4.00	4.59
5	19.5	39.5	78.1	− 33	2	4.0		1.78
					15	3.5		2.50
				0	72	0	4.00	4.00

to the top of the tube. Small amounts of hydrogen are formed at the same time.

Density of $BCl_3 \cdot PH_3$ in the Gas Phase.—40.3 cc. of $BCl_3 \cdot PH_3$ weighs 0.1230 g. The calculated weight of this volume of gas, if complete dissociation is assumed, and the product acted as a perfect gas, would be 0.1340 g.

Decomposition Pressure of $BCl_3 \cdot PH_3$.—The pressure of $BCl_3 \cdot PH_3$ was determined between −11 and +25°, the results being expressed by the equation $\log p = 11.137 - 2810/T$. The maximum deviation of the observed from the calculated pressures does not exceed 0.5 mm.

Reaction of Hydrogen Bromide on Diborane Diphosphine.—Hydrogen bromide reacts in much the same way as hydrogen chloride, the reaction of liquid hydrogen bromide at −78° taking place very rapidly.

Summary

1. Diborane and phosphine react to form a white unstable solid. The reaction takes place in the gas phase above −30° and in the liquid phase above −110°. The properties of the substance were studied and its probable structure discussed.

2. The action of ammonia on diborane diphosphine has been investigated over a temperature range of −75 to +25°. Liquid ammonia has been found to displace from 52 to 58% and gaseous ammonia up to 75% of the phosphine in diborane diphosphine.

3. The action of hydrogen chloride and hydrogen bromide on diborane diphosphine was found to result in the splitting out of hydrogen attached to boron. The compounds $B_2H_4Cl_2 \cdot 2PH_3$, $B_2H_2Cl_4 \cdot 2PH_3$ and $BCl_3 \cdot PH_3$ have been obtained by this reaction.

4. Attempts to prepare a volatile compound $B_3P_3H_6$, the analog of the cyclic compound $B_3N_3H_6$, were unsuccessful.

CAMBRIDGE, MASS. RECEIVED JANUARY 13, 1940

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

Dipole Moment, Induction and Resonance in Tetra-, Penta- and Hexa-substituted Benzenes

BY CHARLES P. SMYTH AND GEORGE L. LEWIS

The dipole moments of a great many poly-substituted benzenes have been measured by numerous investigators, but the loan by Dr. S. O. Morgan of the Bell Telephone Laboratories of fourteen such compounds, only one of which had been previously measured, has given us an unusual opportunity for the study of a large number of closely related compounds obtained from a single source. In the cases of most of the poly-substituted benzenes, departures of the moments from the values calculated as the resultants of the moments produced by the individual substituents have been attributed to mutual repulsion between adjacent atoms, which has since been shown by X-ray and electron diffraction to produce little distortion in most cases, and to mutual induction between adjacent groups, which calculation has shown to be sufficient to account for the observed discrepancies. More recently, the development of our ideas of resonance has brought the explanation not only of differences in moment between mono-substituted aromatic and aliphatic hydrocarbons, but also of a few seeming discrepancies in the moments of poly-substituted benzenes not previously accounted for. Although Groves and Sugden[1] have refined the method of calculating the inductive effect of a dipole upon the various atoms of the molecule containing it, the calculation retains the fundamental uncertainty inherent in the treatment of a distribution of charges as a single dipole located at a point and in the decision as to the proper location of this point. This uncertainty is serious only in calculating the inductive effects of the dipole upon the immediately adjacent atoms, but it is just these effects which make up the major part of the inductive shifts produced by the dipole. Although reasonable and, at times, very satisfactory results have been obtained on the basis of plausible assumptions in both the more and the less refined calculations, the inductive effect will be treated here in an empirical manner, rendered convenient by the number of but slightly differing compounds under examination.

Consideration of the moments obtained in the present work, like that of nearly all poly-substituted benzenes previously treated, loses a certain amount of precision because of the solvent effect, as the low volatility of the substances has

(1) Groves and Sugden, *J. Chem. Soc.*, 1992 (1937).

necessitated their measurement in benzene solution. However, as the dipoles in the fourteen molecules considered here lie in the plane of the benzene ring and as the maximum polarizabilities of the molecules, with a slight deviation in the case of pentachloroethylbenzene, must also lie in this plane and should not vary a great deal with the direction in this plane, the moments observed in benzene solution should be somewhat lower than the gas values,[2] but the small lowering should be relatively much the same for the different molecules, which should, therefore, have rather closely comparable moment values. The difference in solvent effect between these poly-substituted benzenes and those of mono-substituted benzenes should probably be greater than the differences among the solvent effects of the poly-substituted benzenes. However, the moments of mono- and disubstituted benzenes measured in solution will be used in discussing those of the tetra-, penta-, and hexa-substituted molecules. In general accord with what has been said in regard to the lowering of the moment by solvent effect in the more highly substituted benzenes, it may be mentioned that the moments found by Groves and Sugden[3] for the following vapors are higher than those listed by Fuchs and Wolf[4] for the substances in solution by the amount ($\times 10^{18}$) given after each: *m*-$C_6H_4Cl_2$, 0.19; *o*-$ClC_6H_4NO_2$, 0.29; *m*-$ClC_6H_4NO_2$, 0.30; *p*-$ClC_6H_4NO_2$, 0.23. The value reported by Groves and Sugden for *o*-$C_6H_4Cl_2$ vapor is 0.11 lower than the often-measured solution value, 2.27, while, on the basis of the theoretical considerations qualitatively applied and the experimental values just cited as well as the 0.15 lower value of monochlorobenzene in solution, 1.55, than in the vapor, the vapor value might be expected to be higher than that in solution. This single seeming discrepancy does not invalidate our method of approach, but does show the element of uncertainty involved in the comparison of values from different sources.

The solution values of the mono-substituted benzenes, 1.55 for chlorobenzene and 4.00 for nitrobenzene, to be used in the discussion are 0.15 and 0.21 lower than the gas values. The average moment value 0.34 calculated for toluene from the differences between the molar refraction for the D sodium line and the polarizations measured[5] for the pure liquid from -90 to $+90°$ is indistinguishable from the vapor value 0.35 obtained from the variation of polarization with temperature.[6] If, however, the moment is calculated for the vapor from the differences between the molar refraction and the polarization, a constant value 0.45 is obtained, which, probably, represents the upper limit assignable to the toluene moment. The value 0.35 will be used in the calculations of the present paper.

(2) See Higasi, *Sci. Papers Inst. Phys. Chem. Research (Tokyo)*, **28**, 284 (1936).

(3) Groves and Sugden, *J. Chem. Soc.*, 1782 (1937).

(4) Fuchs and Wolf, "Hand- und Jahrbuch der chemischen Physik," Vol. VI, Akademische Verlagsgesellschaft m. b. H., Leipzig, 1935, Appendix.

Experimental Data

As previously indicated, the substituted benzenes were obtained through the kindness of Dr. S. O. Morgan of the Bell Telephone Laboratories and were used without further purification. The benzene used as solvent was purified in the usual manner.[7] The dielectric constants of the solutions were measured at a frequency of 520 kilocycles with a crystal-controlled heterodyne beat apparatus described elsewhere[5] and the densities were measured with an Ostwald–Sprengel pycnometer in the manner previously described.[8] The dielectric constants ϵ and densities d of the solutions containing mole fractions c_2 of solute are given in Table I together with the polarizations P_2 calculated from them and the value P_1 for the solvent. The value of P_∞ for each substance at 25° given in Table II was obtained by extrapolation of the P_2 values to infinite dilution. The dipole moment μ was calculated in the usual manner from the difference between P_∞ and the molar refraction MR_D listed in Table II. As the substances were solid at room temperature, the molar refractions were calculated as additive quantities from the refraction data in "Landolt–Börnstein." The accuracy of these calculated values is equal to that obtainable experimentally in moderately dilute solutions and greater than that obtainable in the most concentrated solutions that could be prepared from the least soluble substances under examination. The smallness of the differences found between P_∞ and MR_D for the symmetrical trichloromesitylene and dichlorodurene give evidence of the accuracy of the MR_D values. The two small moment values calculated from these differences and listed in parentheses are, of course, indistinguishable from zero and indicate zero moments just as do similar small values obtained for liquid carbon tetrachloride and benzene. The somewhat larger moment values of 2,4,6-trichlorotoluene and pentachlorobenzene have probable errors of about 15% and 5%, respectively, because of uncertainty as to atomic polarization, and the remaining values, all higher, have probable errors of about 1%, with the exception of that for the difficultly soluble pentachlorotoluene, which has a probable error of about 5%. In Table II all the substances are named as substituted benzenes, the order of listing being the same as in Table I.

(5) Lewis and Smyth, *J. Chem. Phys.*, **7**, 1085 (1939).

(6) McAlpine and Smyth, THIS JOURNAL, **55**, 453 (1933).

(7) Smyth and Walls, *ibid.*, **54**, 1854 (1932).

(8) Lewis and Smyth, *ibid.*, **61**, 3063 (1939).

TABLE I

DIELECTRIC CONSTANTS AND DENSITIES OF SOLUTIONS IN BENZENE AND POLARIZATIONS AT 25°

c_2	ϵ	d	P_2
Pentamethylchlorobenzene			
0.00000	2.2760	0.87321	(26.672 = P_1)
.01099	2.3310	.87710	124.7
.02077	2.3788	.88062	123.5
.03315	2.4374	.88460	122.5
.03998	2.4690	.88688	121.8
.04448	2.4997	.88861	124.3
.04612	2.490	.88892	121.8
Pentachlorotoluene			
.00354	2.2909	.87823	107.9
.00504	2.2965	.88027	106.1
.00682	2.3027	.88265	104.4
.00856	2.3082	.88490	102.7
.00892	2.3093	.88536	102.5
Pentachloroethylbenzene			
.01440	2.3286	.89296	106.3
.02594	2.3704	.90797	106.6
.02875	2.3807	.91172	106.6
.03657	2.4081	.92239	105.8
.04313	2.4338	.93092	106.4
Pentachlorobenzene			
.00941	2.2893	.88614	64.1
.02469	2.3139	.90618	66.8
.03108	2.3237	.91451	66.8
.04635	2.3472	.93442	66.8
.05737	2.3642	.94854	66.8
1,2,3,4-Tetrachlorobenzene			
.01521	2.3530	.88931	115.0
.02383	2.3892	.89831	110.1
.03033	2.4185	.90516	108.9
.04014	2.4550	.91531	105.2
Trichloromesitylene			
.00544	2.2776	.87781	56.6
.00753	2.2780	.87957	55.6
.01040	2.2790	.88200	55.5
Dichlorodurene			
.00632	2.2789	.87700	57.8
.00887	2.2796	.87861	56.7
.01344	2.2819	.88131	57.2
.01762	2.2833	.88385	56.8
.02133	2.2848	.88605	56.7
.02766	2.2876	.89033	56.3
2,4,6-Trichlorotoluene			
.04429	2.3063	.90357	51.4
.09227	2.3397	.93642	51.2
.15289	2.3803	.97781	50.7
.21281	2.4218	1.01889	50.3
Trichloropseudocumene			
.00636	2.3078	0.87874	122.9
.00779	2.3157	.87994	124.4
.01019	2.3279	.88193	124.4
.01177	2.3359	.88321	124.4
.01392	2.3468	.88493	124.6
Tetrachloro-*o*-xylene			
.00163	2.2932	.87502	204
.00232	2.2998	.87579	199
.00304	2.3072	.87658	199
.00394	2.3171	.87754	202
.00478	2.3238	.87850	195
4,5-Dichloro-*o*-xylene			
.01806	2.5062	.88298	222.4
.03660	2.7291	.89250	211.2
.05009	2.8875	.89943	204.9
.06201	3.0220	.90546	199.3
.07487	3.1641	.91187	194.1
3,4,5-Trichloro-*o*-xylene			
.00613	2.3285	.87807	172.5
.01228	2.3803	.88293	170.2
.01453	2.3976	.88421	169.2
.02369	2.4640	.89089	162.1
Dichloroprehnitene			
.00213	2.3028	.87458	233
.00403	2.3264	.87577	233
.00564	2.3471	.87673	233
.00802	2.3770	.87814	232.2
.00976	2.3990	.87912	231.8
Dinitroprehnitene			
.00201	2.4110	.87480	1009
.00460	2.5857	.87684	977
.00715	2.7584	.87891	947
.01003	2.9571	.88126	914
.01425	3.2416	.88450	873.4
.01941	3.6013	.88857	830.4

TABLE II

MOLAR REFRACTIONS (CALCULATED), POLARIZATIONS (25°), AND MOMENTS

	MR_D	P_∞ (25°)	μ ($\times 10^{18}$)
Pentamethylchlorobenzene	55.0	126.0	1.85
Pentachloromethylbenzene	55.4	105	1.55
Pentachloroethylbenzene	60.1	106.6	1.50
Pentachlorobenzene	50.6	66.8	0.88
1,2,3,4-Tetrachlorobenzene	45.8	120.8	1.90
1,3,5-Trimethyl-2,4,6-trichlorobenzene	55.3	55.8	(0.1)
1,2,4,5-Tetramethyl-3,6-dichlorobenzene	55.6	56.9	(.25)
2,4,6-Trichloromethylbenzene	45.6	51.6	.54
1,2,5-Trimethyl-3,4,6-trichlorobenzene	55.3	124.4	1.83
Tetrachloro-*o*-xylene	55.2	201	2.65
1,2-Dimethyl-4,5-dichlorobenzene	45.8	233	3.01
1,2-Dimethyl-3,4,5-trichlorobenzene	50.4	176	2.46
1,2,3,4-Tetramethyl-5,6-dichlorobenzene	55.0	233	2.93
1,2,3,4-Tetramethyl-5,6-dinitrobenzene	58.2	1035	6.86

Discussion of Results

In discussing the dipole moments in Table II, we are primarily concerned with the effects of the methyl, chloro, and nitro groups upon one another and upon the benzene ring to which they are attached. Unless otherwise indicated, the moment values quoted are taken from the summary of Fuchs and Wolf already referred to.[4]

It is well known that the methyl group is classed with the halogens in its orienting effect

upon substitution in the benzene ring. The small moment of toluene has been attributed by some investigators to the C–H bond moments of the methyl group, it being assumed tacitly and without reason that the aromatic C–H bond moment is zero. The orienting effect of the methyl group shows that it produces some alteration in the distribution of charge in the ring, which should contribute to the moment. That this moment contribution acts in the direction of the C–C bond between the ring and the methyl group, as would be expected, is shown by the fact that the allocation of the entire dipole moment to this axis leads to good agreement between the calculated and the observed moments when additional groups are substituted on the ring. The small moment of the para aromatic H–C bond is included in the value used for each monosubstituted benzene moment and cancels out when these moments are added and subtracted. The fact that the length of the C–C bond between the ring and the methyl group in mesitylene and hexamethylbenzene cannot be distinguished from that of an ordinary aliphatic C–C bond,[9] is consistent with the absence of any very profound disturbance of structure as shown by the smallness of the dipole moment.

The moment values 0.5 and 0.4 determined in solution for *o*- and *m*-xylene respectively differ by no more than the probable errors in their measurement from the values 0.61 and 0.35 calculated by assigning a moment 0.35 to each axis of the ring-to-methyl bonds. The observed moment of *p*-chlorotoluene 1.90 is identical with the value calculated as the sum of the toluene moment 0.35 and the chlorobenzene moment 1.55, the observed value 1.78 for *m*-chlorotoluene agrees well with the resultant 1.75 of the two vectors 0.35 and 1.55, with an angle 120° between them, and the moment of the ortho compound 1.35 is but slightly lower than the value 1.41 calculated with an angle 60° between the two vectors. The agreement between the observed and calculated values of the three bromotoluenes is equally good.

While the *p*- and *m*-dichlorobenzene moments agree well with the calculated values the moment of the ortho compound determined in solution is 15% lower than the resultant of two dipoles of moment 1.55 with an angle 60° between them. This lowering must be attributed to mutual induction since the widening of the angle between the dipoles because of mutual repulsion has been shown by electron diffraction measurements[10] to be only of the order of 1°. It is well known that the moment of monochlorobenzene is lowered through resonance with contributions from structures in which a positively charged chlorine is connected to the ring by a double bond and a negative charge occurs on the para or on one of the two ortho carbons. It would be expected that substitution of additional chlorines on the ring would lessen the occurrence of the double bond between any particular chlorine and the ring and thus increase the dipole moment associated with the bond. The shortening of the carbon–chlorine bond by its partial double bond character has been observed by means of electron diffraction,[10] but the possible variation in this shortening with variation in the degree of double bond character which might be expected to accompany variation in the number of chlorines was not apparent here as it was in the case of the chloroethylenes.[11] The fair agreement between the observed and calculated values of *m*-dichlorobenzene, in which the effect of mutual induction is small shows that any increase of moment caused by decrease in double bond character must be small.

The agreement between the observed and calculated values of the chlorotoluenes and the fact that chloromesitylene has the same moment 1.55 as chlorobenzene while bromomesitylene and bromodurene[12] have moments 1.52 and 1.55, respectively, as compared to 1.52 for bromobenzene, show that the effects of the methyl groups upon the structures contributing to that of chlorobenzene as well as the inductive effect between the halogen and the adjacent methyl are too small to be detected in the moments.

This absence of effect of the methylbenzene upon the chlorobenzene moment is further evidenced by the moments in Table II. In pentamethylchlorobenzene, the moments due to the 2,3-methyl groups should cancel those due to the 5,6-methyl groups, leaving a moment equal to that of *p*-chlorotoluene. The observed value 1.85 is in satisfactory agreement with the observed value of *p*-chlorotoluene 1.90, which has been found identical with the calculated value. Similar treatment of pentachlorotoluene and penta-

(9) Pauling and Brockway, THIS JOURNAL, **59**, 1223 (1937).

(10) Brockway and Palmer, *ibid.*, **59**, 2181 (1937).

(11) Brockway, Beach and Pauling, *ibid.*, **57**, 2693, 2705 (1935).

(12) Birtles and Hampson, *J. Chem. Soc.*, 10 (1937).

chloroethylbenzene would have the moments due to the 2,3-chlorines cancelling those due to the 5,6-chlorines leaving moments equal to those of *p*-chlorotoluene and *p*-chloroethylbenzene, which should be almost identical in value. The observed values 1.55 and 1.50 are considerably lower than that of *p*-chlorotoluene because of induction between the chlorines. Indeed, it is surprising that they are not still lower. This will be clearer after consideration of the moments of tri-, tetra- and pentachlorobenzenes. The previously determined moment of 1,2,4-trichlorobenzene is 1.25. In the absence of inductive effects, the moments due to the 1,4-chlorines should cancel each other leaving a moment equal to that of chlorobenzene 1.55, but the moment of *o*-dichlorobenzene 2.27, 15% lower than the calculated value, has given evidence of strong mutual induction. If the resultant of the 1,2-chlorine moments is taken equal to that of *o*-dichlorobenzene and acting in the line bisecting a 60° angle between the bonds of the 1,2-chlorines, and the usual moment 1.55 is assigned to the 4-chlorine, the resultant moment of the molecule is calculated to be 1.21 in excellent agreement with the observed value 1.25. In 1,2,3,5-tetrachlorobenzene, the 2- and the 5-chlorine moments should, in the absence of induction, cancel one another, while the 1- and 3-chlorine moments should result in a moment equal to that of one, 1.55. However, the three adjacent chlorines give approximately double the opportunity for lowering of moment by induction that is given by two adjacent chlorines and the moment is lowered from 1.55 to 0.65.

At first glance, it would appear that the moment of pentachlorobenzene in Table II should be the same as that of the 1,2,3,5-tetrachlorobenzene, the pair of chlorine moments on one side of the ring cancelling the pair on the opposite side leaving the moment of the central 3-chlorine to determine that of the molecule. However, the 2- and 4-chlorine moments are reduced by the inductive effects of the 1- and 5-chlorines and, consequently, exert a somewhat reduced inductive effect upon the central 3-chlorine, which, therefore, gives a higher moment to the molecule than that found for 1,2,3,5-tetrachlorobenzene. As pentachlorobenzene differs from the two preceding compounds in Table II only in lacking a methyl or ethyl group, one would expect the moments of these latter compounds to be about $0.88 + 0.35 = 1.23$, but they are about 0.3 higher.

The moment of 1,2,3,4-tetrachlorobenzene in Table II can be treated as made up of two vectors with a 120° angle between them and a value equal to that of *o*-dichlorobenzene 2.27, which is reduced 0.41 by the induction between the two chlorines. The resultant of the two vectors 2.27 is, of course, 2.27, but their value will be reduced by the induction between the 2- and 3-chlorines. A reduction of 0.4 gives close agreement with the observed moment 1.90. The apparently small and actually zero moments found for the symmetrical molecules of trichloromesitylene or 1,3,5-trimethyl-2,4,6-trichlorobenzene, and dichlorodurene, or 1,2,4,5-tetramethyl-3,6-dichlorobenzene, indicate that the atomic polarizations of these poly-substituted benzenes are small, probably not over 2 cc. The moment value of 2,4,6-trichlorotoluene, which should be the same as that of toluene in the absence of mutual effects between the methyl group and the chlorines, is higher than that of toluene by an amount which may easily arise from the small atomic polarization.

In the molecule of trichloropseudocumene, or 1,2,5-trimethyl-3,4,6-trichlorobenzene, absence of induction would leave a moment equal to that of *p*-chlorotoluene 1.90. The observed value 1.83 is slightly lower than this, though not distinguishable from the moment of pentamethylchlorobenzene. One would expect the moment to be reduced more than 0.07 by the induction between the 3- and 4-chlorines. Indeed, if the resultant of these two chlorine moments is taken as equal to the moment of *o*-dichlorobenzene 2.27, the moment calculated for the molecule is 1.54, 0.3 lower than the observed as in the cases of methyl- and ethylpentachlorobenzene.

The moment of tetrachloro-*o*-xylene should be equal to the sum of the moments of 1,2,3,4-tetrachlorobenzene 1.90 and *o*-xylene, 0.5 observed, 0.61 calculated. If the calculated value of *o*-xylene is used, the sum obtained is 0.13 lower than the observed value 2.64. The moment of 4,5-dichloro-*o*-xylene should similarly be equal to the sum of the moments of *o*-dichlorobenzene and *o*-xylene, $2.27 + 0.61 = 2.88$. The observed value is higher than this by 0.13. In other words, the tetrachloro-*o*-xylene and the 4,5-dichloro-*o*-xylene moments differ from each other by just the difference between the moments of

1,2,3,4-tetrachlorobenzene and *o*-dichlorobenzene, as they should, but both are slightly higher than the calculated values. Similarly, the moment of 4,5-dibromo-*o*-xylene[13] 2.86 is higher than the value calculated as the sum of the moments of *o*-dibromobenzene and *o*-xylene, 2.00 + 0.61 = 2.61, but the observed moment of 4-bromo-*o*-xylene[13] 2.07 is identical with the calculated value. In 3,4,5-trichloro-*o*-xylene, the moment due to the three chlorines may be calculated roughly by adding 1.55 to the previously mentioned moment of 1,2,3,5-tetrachlorobenzene 0.65. Resolution of the resultant value 2.20 and the moments due to the two methyl groups gives an approximate value 2.74, which is higher than the observed value 2.46 by no more than its possible error. Dichloroprehnitene, or 1,2,3,4-tetramethyl-5,6-dichlorobenzene, should have the same moment as 4,5-dichloro-*o*-xylene. The observed value is 0.08 lower than this latter and only 0.05 higher than the calculated value. As there was originally some uncertainty as to the composition of a substance subsequently found to be 4,6-dichloro-*m*-xylene, the data on it are omitted from Tables I and II. The moment value observed for it, 2.30, is 0.40 higher than the value calculated as the resultant of the individual methyl and chlorine moments.

In the absence of complicating effects, the moment of dinitroprehnitene, or 1,2,3,4-tetramethyl-5,6-dinitrobenzene, should be equal to that of *o*-dinitrobenzene 6.00 plus the resultant 0.61 calculated for two methyl groups ortho to each other. The observed value 6.86 is slightly higher than this calculated value 6.61, although, for a reason to be discussed presently, one might expect it to be slightly lower. Birtles and Hampson[12] have shown that the moments of nitrodurene and aminodurene are lower than those of the corresponding benzene derivatives and close to those of the corresponding alkyl compounds. The moments of aniline and nitrobenzene, through resonance, receive contributions from highly polar structures in which the nitrogen is linked to the ring by a double bond, with the two other atoms of the group lying in the plane of the ring. Birtles and Hampson conclude that the steric repulsion of the adjacent methyl groups in the durenes tends to prevent the atoms attached to the nitrogen from lying in the plane of the ring and, therefore, reduces the contributions from the highly polar structures. No such reduction is evident, at first glance, in the moment of dinitroprehnitene. The moment of *o*-dinitrobenzene is lowered about 13% below its calculated value, as is also the moment of *o*-chloronitrobenzene, while the moment of *o*-dichlorobenzene is lowered 15% below its calculated value. This difference in lowering is far less than in the case of nitroform and chloroform, in the former of which the lowering below the calculated value is 15% as compared to 44% in the latter.[14] As consideration of the dimensions of the nitro and the methyl groups leads to the conclusion that steric repulsion between the two coplanar nitro groups in *o*-dinitrobenzene would be much greater than that between a methyl group and a nitro group in the plane of the ring, it would appear that the 13% reduction of the moment of *o*-dinitrobenzene below the calculated value may be due, to a considerable extent, to the reduction by steric repulsion of the contribution from the coplanar, highly polar structure. Unless the steric repulsion between the two nitro groups were so great that the addition of a methyl group on each side did not increase the steric effect, one would expect a further lowering of the nitro moments in dinitroprehnitene, which is not observed. Further evidence of the lowering of the nitro moment by the proximity of methyl groups is given by the moment of nitromesitylene 3.65 as compared to 4.00 for nitrobenzene and 3.39 for nitrodurene. A slight lowering is also suggested by the fact that the observed moment of *o*-nitrotoluene 3.66 is lower than the calculated value 3.84, while the observed value of *m*-nitrotoluene 4.17 agrees with the calculated 4.18, and the observed value of the para compound 4.44 is higher than the calculated 4.35. The repulsive effect probably should be less in nitromesitylene than in nitrodurene, where the *o*-methyl groups are pushed somewhat toward the nitro group by the methyls on the next carbons, and obviously should be much less in *o*-nitrotoluene, where, however, the apparent lowering may be due, at least in part, to experimental error.

It is evident that the agreement between the observed and calculated values for these polysubstituted benzenes is fairly good, although the observed values tend to be a little higher than the calculated when the latter are unaffected by in-

(13) Sidgwick and Springall, *J. Chem. Soc.*, 1532 (1936).

(14) Lewis and Smyth, THIS JOURNAL, **61**, 3067 (1939).

duction. The toluene moment 0.35 used for the methyl group would seem the most logical value, but, as pointed out previously, it is not impossible that this moment should be as high as 0.45. If this higher value is used for the methyl group moment, some of the calculated values become higher than the observed and the difference between the two is no longer always in the same direction. The moments of pentachlorotoluene and pentachloroethylbenzene, 1.55 and 1.50, still remain appreciably higher than the value 1.33 calculated by adding the methyl group moment 0.45 to the moment of pentachlorobenzene. The discrepancy might be explained by a small lowering of the moment of pentachlorobenzene through a slight bending of the chlorine bonds by steric repulsion between the chlorines. The replacement of the one hydrogen by the larger methyl or ethyl would prevent or even slightly reverse this bending but no such effect is apparent in the relation of the moment of tetrachloro-*o*-xylene to that of 1,2,3,4-tetrachlorobenzene, where it should occur to a slightly smaller extent. Similar discrepancies have been noted in the cases of trichloropseudocumene and of the slightly doubtful 4,6-dichloro-*m*-xylene. It is possible that the somewhat better agreement obtained with the higher value 0.45 for the methyl group moment is not due to incorrectness of the toluene moment 0.35, but is due to reinforcement of the methyl moment by interaction through the ring with the other substituent groups. It may be concluded, however, that, in view of experimental errors and of possible small variations in the effect of solvent upon the moment values, the differences between the observed and calculated values of the moments are too small to give definite evidence of any effects of resonance in the methyl- and chlorine-substituted benzenes other than those occurring in the mono-substituted compounds.

The effects of resonance are so great in nitrobenzene with its large moment that their influence upon the chlorobenzene resonance is apparent in the moment value of *p*-chloronitrobenzene 2.78 found for the vapor,[3] which is 0.26 higher than the value calculated as the difference between the vapor values for chlorobenzene and nitrobenzene. The contribution of one of the polar forms due to each substituent is increased by the presence of the other as in the familiar case of *p*-nitroaniline, where the effect is much greater. The observed value for *m*-chloronitrobenzene vapor[3] 3.69 agrees with the calculated 3.68, as does that of *m*-dichlorobenzene previously noted, and the same is approximately true of the solution value of *m*-nitroaniline in the literature, while resonance again increases the moment of *o*-nitroaniline. Although, as previously concluded, the data in this paper fail to establish definitely the existence of the interaction of resonance effects of methyl and chlorine groups upon the ring, they suggest the possibility of a small increase in moment through the mutual effects of para-substitution upon resonance.

In conclusion, the writers wish to express their gratitude to Dr. B. S. Biggs of the Bell Telephone Laboratories, who prepared the compounds here discussed, and to Dr. S. O. Morgan of the same Laboratories, through whose kindness they were made available for our measurements.

Summary

The dipole moments of fourteen tetra-, penta-, and hexa-substituted benzenes with chlorine and the methyl and nitro groups as substituents have been measured in dilute solutions in benzene. The values are compared with those calculated as the vector sums of the moments of mono-substituted benzenes and the effect of induction between groups is taken care of by using the moment of a di-, tri-, or tetra-substituted molecule as a single vector. On the whole, satisfactory agreement is obtained between the observed and the calculated results. The alteration in the moment due to one group produced by the resonance effects of another group is evident in *p*-chloronitrobenzene, but is too small to detect with certainty in these results where methyl and methyl, methyl and chlorine, or chlorine and chlorine are the groups involved, although an indication of a possible small increase in moment due to such effects is given.

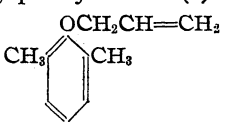
PRINCETON, NEW JERSEY RECEIVED JANUARY 10, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

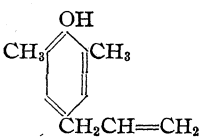
The Claisen Rearrangement. II. A Kinetic Study of the Rearrangement of Allyl 2,6-Dimethylphenyl Ether in Diphenyl Ether Solution

BY D. STANLEY TARBELL AND JOHN F. KINCAID

A recent study[1] of the kinetics of the rearrangement of allyl *p*-tolyl ether in diphenyl ether solution indicated that the reaction is first order and proceeds by some mechanism which does not require catalysis by acids or bases. The case studied involves migration of the allyl group to the free ortho position and might be expected to be a unimolecular reaction. If both ortho positions of an allyl phenyl ether are blocked, however, the allyl group enters the para position on rearrangement, and the reaction might be expected to involve a bimolecular mechanism. We wish to report a study of the rate of rearrangement of a compound of this type, allyl 2,6-dimethylphenyl ether (I).



I



II

The rate of conversion of this compound to 2,6-dimethyl-4-allylphenol (II) in one molar solution in diphenyl ether has been studied at three temperatures, 185.8, 171.6, and 156.9°. At the two higher temperatures the rate of reaction of the pure liquid has been measured, and at 171.6° the effect of dimethylaniline and acetic acid has been studied, as well as the rate in solutions more concentrated and more dilute than one molar.

The structure of the rearrangement product II was proved by the fact that it was identical with the product obtained from direct C-alkylation of 2,6-dimethylphenol with allyl bromide. With allyl bromide and sodium ethylate in alcohol, 2,6-dimethylphenol yielded a mixture of approximately 85% of the ether I and 15% of the C-alkylation product II. In a trial run with allyl bromide and sodium in benzene, the product consisted of 55% of the ether and 45% of the C-alkylation product.

It was found that the phenylurethan of the rearrangement product II could be prepared readily using a trace of dry hydrogen chloride as catalyst; aluminum chloride and bases are also known to catalyze the formation of phenylurethans from phenols.[2]

The isolation of the rearrangement products described in the experimental part was carried out in order to determine whether side reactions occurred during the reaction. The results of the fractionation showed that 95% of the product was pure 2,6-dimethyl-4-allylphenol when the rearrangement of the pure liquid was carried out at 171.6° in the absence of air. Five per cent. of a non-volatile product was formed which was probably a polymer. Since polymerization reactions should be slower in solution than in the pure liquid, it is concluded that the rearrangement in solution is greater than 95% quantitative.

The first order rate constants obtainable from these data by the usual equation, given in Tables I to III, show that the kinetics of the rearrangement are strictly first order. If the slow step in the reaction mechanism were bimolecular, the first order constants for 80% reaction would be only about one-half as great as the initial values, whereas inspection of the table reveals that the constants for the two most dilute solutions do not change greatly with the percentage reaction, while those for the most concentrated solution actually increase with percentage reaction. This increase is very marked for the pure liquid, the rate constant for 77% reaction being 11.85×10^{-5} sec.$^{-1}$ compared to 7.75×10^{-5} sec.$^{-1}$ for 16% reaction. It should be mentioned that these rate constants are not an accurate measure of the specific rate of the rearrangement in the two cases since they were computed from an equation integrated with the condition that k remain constant as the reaction proceeds. Actually the rate of the rearrangement is about three times the initial rate after 80% reaction in the pure liquid. This behavior is similar to that previously noted for allyl *p*-tolyl ether.[1] Although the reaction takes place considerably faster in the pure liquid than it does in solution, the initial values of the rate constants are almost the same. This constancy of the initial values is further proof that the reaction is first order.

(1) Kincaid and Tarbell, THIS JOURNAL, **61**, 3085 (1939).

(2) Leuckart, *Ber.*, **18**, 875 (1885); Claisen, *Ann.*, **418**, 82 (1918).

TABLE I[a]

FIRST ORDER RATE CONSTANTS AT 171.6°

4.30% I and 95.70% diphenyl ether					
2,050	4,450	6,950	12,910	20,360	
13.89	25.26	36.98	55.98	73.44	mean
7.28	6.55	6.65	6.35	6.52	6.67
14.13% I and 85.87% diphenyl ether					
1,970	4,420[b]	4,470	13,480[b]	13,810	
13.21	27.13	27.90	63.76	64.37	mean
7.21	7.16	7.31	7.53	7.47	7.34
17.75% I and 82.25% diphenyl ether					
2,290	4,000	6,900	13,880	21,580	
14.99	25.33	40.15	66.62	83.13	
7.09	7.29	7.44	7.90	8.25	
100% I					
2,200	4,900	8,380	10,000	12,460	
15.68	34.83	58.65	66.44	77.14	
7.75	8.73	10.54	10.92	11.85	
11.23% I, 9.93% dimethylaniline and 78.84% diphenyl ether					
1,790	3,720	6,630	12,820	19,300	
14.35	26.50	42.61	65.76	80.72	mean
8.68	8.30	8.37	8.36	8.53	8.45
13.11% I, 1.07% acetic acid and 85.82% diphenyl ether					
2,740[c]	8,000	12,600	22,320		
22.66	51.73	69.31	88.18		mean
9.38	9.11	9.37	9.56		9.36
11.65% I, 2.05% acetic acid and 86.30% diphenyl ether					
1,940	3,270	5,630	9,380		
18.33	28.70	44.16	63.27		mean
10.42	10.36	10.35	10.68		10.45

[a] The first row gives the time in sec., the second gives the percentage reaction, and the third gives the rate constants in reciprocal seconds times 10^5.

[b] Solution of new materials, 12.46%.

[c] 19.78% I, 0.99% acetic acid and 79.23% diphenyl ether.

TABLE II[a]

FIRST ORDER RATE CONSTANTS AT 185.8°

14.13% I and 85.87% diphenyl ether					
700	1,300	2,290	5,560		
15.51	24.89	39.06	69.84		mean
24.1	22.0	21.6	21.6		22.3
100% I					
700	1,720	2,920	4,180	6,340	
17.24	38.04	58.80	74.98	94.61	
27.0	27.8	30.4	33.1	...	

[a] The first row gives the time in sec., the second gives the percentage reaction, and the third gives the rate constants in reciprocal seconds times 10^5.

The effect of dimethylaniline on the rate was studied in order to determine whether the slow step in the mechanism involved the transfer of a proton. If this were the case, then dimethylaniline should considerably accelerate the rate since it is a far better proton acceptor than diphenyl ether. From Table I it is seen that the addition of 10% of dimethylaniline increases the rate by about 15%. This relatively small increase is interpreted as indicating that a prototropic change is not the slow step in the reaction, although it does not preclude the possibility that such a change is involved somewhere in the mechanism. This 15% increase is, however, to be compared with only a 3% increase for a similar experiment carried out with allyl *p*-tolyl ether.[1]

TABLE III[a]

FIRST ORDER RATE CONSTANTS AT 156.9°

14.13% I and 85.87% diphenyl ether					
5,920	8,440	11,680	22,780	43,420	
12.00	16.78	21.35	43.36	65.80	mean
2.16	2.18	2.06	2.50	2.47	2.27

[a] The first row gives the time in sec., the second gives the percentage reaction, and the third gives the rate constants in reciprocal seconds times 10^5.

The two series of runs in the presence of acetic acid indicate that the reaction is speeded up to some extent by the presence of acids. Thus the rate constant for a 1% solution of acetic acid is 28%, and that for a 2% solution is 42%, greater than that for the reaction in the absence of acids. This effect, although not very great, appears to be definitely beyond any possible experimental error. On the other hand, it appears definite that the reaction as it takes place in the pure liquid or in solution in pure diphenyl ether is not a catalyzed reaction since a much greater increase in the rate would be expected if the reaction could occur *only* in the presence of acids.

The mean rate constants for the 14% solutions at the three temperatures were used to compute the activation energy for the reaction from the Arrhenius equation

$$k = A \exp(-\Delta E/RT) \qquad (1)$$

we obtain $A = 0.583 \times 10^{11}$ sec.$^{-1}$, and $\Delta E =$ 30.3 kcal. per mole. The entropy of activation for the reaction, $\Delta S^{\pm}$, may be obtained from the constant A by means of the equation[3] for the absolute rate of any reaction

$$k = (kt/h)\,\kappa \exp(\Delta S^{\pm}/R) \exp(-\Delta E^{\pm}/RT)$$

Here k is Boltzmann's constant, h is Planck's constant, κ is the transmission coefficient, and $\Delta S^{\pm}$ and $\Delta E^{\pm}$ are the entropy and energy of activation, respectively. By making the usual assumption that κ equals unity, we find that $\Delta S^{\pm}$

(3) H. Eyring, *J. Chem. Phys.*, **3**, 107 (1935).

$= -10.1$ E. U. at 171.6°. This value is to be compared to $\Delta S^{\ddagger} = -9.5$ E. U. for the rearrangement of allyl *p*-tolyl ether.[4] The fact that the entropies of activation for the rearrangement to the ortho and para positions differ by only 0.6 E. U. suggests strongly that the slow step is the same in each case.

Two mechanisms were discussed[1] as possibilities for the rearrangement to the ortho position. The first, the cyclic mechanism, is one in which the γ carbon atom on the allyl group starts to form a bond with the atom in the ring simultaneously with the breaking of the carbon–oxygen bond. The second mechanism proposed, the dissociation mechanism, is one in which the slow step is the breaking of the carbon–oxygen bond, the allyl group being split off as a radical or positive ion. The chemical evidence favors the cyclic mechanism for the rearrangement to the ortho position. This mechanism requires inversion of the allyl group during rearrangement, and this has been observed repeatedly.[5] That the allyl group is never free during the rearrangement to the ortho position is indicated by the work of Hurd and Schmerling,[6] who showed that mixed products are not formed when a mixture of cinnamyl phenyl ether and allyl β-naphthyl ether is rearranged. On the other hand, the chemical evidence favors the dissociation mechanism for the rearrangement to the para position. Thus it has been shown[7] that inversion does not usually occur during the migration of the allyl group to the para position. The chemical evidence for the incorrectness of the cyclic mechanism for the rearrangement to the para position is supported by the use of Fisher-Hirschfelder atomic models. They show that, even in the most favorable orientation, there is still an internuclear distance of more than 4 Å. between the para and γ carbon atoms. Not only is this too great to be favorable for bond formation but the angle is not suitable, being about 120° away from the stable configuration in the plane of the ring.

Thus the chemical evidence appears to indicate that the mechanisms of the migrations to the ortho and para positions are different, while the kinetic studies lead to the conclusion that they are the same. It must, however, be remembered that rate measurements, by themselves, can give information *only* about the slow step in the reaction.

(4) The value previously found for $\Delta S^{\ddagger}$ for the rearrangement of allyl *p*-tolyl ether[1] was −8.1 E. U. However, for purposes of comparison with the present case this must be corrected by $-R \ln 2$ (−1.4 E. U.) due to the fact that there are two ortho positions in the ring available for substitution.

(5) Claisen and Tietze, *Ber.*, **58**, 275 (1925).

(6) Hurd and Schmerling, THIS JOURNAL, **59**, 107 (1937).

(7) Mumm and Müller, *Ber.*, **70**, 2214 (1937); Mumm, Hornhardt and Diederichsen, *ibid.*, **72**, 100 (1939); Mumm and Diederichsen, *ibid.*, **72**, 1523 (1939); Späth and Kuffner, *ibid.*, **72**, 1580 (1939).

Experimental

The technique of carrying out the measurements and analyzing the reaction mixture already has been described.[1]

Allyl 2,6-Dimethylphenyl Ether (I).—Eastman Kodak Co. 2,6-dimethylaniline was purified through the crystalline formyl derivative[8] and 2,6-dimethylphenol prepared from the purified amine by the method of Bamberger.[9] To a solution of 19.5 g. of sodium in 350 cc. of alcohol, 103.5 g. of recrystallized 2,6-dimethylphenol (m. p. 47–48°) was added, followed by dropwise addition of 121 g. of allyl bromide, while heating the solution on the steam-bath. The reaction mixture, which formed a solid precipitate immediately, was heated on the steam-bath for three hours, and poured into 1.5 liters of water. The product was isolated by extraction with 400 cc. of low boiling petroleum ether in two portions; the extract was washed twice with 100-cc. portions of 20% sodium hydroxide solution, dried, the solvent removed, and the product distilled in nitrogen through a modified Widmer column. The main fraction of 63.9 g. had the boiling point of 67–68° at 2 mm., bath temperature 100–105°; d^{25}_4 0.9422, $n^{25}D$ 1.5048. *Anal.*[10] Calcd. for $C_{11}H_{14}O$: C, 81.44; H, 8.69. Found: C, 81.53; H, 8.70. Analysis by the usual method showed that this sample contained 0.4% of 2,6-dimethyl-4-allylphenol (II).

2,6-Dimethyl-4-allylphenol (II).—The sodium hydroxide wash solution of the preceding paragraph yielded on acidification and extraction 34 g. of oil, which was separated by fractionation into two fractions: 10.8 g. of 2,6-dimethylphenol, b. p. 103–115° at 22 mm., and 10 g. of the C-alkylation product, 2,6-dimethyl-4-allylphenol, b. p. 131–138° at 21 mm. The phenylurethan prepared as described below, melted at 139–140.5° after two crystallizations from ligroin, and gave no depression when mixed with the phenylurethan of II produced by rearrangement.

When 8.45 g. of 2,6-dimethylphenol was alkylated with the equivalent amount of sodium and allyl bromide in benzene solution, 2.8 g. of the O-alkylation product I was obtained, and 2.1 g. of the C-alkylation product II.

Isolation of the Products of the Rearrangement.—Forty-three grams of the ether (I) was heated for seven hours at 171.6° in sealed tubes.

The product II (41.3 g.) was distilled in a nitrogen atmosphere through a modified Widmer at a distillation rate of about six drops per minute. At 2 mm. pressure, the boiling point of fractions 2, 3 and 4 varied between 90.5 and 91.4°.

These fractions were analyzed in duplicate for active hydrogen by the usual method, and the molecular weights per active hydrogen are shown in Table IV. The fact

(8) Busch, *ibid.*, **32**, 1008 (1899).

(9) Bamberger, *ibid.*, **36**, 2036 (1903).

(10) Analyses by Dr. L. Weisler.

TABLE IV

Fraction	% Total material	Mol. wt.[a]
1	2.8	
2	55.2	162.8
3	25.5	164.3
4	5.8	162.9
5	9.0	
Total	98.3	

[a] Mol. wt. of 2,6-dimethyl-4-allyl phenol, 162.2.

that these fractions have the expected molecular weight per active hydrogen indicates that they are composed of pure rearrangement product. That fraction 1 was composed almost entirely of the unrearranged ether (I) and its rearrangement product (II) was shown by analyses of samples taken before and after this fraction had been heated for five hours more at the same temperature. The molecular weight per active hydrogen was 296 before and 169.5 after further heating. If fraction 1 is considered to be a mixture of I and its rearrangement product only, these figures are equivalent to a percentage composition of 55% II and 96% II before and after the second heating. These data make it appear probable that no appreciable amount of material formed by side reactions was present in the low boiling fraction.

Fraction 6, the residue left in the still pot, was distilled from a 5-cc. Claisen flask at reduced pressure; 40% of the material distilled at the expected boiling point, but the remainder of this fraction, 5.4% of the original 41.3 g., did not distil. It was evidently polymeric. The portion which distilled had a molecular weight per active hydrogen which agreed with that for (II) to within 0.2%.

The material not accounted for in Table IV, 1.7%, was held up in the still, and by washing out the apparatus with ether a small amount of material was recovered which boiled at the correct place for the rearrangement product. The amount available was insufficient for analysis.

Therefore the only product except the rearrangement product and unreacted ether which could be found was 5.4% of polymeric material in fraction 5. Since polymerization reactions would be expected to be somewhat less rapid in solution than in the pure liquid, it seems certain that the reaction in solution is greater than 95% quantitative. The pure 2,6-dimethyl-4-allylphenol (fractions 2, 3 and 4) has the following properties: b. p. 90.5–91.4° at 2 mm.; d^{25}_4 0.9870; $n^{25}D$ 1.5370.

The **phenylurethan** was prepared from 1 cc. of the phenol and 0.6 cc. of phenyl isocyanate by passing dry hydrogen chloride over the surface of the solution and heating the mixture on the steam-bath for ten minutes. The product, which crystallized on cooling, was recrystallized twice from ligroin, m. p. 141–142.5°, and gave no depression when mixed with samples from the 2,6-dimethyl-4-allylphenol prepared by direct C-alkylation of 2,6-dimethylphenol.

Anal. Calcd. for $C_{18}H_{19}O_2N$: C, 76.84; H, 6.81. Found: C, 76.79; H, 6.78.

Summary

1. Allyl 2,6-dimethylphenyl ether and 2,6-dimethyl-4-allylphenol have been prepared and characterized.

2. The rate of rearrangement of allyl 2,6-dimethylphenyl ether has been measured at 156.9, 171.6 and 185.8°, in the pure liquid at the two upper temperatures, and in diphenyl ether solution at all three temperatures. Measurements covering a four-fold range in concentration in solution showed the reaction to be first order, and the initial values of the rate constants for the pure liquid are the same as those in solution.

3. The reaction rate is not appreciably affected by 10% of dimethylaniline, but 1% and 2% of acetic acid lead to increases in the rate constant of 28% and 42%, respectively.

4. The energy of activation for the reaction is 30.3 kcal. per mole, and the entropy of activation is −10.1 E. U. From a comparison of this value of $\Delta S^{\ddagger}$ with that for the rearrangement to the ortho position, it is concluded that the slow step is the same in each case.

5. The rearrangement has been shown to be at least 95% quantitative in solution.

6. Appreciable amounts of the C-alkylation product are observed in the reaction of allyl bromide and 2,6-dimethylphenol even when the reaction is carried out in alcohol solution in the presence of sodium ethylate.

ROCHESTER, N. Y. RECEIVED DECEMBER 5, 1939

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

Structure of Cannabidiol. II. Absorption Spectra Compared with those of Various Dihydric Phenols

BY ROGER ADAMS, C. K. CAIN AND HANS WOLFF

IN COLLABORATION WITH THE TREASURY DEPARTMENT, NARCOTICS LABORATORY, WASHINGTON, D. C.

The isolation of a new substance, cannabidiol, from the red oil of Minnesota wild hemp was recently described.[1] It proved to be an optically active, resinous, dihydric phenol from which two crystalline derivatives, the *bis*-3,5-dinitrobenzoate and the *bis-m*-nitrobenzenesulfonate, could be obtained. A pure dimethyl ether also was prepared. Oxidation of cannabidiol with formation of *n*-caproic acid indicated the likelihood of the presence of an *n*-amyl group in the phenolic nucleus.

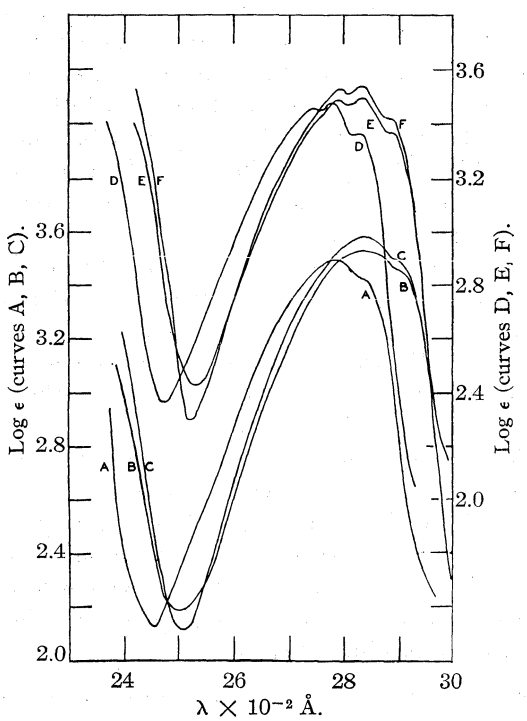
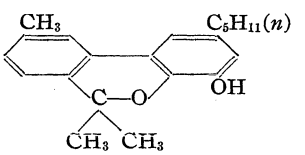
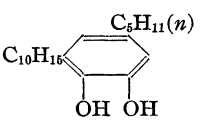


Fig. 1.—A, Catechol; B, 4-methylcatechol; C, 4-*n*-amylcatechol; D, catechol dimethyl ether; E, 4-methylcatechol dimethyl ether; F, 4-*n*-amylcatechol dimethyl ether.

The analyses of cannabidiol and its derivatives revealed the probable formula as $C_{21}H_{30}O_2$, whose similarity to that of cannabinol, $C_{21}H_{26}O_2$, is striking. With the structure of cannabinol (I) satisfactorily established,[2] except for the positions of the hydroxyl and *n*-amyl groups, an analogous structure for cannabidiol might be anticipated, since these two natural products come from essentially the same source.



I



II

Consequently, a tentative formula (II) for cannabidiol was suggested with the postulation that the $C_{10}H_{15}$–group was probably a menthyl residue containing two double bonds.

Information concerning the orientation of the two hydroxyls in the cannabidiol molecule is not readily obtained chemically but through absorption spectra the relationship should be possible to determine. With this end in view a comparison has been made of the ultraviolet absorption spectra of cannabidiol and cannabidiol dimethyl ether with those of catechol, 4-methylcatechol and 4-*n*-amylcatechol and their dimethyl ethers, and with those of resorcinol, 5-methylresorcinol and 5-*n*-amylresorcinol and the corresponding dimethyl ethers.

From Fig. 1 it is apparent that the catechols have one broad peak and one that is much narrower. The introduction of alkyl groups into the catechol molecule in the 4-position causes a shift of the peaks of the spectra toward longer wave lengths with a simultaneous increase in the extinction coefficients at these wave lengths. The dimethyl ethers of these compounds show spectra having three distinct peaks and the variations with introduction of the alkyl groups are similar to those in the unmethylated compounds.

In Fig. 2 are given the spectra of resorcinol and its derivatives. They all show two distinct peaks of about the same breadth. In marked contrast to the catechol derivatives, the introduction of alkyl groups in the 5-position causes a slight shift in the peaks of the spectra toward lower wave lengths and the molecular extinction coefficients at these wave lengths are decreased. The same

(1) Adams, Hunt and Clark, THIS JOURNAL, **62**, 196 (1940).

(2) Cahn, *J. Chem. Soc.*, 986 (1930); 630 (1931); 1342 (1932); 1400 (1933).

general effects are found in the spectra of the dimethyl ethers.

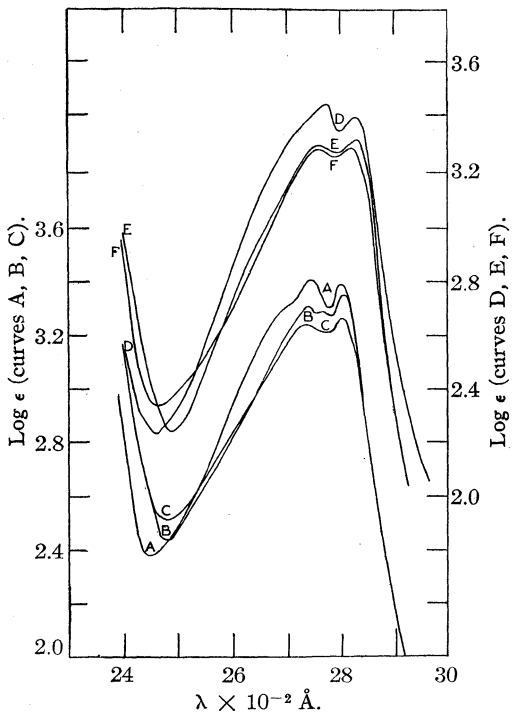


Fig. 2.—A, Resorcinol dimethyl ether; B, 5-methylresorcinol dimethyl ether; C, 5-*n*-amylresorcinol dimethyl ether; D, resorcinol; E, 5-methylresorcinol; F, 5-*n*-amylresorcinol.

A comparison of the spectra of cannabidiol, 5-*n*-amylresorcinol and 4-*n*-amylcatechol shows the striking similarity of the curves of cannabidiol and 5-*n*-amylresorcinol. The peaks in the curve for cannabidiol are shifted toward lower wave lengths and lower extinction coefficients, as was shown to be the effect on the spectra of resorcinol when alkyl groups are introduced. The dimethyl ethers of these three compounds give spectra similarly related.

Confirmation of the deduction that cannabidiol probably is a resorcinol derivative was obtained by infrared absorption spectra (Fig. 4). These were kindly carried out for us by Dr. W. H. Rodebush and Mr. G. W. McMillan of this Laboratory, to whom we are deeply indebted. The spectra of cannabidiol and 5-*n*-amylresorcinol have only single peaks at essentially the same wave length, while that of 4-*n*-amylcatechol shows two distinct peaks at different wave lengths from those shown in the other two spectra.

On the basis of these results, structure II for cannabidiol must be incorrect; it may now be assigned structure III which represents the molecule as a resorcinol derivative. The location of the

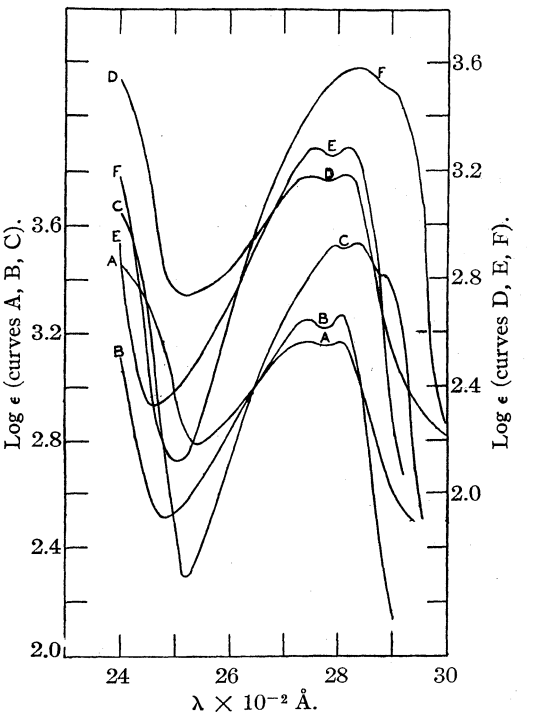


Fig. 3.—A, Cannabidiol dimethyl ether; B, 5-*n*-amylresorcinol dimethyl ether; C, 4-*n*-amylcatechol dimethyl ether; D, cannabidiol; E, 5-*n*-amylresorcinol; F, 4-*n*-amylcatechol.

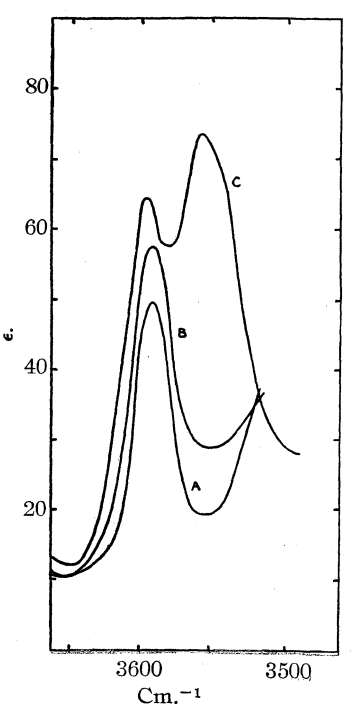
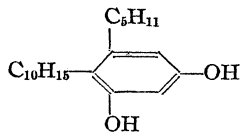


Fig. 4.—A, Cannabidiol; B, 5-*n*-amylresorcinol; C, 5-*n*-amylcatechol.



III

$C_{10}H_{15}$–radical and of the *n*-amyl group in relation to the hydroxyl groups in structure III is purely arbitrary.

Attempts to determine the presence of a resorcinol or catechol orientation of hydroxyls in cannabidiol by means of a variety of color reactions such as have been used in the past for testing for resorcinol, catechol, and red oil, proved negative. No satisfactory correlation was apparent between the color reactions of cannabidiol and 5-*n*-amylresorcinol nor between cannabidiol and 5-*n*-amylcatechol.

Experimental

A Bausch and Lomb medium quartz spectrograph and a Moll type recording densitometer were used for the ultraviolet absorption spectra of solutions of the compounds in ether. The infrared absorption spectra were taken of carbon tetrachloride solutions.

Cannabidiol and cannabidiol dimethyl ether were prepared as previously described.[1]

1,2-Dimethoxy-4-methylbenzene.—This was prepared by the Clemmensen reduction of veratric aldehyde as described by King and l'Ecuyer.[3] The product used boiled at 112° (20 mm.); m. p. 23° (cor.); $n^{25}D$ 1.5250.

1,2-Dihydroxy-4-methylbenzene (4-Methylcatechol).—A mixture of 9 g. of 1,2-dimethoxy-4-methylbenzene and 37 cc. of 48% hydrobromic acid was refluxed for six hours. Water was added followed by sodium bicarbonate until neutral. The compound was ether extracted, the ether solution in turn extracted with 10% aqueous sodium hydroxide, and the alkaline solution which became deeply colored was acidified immediately with dil. sulfuric acid. Subsequent extraction with ether and evaporation of the solvent gave a product which had a b. p. 141–143° (20 mm.). This liquid solidified and was crystallized from a mixture of benzene and petroleum ether (b. p. 40–60°), m. p. 65–66°. Finally it was redistilled before determining the absorption spectra; yield 4.5 g.

1,2-Dihydroxy-4-*n*-pentanoylbenzene.—This was prepared by a method previously described.[4] The observed m. p. 99–100° (cor.) differed slightly from that given by the above authors.[4]

1,2-Dihydroxy-4-*n*-amylbenzene (4-*n*-Amylcatechol).—Miller, Hartung, Rock and Crossley report only a 40% yield by the Clemmensen reduction of 1,2-dihydroxy-4-*n*-pentanoylbenzene, but a 90% yield by a palladium–hydrogen reduction. It has been found that the Clemmensen reduction of the ketone by the modification of Martin[5] gave a 72% yield; b. p. 153–155° (4–5 mm.); $n^{20}D$ 1.5258. The product crystallized in rosets on cooling in ice.

1,2-Dimethoxy-4-*n*-amylbenzene (4-*n*-Amylcatechol Dimethyl Ether).—To a mixture of a solution of 3.6 g. of 4-*n*-amylcatechol in 100 cc. of methanol and 6 g. of dimethyl sulfate was added slowly a 10% ethanolic sodium hydroxide solution until the reaction remained neutral. Another 6 g. of dimethyl sulfate was introduced and the procedure repeated. Most of the color in the solution had disappeared when methylation was complete. The mixture was extracted with ether and the ether solution was washed with aqueous alkali; b. p. 124–126° (4–5 mm.); $n^{20}D$ 1.5084; d^{20}_4 0.9856.

Anal. Calcd. for $C_{13}H_{20}O_2$: C, 75.00; H, 9.62. Found: C, 75.29; H, 9.85.

The resorcinol and orcinol used were purified grades of commercial products. The methyl ethers were prepared in the usual way.

Olivetol dimethyl ether and olivetol were made by the method of Asahina,[6] though more recently the procedure of Suter and Weston[7] for the preparation of these compounds proved to be more satisfactory.

Summary

The ultraviolet and infrared absorption spectra of cannabidiol resemble closely that of olivetol, 1,3-dihydroxy-5-*n*-amylbenzene, and do not resemble that of 4-*n*-amylcatechol. It therefore was concluded that cannabidiol is a resorcinol derivative.

A comparison of the absorption spectra of resorcinol with its 5-methyl and 5-*n*-amyl derivatives indicates that introduction of the alkyl groups causes a slight shift in the peaks toward lower wave lengths and the molecular extinction coefficients at these wave lengths are decreased.

A comparison of catechol and its 4-methyl and 4-*n*-amyl derivatives indicates that introduction of the alkyl groups causes a shift in the peaks toward longer wave lengths and an increase in the extinction coefficients at these wave lengths.

URBANA, ILLINOIS RECEIVED JANUARY 8, 1940

(3) King and l'Ecuyer, *J. Chem. Soc.*, 427 (1937).

(4) Miller, Hartung, Rock and Crossley, THIS JOURNAL, **60**, 7 (1938).

(5) Martin, *ibid.*, **58**, 1438 (1936).

(6) Asahina, *Ber.*, **69B**, 1643 (1936).

(7) Suter and Weston, THIS JOURNAL, **61**, 232 (1939).

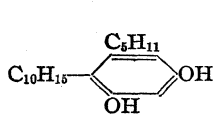
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Structure of Cannabidiol. III. Reduction and Cleavage

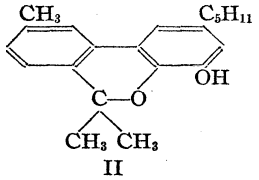
BY ROGER ADAMS, MADISON HUNT AND J. H. CLARK[1]

IN COLLABORATION WITH THE TREASURY DEPARTMENT, NARCOTICS LABORATORY, WASHINGTON, D. C.

On the basis of absorption spectra,[2] cannabidiol (I) appears to be a resorcinol and not a catechol derivative as was first assumed after a consideration of the structure proposed by Cahn[3] for the closely related compound cannabinol (II).



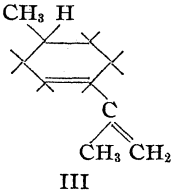
I



II

The C_5H_{11}–group previously has been shown to be normal. New chemical evidence is now submitted to demonstrate that cannabidiol is a resorcinol derivative. Information also has been discovered pertaining to the position of the amyl group in the resorcinol nucleus and to the chemical characteristics and the mode of attachment of the $C_{10}H_{15}$–grouping.

Earlier experiments on catalytic reduction of cannabidiol were variable and hence unsatisfactory for quantitative deductions. These results probably were due primarily to the fact that the cannabidiol used contained traces either of 3,5-dinitrobenzamide or ethyl 3,5-dinitrobenzoate. When pure, cannabidiol reduces rapidly in glacial acetic acid with platinum oxide catalyst and hydrogen at room temperature and 2–3 atm. pressure. Two moles of hydrogen are absorbed before the reduction stops. The product has all of the characteristic color reactions of the original molecule and contains two active hydrogens. It was concluded, therefore, that the amylresorcinol nucleus remained unaffected, and that the reduction had occurred in the $C_{10}H_{15}$–residue with the establishment of the presence therein of two double bonds. In view of the rapidity of hydrogenation under mild conditions, it appears unlikely that the unsaturation consists of one double bond and a three-, four- or five-membered ring such as was suggested as a possibility in the first paper in this series. With these facts in hand and keeping in mind the cannabinol formula, the $C_{10}H_{15}$–group may be postulated as a menthyl residue containing two double bonds (III) which have been assigned the positions indicated fortuitously.



III

The tetrahydrocannabidiol is an essentially colorless, viscous, optically active oil. No crystalline derivatives have as yet been isolated. The product probably is not a pure individual, for reduction of two double bonds in an optically active nucleus is likely to lead to diastereoisomeric tetrahydro derivatives.

Dehydrogenation of cannabidiol was also attempted. The product was optically inactive and analyzed satisfactorily for a biphenyl molecule. No solid derivatives, however, were obtained. In view of the possibility of disproportionation and the small amounts of material taken, these experiments may be used merely as a further indication of the presence of a menthyl group containing two double bonds, which may dehydrogenate, possibly with rearrangement, to a cymyl group. The description of these experiments will be postponed to a later paper.

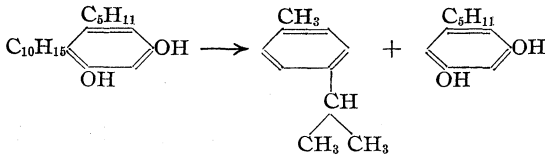
A reaction of cannabidiol which proved to be very informative was its pyrolytic cleavage with pyridine hydrochloride. When heated to 210–230° for three hours, a mixture of cannabidiol and pyridine hydrochloride decomposes and cymene distils. Cymene was proven beyond a doubt by its analysis, physical and chemical properties. Isolation of cymene confirms the previous evidence that the $C_{10}H_{15}$–residue is a menthyl containing two double bonds. From the residual mixture after pyrolysis, was isolated olivetol, 1,3-dihydroxy-5-*n*-amylbenzene, proved by comparison of it and its *bis*-3,5-dinitrobenzoate with au-

(1) An abstract of a thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy in chemistry. Solvay Process Company Fellow, 1939–1940.

(2) (a) Adams, Cain and Wolff, THIS JOURNAL, **62**, 732 (1940); (b) for first paper in this series see Adams, Hunt and Clark, *ibid.*, **62**, 196 (1940).

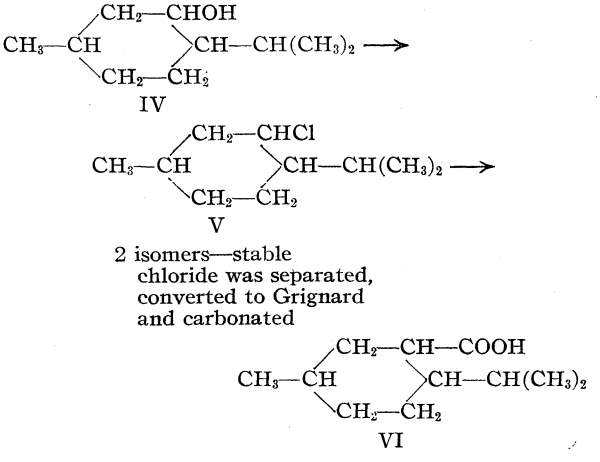
(3) Cahn, *J. Chem. Soc.*, 986 (1930); 630 (1931); 1342 (1932); 1400 (1933).

thentic samples of these products. The equation may be written as follows



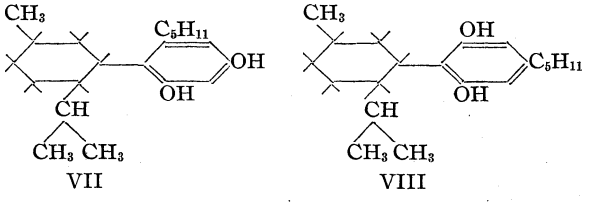
The isolation of olivetol establishes the orientation of the two hydroxyls and the *n*-amyl groups in cannabidiol. The mechanism of this cleavage is not clear and the limited quantity of cannabidiol available excluded further study. It may consist in the primary addition of hydrogen chloride, the hydrogen sufficing to complete the olivetol molecule and the chlorine forming $C_{10}H_{15}Cl$. This latter then is dehydrohalogenated to an olefin linkage which with the other two already present conjugate to a benzene system. On the other hand, the pyridine hydrochloride may function merely as a catalyst in the cleavage. The olivetol then would be formed by removal of a hydrogen from a carbon adjacent to that to which it is attached in the $C_{10}H_{15}$–residue. A new double bond simultaneously would be introduced in the $C_{10}H_{15}$–group thus leading to the completed molecule $C_{10}H_{14}$. Sulfamic acid in place of pyridine hydrochloride gave traces of cymene but the cleavage reaction did not appear to take place readily under these conditions.

Numerous experiments on the oxidation of cannabidiol to obtain one of the two possible olivetol carboxylic acids and thus to establish the position of the $C_{10}H_{15}$–group were unsuccessful. However, oxidation of the tetrahydrocannabidiol gave evidence as to the carbon of the dihydrocymyl residue (III) which was attached to the olivetol. Permanganate in acetone oxidation resulted in a mixture from which sodium bicarbonate solution extracted organic acids. It was obvious by the odor that caproic acid and possibly other low molecular weight aliphatic acids were present. This mixture was converted into the corresponding acid chlorides and then to the anilides. By crystallizing the anilides from benzene a single pure substance was isolated with a melting point of 152–152.5°. Analysis showed $C_{17}H_{25}ON$ and thus the molecule coincided with that of a menthanecarboxylic acid anilide $C_{10}H_{19}CONHC_6H_5$. Of the various theoretically-possible menthane carboxylic acids, one is described, the anilide of which melts at about the same point as that obtained in the above oxidation experiment.[4] This was synthesized by Kurssanow's method. It proved by mixed melting point to be identical with the cannabidiol product. Since the synthetic acid was prepared from *l*-menthol (IV–VI), the configuration of one or more of the asymmetric carbons in tetrahydrocannabidiol probably is similar to the corresponding asymmetric carbons in *l*-menthol



It would appear likely that this acid is the same as that obtained by Bergel[5] from oxidation of reduced red oil. He reported that the anilide of his acid melted at 148.5° (uncor.) but did not identify it. The analyses for this product averaged quite close to the calculated for menthane carboxylic acid anilide (Calcd.: C, 78.72; H, 9.72; N, 5.40. Found: C, 78.56; H, 9.68; N, 6.05).

Significant is the fact that isolation of menthane carboxylic acid anilide establishes the linkage of the $C_{10}H_{15}$–group to the olivetol residue as on the carbon adjacent to that holding the isopropyl group. Consequently, tetrahydrocannabidiol may be formulated as VII or VIII.



Cannabidiol then must be considered as one of these two molecules with two double bonds in the left-hand cycle, the positions of which are now being investigated.

(4) Kurssanow, *J. Russ. Phys.-Chem. Soc.*, **46**, 815 (1914); *C. A.*, **9**, 1751 (1915).

(5) Bergel, *Ann.*, **482**, 72 (1930).

Experimental

Cleavage of Cannabidiol to Cymene and Olivetol.—A mixture of 10 g. of cannabidiol and 12 g. of pyridine hydrochloride was heated for three hours at 210–230°. During the heating a liquid distilled. It was taken up in a little ether, extracted with dilute hydrochloric acid and then with water. After drying with anhydrous magnesium sulfate, the ether was removed by distillation and the product distilled. It boiled very sharply at 176° (cor.) (745 mm.); $n^{20}D$ 1.4900; d^{20}_4 0.8561; yield 2.6 g.

Anal. Calcd. for $C_{10}H_{14}$: C, 89.53; H, 10.51. Found: C, 89.55; H, 10.50.

The same constants were found for an authentic sample of *p*-cymene.

The residue in the reaction flask was treated with a little water and extracted several times with ether. The ether layer was separated, washed with dilute hydrochloric acid and then extracted twice with 10% aqueous sodium hydroxide. The aqueous extracts were acidified with hydrochloric acid and extracted several times with ether. After drying the ether layer with anhydrous magnesium sulfate, the ether was removed and the product distilled. It boiled at 170–175° (2 mm.); yield 3.2 g. The oil was warmed with water and on cooling a white crystalline material, m. p. 41°, was obtained. The crystalline product showed no melting point depression when mixed with an authentic sample of olivetol hydrate, 1,3-dihydroxy-5-*n*-amylbenzene hydrate. Upon drying the hydrate at 50° (2 mm.), anhydrous olivetol was obtained.

Anal. Calcd. for $C_{11}H_{16}O_2 \cdot H_2O$: C, 66.64; H, 9.15. Found: C, 66.69; H, 8.98.

For further identification of the olivetol from the cleavage reaction, it was converted to the *bis*-3,5-dinitrobenzoate by the use of 3,5-dinitrobenzoyl chloride and pyridine. The product was purified from ethanol or ether; white crystals, m. p. 127–128° (cor.).

Anal. Calcd. for $C_{25}H_{20}O_{12}N_4$: C, 52.90; H, 3.54; N, 9.84. Found: C, 52.87, 52.98; H, 3.59, 3.87; N, 10.08.

An identical product was obtained in a similar manner from synthetic olivetol.

Tetrahydrocannabidiol.—A solution of 4.86 g. of cannabidiol in 150 cc. of glacial acetic acid was reduced with hydrogen at 2–3 atm. pressure at room temperature using 0.1 g. of platinum oxide. Hydrogen corresponding to 2.06 moles per mole of cannabidiol was absorbed in fifteen minutes, after which no pressure change was noted in an additional thirty minutes.

The acetic acid was removed *in vacuo* and the tetrahydrocannabidiol, a pale yellowish highly viscous resin, was distilled, b. p. 188–190° (2.5 mm.) (bath temperature 200–215°, $n^{20}D$ 1.5298; yield 4.05 g.).

Rotation. 0.0582 g. made up to 5 cc. with 95% ethanol at 25° gave αD −0.33; *l*, 1; $[\alpha]^{25}D$ −28°.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.18; H, 10.76. Found: C, 78.97; H, 10.52.

Oxidation of Tetrahydrocannabidiol.—To a solution of 2.75 g. of tetrahydrocannabidiol in 100 cc. of acetone was added over a three-hour period a solution of 9.5 g. of potassium permanganate in 500 cc. of acetone at room temperature. During the first ninety minutes of addition, reaction was instantaneous. The flask became warm. The reaction was much slower during the latter part of the addition and unreacted permanganate remained an hour after addition was complete.

The mixture was made slightly acid and the manganese dioxide and excess permanganate were destroyed with sodium bisulfite. After dilution with 500 cc. of water, most of the acetone was removed by distillation. It was then extracted with ether and the ether in turn extracted with aqueous sodium bicarbonate. The bicarbonate layer was acidified and extracted with ether. After removal of the ether the crude bicarbonate-soluble portion amounted to 0.87 g. and the bicarbonate-insoluble, 1.52 g.

The bicarbonate-soluble material, which had an odor of lower fatty acids, was treated with 1.6 g. of thionyl chloride and refluxed overnight on a steam cone. The excess thionyl chloride was evaporated, the resulting mixture dissolved in 10 cc. of benzene, and 4 g. of aniline added. Solid material separated at once. The mixture was heated on the steam cone for two hours, poured into dilute hydrochloric acid solution and extracted with benzene. A product gradually crystallized and was purified by further crystallization from benzene; white crystals, m. p. 152–152.5° (cor.).

Anal. Calcd. for $C_{17}H_{25}ON$: C, 78.72; H, 9.72; N, 5.40. Found: C, 78.79; H, 9.81; N, 5.37.

A mixed melting point with the anilide of *p*-menthane carboxylic acid prepared by the method of Kurssanow[4] showed no depression.

Summary

Cleavage of cannabidiol with pyridine hydrochloride resulted in formation of *p*-cymene and olivetol, demonstrating that cannabidiol probably is a dihydrocymyl group attached to an olivetol residue.

Reduction of cannabidiol resulted in the rapid absorption of two moles of hydrogen with formation of a tetrahydro derivative which showed the same color reactions as cannabidiol. From this experiment it was deduced that the olivetol nucleus was unattacked and confirmed the fact that two double bonds were present in the $C_{10}H_{15}$– grouping.

Oxidation of tetrahydrocannabidiol led to the isolation of a menthane carboxylic acid identical with that which previously has been synthesized from *l*-menthol. The linkage of the $C_{10}H_{15}$–residue thus is established as on the carbon adjacent to that holding the isopropyl group.

Evidence is presented that cannabidiol is a dihydrocymyl olivetol.

URBANA, ILLINOIS RECEIVED JANUARY 8, 1940

[CONTRIBUTION FROM THE LABORATORY OF PHYSIOLOGICAL CHEMISTRY, THE OHIO STATE UNIVERSITY]

Studies on the Chemistry of the Fatty Acids. V. The Preparation of Methyl Ricinoleate and Ricinoleic Acid by Fractional Crystallization Procedures

BY J. B. BROWN AND NAOMA D. GREEN

Ricinoleic acid, $C_{18}H_{34}O_3$, occurs in castor oil to the extent of 80–86% of the total fatty acids.[1,2] The valuable medicinal and commercial properties of this oil are due in large part to this unsaturated hydroxy acid which occurs in the oil as tri-ricinolein and as mixed triglycerides with oleic, linoleic and stearic acids. According to Goldsobel[3] and others[4,5,6,7] ricinoleic acid is 12-hydroxy-*cis*-9-10-octadecenoic acid. Although numerous attempts have been made in the past to prepare the pure acid for use in preparation of derivatives and to study its properties, few, if any, pure preparations, especially of the acid, are described; in most cases analytical criteria of purity are quite inadequate. Methods of preparation up until 1931 have been reviewed by Rider.[8] They have included cold-pressing of the acids of castor oil, and crystallization of the barium soaps of the resultant acids from alcohol; direct alcoholysis of castor oil with methyl alcohol and distillation of the methyl esters; removal of olein, linolein, dihydroxystearin and unsaponifiable from the original oil by repeated extraction with benzine, the final product being 98.5% ricinoleic acid and various combinations of procedures. Rider prepared the pure acid by chilling the fatty acids of castor oil, dissolved in an equal volume of 95% alcohol, to −15° when the solid acids precipitated. The liquid acids were then converted into methyl esters, acetylated with acetic anhydride and the acetylated esters fractionally distilled at 4 mm. The pure acetyl ester was thus isolated. It was converted into ricinoleic acid by saponification. The acid melted at 4–5°. The melting point was the only criterion of purity reported. A more recent preparation by Straus, Heinze and Salzmann[9] employs Rider's method of removing the saturated fatty acids and in addition crystallization of the lead soaps from ether and preparation of the benzoyl methyl ester.

The object of the present work was to apply low-temperature fractional crystallization methods, previously developed in this Laboratory for the purification of oleic, linoleic and linolenic acids,[10] to the preparation of ricinoleic acid and its methyl ester. Since it has long been known that the free acid cannot be distilled without decomposition even at very low pressures, the preparation of pure methyl ricinoleate was first attempted. A specimen of castor oil was converted into methyl esters by direct alcoholysis. The distilled esters were fractionally crystallized from acetone or from methyl alcohol. Fractions were isolated in good yield which analyzed as methyl ricinoleate of high purity. Four such preparations are described. Attempts to prepare pure ricinoleic acid from the pure ester were unsuccessful because the product could not be distilled and because during saponification, even in the cold, the acid was partly dehydrated with the formation of octadecadienoic acids. A specimen of ricinoleic acid of 95% purity was prepared by cold saponification of the crude methyl esters, followed by direct fractional crystallization of the acids from acetone.

Experimental Part

Equipment.—For low temperature work the special equipment described in our previous work was used, namely, a room in which a temperature of −20 to −25° was continuously maintained and a well insulated dry-ice–alcohol apparatus designed to accommodate a 2-liter Erlenmeyer flask. In the latter part of this work, a similarly constructed bath for a 4-liter Erlenmeyer flask was used. All filtrations were carried out by suction in the −20° room.

Procedures. A. Preparation of Pure Methyl Ricinoleate.—(1) One kilogram of castor oil (iodine number 87.9; saponification number 179.7) was esterified with 1500 cc. of methyl alcohol containing 2% dry hydrogen chloride by refluxing on a hot water-bath for twenty-four hours. The crude esters were then distilled at a pressure of 2–3 mm., the boiling point range being 185 to 212°; yield 810 g.

Eighty grams of the esters was dissolved in 4 liters of C. P. acetone in 2-liter Erlenmeyer flasks (more concen-

(1) Eibner and Munzing, *Chem. Umschau. Fette Öle Wachse Harze*, **32**, 153 (1925).
(2) Panjutin and Rapoport, *ibid.*, **37**, 130 (1930).
(3) Goldsobel, *Ber.*, **27**, 3121 (1894).
(4) Kasansky, *J. prakt. Chem.*, **62**, 363 (1900).
(5) Haller and Brochet, *Compt. rend.*, **150**, 496 (1910).
(6) Chonowsky, *Ber.*, **42**, 3339 (1909).
(7) Noorduyn, *Rec. trav. chim.*, **38**, 317 (1919).
(8) Rider, THIS JOURNAL, **53**, 4130 (1931).
(9) Straus, Heinze and Salzmann, *Ber.*, **66B**, 631 (1933).
(10) Brown and Stoner, THIS JOURNAL, **59**, 3 (1937); Brown and Shinowara, *ibid.*, **59**, 6 (1937); **60**, 2734 (1938); Brown and Frankel, *ibid.*, **60**, 54 (1938).

TABLE I

ANALYTICAL DATA ON FOUR SPECIMENS OF METHYL RICINOLEATE

	M. p., °C.	Mean mol. wt.	Iodine number	n^{20}	Acetyl number	$[\alpha]^{32}D$ – Acetone	$[\alpha]^{32}D$	% Purity[a]
Theory, calcd.	...	312.0	81.34	....	137.71	....	....	..
Haller[b]	...	....	...	1.4645^{15}	....	....	+5.3[d]	..
Leathes[c]	...	....	...	....	....	....	+3.8	..
Straus, *et al.*	...	....	...	1.4626^{21}	....	....	....	..
Sample (1)	...	313.44	81.01	1.4627	136.65	....	....	99.2
Sample (2)	...	307.30	82.43	....	135.28	....	....	98.2
Sample (3)	−4.0	303.66	81.05	1.4628	133.75	+7.41°	+4.82°	97.1
Sample (4)	−4.5	311.60	80.71	1.4628	137.05	+5.19°[e]	....	99.5

[a] Purity based on acetyl number. [b] Haller, *Compt. rend. acad. sci.*, **144**, 462 (1907). [c] Leathes, "The Fats," Longmans, Green and Co., New York, N. Y., 1925. [d] At 20°. [e] At 27°.

trated solutions, 4, 8 and 10% were tried and found to give too bulky precipitates for efficient fractionation). No precipitate formed at −20° after standing seventy-two hours. The solution was therefore cooled with constant stirring to −50° at which point a small precipitate (approx. 1%) was removed by suction on a large Buchner funnel (−20°). This fraction was solid at room temperature and probably contained most of the saturated esters. The filtrate was further cooled with vigorous stirring to −60 to −62° and the precipitate at this temperature separated by filtration as above. Solvent was then removed from the precipitate by warming under reduced pressure. The residual product was distilled at 3.6 to 4 mm. pressure in an all-glass apparatus. It was water-white; yield 62 g. Constants on this sample, no. 1, together with those of other specimens of methyl ricinoleate prepared are given in Table I.

(2) In an attempt to find a solvent in which more concentrated solutions could be handled, 400 g. of the original methyl esters was dissolved in 4000 cc. C. P. methyl alcohol and allowed to stand overnight at −20°. The precipitate was filtered off and the filtrate was further cooled with continuous stirring to −40° and a second small precipitate removed. Upon cooling to lower temperatures, it was found that this solution was too concentrated for further fractionation; so it was diluted with an equal volume of methyl alcohol making the solution approximately 5%. A large precipitate came down at −65° and was filtered off. This specimen was treated in a manner similar to the first. The yield of the distilled ester, specimen 2, was 328 g.

(3) Six hundred and forty grams of original esters was dissolved in 32 liters of C. P. acetone in eight 4-liter flasks and treated as sample (1) with the following differences.

The precipitation was carried out in 4-liter flasks in the dry ice–alcohol bath and it was found (perhaps due to slight supercooling with somewhat less efficient stirring in the larger volume of solution) that precipitation corresponding to that in (1) occurred at −55 and −65° instead of −50 and −60° as before. After filtering at −65°, the precipitate was allowed to melt, made up to approximately 2% solution and recrystallized at −65°.

The yield of distilled specimen (3) was 283 g.

(4) An additional sample of methyl ricinoleate was prepared in the same manner as sample (3) except that the recrystallization at −65° was from a 4% solution in acetone instead of 2%.

Analytical data on the four specimens are given in Table I. Molecular weights were determined by saponification; iodine numbers by the Wijs method with one hour reaction time. Acetyl numbers were determined essentially by the method of West and co-workers.[11] The acetyl value was defined as the number of mg. of acetyl radical taken up by 1 g. of sample. In our work we have allowed one and a half hours reaction time and one-half hour decomposition time.

The analytical data in Table I, especially the iodine and acetyl numbers, show the four specimens to be methyl ricinoleate of high purity. The molecular weights by saponification are also in excellent agreement with the theory in specimens (1) and (4). They are not so satisfactory in (2) and (3), which may be due to side reactions with alkali. We have repeatedly obtained low results for molecular weight by the saponification method. In fact it has been difficult with some specimens to obtain checks on this account. From these experiments it may be concluded that it is possible to prepare methyl ricinoleate of high purity by the low temperature crystallization methods described above, either methyl alcohol or acetone being satisfactory solvents.

B. Preparation of Ricinoleic Acid.—It would seem that the preparation of pure ricinoleic acid from the pure ester would be a comparatively simple procedure, but in actual attempts to saponify the ester the resultant acids gave constants which were far from satisfactory. In three such experiments the pure ester was saponified with boiling alcoholic potash, most of the alcohol distilled off, and the soaps decomposed with hot hydrochloric acid. The temperatures of most of these operations were kept below 60°. The resultant acids were analyzed directly or crystallized from ether or acetone at very low temperature. Attempts to distil the acid even at 0.5–1.5 mm. pressure gave products with iodine numbers of 92–113. The undistilled product invariably gave molecular weights by titration 20 to 30 units high, up to 330 (theory 298). Also high iodine

(11) West, Hoagland and Curtis, *J. Biol. Chem.*, **104**, 627 (1934); Hafner, Swinney and West, *ibid.*, **116**, 691 (1936).

numbers were obtained.[12] These high values, however, are not due to abnormal reaction with the Wijs reagent used but to the formation of octadecadienoic acids by the dehydration of methyl ricinoleate or soap during the saponification and subsequent treatment. High molecular weights on the other hand are caused by formation of polyricinoleic acids, to incomplete saponification, or to the presence of residual solvent which is difficult to remove without distillation. Since hot saponification caused definite alteration in the product, two attempts at cold saponification were tried in which the ester was treated with a large excess of alcoholic potash at 0–4° for 101 and 285 hours, respectively. The products again had iodine numbers and mean molecular weights which were indicative of incomplete saponification.

These experiments made it obvious that cold saponification of the pure ester was not complete and hot saponification did not give a pure acid and that the product would have to be fractionally crystallized to remove poly acids and dienoic acids formed in the process. Since fractional crystallization was necessary, obviously it was practical to start with more crude ester which had not been so highly purified. Accordingly a number of samples of less pure methyl ricinoleate were mixed and saponified with hot alcoholic potash. The resultant acids, 359 g., were then dissolved in 7180 cc. of C. P. acetone. No precipitation occurred at −20° and the solution was cooled to −70°. A copious precipitate was removed by filtration and an acid recovered by warming under reduced pressure, taking care to keep the temperature below 60°. Apparently this procedure was successful in removing the last traces of solvent, because the product gave a molecular weight by titration in neutral alcohol of 298 (theory 298.3). The other constants were iodine number (Wijs) 88.52 (theory 85.1), acetyl number 137.9 (theory 144.2), m. p. 5.5°. (The literature reports various melting points from 4–5° (Leathes) to 17°); n^{20} 1.4697 (Straus, Heinze and Salzmann, report 1.4716); $\alpha^{26}D$ (acetone) +7.15°; sp. gr. 27.4°, 0.940. The thiocyanogen number of this specimen of acid was 85.34 (theory 85.09). On the basis of acetyl number, the product was 95.6% ricinoleic acid. On the basis of iodine number and assuming the mixture to consist of ricinoleic and octadecadienoic acids, the purity was 97%.

In the above experiments we have given only a résumé of many of our attempts to prepare ricinoleic acid from its methyl ester and details only in our most successful preparation. We conclude that it is a comparatively simple procedure to prepare the ester in high purity and in very good yield, but, even with pure ester available, it is quite difficult to prepare an acid of satisfactory purity. Ricinoleic acid, itself, appears to be even more difficult to prepare than oleic acid, not because of difficulty of separation from other acids but because of its own reactivity.

(12) *Cf.* Caldwell and Piontkowski, THIS JOURNAL, **56**, 2086 (1934).

Summary

1. Low temperature fractional crystallization procedures have been applied successfully to the preparation of methyl ricinoleate from castor oil.

2. Saponification of methyl ricinoleate and isolation of the resultant acid does not yield a pure ricinoleic acid.

3. Analytical constants of pure methyl ricinoleate and of 95.6% ricinoleic acid are given.

COLUMBUS, OHIO RECEIVED JANUARY 22, 1940

[CONTRIBUTION FROM THE COLLEGE OF PHARMACY OF THE UNIVERSITY OF CALIFORNIA]

N^1,N^4-Nicotinyl Derivatives of Sulfanilamide

BY T. C. DANIELS AND HARRY IWAMOTO

A comparatively large number of N^1 and N^4 acyl derivatives[1] of sulfanilamide have been described and several have been reported to be of pharmacologic interest in the treatment of bacterial infections.[2,3,4] The pharmacologic properties of nicotinic acid and of sulfanilamide suggested the desirability of preparing the nicotinyl derivatives. One of us in 1937 prepared the N^4-nicotinylsulfanilamide. Crossley, Northey and Hultquist[3] have described the N^1-nicotinylsulfanilamide and reported a melting point of 256–257.5°. Our N^4 product had the same melting point and we therefore became interested in ascertaining whether rearrangement had occurred or the melting point of the two derivatives was a coincidence. Partial rearrangement of certain of the N^1-acylsulfanilamides had been observed by Crossley, Northey and Hultquist.[3]

We have prepared the N^4-nicotinyl derivative by two general methods: (1) by the action of nicotinyl chloride[5] on sulfanilamide in anhydrous pyridine, and (2) by treating the anilide of nicotinic acid with chlorosulfonic acid followed by ammonia. The products obtained by the above methods give the same melting point and mixed melting point (257–258°). They do not titrate to a phenolphthalein end-point.

We prepared the N^1-nicotinylsulfanilamide from N^4-acetylsulfanilamide by the method of Crossley, Northey and Hultquist.[3] This product melts at the same temperature as the N^4-nicotinyl derivative (257–258°) but because of its greater acidity titrates quantitatively to a phenolphthalein end-point. A 50% mixture with the N^4-nicotinyl derivative melts at 233–235°. The N^1-derivative after melting can still be titrated quantitatively with sodium hydroxide to a phenolphthalein end-point, which shows that rearrangement does not occur during the melting.

All of the N^4-acyl derivatives of sulfanilamide thus far described, with the exception of the nicotinyl, have a considerably higher melting point than the corresponding N^1 compounds.[2,3]

(1) For nomenclature, see Crossley, Northey and Hultquist, THIS JOURNAL, **60**, 2217 (1938).

(2) Miller, Rock and Moore, *ibid.*, **61**, 1198 (1939).

(3) Crossley, Northey and Hultquist, *ibid.*, **61**, 2950 (1939).

(4) Stuart, U. S. Patent 2,117,260; *C. A.*, **32**, 5160 (1938).

(5) Ingersoll and Robbins, THIS JOURNAL, **48**, 2451 (1926).

The compounds studied crystallized in general as fine needles. Table I gives the analyses and melting points.

TABLE I

N^1 acyl group	N^4 acyl group	Theoretical mol. wt.	Assay, % NaOH	Assay, % Nitrite	Melting points, °C.
Acetyl	Nicotinyl	319.3	99.8	..	255–256
Nicotinyl	Acetyl[a]	319.3	99.8	..	293–294
Nicotinyl	Nicotinyl[b]	383.4	98.4	..	222–248
Nicotinyl[a]	.....	277.3	100.5	..	257–258
.....	Nicotinyl	277.3	...	99.9	257–258

[a] Prepared by the method of Crossley, Northey and Hultquist.[3] [b] Product exists in two forms, one of which melts sharply at 222, the other at 248°.

Pharmacology.—Although the work of Fourneau, *et al.*,[6] indicated that the introduction of acyl groups on the N^4 nitrogen of sulfanilamide greatly reduces the antistreptoccic activity, compounds of this class have since been described which have equal or greater effectiveness.[2,4] The N^4-nicotinylsulfanilamide has been studied by Leake, Karr, Finnegan and Murayama.[7] The preliminary work has indicated an effectiveness greater than that of sulfanilamide in the treatment of experimental hemolytic streptococcal infections and equal to sulfapyridine in experimental pneumococcal infections. The toxicity is much less than that of sulfanilamide or of sulfapyridine. Studies are now in progress on the N^1,N^4-dinicotinylsulfanilamide and on the N^1-acetyl-N^4-nicotinylsulfanilamide. The details of the pharmacologic investigation will be published elsewhere.

Experimental Part

N^4-Nicotinylsulfanilamide.—(1) To 14.2 g. (0.1 mole) of nicotinyl chloride and 17.2 g. (0.1 mole) of sulfanilamide was added 18.0 g. of anhydrous pyridine. The mixture was refluxed on a water-bath for one hour, cooled and several volumes of cold water added. The precipitate was collected on a filter and washed thoroughly with water followed by recrystallization from 50% alcohol; yield 50 to 75%.

(2) To 58.3 g. (0.5 mole) of chlorosulfonic acid in a three-necked flask, equipped with a mechanical stirrer and reflux condenser cooled to 0°, was added 9.9 g. (0.05 mole) of nicotinylanilide in divided portions with continuous agitation. The temperature during the addition was kept below 15°, then gradually raised to 60° on a water-bath

(6) Fourneau, *et al.*, *Compt. rend. soc. biol.*, **122**, 258 (1936).

(7) Leake, Karr and Murayama, unpublished report.

and maintained at this temperature for two hours. The reaction mixture was cooled and treated directly with an excess of cold 28% ammonia solution, adding the ammonia in divided portions with continuous stirring. The stirring was continued for approximately one hour and the precipitate collected and washed several times with water followed by recrystallization from 50% alcohol; yield 40 to 50%. The melting point was identical with that of the product from (1) and gave the same mixed melting point.

N^1-Acetyl-N^4-nicotinylsulfanilamide.—To 25 cc. of acetic anhydride was added gradually 2.8 g. (0.01 mole) of N^4-nicotinylsulfanilamide. The mixture was refluxed for one hour and cooled in an ice-bath. The precipitate was collected and washed with water, then dissolved in sodium hydroxide (*p*H 8), decolorized with activated charcoal and precipitated by the addition of dilute hydrochloric acid to *p*H of 5. The precipitate was filtered, washed and dried; yield approximately 50%.

N^1,N^4-Dinicotinylsulfanilamide.—To 5.5 g. (0.02 mole) of N^4-nicotinylsulfanilamide and 5.7 g. (0.04 mole) of nicotinyl chloride was added 20 cc. of anhydrous pyridine and the product refluxed for one hour. Several volumes of water were added to the cooled reaction product and the solution acidified with dilute hydrochloric acid to a *p*H of 5. The precipitate was collected and washed with several portions of water, redissolved with sodium hydroxide to a *p*H of 8, filtered and reprecipitated by the addition of dilute hydrochloric acid to a *p*H of 5. The product was again washed and dried; yield approximately 40%. The product melts sharply at 222°, resolidifies on heating and melts again at 248°. Titration with sodium hydroxide of the form melting at 248° gives the same equivalent weight as before melting.

Summary

1. The N^4-nicotinylsulfanilamide and N^1,N^4-dinicotinylsulfanilamide are described.

2. The melting points of N^1 and N^4-nicotinylsulfanilamide are the same.

3. The preliminary pharmacologic investigation indicates that the N^4-nicotinylsulfanilamide is effective in the treatment of experimental hemolytic streptococcus infections and also certain types of pneumococcus infections. The toxicity of the N^4-nicotinylsulfanilamide is lower than either sulfanilamide or sulfapyridine.

SAN FRANCISCO, CALIF. RECEIVED JANUARY 2, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY]

α-Furfurylpropylamine and Di-α-furfuryl Tertiary Amines

BY J. E. ZANETTI AND J. T. BASHOUR

α-Furfurylpropylamine has now been synthesized by the same general method as previously used with other secondary α-furfuryl amines.[1] It is a colorless oil with a faint fishy odor boiling at 80–81° under 20 mm. pressure, d^{25}_{25} 0.947, $n^{20}D$ 1.4679. Its hydrochloride melts at 138–140°.

Anal. Calcd. for $C_8H_{13}ON$: N, 10.1. Found: N, 10.2.

Very little has been done in the field of tertiary α-furfuryl amines and only one tertiary amine containing two furfuryl groups has been reported, namely, the tri-α-furfurylamine synthesized by Zanetti and Beckmann.[2] Von Braun and Kohler[3] synthesized several tertiary furfurylamines which, however, contained only one α-furfuryl group and Von Braun and Braunsdorf[4] made an analog of novocaine containing one α-furfuryl group on the tertiary nitrogen.

In our synthesis of secondary α-furfurylamines,[5] tertiary amines were suspected in the small amount of high boiling residue accompanying each preparation. However, in the synthesis of these amines, unfavorable yields are obtained unless the purified secondary amines be made to react with furfuryl bromide.

These tertiary amines are either high boiling liquids or solids and are miscible with most organic solvents. Their properties and the analyses are given in Table I. They are colorless when pure but turn yellow on standing. They have only faint ammoniacal odors. With hydrochloric acid in ether solution they form stable hydrochlorides. As in the case of the secondary furfurylamines, excess of hydrochloric acid must not be used as dark decomposition products will readily form.

Experimental Part

In a flask provided with an air condenser the furfuryl bromide in ether solution is allowed to stand for one to three hours over crushed potassium hydroxide and then the secondary amine is added with agitation. With intermittent shak-

(1) Zanetti and Bashour, THIS JOURNAL, **61**, 3133 (1939).
(2) Zanetti and Beckmann, *ibid.*, **50**, 2081 (1928).
(3) Von Braun and Kohler, *Ber.*, **51**, 86 (1918).
(4) Von Braun and Braunsdorf, *Ber.*, **54**, 2081 (1921).
(5) Zanetti and Bashour, THIS JOURNAL, **61**, 3133 (1939).

TABLE I

Amine, di-α-furfuryl-		Methyl	Ethyl	Propyl	Butyl	Amyl	Phenyl[a]
Boiling point	°C.	100–102	109–110	115–117	126–128	137–139	163–167
	Mm.	5	5	5	5	5	5
Sp. gr., 25/25		1.074	1.055	1.034	1.019	1.005	.....
$n^{20}D$		1.5086	1.5059	1.4978	1.4976	1.4950	.....
Hydrochloride m. p., °C.		153–154	149–151	147–148	105–106	103–105	137–141[b]
Formula		$C_{11}H_{13}O_2N$	$C_{12}H_{15}O_2N$	$C_{13}H_{17}O_2N$	$C_{14}H_{19}O_2N$	$C_{15}H_{21}O_2N$	$C_{16}H_{15}O_2N$
Nitrogen, %	Calcd.	7.3	6.8	6.4	6.0	5.7	5.5
	Found	7.3	7.1	6.5	6.2	5.9	5.7
Carbon, %	Calcd.	...	...	...	72.1	...	75.9
	Found	...	...	...	72.1	...	76.4
Hydrogen, %	Calcd.	...	...	...	8.2	...	5.9
	Found	...	...	...	8.3	...	6.1

[a] Melting point 31–32°; recrystallized from six times the quantity of petroleum ether or methyl alcohol in the ice-bath.
[b] By immersion in preheated baths.

ing the solution rapidly clouds and reaches the boiling point within several minutes to an hour (difurfurylphenylamine developed a dark red color but did not boil). At times excessive heat evolution must be reduced by use of an ice-bath. After twelve hours, the ether is removed and the mixture carried through fractional distillation at reduced pressure in an atmosphere of nitrogen, until successive fractions showed no difference in refractive index. Yields were uniformly about 80% of the theoretical.

The authors are indebted to Mr. Saul Gottlieb for the microanalysis of these compounds.

Summary

1. Six tertiary di-α-furfurylamines were synthesized by the action of furfuryl bromide on secondary α-furfurylamines and their properties reported.

Further work on these amines is being continued in these Laboratories.

COLUMBIA UNIVERSITY
NEW YORK, N. Y. RECEIVED NOVEMBER 23, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF SWARTHMORE COLLEGE]

Sulfonamide Derivatives of Arylureas

BY EDWARD H. COX

The para sulfonamide derivative of phenylurea is in reality a derivative of sulfanilamide. This relationship has prompted the work of preparing some of the arylureasulfonamides with the anticipation that they might possess therapeutic activity comparable to that of sulfanilamide.

The parent substance in the series, *p*-phenylureasulfonamide is then N^4-carbamylsulfanilamide. This compound has been prepared recently by Kolloff[1] and given the name *p*-uraminobenzenesulfonamide. The reaction for its preparation is an application of that reported by Buck and Ferry[2] and involves the action of nitrourea on sulfanilamide in alcohol. The therapeutic activity of the compound was not reported.

In the present work it has been found that the arylureas or their acetyl derivatives can be sulfonated by means of chlorosulfonic acid. The resulting sulfonyl chlorides can then be transformed into the amides or substituted amides. The yields are consistently high throughout the series of reactions.

Some of the N^4-acyl derivatives of sulfanilamide show as high a therapeutic activity[3] as sulfanilamide itself and this is believed to be due to deacylation in the organism with the resultant freeing of the sulfanilamide. In the present case the carbamyl group apparently is not removed *in vivo* and therefore the arylureasulfonamides show no activity in experimental streptococcal infection in mice.[4]

Since it is proposed to continue the work on this series with certain modifications, the author considered it of interest to record the preparation and properties of these arylurea derivatives.

(1) Kolloff, THIS JOURNAL, **60**, 950 (1938).
(2) Buck and Ferry, *ibid.*, **58**, 854 (1936).
(3) Miller, Rock and Moore, *ibid.*, **61**, 1198 (1939); Adams, Long and Johanson, *ibid.*, **61**, 2342 (1939).
(4) The author wishes to thank Dr. Perrin H. Long of The Johns Hopkins Medical School for carrying out the biological tests.

Experimental

The sulfonation of the arylureas and the acetylarylureas presents no difficulties. The resulting sulfonyl chloride derivatives of the arylureas are, however, difficult to purify and no analytical data are listed for them. On the other hand, the acetylarylureasulfonyl chlorides are not difficult to purify and are produced in good yields. The chlorides are converted into the amides by treatment with ammonia or diethylamine. The removal of the acetyl group from the acetylarylureasulfonamides is effected by treating them with boiling hydrochloric acid solution. Mechanical stirring is used in all the reactions carried out, and the temperatures recorded are those for the reaction mixtures.

Acetylation of the Arylureas.—The arylureas are acetylated according to the method of Walther and Wolodowski.[5] To 70 g. of the urea, dissolved or suspended in 200 cc. of pyridine, is added slowly 60 g. of acetyl chloride. During the addition, the reaction mixture is stirred and cooled to 10° below zero. The reaction mixture is then warmed to 30° for one-half hour, poured into cold dilute hydrochloric acid solution, filtered, and washed. Without further purification, the acetylated product is dried and sulfonated. The yields are from 80–90%.[6]

Sulfonation of the Arylureas and the Acetylarylureas.—The procedure is that given in "Organic Syntheses,"[7] except that the temperature during sulfonation of the arylurea is maintained between 0–10°. Higher temperatures tend to darken the reaction product and lower the yields. To 170 cc. of chlorosulfonic acid is added with stirring 70 g. of the arylurea and after the addition the reaction mixture is heated to 50° for one to two hours. The sulfonyl chlorides are filtered, washed and dried before conversion into the amides. Calculated upon air dried aliquots, the yields are 60–70%.

The procedure for the sulfonation of the acetylarylureas is the same as indicated above for the arylureas. The temperature at which the sulfonation is carried out is 10–15° and the amount of the acetylarylureas employed is 90 g. The yields of the crude acetylarylureasulfonyl chlorides are 75–85%. They are crystallized from hot benzene or toluene.

Amide Derivatives.—Fifty grams of the sulfonyl chloride derivatives of the arylureas or the acetylarylureas is treated with 150 cc. of 28% ammonia or 150 cc. of 30% diethylamine. The mixtures are stirred and warmed on a water-bath for one-half hour and then set aside to cool. In some cases the diethylamides remain as oils which are made to solidify by trituration with alcohol. The unsubstituted amides crystallize from hot water or diluted alcohol, while the diethylamides crystallize from a mixture of ethyl acetate and benzene.

Removal of the acetyl group from the acetylarylureasulfonamides is accomplished by treatment with boiling 5 *N* hydrochloric acid solution. The time of hydrolysis, for 40 g. of the various acetyl compounds, using twice the calculated amount of acid and stirring, varies from one-half to two hours. When pure samples of these resulting amides are mixed with the corresponding ones prepared by direct sulfonation and subsequent amidation of the arylureas, no depression in melting points is observed.

The melting points and analytical data are given in tabular review.

TABLE I

p-ACETYLARYLUREASULFONYL CHLORIDES, $CH_3CONHCONH\text{-}Ar\text{-}SO_2Cl$

-Ar-	M. p., °C.	Formula	Nitrogen, % Calcd.	Found
Phenyl	192–193	$C_9H_9O_4N_2SCl$	10.12	10.32
o-Tolyl	197–199	$C_{10}H_{11}O_4N_2SCl$	9.63	9.53
m-Tolyl	199–201	$C_{10}H_{11}O_4N_2SCl$	9.63	9.58

p-ACETYLARYLUREASULFONAMIDES, $CH_3CONHCONH\text{-}Ar\text{-}SO_2NH_2$

Phenyl	246–247	$C_9H_{11}O_4N_3S$	16.33	16.05
o-Tolyl	231–233	$C_{10}H_{13}O_4N_3S$	15.49	15.25
m-Tolyl	226–227	$C_{10}H_{13}O_4N_3S$	15.49	15.30

p-ARYLUREASULFONAMIDES, $NH_2CONH\text{-}Ar\text{-}SO_2NH_2$

Phenyl	206–207	$C_7H_9O_3N_3S$	19.52	19.47
o-Tolyl	223–225	$C_8H_{11}O_3N_3S$	18.33	17.99
m-Tolyl	209–210	$C_8H_{11}O_3N_3S$	18.33	18.05

DIETHYL *p*-ARYLUREASULFONAMIDES, $NH_2CONH\text{-}Ar\text{-}SO_2N(C_2H_5)_2$

Phenyl	148–149	$C_{11}H_{17}O_3N_3S$	15.49	15.47
o-Tolyl	165–167	$C_{12}H_{19}O_3N_3S$	14.72	14.53
m-Tolyl	147–148	$C_{12}H_{19}O_3N_3S$	14.72	14.61

Summary

The preparation and properties of a series of sulfonamide derivatives of some of the arylureas, as well as the intermediate derivatives, are described.

The parent substance, *p*-acetylphenylureasulfonamide (N^4-carbamylsulfanilamide), shows no activity in experimental streptococcal infection in mice.

SWARTHMORE, PA. RECEIVED JANUARY 15, 1940

(5) Walther and Wolodowski, *J. prakt. Chem.*, [2] **59**, 272 (1899).

(6) The acetyl *m*-tolylurea is not found recorded in the literature. It crystallizes from alcohol and melts at 127°. Calcd.: N, 14.58. Found: N, 14.41.

(7) *Org. Syntheses*, Coll., Vol. I, p. 7.

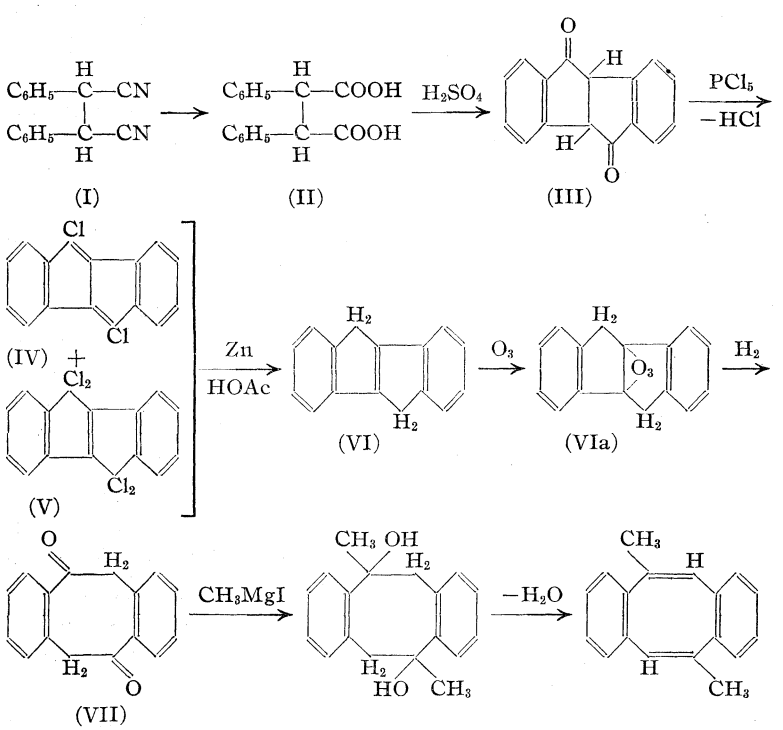
[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

An Attempt to Synthesize a Substituted Cycloöctatetraene[1]

BY STANLEY WAWZONEK

Willstätter[2] has reported the synthesis of cyclooctatetraene. In view of the results obtained by Hurd and Drake[3] in their study of the pyrolysis of bis-quaternary ammonium hydroxides related to 1,2- and 1,3-butenes, and the striking similarity[4] in chemical and physical properties between styrene and its derivatives and the supposed cycloöctatetraene and its derivatives, the structure of the latter compound is questionable.

In the hope that a substituted cycloöctatetraene might be synthesized in an easier manner than cycloöctatetraene itself,[4] the following synthesis[5] of *sym*-dibenzocycloöctatetraene was attempted, and carried out successfully through the formation of the *sym*-dibenzocycloöctanedione-5,11 (VII).



In spite of the failure to complete the synthesis, it was thought that the properties and reactions of the cyclic diketone (VII) were of sufficient interest to be reported.

sym-Dibenzocycloöctanedione-5,11 (VII) is a white solid, difficultly soluble in aqueous alkali and easily soluble in alcoholic alkali to give a yellow solution. To determine the nature of this salt, an alkaline solution was treated with dimethyl sulfate and found to give a product that analyzed for a hydrated dimethyl ether. Since the ether would not brominate and could be cleaved by hydrobromic acid to the diketone (VII), its structure is that given by formula (VIII). The sodium salt is therefore a derivative of the hydrated form of the diketone (IX), a structure which is supported in part by the failure of the salt to react with benzenediazonium sulfate in alkaline solution.

All attempts to cause the diketone (VII) to react with butyl nitrite, *p*-nitrosodimethylaniline, bromine or selenium dioxide were either unsuccessful or gave oily products. That active methylene groups were present in the compound was shown by the formation of a dibenzal compound (X) from benzaldehyde in alcoholic alkali, and by the formation of a substituted quinoline (XI) from isatin in alkali.

The presence of two carbonyl groups was shown by the formation of a dioxime (XII) and a dichlorodiphosphinic acid (XIII) from phosphorus pentachloride. In the Grignard machine the cyclic diketone (VII) showed only one carbonyl group. The Grignard product in turn showed only one active hydrogen. Difficulty in dehydration of the Grignard product indicated that the compound was a dihydropyran (XIV). The formation of such a compound is analogous to the previously reported[6] formation of 2,4,4,6-tetraphenyl-

(1) A portion of a thesis submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy by Stanley Wawzonek, August, 1939.

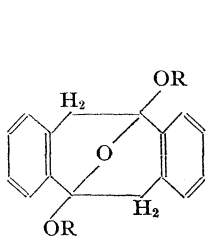
(2) (a) Willstätter and Waser, *Ber.*, **44**, 3433 (1911); (b) Willstätter and Heidelberger, *ibid.*, **46**, 517 (1913).

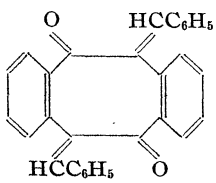
(3) Hurd and Drake, THIS JOURNAL, **61**, 1943 (1939).

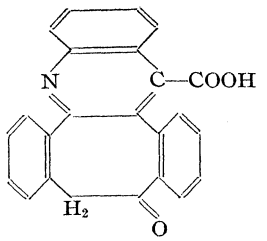
(4) Vincent, Thompson, Jr., and Smith, *J. Org. Chem.*, **3**, 603 (1939).

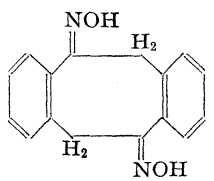
(5) Reactions up through the formation of diphensuccindene-10 (VI) have already been reported in part by Brand and Müller, *Ber.*, **55**, 601 (1922).

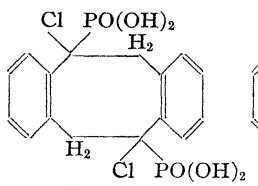
(6) Pere de Carvalho, *Ann. chim.*, **4**, 495 (1935).

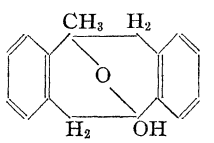

(VIII), R = CH_3
(IX), R = Na

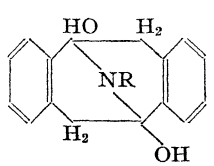

(X)

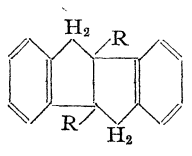

(XI)

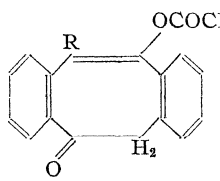

(XII)

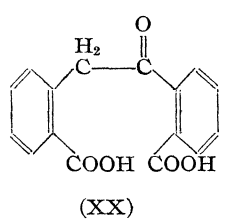

(XIII)

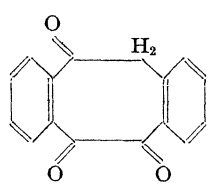

(XIV)

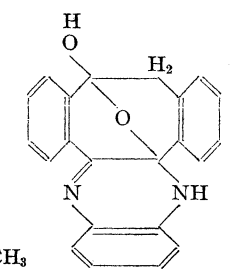

(XV), R = H
(XVI), R = $NHCONH_2$

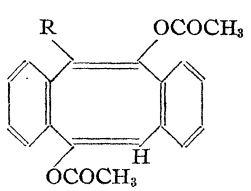

(XVII), R = H
(XVIII), R = OH


(XIX), R = H
(XXI), R = Br


(XX)


(XXII)


(XXIII)


(XXIV), R = H
(XXV), R = Br

2-ethyl-dihydropyran in the reaction between 1,3-dibenzoyl-2,2-diphenylpropane and ethylmagnesium bromide.

With ammonia, ammonia derivatives and reducing agents, the behavior of the diketone (VII) was similar to that of open chained 1,5-diketones in that substituted tetrahydropyridines and glycols, respectively, were formed. The product, (XV) obtained from ammonia, was soluble in dilute hydrochloric acid, and could be converted either by nitrous acid or by melting into the diketone (VII). The compound (XVI) obtained from semicarbazide, upon heating alone or in the presence of powdered potassium hydroxide, gave a mixture of diphensuccindene-10 (VI) and diphensuccindane (XVII). Because of stereochemical reasons, the characteristic loss of water to form pyridines observed with ammonia addition products of open chained 1,5-diketones is impossible with ammonia derivatives of *sym*-dibenzocycloöctanedione-5,11. The glycol (XVIII), formed by the reduction of the diketone (VII) with either amalgamated zinc and hydrochloric acid or zinc and alkali, could be cleaved with lead tetraacetate to the diketone (VII). Treatment of the glycol (XVIII) with either sulfuric or hydriodic acid in acetic acid solution gave a highly insoluble polymer melting above 350°.

That enolic forms were possible was shown in the formation of a mono- and a diacetate by refluxing the diketone (VII) with acetic anhydride in the presence of anhydrous potassium acetate and sulfuric acid, respectively.

The structure of the monoacetate (XIX) was demonstrated by hydrolysis with alkali to the diketone (VII), and oxidation with chromic anhydride to *o,o'*-desoxybenzoindicarboxylic acid (XX). Treatment with bromine in acetic acid caused substitution and the formation of a monobromomonoacetate of structure (XXI), since the product failed to react on refluxing with anhydrous potassium acetate in acetic acid. Further treatment of the monobromomonoacetate (XXI) with bromine in chloroform gave a compound which was not obtained in a pure state, but which contained a smaller percentage of carbon than the starting material. Hydrolysis of the impure product with aqueous alcoholic ammonia gave an orange colored compound which was probably the *sym*-dibenzo-cycloöctanetrione-5,6,11 (XXII), since it formed a bright red hydrated phenazine (XXIII). No reaction could be brought about between the triketone (XXII) and either hydrogen peroxide in alkaline solution, or acetic anhydride in the presence of sulfuric acid or potassium acetate.

The diacetate (XXIV) could be obtained from the monoacetate (XIX) and was hydrolyzed to the cyclic diketone (VII) by alkali. Treatment with bromine in acetic acid gave a monobromodiacetate (XXV), which likewise could be obtained by acetylating the monobromomonoacetate (XXI). No reaction took place between the monobromodiacetate (XXV) and bromine or potassium acetate in acetic acid.

Experimental[7]

α,β-Diphenylsuccinic Acid (II).—The following procedure is a modification of Lapworth and McRae's[8] original directions. A suspension of α,β-diphenylsuccinonitrile (I) (117 g.) in a mixture of concentrated sulfuric acid (333 ml.), water (333 ml.) and glacial acetic acid (166 ml.) was refluxed for eleven hours. The resulting gray suspension was diluted with water, filtered and the acid thus obtained was purified through its potassium salt; yield, 116 g. The product, which was used as such in the next step, melted at 220° when crystallized from acetic acid.

9,12-Dichlorodiphensuccindadiene-9,11 (IV) and 9,9,-12,12-Tetrachlorodiphensuccindene-10 (V).—Brand's original directions[5] were changed in the following manner. Diphensuccindanedione-9,12[9] (III) (24 g.) was heated slowly with phosphorus pentachloride (48 g.) until a clear solution was obtained. The resulting red liquid after cooling was treated with glacial acetic acid (400 ml.) and allowed to stand for twenty-six days. Attempts to accelerate the loss of hydrogen chloride by heating or other means gave less clean-cut reactions. The 9,12-dichlorodiphensuccindadiene-9,11 (IV) that separated out during this time was filtered; yield, 19 g. The filtrate, on pouring into water and extracting with ether, gave a mixture of the red dichlorodiene (IV) and a yellow compound, which, from its analysis and reaction, was 9,9,12,12-tetrachlorodiphensuccindene-10 (V). The red dichlorodiene (IV) obtained in the first step was contaminated by this yellow compound. One gram of starting material (III) was also recovered. 9,9,12,12-Tetrachlorodiphensuccindene-10 (V) crystallized once from a (60–68°) petroleum ether–benzene mixture and once from acetic acid formed yellow prisms melting at 178–179°.

Anal. Calcd. for $C_{16}H_8Cl_4$: C, 56.14; H, 2.34. Found: C, 55.79; H, 2.40.

Diphensuccindene-10 (VI).—9,9,12,12-Tetrachlorodiphensuccindene-10 (V) (0.2 g.) in boiling acetic acid (10 ml.) was treated with zinc dust until the solution became colorless. Upon pouring into water and extracting with ether a white solid (0.08 g.) was obtained melting at 197–204°. When crystallized from ethyl acetate, the solid melted at 204–208° and gave no depression when mixed with diphensuccindene-10 (VI) obtained from 9,12-dichlorodiphensuccindadiene-9,11 (IV).[4]

***sym*-Dibenzocycloöctanedione-5,11 (VII).**—Crude diphensuccindene-10 (VI) (6.06 g.) suspended in pure ethyl acetate (210 ml.) was treated with 12% ozone at −40° until all the diphensuccindene-10 (VI) had gone into solution. Warming to room temperature precipitated the white ozonide (VIa) melting at 191–193° with decomposition but exploding when heated rapidly. The suspension of the ozonide was mixed with 5% Pd·$BaSO_4$ catalyst (0.3 g.) and ethyl acetate (50 ml.) and reduced at room temperature with hydrogen at thirty-five pounds (2.3 atm.) pressure for twenty-four hours. From the resulting solution, after removing the catalyst and unreacted ozonide by centrifuging, and then removing the solvent, there was obtained the white crystalline *sym*-dibenzocycloöctanedione-5,11 (VII) (1.95 g.) melting at 202–204°. The unreacted ozonide and catalyst obtained by centrifuging gave upon further treatment in ethyl acetate (100 ml.) with hydrogen at 1000 pounds pressure and 120° for three hours, an oil from which more of the diketone (VII) (0.29 g.) was isolated. The residual oil, taken up in ether and washed with sodium carbonate, gave upon vacuum distillation an additional 0.35 g. of the diketone (VII); total yield, 2.5 g. The acidic by-products were not investigated further. *sym*-Dibenzocycloöctanedione-5,11 (VII), after four crystallizations from benzene, gave white needles melting at 203.5–204.5°.

Anal. Calcd. for $C_{16}H_{12}O_2$: C, 81.36; H, 5.08. Found: C, 81.30; H, 5.02.

The cyclic diketone (VII) is difficultly soluble in aqueous alkali but easily in alcoholic aqueous alkali to give a pale yellow solution. The yellow solution upon heating turns orange. Upon cooling the original hue returns. Acidification of the solution gives the diketone (VII) back unchanged.

No color change was observed when the diketone (VII) was treated in alcoholic alkali with benzenediazonium sulfate.

The dioxime (XII), obtained by refluxing the diketone (VII) in alcohol for four hours with an excess of hydroxylamine hydrochloride neutralized by sodium carbonate, was crystallized twice from ethanol. It formed white needles melting at 240–243° with decomposition.

Anal. Calcd. for $C_{16}H_{14}O_2N_2$: C, 72.18; H, 5.26; N, 10.53. Found: C, 71.96; H, 5.43; N, 10.50.

Methylation of the Diketone.—The diketone (VII) (0.25 g.) in methanol (4 ml.) was treated alternately with 20% potassium hydroxide and dimethyl sulfate until the solution when basic showed no yellow color. Ether extraction gave a white solid (VIII) (0.25 g.) which, after two crystallizations from ethanol, formed prisms, m. p. 143–144°.

Anal. Calcd. for $C_{16}H_{12}O(OCH_3)_2$: C, 76.60; H, 6.38; OCH_3, 21.67. Found: C, 76.16; H, 6.32; OCH_3, 21.32, 21.29.

The dimethyl ether (VIII) would not brominate but could be cleaved by hydrobromic acid in acetic acid to the diketone (VII).

Dibenzal Derivative of the Diketone (X).—A solution of the diketone (VII) (0.1 g.) in a mixture of ethanol (5 ml.), benzaldehyde (0.5 ml.) and saturated alcoholic potassium hydroxide solution (0.5 ml.) was allowed to stand at room temperature for eight days and then poured into water. Acidification followed by extraction with

(7) Microanalyses by J. W. Opie, C. O. Guss and H. H. Hoehn.
(8) Lapworth and McRae, *J. Chem. Soc.*, **121**, 1699 (1922).
(9) Roser, *Ann.*, **247**, 153 (1888).

ether gave a white solid (X) (0.035 g.) which melted at 244–246° after two crystallizations from toluene.

Anal. Calcd. for $C_{30}H_{20}O_2$: C, 87.37; H, 4.85. Found: C, 86.86; H, 4.23.

Reaction of the Diketone with Isatin.—A mixture of the cyclic diketone (VII) (0.24 g.) and isatin (0.29 g.) in 20% potassium hydroxide solution (5 ml.) was heated for forty-eight hours and the resulting solution then cooled to 0°. Acidification with acetic acid of the insoluble potassium salt formed followed by extraction with ether gave a white solid (XI) (0.115 g.) soluble in both acids and bases. Crystallization twice from ethanol and once from ethyl acetate gave very fine, white crystals which melted at 297° with gas evolution.

Anal. Calcd. for $C_{24}H_{15}O_3N$: C, 78.90; H, 4.10; neut. eq., 365. Found: C, 78.29; H, 4.69; neut. eq., 351, 349.

Reaction of the Diketone with Phosphorus Pentachloride.—A mixture of the diketone (VII) (0.24 g.) and phosphorus pentachloride (1 g.) was heated until completely liquid, cooled and then poured into water. Extraction with ether gave a white solid (XIII) (0.277 g.) which contained both phosphorus and chlorine and melted at 123–126° with gas evolution. Three crystallizations from (60–68°) petroleum ether gave white needles which melted at 123–126° with gas evolution. The residue from melting no longer contained chlorine.

Anal. Calcd. for $C_{16}H_{16}Cl_2P_2O_6$: C, 43.93; H, 3.66. Found: C, 44.14; H, 3.23.

Reaction of the Diketone with Methylmagnesium Iodide.—A solution of the diketone (VII) (0.47 g.) and excess methylmagnesium iodide in ether (10 ml.) and benzene (10 ml.) was refluxed for two hours. Decomposition with ammonium chloride followed by extraction with ether gave the tetrahydropyran (XIV) (0.35 g.) which formed white cubes after two crystallizations from benzene. It melted at 213–215°.

Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.95; H, 6.35. Found: C, 81.24; H, 6.06.

In the Grignard machine the diketone (VII) showed only one carbonyl group.

The Grignard product (XIV) in the Grignard machine liberated only one mole of gas. No dehydration of the Grignard product was observed after six hours of refluxing with a few drops of concentrated sulfuric acid in acetic acid.

Reaction of the Diketone with Ammonia.—A solution of the diketone (VII) (0.12 g.) in concentrated ammonium hydroxide (5 ml.) and ethanol (5 ml.) was refluxed for thirty minutes and poured into water. Extraction with ether gave a white solid (XV) (0.06 g.) soluble in dilute hydrochloric acid. After two crystallizations from benzene and one from a (60–68°) petroleum ether–ether mixture the substituted tetrahydropyridine (XV) melted, if heated rapidly, at 167° with gas evolution, then solidified and melted again at 202–203.5°.

Anal. Calcd. for $C_{16}H_{15}O_2N$: C, 75.88; H, 5.93. Found: C, 75.39; H, 5.55.

The ammonia addition product (XV) when treated with nitrous acid or when heated above its melting point, gave the diketone (VII).

Reaction of the Diketone with Semicarbazide.—A solution of the diketone (VII) (0.12 g.), semicarbazide hydrochloride (0.25 g.) and sodium carbonate (0.06 g.) in ethanol (5 ml.) and water (1 ml.) was refluxed for two hours and the crystalline precipitate (XVI) formed, filtered; yield, 0.105 g., m. p. 207–208° with decomposition. A sample recrystallized twice from methyl cellosolve melted at 210° with decomposition.

Anal. Calcd. for $C_{17}H_{17}O_3N_3$: C, 65.60; H, 5.47. Found: C, 65.50; H, 5.69.

Decomposition of the Semicarbazide Addition Product.—A mixture of the semicarbazide addition product (XVI) (0.35 g.) and powdered potassium hydroxide (0.04 g.) upon heating in a sublimer at atmospheric pressure gave a mixture (0.11 g.) separable by fractional crystallization into diphensuccindene-10 (VI) and diphensuccindane[5] (XVII). A similar behavior was observed when the addition product was heated without potassium hydroxide.

Reduction of the Diketone.—The diketone (VII) (0.24 g.) was refluxed with amalgamated zinc (5 g.) in a mixture of water (5 ml.), concentrated hydrochloric acid (5 ml.) and acetic acid (10 ml.) for seven hours. The glycol (XVIII) (0.125 g.) obtained, after two crystallizations from benzene and one from (60–68°) petroleum ether, gave fine, white needles which melted at 148.5–149°.

Anal. Calcd. for $C_{16}H_{14}O_2$: C, 80.67; H, 5.88. Found: C, 80.99; H, 6.00.

A similar result was obtained by refluxing the diketone (VII) (0.12 g.) in 20% potassium hydroxide (14 ml.) and ethanol (4 ml.) with excess zinc dust until the solution was colorless. Acidification followed by extraction with ether gave the glycol (XVIII) (0.082 g.).

The glycol (XVII) when treated with either sulfuric or hydriodic acid in acetic acid gave a very insoluble yellow compound melting above 350°.

Cleavage of the Glycol.—A mixture of the glycol (XVIII) (0.23 g.) and lead tetraacetate (0.5 g.) in dry benzene (10 ml.) was allowed to stand for six hours at 50° and poured into dilute hydrochloric acid. Extraction with ether gave the cyclic diketone (VII) (0.14 g.).

Monoacetate of the Diketone.—A solution of the diketone (VII) (1.17 g.) in acetic anhydride (15 ml.) was refluxed with anhydrous potassium acetate (0.25 g.) for thirty minutes and then poured into water. Extraction with ether gave a white solid (XIX) (0.85 g.), m. p. 137–140°. Crystallization from ethanol gave white plates melting at 138–139°.

Anal. Calcd. for $C_{18}H_{14}O_3$: C, 77.69; H, 5.04. Found: C, 77.78; H, 5.08.

Alkaline hydrolysis of the monoacetate (XIX) gave the diketone (VII).

Oxidation of the Monoacetate.—A solution of the monoacetate (XIX) (0.14 g.) in acetic acid (10 ml.) was heated with chromic anhydride (0.16 g.) in water (0.2 ml.) at 50–60° for one hour, then poured into water and extracted with ether. A carbonate extraction of the ether layer gave a white solid (0.035 g.) which after crystallization from acetic acid first softened at 180° then melted at 215–220° with all the solid phase disappearing at 245°. This behavior was similar to that of *o,o'*-desoxybenzo-

indicarboxylic acid (XX) prepared according to the directions of Ephraim.[10]

Bromination of the Monoacetate.—A solution of the monoacetate (XIX) (0.28 g.) in glacial acetic acid (10 ml.) was treated with bromine (0.3 g.) in acetic acid (3 ml.) and allowed to stand at room temperature for twelve hours. The white crystals (XXI) (0.2 g.) formed were filtered and recrystallized twice from benzene, m. p. 219–223° with gas evolution. An additional 0.065 g. of the monobromomonoacetate (XXI) could be obtained from the filtrate.

Anal. Calcd. for $C_{18}H_{13}O_3Br$: C, 60.50; H, 3.65. Found: C, 60,10; H, 3.62.

The monobromomonoacetate (XXI) was not affected by refluxing in acetic acid with anhydrous potassium acetate.

Further treatment of the monobromomonoacetate (XXI) (0.25 g.) with bromine (0.5 ml.) in chloroform (10 ml.) at room temperature for thirty-six hours gave a white compound (0.12 g.) that melted at 173–178° with gas evolution. This compound could not be purified.

Anal. Calcd. for $C_{18}H_{13}O_3Br$ (XXI): C, 60.50; H, 3.65. Calcd. for $C_{16}H_{10}O_2Br_2$: C, 48.73; H, 2.54. Found: C, 52.63; H, 3.46.

***sym*-Dibenzocycloöctanetrione-5,6,11.**—The above impure bromo compound (m. p. 173–8°) (0.244 g.) was refluxed with concentrated ammonium hydroxide (2 ml.) and ethanol (7 ml.) for ten minutes and then poured into water. Extraction with ether and chloroform gave an orange solid (XXII) which was purified by sublimation under reduced pressure; yield 0.033 g., m. p. 245–250°. Two crystallizations from ethyl acetate followed by a sublimation at atmospheric pressure gave orange needles melting at 254–256°.

Anal. Calcd. for $C_{16}H_{10}O_3$: C, 76.80; H, 4.00. Found: C, 76.88; H, 3.47.

The triketone (XXII) was not affected by refluxing in acetic anhydride with potassium acetate or sulfuric acid and was stable toward alkaline peroxide.

The hydrated phenazine (XXIII) was obtained by refluxing the triketone (XXII) in absolute ethanol with phenylenediamine and a few drops of acetic acid for five hours. Two crystallizations from ethyl acetate gave bright red needles melting at 283–285°.

(10) Ephraim, *Ber.*, **24**, 2820 (1891).

Anal. Calcd. for $C_{22}H_{16}O_2N_2$: C, 77.64; H, 4.71. Found: C, 77.16; H, 4.57.

Diacetate of the Diketone.—A solution of the diketone (VII) (0.708 g.) in acetic anhydride (10 ml.) was refluxed with one drop of concentrated sulfuric acid for thirty minutes and then poured into water. Extraction with ether gave the diacetate (XXIV) (0.525 g.) melting at 145–148°. Three crystallizations from ethanol gave white plates melting at 150–151°.

Anal. Calcd. for $C_{20}H_{16}O_7$: C, 75.00; H, 5.00. Found: C, 74.98; H, 4.97.

The diacetate (XXIV) could also be obtained from the monoacetate (XIX). Alkaline hydrolysis of the diacetate (XXIV) gave the diketone (VII).

Bromination of the Diacetate.—A solution of the diacetate (XXIV) (0.32 g.) in acetic acid (10 ml.) was treated with bromine (0.4 g.) in acetic acid (4 ml.) and allowed to stand at room temperature for five hours. The crystalline plates (XXV) (0.24 g.) formed were filtered, m. p. 225–229°. An additional 0.055 g. was obtained from the filtrate. Two crystallizations did not change the melting point. A mixture with the monobromomonoacetate (XXI) showed a depression in melting point.

Anal. Calcd. for $C_{20}H_{15}O_4Br$: C, 60.76; H, 3.79. Found: C, 60.66; H, 3.92.

The same monobromodiacetate (XXV) was obtained by refluxing the monobromomonoacetate (XXI) in acetic anhydride with a drop of sulfuric acid.

The monobromodiacetate (XXV) was not affected by refluxing in acetic acid with either anhydrous potassium acetate or excess bromine.

Acknowledgment.—The author wishes to thank Professor C. F. Koelsch for his advice and interest during the course of this research.

Summary

1. The preparation of *sym*-dibenzocycloöctanedione-5,11 from diphensuccindene-10 is described.

2. The properties and reactions of *sym*-dibenzocycloöctanedione-5,11 resemble those of open chained 1,5-diketones.

MINNEAPOLIS, MINN. RECEIVED JANUARY 12, 1940

[CONTRIBUTION NO. 214 FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Identification of Organic Compounds. II. Piperidyl Derivatives of Aromatic Halogenonitro Compounds[1]

BY MARGARET K. SEIKEL[2,3]

The work of this Laboratory on the systematic identification of organic compounds has been extended to the development of standard procedures for the preparation of derivatives of aromatic halogenonitro compounds by means of their reaction with piperidine. This paper reports the results of a study of thirty-seven members of this class. In addition to the application of standard procedures, it includes other observations which are of assistance in identifying the compounds as well as the optimum conditions for preparation and the characterization of all their possible piperidyl derivatives.

As a reagent for the preparation of derivatives of compounds with reactive halogen atoms, piperidine possesses many advantages over other bases such as ammonia, aromatic amines, alkali alkoxides[4] or morpholine.[5] Its main advantage lies in its far greater reactivity, a fact shown quantitatively by workers such as Franzen and Bockhacker[6] and Harradence and Lions.[5] Moreover the main reaction products tend to be more readily crystallized and in general contain fewer by-products.

In preparing piperidyl derivatives no single method applicable to all halogenonitro compounds can be used, both because of the spread in the reactivities of halogen atoms in variously substituted compounds and because of the fact that in certain cases two or more halogen atoms can be replaced successively by careful control of conditions. However, two fairly general reactions have been developed: *i. e.*, procedure A in which the compound is refluxed with piperidine for one hour and procedure B in which an alcohol solution is heated fifteen minutes on the steam-bath. Procedure A yielded derivatives in 65% and identifiable compounds in 79% of the thirty-seven cases studied, the difference in the percentages representing recoveries of original material. The corresponding figures for procedure B are 46 and 74%, respectively.

Initial evidence for the reactivity of the compounds was gained by observing the phenomena occurring on adding piperidine to the solid. Such observations are often valuable in suggesting the identity of an unknown halogenonitro compound. The mildest conditions of time, temperature and solvent for the complete replacement of each halogen atom were determined so that a qualitative comparison of the reactivities of these halogen atoms might be made.

In certain cases replacement of a nitro group in preference to a halogen atom occurs, as Mangini and Deliddo and Le Fèvre and Turner have already shown for the ortho dinitro compounds 19[7,8] and 13.[4] Such replacement is often evidenced by the initial red or red-orange color of the solution of the compound in piperidine and by the failure of any piperidine hydrohalide to precipitate even though the solution boils. The nitro group splits out as nitrosopiperidine for the residual clear yellow oil gives the diphenylamine test for nitrosamines. The presence of this compound in the reaction mixture seems to exert a catalytic effect in continued piperidination because dipiperidination of 13 and 19 occurs more readily than dipiperidination of 15 and 22, which yield the same derivatives, respectively. Although 27 also possesses two nitro groups ortho to each other, successive replacement of the chlorine atoms is the chief result of the reaction.[9] Compound 26 whose structure is intermediate between those of 13 and 27 resembles each of them to a certain extent so that derivatives formed by replacement of one nitro group or of two chlorine atoms were isolated.[10] The somewhat similar

(1) For Articles I and III, see THIS JOURNAL, **62**, 511, 603 (1940).

(2) Research Associate.

(3) This work was assisted by a grant to Ernest H. Huntress from the Warren Fund of the American Academy of Arts and Sciences for which grateful acknowledgment is hereby made.

(4) Le Fèvre and Turner, *J. Chem. Soc.*, 1113–1122 (1927).

(5) Harradence and Lions, *J. Proc. Roy. Soc. N. S. Wales*, **70**, 406–412 (1937).

(6) Franzen and Bockhacker, *Ber.*, **53**, 1174–1179 (1920).

(7) These numbers refer to those assigned the compounds in Tables I and II.

(8) Mangini and Deliddo, *Gazz. chim. ital.*, **63**, 625 (1933).

(9) Some nitro replacement is evidenced by the following facts: nitroso piperidine was detected even in the mildest reactions, crude samples of the dipiperidyl derivative always possessed low broad melting points and the piperidine hydrochloride yield was never higher than 80% for two chlorine atoms replaced.

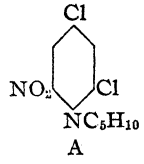
(10) Replacement of chlorine (in preference to nitro) by piperidyl in 26 and 27 is contrary to the results reported for the reaction of these compounds with ammonia; see MacLeod, Pfund and Kilpatrick, THIS JOURNAL, **44**, 2268 (1922), Körner, *Gazz. chim. ital.*, **4**, 353 (1874), and Blanksma, *Rec. trav. chim.*, **27**, 47 (1908).

trinitro compound, 21, however, shows only replacement of the 2-nitro group. Which of the two ortho nitro groups is replaced does not seem to follow any rule as far as can be determined from the compounds under observation. In fact, their reactivities are often so nearly alike that the main reaction product is definitely contaminated with a product resulting from replacement of the other nitro group.[11] Para nitro groups also may be replaced as evidenced by 25.

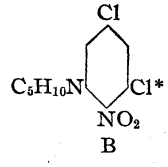
Preparation of all the theoretically possible piperidyl derivatives of each compound was successful in every case with the exception of the monopiperidyl derivative of 32 and the tripiperidyl derivatives of 30 and 33. The derivatives are for the most part readily crystallizable solids melting between 30 and 225°. Some have already been reported as shown in Table I; others, shown in Table II, are new.

The structures of fifteen of the twenty-two new compounds as well as of one already reported may be considered established either by proof, by formation due to replacement of all the halogen in the original compound or replacement of all the halogen atoms which are ortho or para to a nitro group[12] or by evidence as to whether a chlorine atom or a nitro group has been replaced. The structures of the remaining seven compounds as well as of one already reported (the monopiperidyl derivative of 16) are open to some doubt. Footnotes in Table II indicate the assumed structures, whose tentative assignment is based on such facts as the proved structures of amino derivatives of the same halogenonitrobenzenes, the greater reactivity toward amines of halogen ortho to nitro in contrast to halogen para to nitro, and the tendency of the known symmetrical derivatives to be higher melting and more insoluble.

The structures newly established in this work include the following. The identity of the mono- and dipiperidyl derivatives of 19 and 22 limits their structures to N-(3-chloro-6-nitrophenyl)-piperidine and 1-nitro-2,4-di-N-piperidylbenzene. Similarly, 21 and 24 produce the same derivative, indicating that the 2-nitro in 21 is reactive. The monopiperidyl derivative of 26, which forms by replacement of a nitro group, might be either A or B

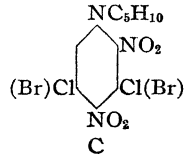


A

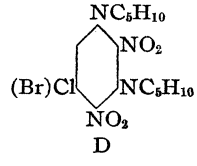


B

It appears to be A as the molecule contains no further reactive chlorine; the Cl* in formula B should be reactive. Also B is believed to be the structure of the monopiperidyl derivative of 30, a compound which melts 15° lower and contains another reactive chlorine atom. The question of the order of replacement of the halogen atoms in the symmetrical trihalogenodinitrobenzenes 16 and 17 has finally been definitely established, at least in respect to the replacement of bromine in 17 by piperidyl. The monopiperidyl derivatives of 16 and 17 already reported have been assigned structure C.[4,13]

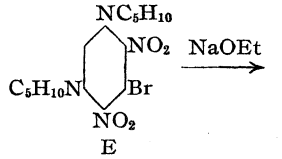


C

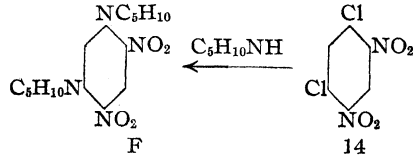


D

The dipiperidyl derivatives have never been prepared before although analogous compounds have been obtained with other amines.[13,14] Borsche's work[13] seemed to show indirectly that the di derivatives were of type D. However, E is definitely the structure of the bromodipiperidyl compound since by reduction with sodium ethylate, similar to the work of Jackson on the establishment of the structures of the two diethoxy derivatives of 17,[15] F is produced which is the known dipiperidyl derivative of 14.



E



F 14

(11) For example, the crude mono- and dipiperidyl derivatives of 19 melt low and over a wide range and the maximum yield of piperidine hydrochloride obtained in the preparation of the latter was 80% no matter how extended the time of reaction. That the presence of nitrosopiperidine in the reaction mixture is not the cause of this reduced yield is proved by the fact that the symmetrical compound 13 produces 100% piperidine hydrochloride yields. Such facts indicate that some replacement of the 4-nitro group accompanies the main replacement of the 3-nitro group.

(12) The complete non-reactivity of halogen atoms meta to nitro groups toward all reagents has been well established.

(13) Borsche and Trautner, *Ann.*, **447**, 1–18 (1926).

(14) Hüffer, *Rec. trav. chim.*, **40**, 451–476 (1921).

(15) Jackson and Warren, *Am. Chem. J.*, **13** 164–193 (1891); Jackson and Koch, *ibid.*, **21**, 510–528 (1899).

This work also proves that C is the structure of the monopiperidyl of 17. The structures of the derivatives of the chloro analog 16 may be assumed to be C and E, respectively, an assumption supported by the similarity in properties, although a reduction such as described above could not be carried out.

The meta substituted compound 20 is characteristically different from all the compounds studied, for it dissolves in piperidine without change in temperature but with the formation of a black-red color. The deep color is believed to be caused by the formation of a molecular addition product since addition of water to a newly mixed solution reprecipitates the original.[16] However, no crystalline addition compound could be isolated. The reaction of *sym*-trinitrobenzene was investigated and found to give analogous results although in this case an unstable mole for mole addition complex could be crystallized.[17] In both cases further deep-seated reactions occur between the nitrobenzene and excess piperidine if allowed to stand or if heated; from the resultant brown powders with indefinite melting points no pure products could be isolated readily.

Experimental

All melting points reported in this paper were taken by the method described in Mulliken's "Identification of Pure Organic Compounds," Vol. I, page 218, on a 360° melting point thermometer immersed in sulfuric acid to the 0° point. All melting points are uncorrected.

Procedure A.—To 0.5 g. of the halogenonitro compound add 1.5 ml. (1.0 ml. for bromo compounds) of piperidine.[18] Observe phenomena such as sputtering (stir to prevent local overheating), boiling, color formation and the time elapsing before piperidine hydrohalide precipitates; these are partially dependent on the quantities used. Reflux the resultant solution or mixture in an oil-bath for one hour, cool, add water and filter. If the product separates as an oil, the following crystallization methods should be tried in order[19]: (a) ice the mixture for an hour with scratching (with few exceptions this method is sufficient); (b) decant the aqueous layer containing excess piperidine and piperidine hydrohalide and wash the oil several times with water; (c) freeze in dry-ice. If no crystallization is then obtained, abandon the experiment. The yields are 90–100% and the crude product will melt sharply provided that the chlorine replacement is complete and decomposition products due to excessive reactivity are not present.

Recrystallize from 85% alcohol using excess if the melting point is low. Certain high melting insoluble compounds require 95% alcohol, acetone, or glacial acetic acid; such cases are mentioned in the footnotes of Table II.

The by-product piperidine hydrohalide yield, an index of the completeness of the reaction, can be determined qualitatively by evaporating the aqueous filtrate of the crude product and weighing the residue. If a nitro group is replaced, this residue is a reddish, acetone-soluble gum, giving a nitrosamine test with diphenylamine reagent.

Procedure B.—Dissolve 0.5 g. of the compound in 5 ml. of boiling alcohol (more if necessary), add 1.5 ml. (1.0 ml. for bromo compounds) of piperidine and heat for fifteen minutes on the steam-bath. If the product does not separate on cooling or icing, force it out with water, crystallizing any oil obtained as described above. If water has not been added before filtering, wash the precipitate with water to remove possible contaminating piperidine hydrohalide. The yields are only 70–90%, but the crystallization from alcohol effects purification.

Modified Procedures.—In most cases the standard procedures do not represent the readiest method of obtaining the derivatives of any one compound, nor can all the theoretically possible derivatives of each compound be prepared by these means. Therefore, modified procedures have been developed. For the most part these consist of applying conditions A or B with a change in the time of heating. These times are noted in Tables I and II; for example, A-2h means that conditions A should be applied for two hours (m is used to represent minutes) and B-0m means that as soon as the piperidine is added to the hot alcohol solution of the compound, the mixture is allowed to cool. The exact number of minutes is critical only in cases where the first of two reactive

(16) Although no addition compounds of 20 and amines have been reported, *m*-dinitrobenzene and certain of its derivatives are known to yield them; see Pfeiffer, "Organische Molekülverbindungen," 1927, p. 360.

(17) Romburgh, *Rec. trav. chim.*, **14**, 68 (1895), obtained the color but could not crystallize the compound.

(18) Monsanto catalytic piperidine with a reboiling range of 104–107° was used for this investigation; see Cook, THIS JOURNAL, **59**, 2661 (1937).

(19) The more laborious crystallization aids suggested by Le Fèvre and Turner,[4] are unnecessary. In fact the ability to dissolve readily in dilute hydrochloric acid is confined to those piperidyl derivatives with few ring substituents.

TABLE I

NEW DATA ON KNOWN PIPERIDYL DERIVATIVES[a]

No.	Halogenated nitrobenzenes[b]	Type of deriv.	Usable[c] stand. proc.	Readiest prepn.[d]
1, 2	1-Chloro- and 1-bromo-2-	Mono[e]	A	A-20m(Cl) A-10m(Br)
3, 4	1-Chloro- and 1-bromo-3-	None	Orig. recov.	
5, 6	1-Chloro- and 1-bromo-4-	Mono[f,g]	A	A-2h(Cl) A-30m(Br)
7, 8	1-Chloro- and 1-bromo-2,4-di-	Mono[f,h,i]	A, B	B-0m[j]
9	1-Chloro-2,6-di-[k]	Mono[l]	A, B	B-0m[j]
10	1-Chloro-2,4,6-tri	Mono[f,m]	B	B-0m[j]
11	1,2-Dichloro-4-	Mono[g]	A	A-20m
12	1,4-Dichloro-2-	Mono[e(1),i]	A	A-20m
13	1,2-Dichloro-4,5-di-[g]	Mono[g]		E-1m[j]
14	1,3-Dichloro-4,6-di-[n]	Mono[g,o]		2M-B-0m[j]
		Di[g]	A, B	B-0m
15	1,2,4-Trichloro-5-[p,q]	Mono[g]		D
16	1,3,5-Trichloro-2,4-di[q,r]	Mono[s]		2M-B-5m
		Tri[g,s,t]	A	A-20m
17	1,3,5-Tribromo-2,4-di-[q,u]	Mono[g,v]		B-2m
		Tri[g,s,t]	A	A-10m
18	*p*-Nitrobenzyl chloride	Mono[w]	A, B	C-2m

[a] In most cases the melting points of the derivatives obtained checked those reported within 2°; wider discrepancies are noted. Compounds 19, 22, 28, 36, and 37, which yielded results completely at variance with the literature, are listed in Table II. Compounds 13, 15, 16, and 17 are in both Tables I and II. [b] Eastman Kodak Co. material unless otherwise stated. [c] "Usable" means that the crude product will be crystalline and purifiable by a maximum of two recrystallizations. [d] Easiest and quickest way of obtaining a pure derivative. Represents the mildest conditions for complete halogen replacement except when footnoted *j*. See Experimental Section for explanation of symbols. [e] (1) Lellmann and Geller, *Ber.*, **21**, 2281–2287 (1888). (2) M. p. 77–77.5°, recorded, [81°]. [f] "Beilstein," Vol. XX, p. 22. [g] Ref. 4. [h] Ref. 20. [i] Fox and Turner, *J. Chem. Soc.*, 1853–1867 (1930). [j] Complete replacement of the halogen occurs at once, *i. e.*, under conditions E-1m. [k] Sane and Joshi, *J. Indian Chem. Soc.*, 9, 60 (1932). [l] Borsche and Rantscheff, *Ann.*, **379**, 166 (1911). [m] 95% alcohol is preferable for recrystallization. [n] Obtained from Fraenkel and Landau. [o] Borsche and Bahr, *Ann.*, **402**, 96 (1914). M. p. 114–114.5°, recorded, [117–118°, 119°]. *Anal.* Calcd. for $C_{11}H_{12}ClN_3O_4$: Cl, 12.4. Found: Cl, 12.4, 12.5. [p] Beilstein and Kurbatow, *Ann.*, **192**, 230 (1878); Holleman and Van Haeften, *Rec. trav. chim.*, **40**, 70 (1921). [q] Carten, Ph.D. Thesis, Massachusetts Institute of Technology, 1939, pp. 116–118. [r] Ref. 14. [s] Ref. 13. [t] Glacial acetic acid is preferable for recrystallization. M. p. 183–184°, recorded, [177–178°, 147–148°]. *Anal.* Calcd. for $C_{21}H_{31}N_5O_4$: N, 16.8. Found: N, 16.9, 16.9. [u] Jackson, *Ber.*, 8, 1172 (1875). [v] M. p. 129–129.5°, recorded, [125–126°]. [w] Lellmann and Pekrun, *Ann.*, **259**, 40 (1890). Best purified by dissolving in 95% alcohol and adding water dropwise so that the oil crystallizes as it forms.

chlorine atoms is being replaced; otherwise it represents the minimum time required for complete halogen replacement as evidenced by piperidine hydrohalide yields. Other procedures are as follows: C, mix the two reactants and add water after the specified time, this representing the simplest method of obtaining a derivative; D, add ice-cold piperidine to the solid compound also iced, continue icing until the initial violent reaction has moderated and then allow the mixture to stand in a water-bath maintained at room temperature, stirring frequently, until the spontaneous evolution of heat ceases (one to two hours); E, dissolve the compound in the least amount of cold alcohol (20–40 ml. for 0.5 g.), add piperidine and after the specified time at room temperature add water to precipitate the product. To prepare monopiperidyl derivatives in cases where dipiperidination is rapid, the amount of piperidine must be limited to the exactly calculated two mols; such procedures are prefixed by 2M. Calculated quantities may be used in other cases to conserve piperidine.

Structure Proofs. Monopiperidyl Derivatives of 1-Chloro-2,3,5-trinitrobenzene (21) and 1,2-Dichloro-3,5-dinitrobenzene (24).—By replacement of a nitro group in 21 a piperidyl derivative was obtained which did not lower the melting point of the monopiperidyl derivative of 24 (which was formed by replacement of a chlorine). Therefore the derivatives must be N-(2-chloro-4,6-dinitrophenyl)-piperidine.

Derivatives of 1-Chloro-3,4-dinitrobenzene (19) and 1,3-Dichloro-4-nitrobenzene (22).—The mono- and dipiperidyl derivatives of 19, formed, respectively, by replacement of one nitro group and a nitro group plus a chlorine, do not lower the melting points of the corresponding derivatives of 22 formed by successive replacements of the chlorines. Therefore, the 3-nitro must be

TABLE II

PREPARATION AND PROPERTIES OF PIPERIDYL DERIVATIVES

No.	Halogenated nitrobenzene[a]	Derivative Pos. of NC_5H_{10}	Formula	Analysis, % Calcd.	Found[b]	Usable[a] stand. proc.	Readiest prepn.[a]	M. p., °C. (uncor.)	Color	Crystal form
19	1-Chloro-3,4-di-[c]	3	$C_{11}H_{13}ClN_2O_2$	Cl, 14.7	14.9	B[d]	E-30m	69–70[e]	Orange	Diamonds
		1, 3	$C_{16}H_{23}N_3O_2$	N, 14.5	14.4		A-4h	77.5–78.5[e]	Yel.-or.	Needles
20	1-Chloro-3,5-di-[f]	See discussion								
21	1-Chloro-2,3,5-tri-[g]	2	Same as 24			A, B	B-0m,[h] C-1m			
22	1,3-Dichloro-4-[i]	3	Same as 19[e]			A, B	C-30m			
		1, 3	Same as 19[e]				A-12h			
23	1,3-Dichloro-5-[j,k]	None formed[l]				Orig. recov.				
24	1,2-Dichloro-3,5-di-[k,m]	2	$C_{11}H_{12}ClN_3O_4$	Cl, 12.4	12.5	A, B	B-0m[h] C-1m	125.5	Yellow	Sheets
13	1,2-Dichloro-4,5-di-[n]	2, 4	Same as 15, see below			A	A			
25	1,3-Dichloro-2,5-di-[g]	2[o]	$C_{11}H_{12}Cl_2N_2O_2$	Cl, 25.8	25.9	A, B	B-0m	86.5–87.5	Yellow	Needles
26	1,3-Dichloro-4,5-di-[k,p]	4	$C_{11}H_{12}Cl_2N_2O_2$	Cl, 25.8	25.8		[q]	57–58	Golden	Plates
		1, 3	$C_{16}H_{22}N_4O_4$	N, 16.7	16.7		[r]	173–173.5	Orange	Ferns
27	1,4-Dichloro-2,3-di-[s]	1	$C_{11}H_{12}ClN_3O_4$	Cl, 12.4	12.4		B-2m	91–92	Red.-or.	Needles
		1, 4	$C_{16}H_{22}N_4O_4$	N, 16.7	16.8	A	A-5m	167–167.5[t]	Crimson	Plates
28	1,4-Dichloro-2,6-di-[s]	1	$C_{11}H_{12}ClN_3O_4$	Cl, 12.4	12.4	A, B	C-1m B-0m[h]	71.5–72.5[u]	Scarlet	Needles
29	1,2,3-Trichloro-4-[v,w]	3[x]	$C_{11}H_{12}Cl_2N_2O_2$	Cl, 25.8	26.1		A-2m	73–74	Orange	Needles
		1, 3	$C_{16}H_{22}ClN_3O_2$	Cl, 11.0	11.3		A-12h	93.5–94	Lemon	Diamonds
15	1,2,4-Trichloro-5-[n]	2, 4	$C_{16}H_{22}ClN_3O_2$	Cl, 11.0	11.0	A	A-2h	103.5–104[y]	Orange	Plates
30	1,3,5-Trichloro-2-[v,w]	1[z]	$C_{11}H_{12}Cl_2N_2O_2$	Cl, 25.8	25.8		[aa]	41–42	Or.-yel.	Powder
		1, 3[z]	$C_{16}H_{22}ClN_3O_4$	Cl, 11.0	11.1		A-4h	88.5–89.5	Yellow	Needles
31	1,2,3,-Trichloro-4,6-di-[w,bb]	1	$C_{11}H_{11}Cl_3N_2O_4$	Cl, 22.2	22.2		2M-B-5m	95–96	Orange	Needles
		1, 3	$C_{16}H_{21}ClN_4O_4$	Cl, 9.61	9.72	A, B	B-0m	188.5–189[t,cc]	Yellow	Cubes
32	1,2,4-Trichloro-3,5-di-[w,bb]	2, 4[dd]	$C_{16}H_{21}ClN_4O_4$	Cl, 9.61	9.48	A, B	B	142.5–143	Orange	Needles
		Stable form			9.48		[ee]	146.5–147.5	Yellow	Needles
16	1,3,5-Trichloro-2,4-di-[n]	1, 5[ff]	$C_{16}H_{21}ClN_4O_4$	N, 15.2	15.2	B	B-10m	190[t]	Lemon	Needles
33	1,3,5-Tribromo-2-[w,gg]	1[hh]	$C_{11}H_{12}Br_2N_2O_2$	Br, 43.9	44.0		A-2½m	70–71	Lemon	Powder
		1, 3[hh]	$C_{16}H_{22}BrN_3O_2$	Br, 21.7	21.7		A-2 to 3h	87.5–88	Golden	Needles
17	1,3,5-Tribromo-2,4-di-[n]	1, 5	$C_{16}H_{21}BrN_4O_4$	Br, 19.3	19.3		D	224–225[t]	Yellow	Needles
34	2-Chloro-6-nitrotoluene	None formed				Orig. recov.				
35	4-Chloro-2-nitrotoluene	None formed				Orig. recov.				
36	*o*-Nitrobenzyl chloride[ii]	ω	$C_{12}H_{16}N_2O_2$	N, 12.7	12.7	B[d]	B-0m	38–39[jj,kk]	Del. yel.	Needles
			$C_{12}H_{15}N_2O_2$·HCl	Cl, 13.8	14.0			210.5–212[kk,ll]	Colorless	Rhomb.
37	*m*-Nitrobenzyl chloride[mm]	ω	$C_{12}H_{16}N_2O_2$	Never dried		A, B[d]	C-1m	10–13[kk,nn]	Yellow	Oil
			$C_{12}H_{16}N_2O_2$·HCl	Cl, 13.8	13.8		B-0m	202.5–205[kk,ll]	Colorless	Cubes

[a] As in Table I. [b] Value reported is mean of two determinations; average deviation of analyses from means is 0.4%. [c] Fraenkel and Landau product recrystallized from 85% alcohol until air evaporation of the alcohol solution deposited crystals and not an oil. *Anal.* Calcd. for $C_6H_3ClN_2O_4$: Cl, 17.5. Found: Cl, 17.5, 17.4. [d] Dry-ice required for crystallization. [e] See discussion in Experimental Section. [f] Bader, *Ber.*, **24**, 1655 (1891), and de Kock, *Rec. trav. chim.*, **20**, 112 (1901). The 3,5-dinitroaniline necessary for the preparation was obtained preferably from 3,5-dinitrobenzoyl chloride, Blanksma and Verberg, *ibid.*, **53**, 988 (1934). [g] In the diazotization of 2,6-dichloro-4-nitraniline and the replacement of the diazo group by a nitro group according to Körner and Contardi, *Chem. Abs.*, **8**, 1761–1762 (1914), and Holleman,[k] the 5% yield of the desired 1,3-dichloro-2,5-dinitrobenzene (25) was accompanied by a 6% yield of 21, the latter being less volatile in superheated steam. It was identified by its melting point, its analysis (Calcd. for $C_6H_2ClN_3O_6$: Cl, 14.3. Found: Cl, 14.5, 14.5) and its piperidyl derivative. [h] Complete replacement of the halogen or nitro group occurs at once, *i. e.*, under conditions E-lm. [i] Roberts and Turner, *J. Chem. Soc.*, 2011 (1925). [j] Holleman, *Rec. trav. chim.*, **23**, 366 (1904). [k] Holleman and Den Hollander, *Rec. trav. chim.*, **39**, 435–480 (1920). [l] A very slow replacement of chlorine occurs, for a trace of piperidine hydrochloride was present in the reaction mixture of procedure A, but its yield amounted to only 10% even after heating four hours. [m] Ullmann and Sané, *Ber.*, **44**, 3734 (1911). [n] See Table I for other derivatives, etc. [o] Structure assumed by analogy with mono-amino derivative, Körner and Contardi, *Chem. Abs.*, **8**, 1762 (1914). [p] Blanksma, *Rec. trav. chim.*, **27**, 46 (1908). [q] Isolated in maximum yield of 15% by recrystallizing once or twice from a large volume of 85% alcohol the oil or gummy solid obtained from conditions E-24h. [r] Isolated in maximum yield of 10% by treating the oil obtained under conditions C-10m with boiling 85 or 95% alcohol until the last few bits of oil crystallized in the hot solution and by allowing the solution to cool slowly. In one case the monopiperidyl derivative separated in a 10% yield from the filtrate after the dipiperidyl derivative had been removed. [s] Page and Heasman, *J. Chem. Soc.*, 3247–3255 (1923). [t] Glacial acetic acid is preferable for recrystallization. [u] Compare with the melting point given by Groves, Turner and Sharp, *J. Chem. Soc.*, 521 (1929). [v] Beilstein and Kurbatow, *Ann.*, **192**, 228–240 (1878). [w] Carten, Ph.D. Thesis, Massachusetts Institute of Technology, 1939, pp. 116–118. [x] Structure assumed by analogy with the mono-amino derivative.[p] [y] The crude product precipitates with piperidine of crystallization and melts around 125°; this is removed by heating for one hour at 110° or by repeated recrystallizations. [z] Structure assumed; compare with derivatives of 33. [aa] Isolated in a 70% yield by recrystallization of the oily product obtained under conditions 2M-A-20m; dry-ice cooling necessary to initiate crystallization even when pure. [bb] Reference 14. [cc] Acetone is preferable for recrystallization. [dd] No monopiperidyl derivative could be obtained; reactions even under the mildest conditions and with only two moles of piperidine produced gums from which only the dipiperidyl derivative

could be isolated in a crystalline state. [ee] By heating the 143° compound for one hour at 125–130° or by remelting it. The 147° compound reverts to the 143° compound on recrystallization. [ff] Structure assumed by analogy with 17. See discussion. [gg] Jackson, *Ber.*, **8**, 1172–1173 (1875). [hh] Structure assumed by analogy with diamino derivative, Körner, *Gazz. chim. ital.*, **4**, 425 (1874). [ii] Fraenkel and Landau material. [jj] If the product is recrystallized from 65% alcohol, a seed must be preserved to initiate crystallization; if it is recrystallized from 60% acetone and seeded by the crust which forms on the edge during icing, it must be filtered ice-cold as in the presence of acetone at room temperature the crystals return to oil. [kk] Compare Lellmann and Pekrun, *Ann.*, **259**, 40–61 (1890). [ll] Recrystallized from absolute alcohol. [mm] Norris and Taylor, THIS JOURNAL, **46**, 756 (1924). [nn] Taken floating in water.

replaced first in 19 and the 3-chloro in 22, followed by the 1-chloro in both. The properties of these derivatives (melting point and color) disagree with those already reported. Mangini[8] only obtained the monopiperidyl derivative of 19 as an oil whose hydrochloride melted at 147–150° (a crude sample of the latter prepared in this work melted at 145–149°). The dipiperidyl derivative of 22 has been described twice by Le Fèvre and co-workers[4,20] as red-orange, m. p. 67–68°; these properties as well as the method of preparation are more consistent with those given in Table II for the monopiperidyl derivative.

Monopiperidyl Derivative of 1,3-Dichloro-4,5-dinitrobenzene (26).—Analysis showed that piperidyl had replaced nitro. When 20 mg. of this derivative was subjected to the treatment A-4h, it was quantitatively recovered in pure form, m. p. 56–57° [57–58°], and did not lower the melting point of the analyzed sample; the filtrate contained only the merest traces of ionized chlorine. Therefore, this derivative contains no replaceable chlorine and must possess Structure A. Under the same conditions the monopiperidyl derivative of 30, m. p. 41–42°, and believed to possess structure B, yielded the dipiperidyl derivative which melted at 89–89.5° after one recrystallization [88.5–89.5°] and did not lower the melting point of an analyzed sample.

Mono- and Dipiperidyl Derivatives of 1,3,5-Tribromo-2,4-dinitrobenzene (17).—The structures of these derivatives were proved to be C and E, respectively, by the following reduction of the dipiperidyl derivative with sodium ethylate to F. The dipiperidyl derivative (0.5 g., 0.0012 mole) was dissolved by heating in 50 ml. of absolute alcohol and treated with 0.27 g. of sodium (10 × 0.0012 mole) dissolved in 10 ml. of absolute alcohol. The yellow solution was refluxed on the steam-bath for fifteen minutes, the color changing very slowly at first and then rapidly to orange, red and finally dark red. The dark red solution was evaporated almost to dryness by air, leached with water (which dissolved the red by-product) and filtered. The mustard colored crude (yield 50%, m. p. 120–126°) was recrystallized once or twice from 85% alcohol using Norite decolorizing carbon, m. p. 130–130.5°. Shorter reaction times, even ten minutes, produced very little reduction and, coupled with other observations, this seems to indicate that the red by-product catalyzes the reduction. Longer reaction times did not change the yields or the melting point. The identity of this product as 1,3-dinitro-4,6-di-N-piperidylbenzene was proved by a mixed melting point with authentic material, m. p. 130–131° (obtained by the action of piperidine on 14) and by analysis.

Anal. Calcd. for $C_{16}H_{22}N_4O_4$: N, 16.7. Found: N, 16.7, 16.9.

(20) Le Fèvre, Saunders and Turner, *J. Chem. Soc.*, 1171 (1927).

Dipiperidyl Derivative of 1,3,5-Trichloro-2,4-dinitrobenzene (16).—An attempt to reduce this compound to F with sodium ethylate and hence prove its structure failed. When it was subjected to the same treatment as its bromo analog (see under 17), the color change shifted only to orange-yellow after refluxing for one-half hour and a sample of the product melted at 150–165°. The ethylate concentration was tripled and the refluxing continued until the dark red color formed (three-quarter hour more). The 70% yield of product, m. p. 167–170°, crystallized from 80% acetic acid in orange-yellow needles, m. p. 173–174°. It contained no chlorine and is believed to be 1-ethoxy-2,6-dinitro-3,5-di-N-piperidylbenzene.

Anal. Calcd. for $C_{18}H_{26}N_4O_5$: N, 14.8. Found: N, 14.8, 14.9.

Lack of material prevented further investigation. The formation of this ethoxy derivative may indicate that the compound has structure D instead of E as its bromo analog, but undoubtedly the chlorine atom is more resistant to reduction than the bromine atom.

Addition Compounds with Piperidine. 1,3,5-Trinitrobenzene.—When *sym*-trinitrobenzene, m. p. 119–121, and piperidine are mixed mole for mole, a thick black-red solution forms at first with slight if any change in temperature. This thickens at once and becomes crystalline, the dark dull red product melting at 60–62° with gas evolution between 110–120°. The formation of this addition compound occurs so readily that if a few crystals of trinitrobenzene are floated on a 0.05% aqueous piperidine solution, the solution slowly acquires a very slight pink tinge. However, it is unstable in two directions. First, it decomposes into the original components whenever exposed to air, the surface fading to a light pink; solvents, while dissolving enough to produce a red solution, decompose it for the most part. Therefore it cannot be recrystallized and can be preserved only by stoppering tightly with a minimum of space. In an atmosphere saturated with piperidine it deliquesces. Second, deep-seated reactions occur slowly so that a well-stoppered sample cannot be kept for more than an hour or two before the melting point begins to drop and broaden; in three or four days the material becomes a black liquid. In fact even if the addition product were decomposed immediately

after forming, the recovered trinitrobenzene was light raspberry colored, although even two days of standing had little effect on the melting point of the recovered material. The identification of any further products was not undertaken as the material obtained from long standing or from heating the trinitrobenzene in excess piperidine consisted of brown crystallized gums, completely soluble in concentrated hydrochloric acid but not responding to any simple method of purification.

1-Chloro-3,5-dinitrobenzene (20).—This exhibited the same color phenomena with piperidine as *sym*-trinitrobenzene, but no crystalline addition product could be prepared although various ratios of piperidine to chloronitrobenzene were tried and the thick red liquids cooled in dry-ice until they hardened to glasses. This addition product does not form as readily, for although 20 deliquesces in saturated piperidine vapor, it will not produce color with aqueous piperidine. The same deep-seated reactions occur, but no pure product could be isolated from the brown powders by fractional precipitation from either the concentrated hydrochloric acid solution or from acetone solution.

Relative Reactivities.—A qualitative determination of the relative reactivities of the various compounds was made both very roughly by observing the phenomena occurring when piperidine is added to the solids and more accurately by determining the mildest conditions for complete replacement of each halogen atom as well as by certain comparative experiments not discussed. The following list is in order of decreasing reactivity in respect to monopiperidination only: A. Compounds producing sputtering as simultaneous precipitation of the piperidine hydrohalide and boiling of the red or orange liquid occurs (sp) or boiling of the red or orange solution without salt precipitation (b), (1) reactions instantaneous in cold alcohol solution [10 (sp), 7 (sp), 8 (sp), 14 (sp), 28 (sp), 24 (sp), 9 (sp), 21 (b) and 13 (b)], (2) reactions not instantaneous in cold alcohol solution, 19 (b), 25 (b), 27 (sp), [16 (sp) and 31 (sp)], 26 (b, sp), 32 (sp); B. Compounds forming clear yellow solutions from which piperidine hydrohalide precipitates in the cold in a few minutes (Xm) generally accompanied by liberation of heat, [36(0m), 37(0m) and 18(0m)], 15(0m), 17(0-1m), 22(1m), 29(1-2m), 30($2^1/_2$m), 12(5m), 33(15m); C. Compounds dissolving in piperidine with absorption of heat and producing clear yellow solutions, 2, 11, 1, 6, 5, 23, [3, 4, 34 and 35].

Summary

1. Two standard procedures for the preparation of piperidyl derivatives of aromatic halogenonitro compounds have been developed.

2. All possible piperidyl derivatives of the compounds studied have been isolated and the most favorable conditions for their preparation determined.

3. The structures of certain derivatives have been proved.

CAMBRIDGE, MASS. RECEIVED NOVEMBER 28, 1939

[CONTRIBUTION NO. 210 FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

The Deepening of Color of Sodium Nitrophenolate Solutions with Elevation of Temperature

BY TENNEY L. DAVIS AND JOSEPH L. RICHMOND

The yellow color of solutions of the salts of *m*-nitrophenol is of significance in discussions of theories of color and constitution. Satisfactory quinoid formulas may be written for the colored salts of *o*- and *p*-nitrophenol, as Armstrong[1] pointed out, and the parent substances may be supposed to exist in tautomeric quinoid forms. Hantzsch[2] accepted the view of Armstrong and suggested formulas for the colored salts of *m*-nitrophenol. Later he[3] succeeded in preparing colored and colorless esters of *o*- and *p*-nitrophenol, but not of the *m*-compound, and concluded that the free *m*-quinone is not capable of existence; or, as we should say, that *m*-nitrophenol is not capable of tautomerizing to a quinoid form, but that the colored salts of *m*-nitrophenol are nevertheless quinoid, the *m*-

(1) Armstrong, *J. Chem. Soc.*, 101 (1892).
(2) Hantzsch, *Ber.*, **39**, 1095 (1906).
(3) Hantzsch, *ibid.*, **40**, 339 (1907).

quinone structure being stable in electronegative radicals present in an electrolyte along with positive ions of the metal. Hantzsch's *m*-quinoid formulas have not met with general acceptance, for they represent atomic arrangements which are thought to be unstable. The problem has been complicated further by the absence from the literature of any clear cut definition of quinones and of an understanding or an agreement as to what the structure of *m*-quinones, if they exist, would be.[4]

Hirsch[5] reported that solutions of the sodium salts of *o*- and *p*-nitrophenol become more deeply colored when they are warmed, and stated wrongly that the colors of the solutions on cooling revert only slowly to the original shades. We find that the changes of color intensity are as rapid as the changes of temperature, and we find, contrary to the observation of Hirsch, that solutions of sodium *m*-nitrophenolate behave in the same general way as those of the *o*- and *p*-compounds. The change appears to be solely a change in color intensity, for the color of a short column of warm solution matches perfectly with the color of a longer column of cold solution.[6]

The colors of solutions of the three sodium nitrophenolates are sensibly the same to the eye. Measurements of the thermotropic color intensifications have shown that the three substances differ from one another in respect to this property no more than substances of similar but not wholly identical structure would be expected to differ.

(4) The common practice in textbooks appears to be to describe the production of *p*-benzoquinone by the oxidation of hydroquinone, to discuss the peculiar chemical and structural properties of this substance, and then to use these properties as a basis for outlining, but not for defining, the class of quinones. The definition of quinones as oxidation products of benzene derivatives is not satisfactory; quinone dioxime, an undoubted quinone, is oxidized by strong nitric acid to yield *p*-dinitrobenzene. For a number of years T. L. D. has been accustomed in his classes to define quinones as substances in which two atoms attached to an aromatic ring (or ring system) are the terminal atoms of a conjugate system through the aromatic ring (or ring system). (An aromatic ring is conceived and defined as a six-membered carbon ring, each carbon atom of which has one residual valence.) This definition is believed to include all substances which are recognized to be quinones, and to exclude all those which are not now classed as such. It has the advantage that it unifies the reactions of quinones, in which the side chain conjugated into the ring acts in many cases to make the ring accessible to reagents which do not affect the ring of other aromatic substances. It excludes the possibility of *m*-quinones, but leaves open for study the question of what structures result when two hydrogen atoms are removed from *m*-diphenols.

(5) Hirsch, *Ber.*, **36**, 1893 (1903).

(6) Hantzsch, *ibid.*, **39**, 1084 (1906), reported observations on the colors of the dry salts, that they intensified on warming and after cooling later faded again. Goddard, *J. Chem. Soc.*, 54 (1922), found that the hydrated sodium salts of the nitrophenols lose water to form the anhydrous compounds which are darker in color, and that these on standing in the air take up water to form the lighter hydrated salts.

The results of our experiments with 0.1 *N* solutions of the sodium nitrophenolates are plotted in Fig. 1, where each curve summarizes the results from two or from three runs, and the spread of the data indicates the approximation or error with which we have been able to match the colors.

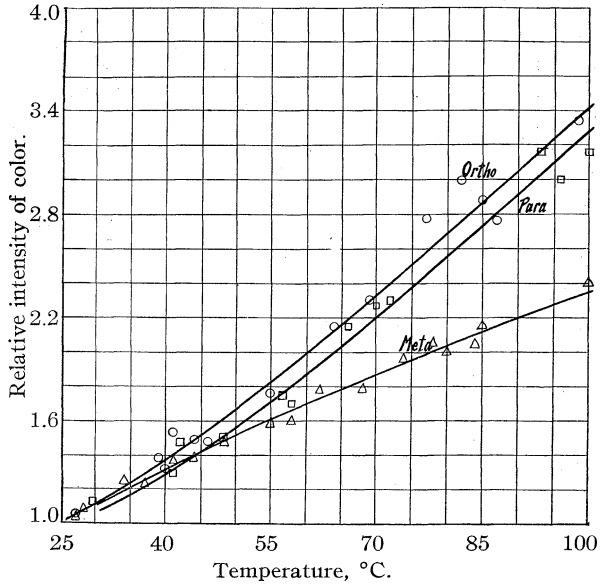


Fig. 1.—Intensity of color of warm 0.1 *N* sodium nitrophenolate solutions compared with the color of the same solutions at 25°: ○, ortho; □, para; △, meta.

The curves for the *o*- and *p*-compounds are close together; the color of the solution of the ortho compound is about 3.4 times as intense at 100° as at 25°; that of the para compound about 3.3 times. The curve for the *m*-compound slopes upward less sharply but is of the same general form as the curves for its isomers; the color of 0.1 *N* sodium *m*-nitrophenolate is about 2.3 times as intense at 100° as at 25°. In other experiments to determine the effect of alkalinity, sodium carbonate was added to 0.1 *N* *m*-nitrophenol solution in amounts corresponding to 0.02, 0.2, 1.0 and 2.0 *N* concentration of sodium ion. The results, plotted in Fig. 2, show that the thermotropic color intensification is lessened by increasing amounts of alkali, hence, since the alkali may be presumed to reduce the ionization of the salt, that the effect is due to a property of the ion.

An hypothesis to account for the behavior of the three nitrophenolates must assign similar structures to the ions of all of them, and will have additional plausibility if it relates the structure of the *m*-nitrophenolate ion to the known

facts relative to the existence, or non-existence, of *m*-quinone.

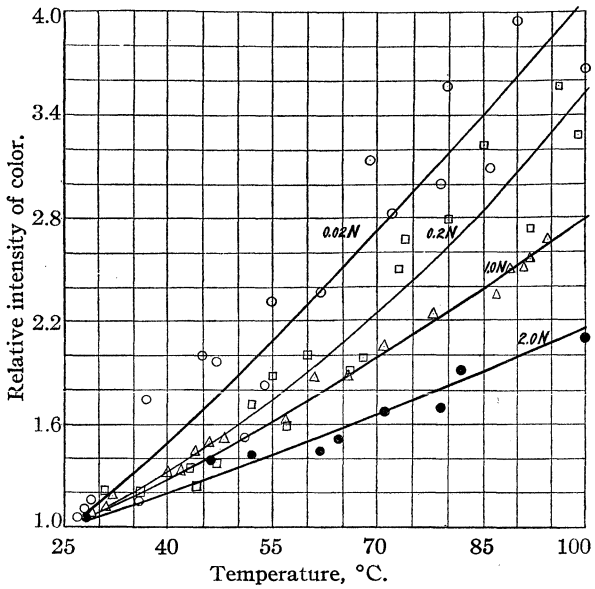


Fig. 2.—Effect of sodium carbonate upon thermotropic color intensification of 0.1 *N* *m*-nitrophenol solutions: ○, 0.02 *N* sodium carbonate; □, 0.2 *N*; △, 1.0 *N*; ●, 2.0 *N*.

Experimental Results

A colorimeter was constructed in which two beams of light from a single source were made to pass respectively through two tubes, one of which contained a column of solution at room temperature the length of which could be varied while the other contained a column of constant length enclosed in a jacket through which water was circulated into which steam or warm water or cold water was injected as required. The temperature of the second column of solution was determined by means of a thermocouple which, it was found, did not interfere with the optical path. The light after passing through the two tubes was reflected upon a single target as two semicircular spots so placed as to form a complete circle with each other. The length of the column of liquid at room temperature was then adjusted until the two halves of the circular spot were indistinguishable. The runs were started with the same solution in both tubes in columns of equal length. The temperature of the jacketed column was then raised a convenient amount. When the potentiometer readings showed that the temperature had become constant, the length of the column in the other tube was adjusted until the colors matched and the ratio of the length of the cold column to the length of the warm column was recorded as the relative intensity of the color of the solution at the temperature in question as compared with the color at room temperature. Similar readings were made at intervals while the temperature was raised to about 100°, then while the temperature was lowered to that of tap water, and the relative color intensities were calculated in comparison with the color at 25°. There was no perceptible lag in the intensification of the color on warming or in the fading of the color on cooling; the relative intensities of color were found to be the same whether measured while going up or while going down the temperature scale. At each concentration two or generally three runs were made, and the results were plotted in a single curve. The results at the even temperatures read from such curves, for 0.1, 0.02, 0.01 and 0.005 *N* solutions of the three nitrophenolates are summarized in Table I. From these data it is evident that the difference between the isomers is less in the more dilute solutions.

In another series of experiments sodium carbonate in amounts corresponding to 0.02, 0.2, 1.0 and 2.0 *N* concentration was added to 0.1 *N* solutions of *m*-nitrophenol, and the thermotropic color intensifications of these solutions, containing, respectively, one-fifth, twice, ten times, and twenty times the equivalent amount of sodium ion, were determined. The data lay closest to smooth curves in the experiments in which the more sodium carbonate was used. Other experiments were carried out with 0.01 *N* solutions of *m*-nitrophenol containing one-fifth, twice, ten times and twenty times the equivalent amount of

TABLE I

INTENSITY OF COLOR OF WARM SODIUM NITROPHENOLATE SOLUTIONS COMPARED WITH THE COLOR OF THE SAME SOLUTIONS AT 25°

	o-Nitrophenolate, *N*				*m*-Nitrophenolate, *N*				*p*-Nitrophenolate, *N*			
Temp. °C.	0.1	0.02	0.01	0.005	0.1	0.02	0.01	0.005	0.1	0.02	0.01	0.005
25	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
30	1.12	1.11	1.06	1.10	1.10	1.04	1.06	1.08	1.05	1.04	1.04	1.02
35	1.24	1.23	1.15	1.22	1.21	1.11	1.13	1.17	1.16	1.09	1.16	1.06
40	1.37	1.35	1.25	1.34	1.32	1.20	1.22	1.28	1.28	1.14	1.25	1.11
45	1.52	1.48	1.36	1.47	1.42	1.30	1.33	1.40	1.42	1.20	1.36	1.16
50	1.67	1.60	1.49	1.60	1.52	1.39	1.44	1.51	1.56	1.28	1.47	1.23
55	1.83	1.74	1.63	1.75	1.61	1.51	1.55	1.62	1.71	1.38	1.60	1.32
60	1.99	1.90	1.79	1.89	1.70	1.66	1.68	1.74	1.87	1.50	1.75	1.43
65	2.16	2.06	1.85	2.06	1.78	1.80	1.82	1.88	2.03	1.63	1.90	1.59
70	2.33	2.25	2.11	2.21	1.87	1.93	1.96	2.03	2.20	1.78	2.08	1.76
75	2.50	2.45	2.28	2.37	1.95	2.07	2.12	2.19	2.37	1.98	2.27	1.87
80	2.68	2.64	2.46	2.44	2.03	2.21	2.32	2.35	2.55	2.17	2.48	2.16
85	2.86	2.86	2.65	2.63	2.12	2.38	2.51	2.49	2.73	2.38	2.70	2.40
90	3.05	3.10	2.90	2.82	2.19	2.55	2.70	2.64	2.90	2.64	2.98	2.62
95	3.23	3.38	3.18	3.12	2.27	2.72	2.87	2.81	3.10	2.89	3.20	2.84
100	3.41	3.66	3.46	3.32	2.35	2.90	3.06	2.98	3.28	3.20	3.43	3.10

TABLE II

EFFECT OF SODIUM CARBONATE ON THERMOTROPIC COLOR INTENSIFICATION OF *m*-NITROPHENOL SOLUTIONS AT VARIOUS CONCENTRATIONS

m-Nitrophenol, *N*	0.1	0.1	0.1	0.01	0.01	0.01	0.01	0.01	0.001	0.001
Na_2CO_3, *N*	0.02	0.2	1.0	2.0	0.002	0.02	0.1	0.2	0.01	0.02
Temp. °C.										
25	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
30	1.15	1.10	1.08	1.06	1.08	1.06	1.04	1.05	1.06	1.04
35	1.32	1.21	1.18	1.13	1.16	1.10	1.09	1.10	1.11	1.08
40	1.50	1.33	1.28	1.20	1.22	1.18	1.16	1.17	1.16	1.12
45	1.69	1.47	1.38	1.27	1.34	1.28	1.23	1.25	1.22	1.16
50	1.89	1.60	1.50	1.35	1.44	1.40	1.30	1.34	1.28	1.20
55	2.19	1.75	1.61	1.42	1.56	1.52	1.38	1.42	1.34	1.25
60	2.30	1.90	1.74	1.50	1.69	1.66	1.45	1.51	1.40	1.32
65	2.51	2.07	1.86	1.58	1.83	1.80	1.53	1.61	1.46	1.38
70	2.73	2.24	1.99	1.66	1.97	1.92	1.62	1.73	1.53	1.46
75	2.95	2.43	2.11	1.74	2.11	2.08	1.74	1.86	1.62	1.55
80	3.17	2.63	2.25	1.82	2.26	2.22	1.85	2.00	1.70	1.65
85	3.40	2.85	2.38	1.90	2.41	2.38	2.00	2.12	1.79	1.76
90	3.62	3.07	2.51	1.98	2.57	2.54	2.18	2.29	1.88	1.87
95	3.84	3.30	2.65	2.07	2.74	2.68	2.40	2.42	1.98	1.99
100	4.05	3.54	2.79	2.15	2.91	2.82	2.65	2.59	2.07	2.10

sodium ion, and with 0.001 *N* solutions containing ten and twenty times the equivalent, respectively. The results read from the curves are summarized in Table II. The data from the experiments with the more dilute solutions are probably the least precise because of the difficulty of matching the fainter colors.

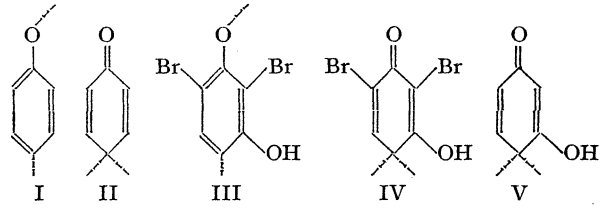
m-Nitrophenol, prepared by the method of Adams and Wilson,[7] was purified by vacuum distillation and finally by sublimation in vacuum, almost white crystals melting sharply at 96°. The sodium salt, prepared in the usual way and recrystallized from alcohol and from water, consisted of orange colored small crystals containing two molecules of water of crystallization. *Anal.* Sodium found, 11.4, 11.5. Calcd. for $C_6H_4O_3NNa \cdot 2H_2O$: Na, 11.6.

Sodium *o*-nitrophenolate, recrystallized from alcohol and from water, consisted of anhydrous bright red needles. *Anal.* Sodium found, 14.6, 14.5. Calcd. for $C_6H_4O_3N$-Na: Na, 14.3.

Sodium *p*-nitrophenolate crystallized from water in bright canary-yellow crystals containing two molecules of water of crystallization. *Anal.* Sodium found, 11.6.

Interpretation of Results

The work of Hunter and his co-workers[8] has shown that the oxidation of phenol occurs through the intermediate production of a radical having formulas I and II below (which formulas we regard as equivalent), while that of Davis and Hill[9] has shown that tribromoresorcinol similarly passes through the stage represented by formulas III and IV. Davis and Harrington[10] have shown that the quinyl radical, formula IV, is probably intermediate in many of the reactions of tribromoresorcinol, being formed by the spontaneous splitting off of hydrogen bromide from the tautomeric form of that substance. This formula



I II III IV V

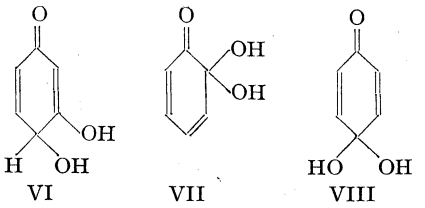
corresponds to the removal of two hydrogen atoms from dibromoresorcinol and may be regarded, if the language is permitted, as representing dibromo-*m*-quinone. The comportment of *m*-diphenols in general, on oxidation and in other reactions, may be interpreted by supposing the intermediate existence of such *m*-quinones, and formula V may be taken as representing *m*-quinone itself; which is thus a *p*-quinyl radical, probably incapable of an independent existence but ready, according to the environment in which it exists momentarily, to form resorcinol by reduction, hydroxy-*p*-quinone by oxidation, or by doubling-up under conditions which are neither oxidizing nor reducing to form dihydroxydiphenoquinone. If *m*-quinone may hydrate, formula VI, as *o*- and *p*-quinone presumably hydrate, formulas VII and VIII, then the hydrated quinones will exhibit similar unsaturated and resonating structures and will supply a common basis for discussions of color and constitution. The fact that formula VI represents one of the tauto-

(7) Adams and Wilson, "Organic Syntheses," Vol. 3, John Wiley and Sons, Inc., New York, N. Y., 1923, p. 87.

(8) Hunter, *et al.*, THIS JOURNAL, **38**, 1761 (1916); **39**, 2640 (1917); **43**, 131, 135, 151 (1921); **48**, 1608, 1615 (1926).

(9) Davis and Hill, *ibid.*, **51**, 493 (1929).

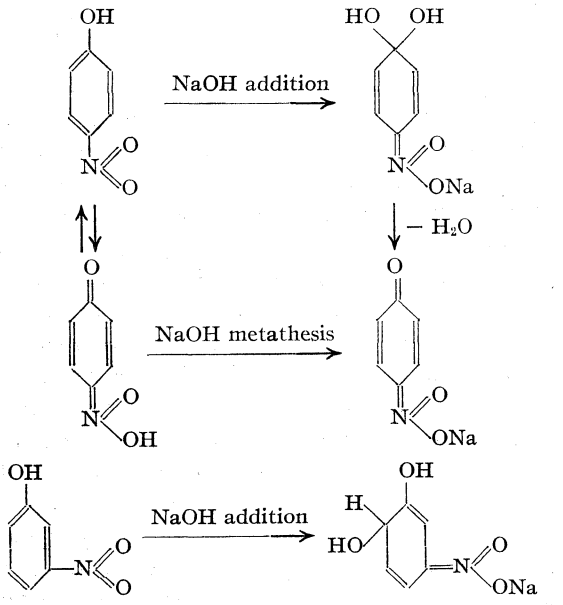
(10) Davis and Harrington, *ibid.*, **56**, 129 (1934).



VI VII VIII

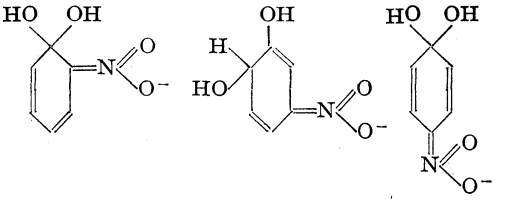
meric forms of 1,2,4-trihydroxybenzene suggests that the latter substance may perhaps be procurable from resorcinol by oxidation under appropriate conditions. For our present purpose however it is not necessary to suppose that the simple quinones hydrate. The formulas are illustrative. Our hypothesis supposes only that quinoid (not quinone) ions may exist which correspond to the three hydrated quinones.

o- and *p*-nitrophenol are both capable of tautomerizing, and may form sodium salts by the replacement of hydrogen atoms in the tautomers. *m*-Nitrophenol cannot do this. The same sodium salts of *o*- and *p*-nitrophenol, however, may be formed by a different mechanism; it is possible that the sodium hydroxide may add to the benzene derivative to form a quinoid compound[11] from which water may subsequently split off. But there is no evidence that the water does split off in aqueous solution. The colored ions may in fact be hydrated. *m*-Nitrophenol likewise may



(11) The addition of alkali to nitro compounds in this manner, the alkali metal to the nitro group and the rest of the adding molecule to the *p*-position of the ring, has been shown to be probable in many instances, particularly by the work of Jackson and his collaborators in their investigations of the reactions of picryl chloride and of trinitroanisole and trinitrophenetole with sodium alcoholates, *Am. Chem. J.*, **20**, 448 (1898); **23**, 294 (1901).

combine directly with sodium hydroxide to form a *p*-quinoid compound (a hydrated *m*-quinone) from which, however, water cannot split off, and, as far as the formation of hydrated salts, and of colored hydrated ions, is concerned, all three of the nitrophenols are alike. We suppose therefore that the colored ions of the three nitrophenolates are the hydrated quinoid ions indicated. By this



hypothesis the structure assigned to the *m*-nitrophenolate ion has the same relationship to the structure of *m*-quinone as that of the *p*-nitrophenolate ion has to the structure of *p*-quinone. The three nitrophenolate ions are supposed to be of similar structure and hence are expected to behave in similar manners. We are not prepared to offer an hypothesis to explain how the quinoid structure accounts for the thermotropic intensification of the colors of the solutions, except by the general supposition that the increase of temperature increases the resonance of the conjugate system of the ions, for we suppose that it is not the quinoid structure merely, but the possibilities of resonance which that structure provides, which make the basis for the quinone theory of color and constitution. The resonating system of the ions extends only into the rings, but not through them and beyond as in many of the dyestuffs, and this circumstance, in some way, may perhaps be associated with the phenomenon of color intensification.

Summary

The colors of warm solutions of the three sodium nitrophenolates have been measured by comparison with the colors of the same solutions at 25°. The thermotropic color intensifications of the three isomers appear to conform to the same general law, but the effect is least in the case of the *m*-compound.

The effect of various concentrations of sodium carbonate in solutions of *m*-nitrophenol has been studied. Alkali retards the color intensification, confirming the opinion that the effect is due to a property of the ion.

An hypothesis has been offered which assigns similar hydrated quinoid structures to the *o*-,

m-, and *p*-nitrophenolate ions, and is, at the same time, in harmony with the known facts concerning *m*-quinone and the oxidation of *m*-diphenols.

CAMBRIDGE, MASS. RECEIVED DECEMBER 28, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Cyanates of Silicon, Phosphorus and Boron. Instability of Certain Ternary Boron Compounds

BY GEORGE S. FORBES AND HERBERT H. ANDERSON

Reynolds[1] prepared stable silicon thiocyanate (b. p. 314°) from silicon tetrachloride and lead thiocyanate in benzene. Two years later, Cocksedge,[2] upon treating boron bromide with silver thiocyanate, obtained boron thiocyanate as a white crystalline solid which grew dark even at 100°. Both offered some evidence that sulfur, not nitrogen, was linked to the non-metallic element. Dixon[3] reported the isolation of phosphorous thiocyanate from lead thiocyanate and phosphorus trichloride in commercial benzene as "a reddish-yellow, clear, dense oil which gave the reactions for thiocyanate, thiocarbimide and phosphorus." At 170° the contents of the flask "suddenly changed, without evolution of gas, to a sticky black solid which presently became hard and brittle." Dixon thought that this might be a polymer of $P(NCS)_3$, but was unable to substantiate his opinion.

It occurred to us to inquire whether these weakly electronegative elements would form stable cyanates, or isocyanates or both. Preparations were undertaken to obtain evidence bearing upon this issue.

Silicon Isocyanate and Cyanate

Preparation.—Eighty grams of silicon chloride was added with vigorous shaking, over a period of fifteen minutes to 250 cc. of pure benzene in which 290 g. of finely powdered silver (iso)cyanate was suspended. The flask was then heated on the steam-bath for half an hour. After filtration, and several washings with benzene, the solvent was distilled off at atmospheric pressure. The yield of crude liquid product, 72 g., was 78% referred to cyanate. Potassium and lead cyanates were much less reactive and led to much smaller yields even after forty hours of refluxing. A second preparation, starting with excess of silicon chloride, afforded a yield of 86%. After expulsion of silicon tetrachloride and benzene, the colorless liquid product was distilled under 25 mm. pressure. The boiling point rose sharply at the end, and the residue, a very pale yellow liquid, was found to be 2.5% of the whole.

(1) Reynolds, *J. Chem. Soc.*, **89**, 397 (1906).
(2) Cocksedge, *ibid.*, **93**, 2177 (1908).
(3) Dixon, *ibid.*, **79**, 541 (1901).

Anal. Weighed portions of each fraction were converted into silica by hydrolysis, evaporation and ignition to constant weight all in the same crucible. The results follow.

Fraction of b. p. 185.6°, silicon found 14.22, 14.27, 14.46, 14.47%, average 14.35%.

Fraction of b. p. 247.2°, silicon found 14.06 and 14.56%, average 14.31%.

Calculated for $Si(NCO)_4$ and $Si(OCN)_4$, 14.32%.

The molecular weight of each fraction was determined in Dumas bulbs of about 50 cc. capacity, with the usual precautions.

186° fraction, mol. wt. found 202.5, 205.7, average 204.1.

247° fraction, mol. wt. found 211.9.

Calculated for $Si(NCO)_4$ and $Si(OCN)_4$, 196.1.

In addition, the molecular weight of the 186° fraction was determined by the freezing point method in benzene solution to be 204.1 and 194.4, average 199.2. Not enough of the higher boiling fraction for this determination remained.

Properties.—The boiling points were measured at various pressures by a dynamic method described, among others, by Mack and France.[4] Rubber connections were avoided by fused joints. The thermometers for these and other definitive measurements were standardized in the same apparatus with water, aniline and benzoic acid as primary standards, also with bromobenzene and benzoyl chloride. The plot of $\log_{10} p$ (mm.) for each liquid, against $1/T$ was a satisfactory straight line, and the logarithmic equations predicted the data within three millimeters, assuming the correctness of the temperatures. Densities at 20° were determined only by weighing the contents of a pipet. The index of refraction (white light), also at 20°, was measured with an

TABLE I

	$Si(NCO)_4$	$Si(OCN)_4$
B. p., °C., 760 mm.	185.6 ± 0.3	247.2 ± 0.5
M. p., °C.	26.0 ± 0.5	34.5 ± 0.5
$\log_{10} p$ (mm.)	$9.0198-2816/T$	$9.8211-3611/T$
λ_V, cal.	12,900	16,500
λ_V/T, cal./°	26.5	31.7
d, g./cc.	1.409, 1.413 ± 0.005	1.414 ± 0.005
n	1.4610 ± 0.0003	1.4646 ± 0.0003

(4) Mack and France, "Laboratory Manual of Physical Chemistry," D. Van Nostrand Co., Inc., New York, 1934, p. 77.

Abbe refractometer with thermostated prism. Table I summarizes the data obtained.

The above identification of the two silicon cyanates rested mainly upon analogies with ethyl isocyanate and cyanate, respectively. The structures of the latter were established by Anschütz[5] and Ponomareff[6] who showed that hydrolysis of the first yielded diethylurea and carbon dioxide, hydrolysis of the second urethan. The difference between their boiling points, 60 and 160°, respectively, agrees with that of the two silicon cyanates. Further evidence was available from their respective behavior when hydrolyzed. The reaction of the low-boiling liquid, presumably

$$Si(NCO)_4 + 4H_2O \longrightarrow H_4SiO_4 + 4HNCO$$

was vigorous, and the silica was largely coagulated due to its formation in acid solution. But the reaction of the high-boiling liquid, presumably

$$Si(OCN)_4 + 12H_2O = H_4SiO_4 + 4NH_4HCO_3$$

was slow, and silica was obtained in the form of a sol, which proved extremely hard to dehydrate.

The prospect of a decisive proof of the structures of our silicon cyanates, as well as those of boron and phosphorus by purely chemical methods, appears less bright than by Raman spectra or electron diffraction data. It is hoped that such studies may be undertaken, at a later date, in this Laboratory.

Phosphorous Isocyanate

Preparation.—Ninety grams of phosphorus trichloride reacted with 230 g. of silver (iso)cyanate in 300 cc. of warm benzene. After filtration and expulsion of the solvent, 62 g. of liquid remained, nearly 80% of the theoretical yield based on cyanate. After several distillations a colorless liquid was obtained boiling at 167° (uncorrected) under 755 mm. There was a higher boiling fraction of about 2% which decomposed yielding a dark residue. This residue, observed in each of two runs, was hydrolyzed by water.

Anal.—The redistilled product contained no chloride. Weighed samples were hydrolyzed to phosphorous and (iso)cyanic acids. A known volume of standard iodine solution was added, and the solution made about 3 *N* in hydrochloric acid. After an hour on the steam-bath, the oxidation of phosphorous to phosphoric acid was assumed to be complete. The excess of iodine was then titrated with standard thiosulfate. Phosphorus found, 20.02 and 20.11%. Calculated, 19.75%. The molecular weight of the vapor, by the Dumas method, was 159.0 and 158.6. Calculated for $P(NCO)_3$, 157.1.

Properties.—Our data for the more important physical properties were as follows: boiling point at 760 mm., 169.3 ± 0.3°; melting point, −2 ± 0.5°; vapor pressure, $\log_{10} p$ (mm.) = 8.7455 − 2595/T; λ_v = 11,900 cal.; λ_v/T = 26.8 cal./deg.; density 1.439 g./cc.; refractive index (white light) n, 1.5352.

Our identification of the product as isocyanate rests largely upon its normal boiling point, 169.3°, which is even lower than that of phosphorus tribromide, 172.9°, and far below that which would be predicted for a normal cyanate, judging from corresponding ethyl and silicon compounds. The Trouton constant, also, agrees with that of silicon isocyanate in a clean-cut fashion.

The purest product displayed some unexpected phase relationships. The distillate boiling at 169.3° stood for two weeks at room temperature without visible change. Upon supercooling it to −20°, a white solid appeared having a melting point of −2°. The resulting liquid, held at room temperature for three days, turned into a white solid, melting at about 80°, and insoluble in benzene, ether, chloroform and carbon tetrachloride. Sidgwick[7] has summarized various investigations upon polymers of cyanic acid. Cyanuric acid, soluble in ordinary solvents, can be converted to cyanic acid, which repolymerizes to cyanelide, a solid insoluble in the same solvents. Without attempting to press the analogy too far, we consider the behavior of our phosphorous isocyanate rather similar to the above. Our insoluble solid melting at 80° yielded a liquid boiling at 169.3° like the original liquid, but another sample held at room temperature yielded once more the supposed polymer, melting this time at 95°. Possibly the polymerization was more nearly complete than in the solid melting at 80°.

Boron Cyanate

Preparation.—Forty grams of silver (iso)cyanate, 8 g. of boron bromide and 125 cc. of warm benzene were shaken in a flask. The resulting solution contained about one-quarter of the expected boron cyanate and extraction of the solid residue with benzene removed but little more. A large box was provided with a glass cover, a built-in steam coil, and holes in the sides with wristlets having elastic bands to fit snugly over the operator's gloves. Air was expelled by tank nitrogen, and a slow current maintained during filtration, evaporation to a small volume, drying of the crystals, and sampling. Hydrolysis of the solid was negligible under these conditions.

Anal. The white solid decomposed with evolution of carbon dioxide in water and in dilute sulfuric acid, thus

(5) Anschütz, *Ann.*, **359**, 210 (1908).

(6) Ponomareff, *Ber.*, **15**, 513 (1882).

(7) Sidgwick, "Organic Chemistry of Nitrogen," revised by Taylor and Baker, Clarendon Press, Oxford, 1937, pp. 322–326 and 331.

indicating presence of cyanate. No bromide was detected in the resulting solution. Four samples, ranging from 0.1071 to 0.3592 g., were weighed under dry nitrogen and hydrolyzed in dilute sulfuric acid.

$$2B(OCN)_3 + 3H_2SO_4 + 12H_2O \longrightarrow 2H_3BO_3 + 3(NH_4)_2SO_4 + 6CO_2$$

After expulsion of carbon dioxide, standard sodium hydroxide was added to a methyl red end-point. Enough mannite was added to yield a 10% solution, and titration followed to a phenolphthalein end-point. In a blank experiment with an equal weight and concentration of ammonium sulfate the proper correction for its buffering action was evaluated. Boron found was 8.12, 7.94, 7.87 and 8.05%, average 7.99%; the calculated value is 7.91%.

Properties.—Boron cyanate, like boron thiocyanate, was isolated from benzene in tiny crystals. Its solubility in benzene, ether, chloroform or dioxane is roughly 2 g. per 100 cc. Anhydrous ethanol dissolves it with rapid decomposition. Bromine is unreactive at 25° and at 200°. An attempt was made to sublime it in a good vacuum, with cautious heating, but the substance merely became brown to black in color. The fact that our product had no melting point, and could not even be sublimed, suggested that its structure was analogous to that of boron thiocyanate as established by Cocksedge.[2]

Instability of Certain Ternary Boron Compounds

Before preparing the cyanates, efforts were made to obtain boron chlorobromides, analogous to the silicon chlorobromides previously studied by one of us.[8] Besson[9] had reported the existence of boron bromoiodides, but his evidence that the scanty products were single definite compounds left much to be desired. On the other hand, Poggiale[10] obtained only boron chloride from boron bromide treated with chlorine. Gustavson[11] and Tarible[12] employing carbon tetrachloride and arsenic trichloride, respectively, reported the same outcome. Amorphous boron, from boric oxide and magnesium, was treated with bromine vapor at 800°. The resulting boron bromide was purified by distillation. We employed a three-necked flask with stirrer, separatory funnel and a column leading to a condenser. In successive experiments boron bromide was treated separately with sulfur monochloride, stannic chloride and titanium tetrachloride. The vapors, upon leaving the heated zone, were cooled by dry ice. Sulfur monochloride yielded only boron chloride mixed with unchanged boron bromide, and the flask contained sulfur monobromide. Titanium tetrachloride and stannic chloride reacted quantitatively with boron bromide. Next, hydrogen chloride was bubbled through boron bromide at 65° and the mixed vapors passed through a tube heated to 800° over a length of 70 cm., but boron bromide and chloride, only, were recovered. It was hoped that silicon dichlorodibromide might yield boron dichlorobromide, but boron trichloride was the only low-boiling product obtained at 800°, with a yield of 10%.

In addition, simple products only were obtained from the following reactions: (1) boron with mixed chlorine and oxygen, the temperature of the reaction zone being gradually lowered from 800 to 650°; (2) boron with mixed chlorine and bromine at 800°; (3) boron bromide and oxygen at 800°; and (4) boron bromide and antimony trifluoride at 90°.

(8) Schumb and Anderson, THIS JOURNAL, **59**, 651 (1937).
(9) Besson, *Compt. rend.*, **112**, 1002 (1891).
(10) Poggiale, *ibid.*, **22**, 124 (1846).
(11) Gustavson, *Ann. chim. phys.* (5) **2**, 228 (1874).
(12) Tarible, *Compt. rend.*, **132**, 207 (1901).

Summary

1. Silver (iso)cyanate reacts with silicon tetrachloride, phosphorus trichloride and boron bromide in benzene far more completely than does potassium cyanate or lead cyanate.

2. Ninety-eight per cent. of the product obtained from silicon tetrachloride appears to be $Si(NCO)_4$, m. p. 26.0° and b. p. 185.6°; the remainder was $Si(OCN)_4$, m. p. 34.5° and b. p. 247.2°. Our identification rests mainly upon analogies with ethyl isocyanate and cyanate. Various physical properties were quantitatively investigated.

3. Phosphorus trichloride yielded $P(NCO)_3$ as the only volatile product, m. p. −2.0°, b. p. 169.3°. Samples once frozen, on standing at room temperature, were converted into a solid insoluble in ordinary organic solvents which reverted to the original (soluble) liquid on heating.

4. Boron trichloride yielded a white solid of low solubility which decomposed on moderate heating. Its analysis, as well as its properties, indicated that it was $B(OCN)_3$.

5. Boron chlorobromides, fluorobromides, oxychloride and oxybromide were not obtained in a series of experiments in which both reactants and temperatures were widely varied.

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RECEIVED DECEMBER 30, 1939

[CONTRIBUTION FROM THE COLLEGE OF ST. THOMAS]

The Mercurous Bromide Electrode

BY W. D. LARSON

There are available in the recent literature only a few measurements from which the standard potential of the mercury–mercurous bromide electrode can be calculated. Gerke[1] measured the cell

$$H_2/HBr/Hg_2Br_2/Hg \qquad (1)$$

at an acid molality of 0.10015. Ishikawa and Ueda[2] measured cell (1) at a molality of 0.1012.

In the present study are presented data on the cell

$$Ag/AgBr,\ KBr,\ Hg_2Br_2/Hg \qquad (2)$$

at 20, 25, and 30°. These data allow the calculation of the standard potential of the mercury–mercurous bromide electrode, since the corresponding value for the silver–silver bromide electrode is well known at the various temperatures.[3] Harned[3e] has pointed out that $E^0 = 0.07115 \pm 0.00015$ v. includes the results of all the investigators listed in reference (3). The value of Harned and Donelson,[3e] namely, $E^0 = 0.07131 - 4.99 \times 10^{-4}(t - 25) - 3.45 \times 10^{-6}(t - 25)^2$ has been chosen for the calculation of the standard potentials reported in this paper.

Experimental

The cell vessels were of a modified H type arranged so that solutions free from air (and saturated with nitrogen) could be used in them. There was a stopcock between the two electrodes. Measurements were made with the stopcock open, but it was kept closed at all other times.

Mercury was purified by spraying through a tower of diluted nitric acid, and washing with water. It was then distilled in a slow current of air, and redistilled *in vacuo*.

Mercurous bromide was prepared by precipitation from approximately 0.1 *N* solutions of potassium bromide and mercurous nitrate. Br^- was kept in excess. Especial care was taken that no chloride was present in the potassium bromide; it was prepared from a chlorate and chloride-free preparation of potassium bromate by decomposition with heat followed by three crystallizations from "conductivity" water. The mercurous nitrate solution was made up without the addition of nitric acid.[4] Preliminary experiments showed that constant and reproducible e. m. f. readings could be obtained with aged mercurous bromide. Preparations of the salt allowed to stand in the dark under water for at least one week after thorough rinsing gave e. m. f. readings which were constant within a few hours after the cells were made up. The thickness of the layer of mercurous bromide on the mercury in the electrode made no difference in the values obtained.

The silver–silver bromide electrodes were prepared according to the directions of Keston[3b] for the thermal type electrodes. In order to compare an electrolytic type electrode, several silver–silver bromide electrodes were prepared according to Carmody[5] for silver–silver chloride electrodes. Electrodes prepared by these two methods had potentials which differed by about 0.1 mv. on the average. The greatest variation observed was 0.4 mv.

Electromotive force measurements were made with a L. & N. type K potentiometer and either a type R or a type 2520-c L. & N. galvanometer. An Eppley unsaturated Weston cell certified by the manufacturers was the standard of e. m. f. The cells were kept in a water thermostat. Temperature control at 25° was within 0.04° and within 0.06° at 20 and 30°. The temperatures were determined by reference to a mercury in glass thermometer certified by the Bureau of Standards, and were known to be accurate to within 0.05°.

Cells were measured for not less than five days, and some were kept for over a month. Any cell which showed wide variations in e. m. f. after the first few days was discarded.

Concentrations of the electrolyte, KBr, varied from 0.02 to 0.15 molar. No differences in e. m. f. due to concentration of the bromide were observed.

Results

The Standard Potential.—The measurement of eleven cells containing silver–silver bromide electrodes prepared electrolytically gave a mean value of 0.06831 v. at 25°. The average error was 0.15 mv. The greatest deviation from the mean value amounted to 0.38 mv. for these cells. For the cells containing thermally prepared silver–silver bromide electrodes, the e. m. f. was 0.06839 v. at 25°. The average error and greatest individual deviation from the mean for these latter cells were 0.11 mv. and 0.18 mv., respectively. Table I summarizes the results obtained at 20, 25, and 30°.

TABLE I

THE VALUES OF THE E. M. F. OF CELL (2) AT VARIOUS TEMPERATURES

Temp., °C.	E. m. f., volts	Number of cells	Type of AgBr electrode
20	0.06630 ± 0.00014	5	Thermal
25	.06831 ± .00015	11	Electrolytic
25	.06839 ± .00011	9	Thermal
30	.07048 ± .00012	5	Thermal

(1) Gerke, *J. Phys. Chem.*, **31**, 886 (1927).

(2) Ishikawa and Ueda, *J. Chem. Soc. Japan*, **51**, 59 (1930).

(3) (a) Jones and Baeckstrom, THIS JOURNAL, **56**, 1524 (1934); (b) Keston, *ibid.*, **57**, 1671 (1935); (c) Harned, Keston and Donelson, *ibid.*, **58**, 989 (1936); (d) Owen and Foering, *ibid.*, **58**, 1575 (1936); (e) Harned and Donelson, *ibid.*, **59**, 1280 (1937).

(4) Kolthoff and Larson, *ibid.*, **56**, 1881 (1934).

(5) Carmody, *ibid.*, **54** 188 (1932).

The cells with thermal type silver–silver bromide electrodes gave better agreement among themselves than those containing electrolytically prepared electrodes. For this reason the calculations are based on the cells made with thermal silver bromide electrodes.

At 20, 25, and 30°, the standard potential of the mercury–mercurous bromide electrode has the values 0.14001, 0.13970, and 0.13921 v., respectively. These figures are obtained by adding the standard potentials of the silver–silver bromide electrode as reported at these temperatures by Harned and Donelson[3e] to the observed electromotive forces. These results may be expressed by the equation

$$E^0 = 0.13970 - 8.1 \times 10^{-5}(t - 25) - 3.6 \times 10^{-6}(t - 25)^2 \quad (3)$$

Values calculated by means of this equation agree with the experimental ones to less than 0.1 mv.

The value 0.1397 v. at 25° obtained in this study may be compared with 0.1396 v. reported by Gerke[1] and 0.1395 v. which may be calculated from the measurements of Ishikawa and Ueda[2] if one uses the activity coefficient for 0.1 molal hydrobromic acid given by Harned, Keston and Donelson.[3c] Latimer[6] gives 0.1397 v., based also on the measurement of Ishikawa and Ueda. It seems likely that a somewhat different activity coefficient may have been used by Latimer in this computation. In addition, there is the value 0.1385 v. given by Gerke in the "I. C. T."[7] This value apparently is based on Gerke's own measurement.[1] Finally, there are the values of the author[8] from measurements of cell (1) over a wide concentration range at 25°. When these results are recalculated using the activity coefficients of Harned, Keston and Donelson, one obtains 0.1389 v. as the standard potential at 25°.

Since the cells measured in this study were not as sensitive to oxygen or to light as are cells containing mercurous bromide in an acid solution, and in view of the agreement between the result obtained in this study and the value calculated from thermal measurements (see Latimer[6]), it seems reasonable that the most reliable value for the standard potential is 0.1397 v.

The Entropy of Mercurous Bromide.—From the value of the temperature coefficient of the standard electrode potential, which may be computed from eq. (3) by differentiation, one may calculate the standard entropy change for the reaction $2Hg + 2H^+ + 2Br^- \rightarrow Hg_2Br_2 + H_2$, using the familiar equation

$$\Delta S^0_{298} = nF(dE/dT) = 2 \times 23070 \times 0.000081 = 3.7 \text{ e. u.}$$

ΔS^0_{298} is also given by

$$\Delta S^0_{298} = S^0_{H_2} + S^0_{Hg_2Br_2} - 2S^0_{Hg} - 2S^0_{H^+} - 2S^0_{Br^-}$$

Using the values for the entropy of the substances involved which are given by Latimer,[6] the value of $S^0_{Hg_2Br_2}$ is found to be 48.9 e. u. at 25°.

To be compared with this is the value 52.8 given by Latimer. This value is based on the measurement of Ishikawa and Ueda[2] and on the thermal data of Kelley.[9] The temperature coefficients obtained in this study agree very well with those of Ishikawa and Ueda. Since Kelley also used the entropies of liquid mercury and of liquid bromine in computing the entropy of mercurous bromide, it is well to compare the entropy calculated on the basis of the reaction $2Ag + Hg_2Br_2 \rightarrow 2AgBr + 2Hg$ which is the cell reaction of cell (2). The e. m. f. of cell (2) is given by $E = 0.06839 + 0.000418(t - 25)$ over the range 20–30°. From this, the value of the temperature coefficient is 0.000418, giving for the standard entropy change of the reaction $2Ag + Hg_2Br_2 \rightarrow 2AgBr + 2Hg$, 19.3 e. u. If this value is combined with the entropies of AgBr, Hg, and Ag given by Latimer, one finds that the standard entropy of mercurous bromide is 48.5 e. u. This is in excellent agreement with the value calculated using the values given by Latimer for the entropy of Br^-, H_2, and Hg. This result would seem to indicate that the discrepancy may be due to the value of the entropy of liquid bromine used by Kelley.

Summary

1. The standard potential of the mercury–mercurous bromide electrode was determined by measurements of the cell Ag / AgBr, KBr, Hg_2Br_2 / Hg. The standard potential of the mercury–mercurous bromide electrode is 0.1397 v. at 25°.

2. From temperature coefficient measurements the standard entropy of mercurous bromide was computed. The standard entropy of solid mercurous bromide computed was 48.7 cal. deg.$^{-1}$ mole^{-1}.

ST. PAUL, MINNESOTA RECEIVED JANUARY 23, 1940

(6) Latimer, "Oxidation Potentials," Prentice-Hall, Inc., New York, N. Y., 1938.

(7) "I. C. T.," Vol. VI, McGraw-Hill Book Co., New York, N. Y., 1930, p. 332.

(8) W. D. Larson, M. S. Thesis, Michigan State College, 1931.

(9) Kelley, U. S. Bureau of Mines Bull. 394 (1935).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, ST. LOUIS UNIVERSITY SCHOOL OF MEDICINE]

A Study of Some Reactions between Dry Inorganic Salts. V. Reactions below the Fusion Point[1]

BY HAROLD L. LINK WITH LYMAN J. WOOD

It has been demonstrated[2] that when the sixty reciprocal pairs of the alkali halides were fused and the molten masses quenched the resultant mixtures contained, in almost every case, respectively, the heavy cation united with the heavy anion and the light cation united with the light anion. This pair of salts which has been called the stable pair might, for some purposes, be more conveniently called the pair of balanced mass. In only three cases was any evidence found for incomplete reaction of the reciprocal (unstable) pair when reacting to form the stable pair of balanced mass. When the chlorides, bromides and iodides of sodium, potassium, rubidium and cesium (reactions 1–18 of the series described above) were heated for long periods of time under the fusion point several stable pairs of balanced mass were found to be partially converted to the reciprocal pairs.[3] It was shown in this last paper that some of these reversals resulted in a chemical equilibrium which appeared to follow the mass law. Not much reaction was found to occur in the solid state unless the reaction temperature was within 100° of the fusion temperature.

The purpose of this paper is to report further studies on (1) the relationship between temperature and reaction in the solid state, (2) a study of the remaining 42 reactions of the alkali halide reactions (numbers 19 to 60), and (3) a further study of chemical equilibrium in the solid state.

Apparatus, Materials and Methods.—The salt mixtures were heated in the same furnace and in the same manner as previously described.[3] The X-ray apparatus used for analyzing the mixtures after heating was the one used by Thomas and Wood.[2] The lithium, sodium and potassium salts were Analytical Reagent quality. Rubidium and cesium chlorides, bromides and iodides were C. P. stock supplies from the Maywood Chemical Company. The fluorides of both rubidium and cesium were prepared by dissolving the respective carbonates in hydrofluoric acid. The pure salts were fused and kept over phosphorus pentoxide until needed. The lithium salts were fused in an atmosphere of carbon dioxide.

In order to study further the relationship between the extent of the reaction in the solid state at a given temperature and the melting range it was first necessary to determine the melting ranges for the various salt pairs. This was accomplished by heating the salt pairs in a small wire wound electric furnace and measuring the temperature with a thermocouple which had been calibrated by comparison with the melting points of ten pure chemicals which covered the range of temperatures involved in this investigation. No effort was made to obtain highly accurate results since such were not necessary. Approximately the same results were obtained regardless of whether the reciprocal or stable pair was heated.

Experimental Results

After the melting ranges of the first 18 reactions had been determined several salt pairs which were known to react with each other were heated for thirty-six hour periods at various temperatures. It was found in general that if the reaction temperature was more than 200° under the melting range very little reaction occurred while if the reaction temperature was within 100° of the melting range the extent of the reaction was quite considerable. Results obtained for reaction 4 (NaI–KCl) and reaction 7 (NaI–KBr) showed[3] that reaction in the solid state may be quite rapid if the reaction temperature is only a few degrees under the fusion temperature.

With these general rules in mind the remaining 42 reactions of this series (reactions 19–60 as numbered by Thomas and Wood[2]) were divided into 6 groups and heated for thirty-six hour periods at the various reaction temperatures described in Table I. In this way it was found possible to make most of the reaction temperatures within approximately 100° of the respective melting ranges. The difference was a little more than 100° for a few of the reactions heated at 550°. With the exception of cesium fluoride the accepted cube edges for the various alkali halides, with which the values in Table I are to be compared, have been listed in the above-mentioned papers[2,3] and are not repeated here. The accepted cube edge value for cesium fluoride is 6.008 Å. For convenience the reactions described in Table I have been divided into two groups, *viz.*, reactions 19–42 which include all

(1) This communication is part of a doctoral thesis presented by Harold L. Link to the Faculty of St. Louis University, June, 1939.

(2) (a) E. B. Thomas with Lyman J. Wood, THIS JOURNAL, **56**, 92 (1934); (b) **57**, 822 (1935); (c) **58**, 1341 (1936).

(3) H. L. Link and Lyman J. Wood, *ibid.*, **60**, 2320 (1938).

TABLE I

SHOWING THE RESULTS OBTAINED BY HEATING VARIOUS SALT PAIRS AT APPROXIMATELY 100° BELOW THE FUSION TEMPERATURE FOR THIRTY-SIX HOURS

No.	Temp., °C.	Stable pair: Initial		After heat treatment: a in Å.[a]		Patterns	Reciprocal pair: Initial		After heat treatment: a in Å.[a]		Patterns
19	550	LiF	NaCl	4.016	5.630	LiF, NaCl	LiCl	NaF	4.014	5.625	LiF(w),[b] NaCl(s), NaF(w)[c]
20	550	LiF	KCl	4.009	6.276	LiF, KCl	LiCl	KF	4.016	6.275	LiF(s), KCl(s)
21	550	LiF	RbCl	*d*	6.572	LiF(w), RbCl	LiCl	RbF		6.570	RbCl(s)
22	550	LiF	CsCl		4.111	CsCl(s)	LiCl	CsF	4.010	4.110	LiF(w), CsCl(s)
23	550	LiF	NaBr	*d*	5.949	LiF(w), NaBr	LiBr	NaF		5.939	NaBr(s)
24	550	LiF	KBr		6.570	KBr	LiBr	KF	4.016	6.590	LiF(w), KBr(s)
25	550	LiF	RbBr		6.858	RbBr	LiBr	RbF		6.862	RbBr
26	550	LiF	CsBr	4.010	4.291	LiF, CsBr	LiBr	CsF		4.290	CsBr(s)
27	450[e]	LiF	NaI	*d*	6.462	LiF(w), NaI(s)	LiI	NaF	*d*	6.467	LiF(w), NaI(s)
28	550	LiF	KI		7.048	KI(s)	LiI	KF		6.525	LiI–KI[f]
29	550	LiF	RbI		7.321	RbI	LiI	RbF		7.319	RbI
30	550	LiF	CsI		4.562	CsI(s)	LiI	CsF		4.559	CsI(s)
31	450[e]	LiCl	NaBr	5.213	5.759	LiCl–LiBr,[f] NaCl–NaBr[f]	LiBr	NaCl	*d*	5.750	LiCl–LiBr,[f] NaCl–NaBr[f]
32	300	LiCl	KBr	*d*	6.567	LiCl(w), KBr(s)	LiBr	KCl	*d*	6.565	LiBr(w), KBr(s)
33	200	LiCl	RbBr		6.857	RbBr(s)	LiBr	RbCl	*d*	*d*	LiCl(w), RbBr(w), RbCl(w)[d]
34	200	LiCl	CsBr		4.291	CsBr(s)	LiBr	CsCl		4.266	CsCl–CsBr[f]
35	400	LiCl	NaI	5.127	6.463	LiCl(w), NaI(s), NaCl(s)[g]	LiI	NaCl	6.457	5.628	NaI, NaCl
36	400	LiCl	KI	5.133	7.052	LiCl, KI(s), KCl[h]	LiI	KCl	*d*	6.278	LiI(w), KCl(w), KI(s)[i]
37	300	LiCl	RbI		6.569	RbCl	LiI	RbCl	7.318	6.574	RbI(s), RbCl
38	250	LiCl	CsI	5.140	4.109	LiCl, CsCl(s)	LiI	CsCl		4.561	CsI
39	400	LiBr	NaI	6.432	5.943	NaBr–NaI,[f] NaBr(s)	LiI	NaBr	*d*	5.933	LiI(w), NaBr
40	200	LiBr	KI		7.050	KI	LiI	KBr		6.569	KBr
41	200	LiBr	RbI	*d*	*d*	RbI–RbBr[j]	LiI	RbBr	*d*	*d*	RbI–RbBr[j]
42	300	LiBr	CsI	*d*	4.290	LiI(w), CsBr	LiI	CsBr		*d*	CsI phase
43	550	NaF	KCl	4.623	6.278	NaF, KCl	NaCl	KF	4.620	6.278	NaF(s), KCl(s)
44	550	NaF	RbCl		6.571	RbCl	NaCl	RbF		6.564	RbCl
45	550	NaF	CsCl	4.614	4.109	NaF, CsCl(s)	NaCl	CsF	4.109	5.621	CsCl, NaCl, NaF(w)[d]
46	550	NaF	KBr		6.566	KBr(s)	NaBr	KF	6.569	5.944	KBr, NaBr, NaF(w)[d]
47	550	NaF	RbBr	4.621	6.859	NaF, RbBr	NaBr	RbF		6.863	RbBr(s)
48	550	NaF	CsBr	4.619	4.289	NaF, CsBr	NaBr	CsF		4.279	CsBr
49	550	NaF	KI	4.610	7.054	NaF(w), KI(s)	NaI	KF	7.052	*d*	KI(s), NaI(w)
50	550	NaF	RbI		7.322	RbI	NaI	RbF	*d*	7.322	NaF(w), RbI(s)
51	550	NaF	CsI	*d*	4.563	NaF(w), CsI(s)	NaI	CsF		4.563	CsI(s)
52	450	KF	RbCl	*d*	6.568	KF(w), RbCl(s)	KCl	RbF	*d*	6.493	KF(w), KCl–RbCl
53	400	KF	CsCl	5.325	4.111	KF(s), CsCl(s)	KCl	CsF	5.335	4.111	KF, CsCl, KCl[k]
54	450	KF	RbBr		6.855	RbBr(s)	KBr	RbF		6.816	KBr–RbBr[f]
55	450	KF	CsBr	5.334	4.289	KF, CsBr	KBr	CsF	*d*	4.292	KF(w), CsBr(s), KBr[l]
56	450	KF	RbI	*d*	7.320	KF(w), RbI	KI	RbF	*d*	7.318	KF(w), RbI(s)
57	450	KF	CsI		4.562	CsI(s)	KI	CsF	4.562	7.051	CsI(s), KI(w)
58	400	RbF	CsCl	*d*	4.111	RbF(w), CsCl(s)	RbCl	CsF	*d*	4.110	RbF(w), CsCl(s), RbCl[m]
59	400	RbF	CsBr		4.289	CsBr(s)	RbBr	CsF	*d*	4.290	RbF(w), CsBr(s), RbBr(w)[d]
60	400	RbF	CsI		4.561	CsI(s)	RbI	CsF	4.561	*d*	CsI(s), RbI

[a] Cube edge. [b] w = "weak"; s = "strong." [c] $a = 4.620$. [d] Pattern observed by direct comparison with standard lines. No accurate value for the cube edge could be obtained. [e] Heated for 75 hours. [f] Solid solution. [g] $a = 5.621$. [h] $a = 6.285$. [i] $a = 7.054$. [j] Two solid solutions; one rich in RbI, the other rich in RbBr. [k] $a = 6.281$. [l] $a = 6.578$. [m] $a = 6.578$.

of the reaction mixtures containing lithium salts and reactions 43–60 which do not involve lithium salts. When the stable or balanced pairs of this last group of reactions were heated at the reaction temperatures indicated in Table I, no evidence for any reversal to the reciprocal pair was obtained. On the other hand, when the reciprocal pairs were heated all of them were converted partially or completely to the stable pairs. Evidence for incomplete reaction was obtained for reactions 45, 46, 49, 52, 53, 54, 55, 57, 58, 59 and 60. It was found possible to calculate the extent of the reaction for the reciprocal pairs of reactions 52 and 54 because of the formation of solid solutions. The cube edge of 6.493 Å. reported for reaction 52 corresponds to a solid solution of 26.5 mole per cent. potassium chloride and 73.5 mole per cent. rubidium chloride. The cube edge value of 6.816 Å. reported for reaction 54 corresponds to a solid solution of 15.2 mole per cent. potassium bromide and 84.8 mole per cent. rubidium bromide. The reciprocal pairs of reactions 43, 44, 47, 48, 50, 51 and 56 appeared to go to completion in the direction of the stable pairs. Only in the case of reaction 56 would solid solutions be expected to form if reaction were incomplete.[2,3] The X-ray diffraction patterns obtained corresponded to those of pure rubidium iodide and potassium fluoride and are to be taken as evidence that the reciprocal

TABLE II

RESULTS OF SOLID SOLUBILITY STUDIES OF KCl–KBr AND CsCl–CsBr

Composition, mole %		Temp., °C.	Time, hr.	Cube edge, Å. Obsd.	Theory	Remarks
KCl 50	KBr 50	400	36	6.280		Immiscible
				6.570		
KCl 50	KBr 50	480	36	6.425	6.425	Miscible
KCl 33	KBr 33	400	72	6.347		23%KBr–77%KCl
	CsCl 33			4.241		25%CsCl–75%CsBr
CsCl 50	CsBr 50	360	36	4.200[a]	4.200	Miscible
CsCl 50	CsBr 50	400	36	4.209	4.200	Miscible
CsCl 25	CsBr 75	400	84	4.243	4.245	Miscible
CsCl 75	CsBr 25	400	84	4.156	4.155	Miscible

[a] Result taken from F. Meyer, B.S. Thesis, St. Louis University, June, 1938.

pair has been completely converted to the stable pair. In the other cases the same conclusion is based on the absence of any diffraction patterns corresponding to the reciprocal pairs.

The 24 reactions numbered 19–42 are of considerable interest since all of the reaction mixtures contain lithium salts. In the studies above the fusion point it was found that the stable pair always contained the highest melting compound in the case of each reaction except the reaction mixtures containing lithium salts. In the case of the lithium reactions, only the stable pairs of reactions 21, 22, 25, 26, 29 and 30 contained the highest melting compounds. Referring to Table I it will be seen that no evidence was obtained for any reversal of the stable pairs of reactions 19–30. In six of these reactions the stable pair contains the highest melting compound and in six the reciprocal pair. The only common factor that has been discovered is that each stable pair contains lithium fluoride.

The reciprocal pairs of the other twelve reactions (31–42) all contain the highest melting compound and the stable pairs of most of the reactions showed some reversal to the reciprocal pair when heated at the temperatures indicated in Table I. No evidence of any reversal of stable pairs for reactions 32, 33, 34 and 40 was observed.

Reaction No. 11.—In a previous study[3] of reaction number 11 at 480° (under the fusion temperature) it was found that when either the reciprocal or stable pair was heated an equilibrium was formed as represented by the equation

$$CsCl + KBr \rightleftarrows CsBr + KCl$$

and that when the composition of the reacting mixture was changed the equilibrium shifted in accordance with the demands of the mass law. Further studies of this reaction have been made at 440, 400 and 360°. The observations, though not yet fully completed, indicate that the reaction proceeds to equilibrium at each temperature and that the composition of the equilibrium mixture changes with the composition of the reaction mixture in accordance with the demands of the mass law. Efforts to calculate ΔH for reaction 11 by means of van't Hoff's reaction isochor after the manner of Tubandt and Reinhold[4] when working with the solid reactions occurring between the pairs Ag_2S–CuI and Ag_2S–Cu_2Se gave values for ΔH of the correct sign but several times as large as was to be expected from the best available experimental values. A detailed description of these and other similar studies is being made the subject of a future report.

In Table II are to be found the results of solid solution studies made necessary by the investigation of reaction 11 described above. Table III shows in detail the X-ray diffraction data for a CsCl–CsBr solid solution formed at 360°. Other

TABLE III

SHOWING THE INTERPLANAR DISTANCES OF THE 50–50 CsCl–CsBr SOLID SOLUTION FORMED AT 360°

Line no.	I	*hkl*	*d* Obsd.	*d* Calcd.	*a* Obsd.	*a* Calcd.
1	2	100	4.23	4.200		
2	10	110	2.96	2.970		
3	1	111	2.41	2.425		
4	5	200	2.09	2.100		
5	3	210	1.873	1.878		
6	9	211	1.714	1.715	4.198	4.200
7	6	220	1.484	1.485	4.198	4.200
8	1	300 or 221	1.400	1.400	4.200	4.200
9	7	310	1.329	1.328	4.203	4.200
10	1	311	1.266	1.266	4.199	4.200
11	v w	222	1.203	1.213		
12	v w	320	1.162	1.165		
13	7	321	1.123	1.122	4.202	4.200
14	w	322	1.014	1.019		
15	1	330	0.990	0.990	4.200	4.200
					Av. 4.200	4.200

(4) Tubandt and Reinhold, *Z. physik. Chem.*, **140A**, 291 (1929).

similar data are summarized in Table II. Particular attention should be called to the results obtained from heating an equimolar mixture of potassium chloride, potassium bromide and cesium chloride (Table II). When potassium chloride and potassium bromide are heated together at 400° no solid solution results. However, when cesium chloride is heated with potassium chloride and potassium bromide at 400°, a solid solution of potassium chloride and potassium bromide results. The cube edge obtained for this solid solution indicates that only the potassium chloride formed by the interaction of the cesium chloride and potassium bromide dissolves in the residual potassium bromide. The cesium bromide in the CsCl–CsBr solid solution is less than when an equimolar mixture of cesium chloride and potassium bromide is heated and very nearly the same as when 2 moles of potassium chloride and 1 mole of cesium bromide are heated together (Table IV). Within the limits of experimental error, the extent of the reaction is, in each case, in agreement with the demands of the mass law.

TABLE IV

EQUILIBRIUM MIXTURES OF REACTION 11 AT 400°

Before heating	100		100				100
	CsCl	+	KBr	⇄	CsBr	+	KCl
After heating	25		25		75		175
Before heating					100		200
	CsCl	+	KBr	⇄	CsBr	+	KCl
After heating	25		25		75		175
Before heating	100		100				
	CsCl	+	KBr	⇄	CsBr	+	KCl
After heating	19		19		81		81

Summary

Reactions occurring between the alkali halides in the solid state have been studied. Salt pairs corresponding to all sixty of the possible reactions have been heated for long periods of time below the fusion point and the resulting mixtures analyzed by the method of X-ray crystal analysis. The reaction mixtures of the forty-two reactions included in this report contained lithium salts or fluorides or both, the remaining eighteen reactions having been previously reported.[3]

1. Twelve of the reaction mixtures contained both lithium salts and fluorides. The highest melting component was contained in the stable pair in six cases and in the reciprocal pair in six cases. In each case lithium fluoride was a member of the stable pair. No evidence was found for the reversal of any of the stable pairs to the corresponding reciprocal pairs.

2. Twelve of the reaction mixtures contained lithium salts but no fluorides. The highest melting component was contained in the reciprocal pair in each case. Eight of these stable pairs showed some tendency toward reversal to the reciprocal pair and four did not.

3. Eighteen of the reaction mixtures contained fluorides but no lithium salts. The highest melting component was contained in the stable pair in each case and no evidence was obtained for the reversal of any of the stable pairs to the reciprocal.

4. Evidence for partial or complete conversion of the reciprocal to the stable pair was obtained for forty of the forty-two reactions.

5. It was found that in general there was very little reaction in the solid state if the reaction temperature was more than 200° below the melting range and that there was likely to be considerable reaction if the reaction temperature was within 100° of the melting range.

ST. LOUIS, MO. RECEIVED OCTOBER 24, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF ILLINOIS AND INDIANA UNIVERSITY]

Carbon Suboxide in the Friedel–Crafts Reaction. I

BY JOHN H. BILLMAN,[1] GEORGE E. TRIPP AND R. VINCENT CASH

It was first shown by Hurd[2] that ketene would react with aromatic hydrocarbons or aromatic ethers in the presence of aluminum chloride to form primarily simple ketones according to the equation

$$C_6H_6 + H_2C{=}C{=}O \xrightarrow{AlCl_3} C_6H_5{-}\overset{\overset{O}{\|}}{C}{-}CH_3 \quad (1)$$

Since Hurd's discovery, several investigators[3] have studied ketene more extensively in an endeavor to increase the yield of the expected ketone or to identify the other products formed in some of the reactions. Recently Boese[4] has found that diketene also would react in a manner similar to ketene, for with benzene and aluminum chloride he was able to prepare benzoylacetone.

As the above ketenes are the only two ketenes that have been tried in a Friedel–Crafts reaction, we felt that it would be of value to extend this type of reaction using carbon suboxide as the ketene, for in carbon suboxide there is a duoketene structure which should offer double the possibility for reaction and thereby lead to the formation of an entirely different series of products than could be obtained from any other simple ketene.

If carbon suboxide should react with benzene in the presence of aluminum chloride exactly as does ketene, then one would expect to obtain dibenzoylmethane. However, if only one of the two ketene functional groups participated in the Friedel–Crafts reaction, then benzoylacetic acid, or acetophenone by decarboxylation of the latter, would be anticipated.

$$C_6H_6 + O{=}C{=}C{=}C{=}O \xrightarrow{AlCl_3} C_6H_5COCH_2COOH \quad (2)$$

$$C_6H_5COCH_2COOH \longrightarrow C_6H_5COCH_3 + CO_2 \quad (3)$$

Except for a large amount of polymerized carbon suboxide, the only product identified in the reaction after hydrolysis by dilute acids was acetophenone. This ketone must have come by way of benzoylacetic acid, which is known[5] to undergo decarboxylation in the presence of dilute acids, whereas dibenzoylmethane is stable in this medium.

Despite the fact that all of the runs were carried out at nearly ice temperature, polymerization of carbon suboxide could not be prevented. As it has been shown that in certain instances anhydrous stannic chloride causes less polymerization than aluminum chloride,[6] the former condensing agent also was used. However, no difference in the results could be observed.

Whereas previous workers have reported the liberation of hydrogen chloride during the condensation of ketenes with aromatic hydrocarbons, in the presence of aluminum chloride, we were unable to detect any of the gas. Only upon refluxing the mixtures was hydrogen chloride evolved.

Further work is being done in this Laboratory on carbon suboxide in the Friedel–Crafts reaction.

Experimental

Preparation of Carbon Suboxide.—The carbon suboxide used in our experiments was prepared by a method similar to that used by Hurd[7] in which diacetyltartaric anhydride was pyrolyzed by heating in an electric furnace to 625°. The gas, as it formed, was collected in a trap cooled to −78° by solid carbon dioxide and acetone. Before using the liquid carbon suboxide it was first distilled to free it from the dark colored impurities that also collected in the trap. The carbon suboxide, as it distilled over, was run directly into a calibrated receiver containing dry benzene cooled to approximately 4°. At the completion of the distillation, a measured volume of the benzene solution was removed and treated with an excess of aniline. From the amount of malonanilide formed, the amount of carbon suboxide in solution was determined.

Procedure.—Seven and five-tenths grams (0.12 mole) of carbon suboxide dissolved in 400 cc. of benzene, as prepared above, was added to 200 cc. of benzene and cooled to approximately 4°. Forty grams (0.27 mole) of aluminum chloride was then added slowly with vigorous stirring. A deep reddish-brown precipitate formed immediately. After all of the aluminum chloride had been added it was found that there was no noticeable odor of carbon suboxide in the reaction flask. The mixture was then refluxed, at which time large amounts of hydrogen chloride were evolved. Hydrolysis was accomplished by the addition of ice and water and the mixture allowed to stand over-

(1) Present address: Indiana University, Bloomington, Indiana.

(2) Hurd, THIS JOURNAL, **47**, 2777 (1925).

(3) (a) Ploeg, *Rec. trav. chim.*, **45**, 342–344 (1926); (b) Packendorff, Zelinsky and Leder-Packendorff, *Ber.*, **66**, 1069 (1933); (c) Spring and Vickerstaff, *J. Chem. Soc.*, 1873 (1935); (d) Williams and Osborn, THIS JOURNAL, **61**, 3438 (1939).

(4) Boese, *Ind. Eng. Chem.*, **32**, 16 (1940).

(5) Beckmann and Paul, *Ann.*, **266**, 17 (1891).

(6) *Org. Syntheses*, **28**, 2 (1938).

(7) Hurd and Pilgrim, THIS JOURNAL, **55**, 757–759 (1933).

night. When hydrolysis was complete the mixture was worked up in the usual manner. A small amount of an oil with the odor of acetophenone was found after evaporation of the benzene layer. A similar product was obtained by steam distillation of the water layer. This oil solidified at approximately 19° and formed a semicarbazone melting at 195–196°, which corresponds to that of acetophenone. An authentic sample of the semicarbazone of acetophenone also melted at 195–196°; a mixed melting point evidenced no lowering of this value.

Summary

1. It has been shown that carbon suboxide will undergo a Friedel–Crafts reaction with benzene.
2. We conclude that benzoylacetic acid was formed as an intermediate in the reaction.
3. Acetophenone was isolated from the reaction mixture.

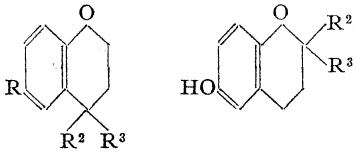
RECEIVED JANUARY 23, 1940

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

Polymethylbenzenes. XXV. The Reaction between Dimethylacrylic Acid and the Trimethylbenzenes[1]

BY LEE IRVIN SMITH AND WILLIAM W. PRICHARD[2]

The work described in this paper was begun as an attempt to synthesize some 4,4-disubstituted chromans (I) or hydrocoumarins (III) in which the 6-position was occupied by a hydrogen atom or hydroxyl group.



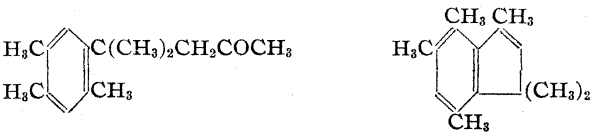
I, R = H or OH; R^2 and R^3 = alkyl

II

III

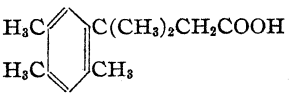
Such compounds were of interest because of their relationship to the tocopherols (vitamin E) which are analogous 2,2-dialkyl chromans, II. Very few examples of 4,4-disubstituted chromans are known,[3] and there is only a single example (III) of the synthesis of a 4,4-disubstituted hydrocoumarin.[4]

The difficulty in the synthesis of these substances appeared to be the introduction of the quaternary carbon atom,[5,6] hence attention was turned to methods for closing the chroman and hydrocoumarin rings after introduction of the quaternary carbon atom. The necessary intermediates, however, proved impossible to prepare. Appropriate alkylation of malonic ester failed because dimethyl - *o* - hydroxyphenylcarbinol[7,8] could not be converted to the chloride. Likewise unsuccessful were all attempts to obtain any crystalline products when mesityl oxide in the presence of aluminum chloride was condensed with any of a number of substituted phenols and hydroquinones or their ethers,[3a,9] and it appeared that the unsaturated ketone could be condensed successfully only with hydrocarbons.[7] It was known that β-[2,4,5-trimethylphenyl]-propionic acid could be converted into a quinone and then to a 6-hydroxyhydrocoumarin[10] and the analogous propionic acid, completely substituted in the β-position, should be accessible through the ketone IV resulting from the condensation of pseudocumene and mesityl oxide. The result of this condensation, however, was an indene V, although in view of the rearrangements described below the orientation of the methyl groups in the benzene ring of this compound is not certain.



IV

V



VI

The possibility remained that the condensation of pseudocumene with β,β-dimethylacrylic acid might lead to the acid VI, in which case the series of reactions could be carried out as planned. The product of this condensation was a mixture of

(1) Polymethylbenzenes, XXIV, THIS JOURNAL, **61**, 989 (1939).

(2) Abstracted from a thesis by W. W. Prichard, presented to the Graduate Faculty of the University of Minnesota, in partial fulfillment of the requirements for the Ph.D. degree, October, 1939.

(3) (a) Niederl, THIS JOURNAL, **51**, 2426 (1929); (b) Dianin, *J. Russ. Phys.-Chem. Soc.*, **46**, 1310 (1914).

(4) John, Günther and Schmeil, *Ber.*, **71**, 2617 (1938).

(5) Kostanecki, *et al.*, *Ber.*, **35**, 861, 2889 (1902); **37**, 774 (1904).

(6) Hill, *Chem. Rev.*, **19**, 25 (1936).

(7) Hoffman, THIS JOURNAL, **51**, 2542 (1929).

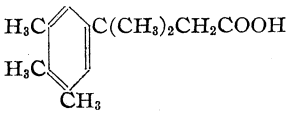
(8) Béhal and Tiffeneau, *Bull. soc. chim.*, [4] **3**, 315 (1908).

(9) Liebermann and Hartmann, *Ber.*, **24**, 2586 (1891).

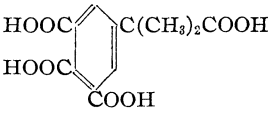
(10) Smith and Denyes, THIS JOURNAL, **58**, 304 (1936).

acids from which there was isolated 50–60% of a pure acid which melted at 111–112° and which had the composition required by formula VI.

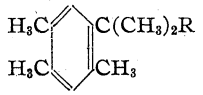
However, investigation of this acid soon showed that it could not be the substance VI, but must be an isomer having the structure VII. Oxidation to a known benzenetetracarboxylic acid failed because the quaternary carbon atom was resistant to oxidation,[11] and the oxidation product was an unknown tricarboxyphenylisobutyric acid, VIII. It was necessary, therefore, to use other methods in determining the orientation of the substituents, and as a first approach VI was synthesized from 5-acetopseudocumene by the method Hoffman[7] used in synthesizing β-phenylisovaleric acid.



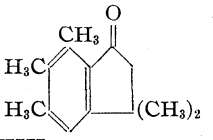
VII



VIII



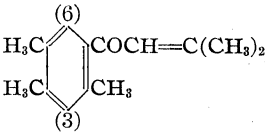
IX, R = OH
X, R = Cl
XI, R = $CH(COOC_2H_5)_2$
XII, R = $CH(COOH)_2$



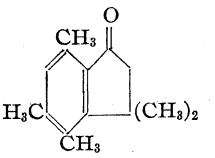
XIII
XIV, Oxime of XIII

Methylmagnesium iodide was added to 5-acetopseudocumene to give the carbinol IX; the ketone is enolized to the extent of 25% by the Grignard reagent[12] and consequently the product contained much of the starting material. Since the carbinol could not be crystallized, and the risk of dehydration precluded distillation, this product was subjected to the action of hydrochloric acid at 0° and the mixture containing the chloride X was used to alkylate sodium malonic ester. The product of this reaction was saponified and a malonic acid (XII) was isolated in 5–10% yield. This malonic acid melted with decomposition to give a monobasic acid VI isomeric with, but different from, the acid VII.

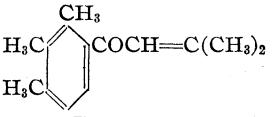
The acid VII, in contact with sulfuric acid, was readily converted to the hydrindone XIII, which gave an oxime XIV with ease. Since acetyl chloride condensed readily with pseudocumene in the 5-position, it seemed likely that any other acid chloride would attack the same position. Accordingly β,β-dimethylacrylic acid chloride was condensed with pseudocumene in the presence of aluminum chloride. The product XV was obtained in good yield, and shown to have this structure by oxidation to pyromellitic acid.



XV

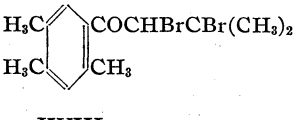


XVI

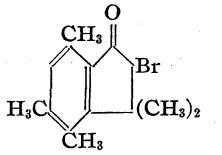


XVII

The ketone XV was then cyclized by aluminum chloride[13] to the hydrindone XVI, in quantitative yield. This hydrindone XVI was an *isomer* of XIII, and since the acyl group in XV was known to be in position 5, cyclization of XV must have involved position 6 in this compound. Consequently the condensation of pseudocumene with β,β-dimethylacrylic acid could not have involved the 6-position of the aromatic nucleus, for this would also have led ultimately to the indone XVI. Since the synthetic acid VI was different from VII, neither could this condensation have involved the 5-position. Condensation in the 3-position of pseudocumene would lead to an acid which could not be converted to a hydrindone. Hence it followed that VII could not be a derivative of pseudocumene; nor could it be a derivative of mesitylene, for the acid analogous to VI and VII, derived from mesitylene, likewise would not be convertible to a hydrindone. The only possibility remaining was that VII was a derivative of hemimellitene. The ketone XV gave a dibromide XVIII, identical with the product obtained by condensing α,β-dibromoisovaleryl chloride with pseudocumene. This dibromide XVIII was cyclized by aluminum chloride, giving the bromohydrindone XIX.



XVIII



XIX

Condensation of 1,2,3-trimethylbenzene with dimethylacrylic *acid chloride* under the same conditions used in the synthesis of XV, produced the ketone XVII. Oxidation of XVII gave benzene-1,2,3,4-tetracarboxylic acid, proving the orienta-

(11) Tiemann and Kruger, *Ber.*, **26**, 2685 (1893); Bogert and Applebaum, THIS JOURNAL, **60**, 930 (1938).

(12) Smith and Guss, *ibid.*, **59**, 804 (1937).

(13) Kohler, *Am. Chem. J.*, **42**, 376 (1909).

tion of the groups in the ketone. Cyclization of XVII with aluminum chloride gave the hydrindone XIII, identical with the product obtained by cyclizing VII. The structure of VII, therefore, must be β-[3,4,5-trimethylphenyl]-propionic acid. The only weakness in this argument is the fact that aluminum chloride was used in cyclizing the ketone XVII, and a rearrangement in this step was possible. Against this is the fact that the ketone XV gave an isomeric hydrindone on similar treatment and hence if rearrangement had occurred in either case both ketones should have given the same hydrindone, *i. e.*, the one stable in the presence of aluminum chloride. Moreover, the cyclizations gave pure hydrindones, while if rearrangement had occurred, a mixture would have been more likely.

As a further proof of the structure of VII, hemimellitene and β,β-dimethylacrylic *acid* were condensed under conditions identical with those used in the condensation of pseudocumene. The result was a single acid, obtained in almost quantitative yield, identical in every way with VII. Thus the interesting fact emerges that hemimellitene condenses with an acid chloride in the 4-position, while the product obtained by adding the hydrocarbon to the conjugated system in dimethylacrylic acid has the acid residue in the 5-position. These results are in agreement with those of Nightingale[14] and Perry[15] who found that *t*-butyl chloride condensed with *m*-xylene in the 5-position, while acetyl chloride condensed in the 4-position. The β-phenylisovaleric acids may be regarded as *t*-butyl derivatives, and hence they should behave toward aluminum chloride in a manner similar to that of the hydrocarbons themselves, and Nightingale, as well as Perry, have shown that 4-*t*-butyl-*m*-xylene rearranges readily in the presence of aluminum chloride to give 5-*t*-butyl-*m*-xylene. The formation of VII, a 1,2,3,5-tetrasubstituted benzene, in the presence of aluminum chloride is also in accord with experience obtained in methylating xylene and other hydrocarbons in the presence of aluminum chloride; in these reactions, little if any 1,2,3-trimethyl- and 1,2,3,4-tetramethyl-benzenes are formed.[16] With these facts in mind, it was of interest to subject the 1,2,4,5-acid VI (m. p. 77–79°) to the action of aluminum chloride. The product was a mixture having the same melting point range as that of the mixture of acids obtained by condensation of pseudocumene with β,β-dimethylacrylic acid; because of the small amount of material available, it was not possible to isolate the 1,2,3,5-acid VII from this mixture in an entirely pure state. However, the impure acid obtained in this way (m. p. 101–107°) when mixed with pure VII (m. p. 111–112°) melted at 104–108°. It was thus established that aluminum chloride would bring about rearrangement of acid VI, and that the product, if not quite entirely VII, contained a large proportion of it. While not strictly comparable to the rearrangement of VI, migrations of this type have been noted by v. Auwers in connection with his studies on the Fries rearrangement.[17] Thus the acetates of pseudocumenol-5 and -6, of mesitol and of hemimellitenol-4 all give 4-hydroxy-5-acetohemimellitene, the first three with rearrangement of the methyl groups, and the last with no such rearrangement.

It was not possible to determine all of the constituents of the mixture of acids obtained when pseudocumene was condensed with dimethylacrylic acid. Saponification of the lower boiling fractions of the ester made from the crude acid product gave a mixture of acids melting at 68–90°. It is likely that these are dimethylphenylisovaleric acids, since a part of the pseudocumene used was always converted into durene. Hence some xylenes must also have been formed, and as no xylenes could be obtained from the alkali-insoluble portion of the product, these must have condensed with the acrylic acid. Several crystallizations of the residue from which most of the acid VII had been removed gave an acid melting at 85–89°, but repeated crystallization failed to give a product with a sharper melting point.

p-Xylene condensed readily with dimethylacrylic acid to give a dimethylphenylisovaleric acid. If no migration of methyl groups occurred, this acid could have but one structure, that in which the methyl groups are in positions 2 and 5. But in view of the rearrangement of the butyl xylenes and of acid VI in the presence of aluminum chloride, this product may well be the 3,5-dimethyl compound. The orientation of the methyl groups in this compound was not established, but the acid was readily cyclized to a hydrindone.

(14) Nightingale and Smith, THIS JOURNAL, **61**, 101 (1939).
(15) Smith and Perry, *ibid.*, **61**, 1411 (1939).
(16) Moyle and Smith, *J. Org. Chem.*, **2**, 114 (1937).
(17) (a) v. Auwers, Bundesmann and Wieners, *Ann.*, **447**, 162 (1926); (b) v. Auwers and Mauss, *ibid.*, **460**, 240 (1928); (c) v. Auwers and Dersch, *ibid.*, **462**, 112 (1928); (d) v. Auwers and Bergmann, *ibid.*, **472**, 287 (1929); (e) v. Auwers and Janssen, *ibid.*, **483**, 44 (1930).

Mesitylene also condensed with dimethylacrylic acid. The product was a mixture, from which a pure dimethylphenylisovaleric acid was isolated in poor yield. This acid likewise was readily cyclized to a hydrindone. It is interesting that acid VII, the acid from *p*-xylene and the acid from mesitylene all melt at about 110–112°, yet a mixture of any two of them exhibits a marked depression in melting point.

Experimental Part[18]

β-[3,4,5-Trimethylphenyl]-isovaleric Acid, VII.—Dimethylacrylic acid (10 g., 0.1 mole) was dissolved in pseudocumene (44 g., 0.36 mole). The solution was cooled (−10°) and stirred, and aluminum chloride (26.6 g., 0.2 mole) was added at such a rate that the temperature did not exceed −10°. The mixture became viscous and dark red, and there was a slight evolution of hydrochloric acid. Stirring at −10° was continued for two hours after all the catalyst was added; the mixture was then poured over a large amount of iced hydrochloric acid. The organic layer was removed and the aqueous layer was extracted three times with ether (30 cc. each time). These extracts were combined with the organic layer and were washed thoroughly with water and then were extracted with carbonate (10%) until the aqueous washings were strongly alkaline. The alkaline solution was warmed gently to remove dissolved ether and then was made strongly acid with hydrochloric acid. The oil which separated soon solidified; the crude acid so obtained weighed 20.8 g. and melted at 84–96°. Repeated recrystallization from dilute alcohol or dilute acetic acid gave a product melting at 111–112° (VII), but the losses were great and it was much better to esterify the crude product and fractionate the ester.

Anal. Calcd. for $C_{14}H_{20}O_2$: C, 76.36; H, 9.09; n. e., 220. Found: C, 75.72, 76.79; H, 8.73, 8.96; n. e., 217.7, 217.9, 216.2.

The carbonate insoluble portion of the reaction mixture was fractionated under 11 mm. pressure. There resulted 26 g. of a liquid boiling at 52–53° (pseudocumene) and a residue (4 g.) of a white solid (durene, m. p. and mixed m. p., 76–78°).

Methyl Ester.—The crude acid VII (63.5 g., m. p. 99–102°) was refluxed for two hours in methanol (300 cc.) containing sulfuric acid (10 cc.). The reaction mixture was diluted with water (600 cc.). The ester layer was removed and the aqueous layer extracted three times with benzene (30 cc. each time). The combined organic layers were washed with water, then twice with carbonate (10%) and again with water. The benzene was removed under reduced pressure on the water-bath and the residual oil was fractionated under 4 mm. pressure through a 30-inch (76-cm.) Fenske column. The products were: A, 4.0 g., b. p. 111–118.5°; B, 8.7 g., b. p., 118.5–123°; C, 3.0 g., b. p. 124–129°; D, 41.5 g., b. p. 129–130°; E, 6.0 g., residue. Hydrolysis of fraction D gave crude acid VII, m. p. 103–107°. After two crystallizations from dilute alcohol, the acid weighed 28 g. and melted at 111–112°. A portion of this purified acid (10.4 g.) was re-esterified, giving 13.3 g. of methyl ester, practically all of which boiled at 130–130.5° under 6 mm. pressure.

Anal. Calcd. for $C_{15}H_{22}O_2$: C, 76.87; H, 9.16. Found: C, 76.92, H, 9.40.

Hydrolysis of fraction B (2 cc.) gave 2.0 g. of a crude acid which melted at 68–90°. Crystallization of this acid from dilute ethanol gave a product melting at 85–90°; several more crystallizations did not give a product with a higher melting point. A mixture of this acid and the pure acid VII melted at 79–87°.

Acid VII from Hemimellitene.—Dimethylacrylic acid (2.5 g.) and hemimellitene (6 g.) were condensed at −10° with aluminum chloride (6.65 g.) as described above. The crude product, isolated as described above, weighed 5.4 g. and melted at 106–107°; when mixed with the pure acid VII from pseudocumene, the substance melted at 109–110°. One crystallization of this product from dilute ethanol gave a product melting at 111–112°; it was not necessary to convert the acid made from hemimellitene into the ester in order to purify it, and from the yield and purity of the crude product, it is apparent that this condensation gives a single substance, VII.

3,4,5-Tricarboxyphenylisobutyric Acid, VIII.—The acid VII (1.0 g.) was refluxed with potassium permanganate (11.1 g.) in water (210 cc.) containing potassium hydroxide (20 cc., 20%) for eighteen hours. Ethanol was added to decolorize excess permanganate, the precipitated manganese dioxide was filtered off and the filtrate was concentrated to 20 cc. and made faintly acid with acetic acid. Barium chloride (saturated solution) was added to the hot solution until no more precipitate formed. The barium salt was removed and dissolved in hydrochloric acid (4 *N*, 8 cc.). The barium was precipitated with sulfuric acid (6 *N*), care being taken to avoid an excess of the acid. The barium sulfate was removed and the acid VIII was isolated from the filtrate. After crystallization from 6 *N* hydrochloric acid, the substance melted at 192–194°. It did not correspond in melting point with any of the known tri- or tetracarboxybenzenes. Repetition of the oxidation, refluxing for thirty hours, gave the same product.

Anal. Calcd. for $C_{13}H_{21}O_8$: C, 52.70; H, 4.02. Found: C, 52.78, 52.24, 52.99; H, 4.99, 5.27, 4.84.

A small amount of the acid was esterified with diazomethane in ether, but the methyl ester was an oil which could not be crystallized.

β-[2,4,5-Trimethylphenyl]-isovaleric Acid, VI.—5-Acetopseudocumene (16.2 g., 0.1 mole) was added to a solution of methylmagnesium iodide (magnesium 2.5 g., methyl iodide 16 g.) in ether (60 cc.) under nitrogen. The mixture was refluxed for an hour and then decomposed with iced ammonium chloride solution. The product was removed by several ether extractions and the ether solution was washed with water, then with dilute bicarbonate and again with water and dried over sodium sulfate. Removal of the ether under vacuum left a light yellow oil (18 g.) which could not be crystallized. It was a mixture of acetopseudocumene and the carbinol IX. This oil was dissolved in petroleum ether (20 cc., b. p. 38–40°) and the solution was saturated with dry hydrogen chloride at 0°; a layer of water separated. After standing for thirty minutes,

(18) Microanalyses by J. W. Opie, C. O. Guss and H. H. Hoehn.

the product was washed several times with water and dried over sodium sulfate. This solution of the chloride X was added to sodium malonic ester (ethyl malonate 16.5 g., sodium 2.3 g.) in dry ether (100 cc.) and the mixture was refluxed for two and one-half hours. The mixture was poured into water and the organic layer was removed and washed first with water, then with dilute hydrochloric acid, and again with water. The solvent was removed and the residual oil (XI) was refluxed for five hours with potassium hydroxide in methanol (75 cc., 30%). Water was added and the solution was extracted thoroughly with ether. The aqueous layer was then acidified; a yellow oil (1.3 g.) formed, which was removed, taken up in ether, and then extracted from the ether solution with dilute carbonate. Acidification of the carbonate regenerated the oil, which was again taken up in ether and dried over Drierite. Removal of the solvent left an oil which slowly crystallized. Recrystallization from dilute alcohol gave a white crystalline product melting at 143.5–148.5° with decomposition. This was the malonic acid XII. It was not analyzed, but was decarboxylated by heating it in a test-tube to 160°. The escaping gas was identified as carbon dioxide; the melt solidified on cooling. After crystallization from dilute ethanol, the product, VI, melted at 79–81°. A mixture with the acid VII (m. p. 111–112°), melted at 67–69°.

Anal. Calcd. for $C_{14}H_{20}O_2$: C, 76.36; H, 9.09. Found: C, 76.39; H, 9.02.

Rearrangement of VI to VII.—The acid VI (0.085 g.) was dissolved in carbon disulfide (3 cc.) and aluminum chloride (0.10 g.) was added. A vigorous reaction occurred and a red oil precipitated. The mixture was refluxed for fifteen minutes, after which the solvent was removed. The residual oil was decomposed with dilute hydrochloric acid and the resulting white solid was extracted with ether (5 cc.). The ethereal solution was washed with water and then extracted with carbonate. Acidification of the carbonate solution produced a solid melting at 78–95°. After two crystallizations from dilute alcohol, the substance (VII) melted at 101–107°. A mixture of this and pure VII (m. p. 111–112°) melted at 104–108°; a mixture of this specimen of VII and the starting material VI melted at 65–69°.

3,3,5,6,7-Pentamethylhydrindone, XIII.—The acid VII (4.4 g.) was dissolved in concd. sulfuric acid (30 cc.) and allowed to stand for four hours at room temperature. The mixture was poured over cracked ice and the hydrindone (4 g., 99%, m. p., 100–101°) was removed and crystallized from dilute ethanol. It formed long white needles which melted at 103.5–104°.

Anal. Calcd. for $C_{14}H_{18}O$: C, 83.16; H, 8.91. Found: C, 83.21; H, 8.70.

Oxime XIV.—The hydrindone XIII (3.82 g.) was dissolved in ethanol (50 cc.) and a solution of hydroxylamine hydrochloride (4.0 g.) and sodium acetate (8.0 g.) in water (10 cc.) was added. The mixture was refluxed for thirty minutes and then cooled. The solid (3.12 g., m. p. 179–185°) was removed and crystallized from dilute ethanol. It was white, and melted at 196–196.5°.

Anal. Calcd. for $C_{14}H_{19}ON$: C, 77.42; H, 8.75. Found: C, 76.08, 76.65; H, 8.51, 8.62.

Isopropylidene - 2,3,4 - trimethylacetophenone, XVII.—Hemimellitene (6 g., 0.05 mole) and dimethylacrylic acid chloride (5.0 g., 0.042 mole) were dissolved in carbon disulfide (15 cc.). Aluminum chloride (5.64 g., 0.042 mole) was slowly added to the rapidly stirred, cooled (−10°) solution. After nearly all of the catalyst had been added, a vigorous evolution of hydrogen chloride began. The reaction mixture was allowed to warm to room temperature (twelve minutes) and was then immediately poured over iced hydrochloric acid. The organic layer was removed and the aqueous layer was extracted three times with ether (10 cc. each time). The extracts were combined with the main organic layer and the whole was washed several times with water, then with dilute carbonate, and again with water. Solvent and unchanged hydrocarbon were removed by steam distillation (total distillate 100 cc.). The residue was extracted with ether and the extract was dried over Drierite. After removal of the solvent, the residual oil was distilled under reduced pressure (6 mm.) through a six-inch (16-cm.) column packed with glass helices. After a small forerun (0.8 g.) boiling at 136–138°, the bulk of the product (3.4 g.) came over at 138–139°.

Anal. Calcd. for $C_{14}H_{18}O$: C, 83.16; H, 8.91. Found: C, 82.63; H, 8.90.

Oxidation of the ketone (1.0 g.) by permanganate (14.6 g. in 300 cc. of water) and alkali (20% KOH, 30 cc.) was accomplished by refluxing the mixture for six hours. The product was isolated through the barium salt as described above in the preparation of VIIIa from VIII. **Benzene-1,2,3,4-tetracarboxylic acid** was obtained but the specimen melted indefinitely about 170°. It accordingly was converted into the tetramethyl ester by action of diazomethane; after crystallization from dilute methanol, the ester melted at 130–130.5° alone or when mixed with an authentic specimen.

Hydrindone, XIII.—The ketone XVII (1 g.) was dissolved in carbon disulfide (5 cc.) and aluminum chloride (0.7 g.) was added. The solution was saturated in the cold with dry hydrogen chloride and then refluxed for forty minutes. The solvent was evaporated and the residual red oil was decomposed with iced hydrochloric acid. A white solid (0.90 g.) formed at once; it melted at 90–95°. Crystallized once from dilute ethanol, it separated in long white needles which melted at 103.5–104°, alone or when mixed with a specimen of XIII prepared from the acid VIII.

Isopropylidene - 2,4,5 - trimethylacetophenone, XV.—Pseudocumene (15 g., 0.10 mole) was condensed with dimethylacrylic acid chloride (10.5 g.) in carbon disulfide (25 cc.), using aluminum chloride (13.3 g.) in exactly the same manner described above for the preparation of XVII. The product (8.5 g.) isolated and purified in the same way, boiled at 131–131.5° under 6 mm. pressure.

Anal. Calcd. for $C_{14}H_{18}O$: C, 83.16; H, 8.91. Found: C, 82.27; H, 9.12.

Oxidation of this ketone (1.0 g.) using the procedure described above for oxidation of XVII gave **pyromellitic acid** (0.4 g.) melting with decomposition at about 225°. Esterification of this acid by diazomethane gave the tetramethyl ester, m. p. 138–139°, alone or when mixed with an authentic specimen.

3,3,4,5,7-Pentamethylhydrindone, XVI.—The ketone XV (2 cc.) was cyclized with aluminum chloride (1.3 g.) in carbon disulfide (10 cc.) by the procedure used in cyclizing XVII. The hydrindone XVI, obtained in quantitative yield, crystallized in flat plates from dilute ethanol. It melted at 54–55.5°.

Anal. Calcd. for $C_{14}H_{18}O$: C, 83.16; H, 8.91. Found: C, 83.37; H, 9.05.

2,4,5-Trimethyl-α,β-dibromoisovalerophenone, XVIII.—A solution of the ketone XV (1.0 g.) in dry ether (10 cc.) was brominated by liquid bromine (0.79 g.). The color was discharged instantly and no hydrogen bromide was evolved. Evaporation of the solvent left an oil which solidified rapidly. After crystallization from ethanol, the substance melted at 74–76°.

Dimethylacrylic acid (15 g.) in carbon disulfide (25 cc.) was brominated with liquid bromine (7.7 cc.) at 0°. The solvent was pumped off and the solid residue was suspended in benzene (25 cc.). Phosphorus pentachloride (31.2 g.) was added slowly to the cooled (0°) solution. The acid gradually dissolved, and after solution was complete the volatile materials were pumped off and the residue was distilled. The acid chloride (27 g., 66%) boiled at 77–82° under 5 mm. pressure; there was some decomposition during the distillation. The acid chloride was dissolved in pseudocumene (16.5 g., 0.11 mole) and carbon disulfide (25 cc.). The solution was cooled to −10° and aluminum chloride (14.6 g., 0.11 mole) was added with stirring. As soon as all of the aluminum chloride was added, the reaction mixture was poured into iced hydrochloric acid.

The solvent was removed by steam distillation and the residue was extracted with ether. Removal of the ether left an oil which solidified. This solid (XVIII), crystallized from ethanol, melted at 74–76° and was identical with the product obtained by brominating the ketone XV. The yield was 12 g. (33%); a large amount of a greenish oily by-product was also formed.

Anal. Calcd. for $C_{14}H_{18}OBr_2$: C, 46.42; H, 4.97. Found: C, 46.41; H, 5.09.

2-Bromo-3,3,4,5,7-pentamethylhydrindone, XIX.—The dibromo ketone (0.5 g.) was mixed with aluminum chloride (1.0 g.) in a test-tube and the mixture was warmed to 50°. A vigorous reaction occurred, with evolution of hydrogen bromide. The melt was decomposed with ice and the solid product was removed and crystallized from ethanol. It melted at 102–104°.

Anal. Calcd. for $C_{14}H_{17}OBr$: C, 59.79; H, 6.05. Found: C, 59.75; H, 6.52.

β-[2,5-Dimethylphenyl]-isovaleric Acid.—Dimethylacrylic acid (5.0 g.) dissolved in *p*-xylene (8.0 g.) was added slowly with stirring to a cooled (0°) solution of aluminum chloride (16 g.) in *p*-xylene (12 g.). After stirring for one and one-half hours at 0°, the mixture was poured into iced hydrochloric acid. The product, isolated and purified as described for other similar condensations above, weighed 4.12 g. and melted, after crystallization from dilute acetic acid, at 93–100°. After two crystallizations from dilute ethanol, the product melted at 108–110°. Analysis showed that this substance was a dimethylphenylisovaleric acid, but the orientation of the methyl groups in the benzene ring is not certain.

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.72; H, 8.71; n. e., 206. Found: C, 75.50; H, 8.60; n. e., 205.7.

3,3,4,7-Tetramethylhydrindone.—The above acid (1.0 g.) was allowed to stand in sulfuric acid (20 cc.) for one hour. The mixture was poured onto ice and the solid was removed and crystallized from dilute ethanol. It melted at 52–53°. The position of the methyl groups in the benzene ring is not certain.

Anal. Calcd. for $C_{13}H_{16}O$: C, 82.99; H, 8.52. Found: C, 82.73; H, 8.79.

Condensation of Mesitylene with Dimethylacrylic Acid.—The hydrocarbon (31.5 g.) was condensed with the acid at 0° by adding aluminum chloride and the product was isolated as described above in similar experiments. A small yield (3.0 g.) of solid resulted. This solid was crystallized successively from dilute methanol, petroleum ether (b. p. 28–35°), dilute ethanol (twice) and dilute acetic acid. It then melted at 110–111°. Although it was a dimethylphenylisovaleric acid, it was not identical with the product (m. p. 108–110°) obtained in a similar manner from *p*-xylene; a mixture of the two substances melted at 85–90°.

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.72; H, 8.71. Found: C, 75.53; H, 8.90.

When this acid (0.10 g.) was cyclized with sulfuric acid in the usual way, the product was a **tetramethyl hydrindone** melting at 62–63° which likewise was different from the product similarly derived from *p*-xylene.

Anal. Calcd. for $C_{13}H_{16}O$: C, 82.99; H, 8.52. Found: C, 82.16; H, 8.65.

1,1,3,4,5,7-Hexamethylindene, V.—Pseudocumene (12 g., 0.1 mole) was cooled to 0° and aluminum chloride (15 g., 0.11 mole) was slowly added. To this mixture at 10°, mesityl oxide (8 g., 0.08 mole) was added slowly. The aluminum chloride gradually dissolved to give a cherry-red solution which was allowed to stand at room temperature for three hours. It was decomposed by iced hydrochloric acid, the organic layer was separated and the aqueous layer was extracted with ether. The organic layers were combined, washed first with water and then with carbonate, and dried over calcium chloride. The solvent was removed and the residue was distilled under 11 mm. pressure. Pseudocumene and mesityl oxide (12 g.) came over at 42–50°; the boiling point then rose to 145–146° and 4 g. of distillate which solidified at once was collected. When crystallized from ethanol, this material melted at 87.5–88.5°. No carbonyl derivatives could be obtained, nor could any acid be isolated when the substance was oxidized with hypobromite. The product instantly decolorized bromine in carbon tetrachloride, with evolution of hydrogen bromide.

Anal. Calcd. for $C_{15}H_{20}$: C, 90.00; H, 10.00. Found: C, 90.08; H, 10.40.

Phenol and Mesityl Oxide.—The ketone (9.9 g.) and phenol (9.4 g.) were mixed and concd. sulfuric acid (10 cc.) was added slowly at 0°. The light red solution stood at room temperature for six days and was then poured into ice. The viscous product was triturated with water and then taken up in 20% potassium hydroxide. The alkaline solution was extracted with ether, and then saturated with carbon dioxide. A yellow amorphous solid precipi-

tated. This solid could not be crystallized from any of a number of solvents tried; the usual result was a brown sirup. A portion of this sirup was subjected to high vacuum distillation. It started to evolve gas at about 78° and at 100° a sublimate slowly formed. This sublimate resembled shellac, and it could not be crystallized. Repetition of the experiment, using acetic acid as a diluent and a temperature of 85° for one hour, gave the same results.

Pseudocumenol-6 and Mesityl Oxide.—The same treatment converted the mixture of these substances into a brown oil, soluble in potassium hydroxide. Carbon dioxide precipitated from the alkaline solution a tan solid containing some unchanged phenol. This solid, after repeated precipitation from dilute alcohol and dilute acetic acid, melted at 63–70° but it was not crystalline and it could not be purified further.

***p*-Bromophenol and mesityl oxide** likewise gave only amorphous products.

Hydroquinone Dimethyl Ether and Mesityl Oxide.—The ether (6.9 g.) and the ketone (4.95 g.) were dissolved in carbon disulfide (50 cc.) and aluminum chloride (20 g.) was added. After refluxing for one hour, the mixture was decomposed with iced hydrochloric acid. No alkali-soluble product was obtained and 85% of the ether was recovered.

***p*-Chlorophenol** (3.4 g.) and **mesityl oxide** (2.97 g.) were similarly treated with aluminum chloride (4 g.) at 100° for three hours. The product was separated into alkali-soluble and -insoluble parts but nothing but starting materials could be isolated from these.

***p*-Chloroanisole** (4.26 g.) and **mesityl oxide** (2.97 g.) were mixed in nitrobenzene (15 cc.) and heated for two and one-half hours at 100° with aluminum chloride (4.0 g.). Distillation of the steam volatile part of the product showed nothing but the starting materials to be present.

***o*-Hydroxyphenyldimethylcarbinol.**—Methylmagnesium iodide (0.194 mole) was prepared in the usual manner. Methyl salicylate (9.8 g., 0.0645 mole) in ether (40 cc.) was added to the Grignard solution. The mixture was allowed to stand overnight and was then worked up in the usual manner, every precaution being taken to prevent dehydration of the product. The carbinol was obtained in 64% yield; after crystallization from petroleum ether, it melted at 43–44°.

The carbinol (8.85 g.) was dissolved in benzene and a little Drierite was added. The mixture was saturated with dry hydrogen chloride. A layer of water formed. The benzene layer was removed and washed repeatedly with water. Removal of the solvent under reduced pressure left an oil which solidified on standing. This solid (m. p. 95–96°) did not contain halogen, gave a very weak Folin phenol test, and rapidly decolorized bromine in carbon tetrachloride. An orange-yellow color was produced with sulfuric acid. The solid was insoluble in aqueous potassium hydroxide, hot or cold.

Summary

1. In the presence of aluminum chloride, the condensation of pseudocumene with dimethylacrylic acid is accompanied by a rearrangement of the alkyl groups. The product does not have the substituents in positions 1, 2, 4 and 5 (VI) but is β-[3,4,5-trimethylphenyl]-isovaleric acid, VII.

2. Pseudocumene condenses normally with dimethylacrylic acid chloride in the presence of aluminum chloride, the acyl group entering the 5-position.

3. Hemimellitene condenses with dimethylacrylic acid to give the isovaleric acid VII in 95% yield, condensing in the 5-position.

4. Hemimellitene condenses with dimethylacrylic acid chloride, however, in the 4-position.

5. These ketones and acids were converted to hydrindones, and the relationship existing between the different hydrindones thus obtained is discussed.

6. β-[2,4,5-Trimethylphenyl]-isovaleric acid (VI) was synthesized and found to rearrange to the 3,4,5-trimethylphenyl compound in the presence of aluminum chloride.

MINNEAPOLIS, MINNESOTA

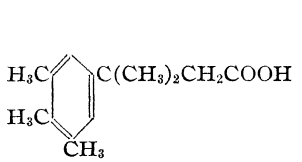
RECEIVED NOVEMBER 15, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

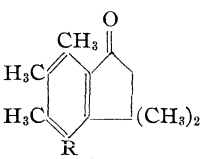
3,3,5,6,7-Pentamethylhydrindone and 4,4,5,6,8-Pentamethylhydrocarbostyril

BY LEE IRVIN SMITH AND WILLIAM W. PRICHARD[1]

In the preceding paper[2] there were outlined the general lines of attack by means of which 4,4-dialkyl-6-hydroxychromans might be prepared. The reactions chosen for this purpose failed to produce the proper intermediates, because when

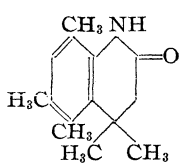


I

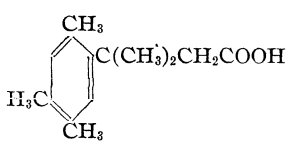


II, R = H
III, Oxime of II
V, R = NO_2
VI, R = NH_2
VII, R = OH
VIII, Oxime of VII

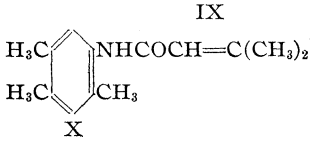
pseudocumene was condensed with dimethylacrylic acid, rearrangement occurred and a derivative of hemimellitene (I) resulted. In the early stages of this work it was discovered that the acid I could be converted readily into a hydrindone.



IV



IX



X

Although not convertible to a 6-hydroxychroman, this hydrindone II was studied in some detail, and for comparison, the hydrocarbostyril IV, although likewise not convertible to a 6-hydroxychroman, was synthesized.

The hydrindone II gave a good yield of the oxime III, but this oxime gave very unsatisfactory results when attempts were made to carry out a Beckmann rearrangement. Frequently a small amount of solid product was obtained, but this product was a mixture from which, in no case, could any pure substance be isolated. These results were surprising in view of the fact that the unsubstituted hydrindone oxime can be rearranged to a hydrocarbostyril (although in poor yield) by refluxing it in ether with phosphorus pentachloride,[3] while fluorenone oxime gives a 90% yield of product when rearranged with phosphorus pentachloride in phosphorus oxychloride.[4]

Since no pure product could be obtained by rearrangement of the oxime III, it was decided to introduce the hydroxyl group into the hydrindone II and then attempt the Beckmann rearrangement of the phenolic oxime VIII. The hydrindone was readily nitrated to a mono nitro compound V which was reduced to the amino hydrindone VI. Replacement of the amino group by hydroxyl was accomplished by diazotization in the usual way. The phenolic hydrindone VII formed an oxime VIII, but this oxime could not be rearranged to a crystallizable product, either by the method of Kipping[3] or by that of Huntress.[4]

In order to examine the properties of the hydrocarbostyrils which should result from the rearrangement of hydrindone oximes, the hydrocarbostyril IV was synthesized from pseudocumidine-5 via the trimethyl anilide of dimethylacrylic acid (X). It was hoped also that this hydrocarbostyril IV could be converted into the phenylisovaleric acid IX which would also have been the product had the condensation of dimethylacrylic acid with pseudocumene involved the 6-position of the hydrocarbon. The amide X was readily prepared, and in the presence of aluminum chloride this amide was converted into an excellent yield of the hydrocarbostyril IV. This reaction is of interest, since Mayer, van Zütphen and Phillips[5] found that the N-methylanilide of acrylic acid did not give the corresponding hydrocarbostyril with aluminum chloride while several substituted anilides of β-chloropropionic and β-chlorobutyric acids gave excellent yields of hydrocarbostyrils. These authors concluded therefore that the ring closure occurred by loss of hydrogen chloride from the β-chloroanilides and that the α,β-unsaturated anilide was not involved. The easy cyclization of the unsaturated amide X apparently refutes this argument, but it is of course possible that cycliza-

(1) Abstracted from a thesis by W. W. Prichard, presented to the Graduate School of the University of Minnesota, in partial fulfillment of the requirements for the Ph.D. degree, October, 1939.

(2) Smith and Prichard, THIS JOURNAL, **62**, 771 (1940).

(3) Kipping, *J. Chem. Soc.*, **65**, 490 (1894).

(4) Huntress, THIS JOURNAL, **49**, 2618 (1927).

(5) Mayer, van Zütphen and Phillips, *Ber.*, **60**, 858 (1927).

tion of X by aluminum chloride is preceded by the addition of hydrogen chloride to the double bond.

Mayer, Phillips, Ruppert and Schmitt[6] succeeded in opening the heterocyclic ring of their hydrocarbostyrils by action of aqueous barium hydroxide at 150°. In this Laboratory, Mayer's method had been used with success in an analogous situation[7] but all attempts to open the ring of the hydrocarbostyril IV failed and it appears that when the anilides of α,β-unsaturated acids have two substituents in the β-position, ring closure to the hydrocarbostyril is particularly easy and the heterocyclic compound, once formed, is particularly stable.

Experimental Part[8]

3,3,5,6,7-Pentamethylhydrindone, II, and its Oxime, III.—Preparation of these substances is described in the previous paper.[2]

Beckmann Rearrangement of Oxime III.—The oxime (0.34 g.) was dissolved in a mixture of phosphorus pentachloride (1.0 g.) and phosphorus oxychloride (5.0 g.). A vigorous reaction occurred, accompanied by evolution of hydrogen chloride. The mixture was refluxed for twenty minutes and then poured over ice. The product, a sticky brown material, was taken up in chloroform. Removal of the solvent left a brown gum, whose solution in dilute ethanol deposited a small amount of a somewhat gummy solid melting at about 85°. This substance could not be purified further. Repetitions of the experiment always gave products of the same gummy nature; on one occasion a small amount of crystalline product melting at 150–170° was obtained. This was a mixture which could not be separated.

3,3,5,6,7-Pentamethyl-4-nitrohydrindone, V.—The hydrindone II (3.0 g.) was dissolved in chloroform (20 cc.) and the solution was cooled (−5°) and stirred with sulfuric acid (50 cc.) while a solution of sodium nitrate (1.3 g.) in sulfuric acid (10 cc.) was slowly added. The solution was cooled and stirred for ten minutes longer and then poured on ice. The chloroform layer was removed and the acid layer was extracted thoroughly with chloroform. The combined chloroform solutions were washed with water, dilute carbonate and again with water. The solvent was removed at about 50° under reduced pressure, and the residual oil was crystallized from dilute methanol. The nitrohydrindone (1.14 g.) melted at 94–94.5°; the mother liquor, when concentrated, deposited a second crop (0.4 g.) melting at 92–93°. The remainder of the product was a red oil.

Anal. Calcd. for $C_{14}H_{17}O_3N$: C, 68.01; H, 6.88. Found: C, 68.74; H, 6.98.

3,3,5,6,7-Pentamethyl-4-aminohydrindone, VI.—The nitrohydrindone V (1.10 g.) was dissolved in acetic acid (10 cc., 60%) and the solution was warmed with zinc (20 mesh, 1.0 g.) for ten minutes after the initial vigorous reaction subsided. Dilution of the solution with ice precipitated the amine (0.90 g.) as a white solid which melted sharply at 81–82°. Two crystallizations from dilute methanol gave a product melting at 101–102°. Investigation showed that this compound had two melting points. A fairly large crystal of the substance was powdered and packed into two melting point capillary tubes. One of these was placed in a bath the temperature of which was raised at a moderate rate. This specimen was completely liquefied at 84°; it then re-solidified and melted again sharply at 101–102°. The other tube was placed in the bath at 70° and the temperature was raised very slowly. There was no evidence of softening until a temperature of 100° was reached; the sample then melted sharply at 101–102°. A similar dimorphism was shown by some of the other compounds in the series.

Anal. Calcd. for $C_{14}H_{19}ON$: C, 77.42; H, 8.76. Found: C, 75.74; H, 8.89.

3,3,5,6,7-Pentamethyl-4-hydroxyhydrindone, VII.—The amino compound VI (0.46 g.) was dissolved in sulfuric acid (10%, 10 cc.) by warming. The solution was cooled to 0°, and to the resulting suspension there was slowly added a solution of sodium nitrite (0.15 g.) in water (2 cc.). The mixture was allowed to stand for thirty minutes. Copper sulfate (saturated solution, 5 cc.) and sulfuric acid (1 cc.) were added and the mixture was refluxed for twenty minutes. Nitrogen was evolved and a white solid (0.40 g.) separated. This was removed and crystallized from dilute methanol. The substance melted at 183–185° and was completely soluble in cold Claisen alkali.

Anal. Calcd. for $C_{14}H_{18}O_2$: C, 77.07; H, 8.26. Found: C, 77.02; H, 8.60.

Oxime, VIII.—The oxime was prepared from the hydrindone in dilute methanol in the usual way with hydroxylamine hydrochloride and sodium acetate. After crystallization from dilute methanol, it melted at 183–185° to a dark liquid. When mixed with the hydrindone VII (m. p. 183–185°) the substance melted at 165–170°.

Anal. Calcd. for $C_{14}H_{19}O_2N$: C, 72.10; H, 8.15. Found: C, 71.70; H, 8.90.

The oxime (0.1 g.) in ether (5 cc.) was refluxed with phosphorus pentachloride (0.5 g.) for four hours. The ether solution was washed with water and dilute carbonate and dried over Drierite. Removal of the solvent left a yellow oil containing chlorine. The oxime (0.15 g.) in phosphorus oxychloride (3 cc.) was refluxed with phosphorus pentachloride (0.5 g.) for one hour. Addition of water slowly precipitated an amorphous solid which could not be crystallized from dilute alcohol, although the expected hydrocarbostyril (synthesized in another way; see next paper) crystallized readily from this solvent.

2,4,5-Trimethyl Anilide of Dimethylacrylic Acid, X.—Pseudocumidine-5 (11.1 g.) was dissolved in benzene (50 cc.) and a solution of dimethylacrylic acid chloride (4.85 g.) in benzene (15 cc.) was slowly added. The amine hydrochloride precipitated at once. The mixture was refluxed for thirty minutes and the suspended solid was filtered off. The benzene filtrate was extracted several

(6) Mayer, Phillips, Ruppert and Schmitt, *Ber.*, **61**, 1966 (1928).
(7) Smith and Denyes, THIS JOURNAL, **58**, 304 (1936).
(8) Microanalyses by J. W. Opie, H. H. Hoehn and C. O. Guss.

times with dilute hydrochloric acid, washed with water and then concentrated to about 40 cc. On cooling, a solid was deposited. Petroleum ether (100 cc., b. p. 28–35°) was added and the solid was filtered off. It weighed 7.1 g. (80%) and melted at 107.5–108°.

Anal. Calcd. for $C_{14}H_{19}ON$: C, 77.42; H, 8.76. Found: C, 76.90; H, 9.08.

4,4,5,6,8-Pentamethylhydrocarbostyril, IV.—The anilide X (3.0 g.) was mixed with aluminum chloride and the dry mixture was warmed on the water-bath for twenty-five minutes. Ice was added, and the nearly white solid (2.9 g.) which separated was removed. It melted at 207–209°. Crystallization from ethanol gave a slightly yellow product which melted at 209–210°.

Anal. Calcd. for $C_{14}H_{19}ON$: C, 77.42; H, 8.76. Found: C, 77.18; H, 9.09.

One gram portions of the hydrocarbostyril were heated to 150, 200 and 250° for fifteen, ten and eight hours, respectively, in a bomb with barium hydroxide (3.0 g.) and water (15 cc.). In each case the starting material was recovered unchanged, and the alkaline solution contained no organic matter.

Summary

1. This paper contains a description of the conversion of 3,3,5,6,7-pentamethylhydrindone II to 3,3,5,6,7-pentamethyl-4-hydroxyhydrindone VII via the nitro compound and the amine.

2. Neither the oxime of II, nor that of VII, could be made to undergo a Beckmann rearrangement.

3. The 5-pseudocumidide of dimethylacrylic acid, X, is converted smoothly to 4,4,5,6,8-pentamethylhydrocarbostyril IV by action of aluminum chloride. The heterocyclic ring in IV is extremely stable; it is not opened by treatment with barium hydroxide at 250°.

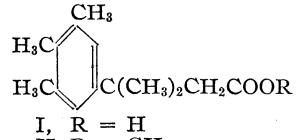
MINNEAPOLIS, MINNESOTA RECEIVED NOVEMBER 15, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

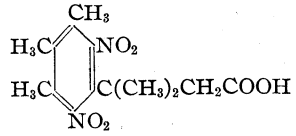
The Nitration of β-[3,4,5-Trimethylphenyl]-isovaleric Acid and its Methyl Ester I. Formation of 4,4,6,7,8-Pentamethyl-5-nitrohydrocoumarin

BY LEE IRVIN SMITH AND WILLIAM W. PRICHARD[1]

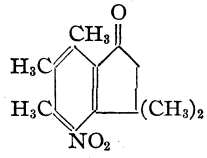
In the preceding papers[2] it was established that condensation of dimethylacrylic acid with pseudocumene was accompanied by rearrangement of the methyl groups and that the resulting β-[trimethylphenyl]-isovaleric acid had structure I, with the methyl groups in positions 3, 4 and 5.



I, R = H
II, R = CH_3



III



IV

The acid I, obtained in good yield, offered a suitable material for model researches on the conversion of such β-phenylisovaleric acids into 4,4-dimethylhydrocoumarins. Accordingly it was planned to carry out this transformation by the series of reactions already used for this purpose[3] which involved reduction of the nitro compound to the amine or hydrocarbostyril, and conversion of the latter to the hydrocoumarin by the method of Mayer, Phillips, Ruppert and Schmitt.[4]

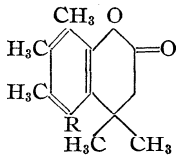
Astonishingly, nitration of the acid I by the method of Smith and Denyes[3] produced neither the dinitro compound III nor the known nitrohydrindone IV[2b] but the nitrohydrocoumarin V, $C_{14}H_{17}O_4N$, melting at 152.5–153°. The yield of this substance was very poor, but when the methyl ester II was nitrated by a solution of sodium nitrate in sulfuric acid there resulted in almost quantitative yield a mixture of two substances, one of which was the compound $C_{14}H_{17}O_4N$, m. p. 152.5–153°. These two nitration products crystallized well, but their solubilities were so nearly identical that the separation was very difficult and was effected only after repeated crystallization supplemented by manual separation of the two types of crystals. The nitrohydrocoumarin V was neutral, but dissolved in strong alkali after continued boiling, giving a bright cherry-red solution, and it was precipitated unchanged when this alkaline solution was satu-

(1) Abstracted from a thesis by W. W. Prichard, presented to the Graduate Faculty of the University of Minnesota, in partial fulfilment of the requirements for the Ph.D. degree, October, 1939.

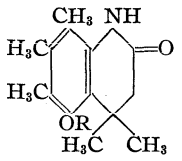
(2) (a) Smith and Prichard, THIS JOURNAL, **62**, 771 (1940); (b) **62**, 778 (1940).

(3) Smith and Denyes, *ibid.*, **58**, 304 (1936).

(4) *Ber.*, **61**, 1966 (1928).



V, R = NO_2
VI, R = NH_2
IX, R = I (iodine)
X, R = OH
XI, R = OCH_3



VII, R = H
VIII, R = Ac

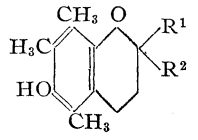
rated with carbon dioxide. Reduction of V produced an amine VI which dissolved readily in hot dilute mineral acids, and which crystallized as the hydrochloride or sulfate when the solutions were cooled. The amine VI also dissolved readily in strong alkalies, but it could not be recovered from these solutions. When the solution of VI in alkali was saturated with carbon dioxide, there resulted an isomer of VI, the hydroxyhydrocarbostyril VII. The hydroxyhydrocarbostyril VII was soluble in alkali and was precipitated unchanged when the solution was acidified; it was insoluble in dilute acids, however, and formed no salts with them, but it could be converted into a monoacetyl derivative, VIII. While the amine VI was readily diazotized and coupled with naphthols to give colored azo compounds, the hydrocarbostyril VII could not be diazotized. This hydroxyhydrocarbostyril is the one which should result from a Beckmann rearrangement of the oxime of 4-hydroxy-3,3,5,6,7-pentamethylhydrindone[2b] but unfortunately no crystalline material could be obtained from the rearrangement product of this oxime.

The diazonium salt from the amine VI reacted with potassium iodide to give the iodo compound IX which slowly dissolved in boiling alkali to give a red solution. This solution contained ionic iodine, but acidification gave no pure products. When the diazonium sulfate derived from VI was refluxed with a little copper sulfate, there resulted the hydroxyhydrocoumarin X. This substance dissolved readily in alkali and was recovered unchanged when the solution was acidified. Various attempts to convert X into a dimethoxy methyl ester by action of methyl sulfate and alkali invariably gave the monomethyl ether XI and no product resulting from opening of the hydrocoumarin ring could be obtained. However, this ether XI slowly dissolved in boiling alkali, indicating either that the ring had opened under these condition, or else enolization of the carbonyl group had occurred. No benzoyl derivative resulted when the alkaline solution of XI was shaken with benzoyl chloride, nor was it possible, by any means tried, to recover anything from the alkaline solutions except the ether XI.

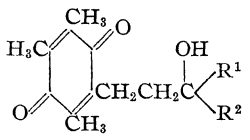
Previous work on some similar hydrocoumarins without the two methyl groups in the 4-position[5] has indicated that it is extremely difficult to open the rings in these compounds; introduction of the two methyl groups in position 4 adjacent to the benzene ring apparently results in rings of even greater stability. Solubility of many of these compounds in alkali indicates that although salts of open chain derivatives may be formed in alkaline solutions, these revert at once to the cyclic compounds as soon as the strong alkali is removed, even when the alkaline solutions are shaken with methyl sulfate. The easy conversion of the amino hydrocoumarin VI into the hydroxyhydrocarbostyril VII must involve at least a momentary opening of the hydrocoumarin ring, although the reverse transformation, from VII to VI, cannot be brought about even partly. No compounds analogous to open chain derivatives of VI, VII or X are known with certainty. Niederl,[6] who condensed mesityl oxide with phenol, oxidized the product and described the resulting substance as β-[*o*-hydroxyphenyl]-isovaleric acid, but he gave no properties nor analysis of his compound, and consequently exact information is lacking. John, Günther and Schmeil,[7] who prepared 4,4,5,7,8-pentamethyl-6-hydroxyhydrocoumarin, did not give any discussion of the properties of this compound nor were any derivatives of it cited which resulted from reactions in which the ring was opened.

The surprising formation of the hydrocoumarin V by nitration of the acid I or its ester II and which involves the equivalent of hydroxylation at position 6, finds a parallel in a reaction discovered in connection with α-tocopherol, a 2,2-dialkyl-6-hydroxychroman (XII). When α-tocopherol is subjected to the action of any of a number of mild oxidizing agents, the first products formed are yellow *p*-quinones, such as XIII.[8] When, however, certain silver salts, notably silver nitrate, are used and the action is prolonged, oxidation proceeds beyond the yellow stage and

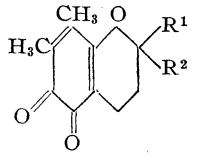
(5) Smith and Tenenbaum, THIS JOURNAL, **59**, 667 (1937).
(6) Niederl, *ibid.*, **51**, 2426 (1929).
(7) John, Günther and Schmeil, *Ber.*, **71**, 2617 (1938).
(8) (a) John, Dietzel and Emte, *Z. physiol. Chem.*, **257**, 173 (1939); (b) Karrer, Fritzsche and Escher, *Helv. Chim. Acta*, **22**, 661 (1939).



XII



XIII



XIV

brilliant red solutions result.[8,9] These red solutions also result when nitric acid in ethanol is used as the oxidizing agent.[8b,10] Crystalline red compounds have been isolated as nitric acid oxidation products of simple model substances having structure XII, and it has been shown that these red substances are *o*-quinone derivatives such as XIV.[11] The transformation of XII into XIV thus involves the equivalent of hydroxylation of the ring by nitric acid or a silver salt and it is comparable to the transformation of the acid I into the nitrohydrocoumarin V. There are considerable differences between the two cases, however. Formation of orthoquinones from coumaran and chroman compounds results only when the hydroxyl group para to the bridge oxygen is present; it takes place via the yellow *p*-quinone intermediate and is accompanied by elimination of the group adjacent to the carbon junction of the two rings. Moreover, 6-hydroxyhydrocoumarins do not give the reaction.[11] In the transformation of I into V, no group is eliminated, the reaction is accompanied by nitration, and the position para to the bridge oxygen is blocked by a methyl group. Whether or not the two series of reactions have a common mechanism remains to be decided.

As stated above, nitration of the ester II gave two products, one of which was V. The other product, melting at 125–125.5°, was a substance having the composition $C_{15}H_{20}O_6N_2$. This composition corresponds to that of the methyl ester of III; but the properties of the substance indicate quite clearly either that it does not have this structure, or, if it does, that the methyl ester of III is a most remarkable substance. Reduction of this substance results in the loss of two carbon atoms and most of the oxygen, giving a compound $C_{13}H_{20}ON_2$. The structure and properties of this second nitration product are still under investigation and the results will form the subject of a later paper.

(9) (a) Evans, Emerson and Emerson, *Science*, **88**, 38 (1938); (b) John and Emte, *Z. physiol. Chem.*, **261**, 24 (1939); (c) Karrer, Escher and Rentschler, *Helv. Chim. Acta*, **22**, 1287 (1939).

(10) Furter and Meyer, *ibid.*, **22**, 240 (1939).

(11) Smith, Irwin and Ungnade, THIS JOURNAL, **61**, 2424 (1939).

Experimental Part[12]

β-[3,4,5,-Trimethylphenyl]-isovaleric Acid, I, and its Methyl Ester, II.—The preparations of I, m. p. 111–112°, and of II, b. p., 130–130.5° under 6 mm., are described in a previous paper.[2a]

4,4,6,7,8-Pentamethyl-5-nitrohydrocoumarin, V. A. By Nitration of the Ester II.—The ester (10.41 g., 0.045 mole) was dissolved in chloroform (30 cc.) and stirred with sulfuric acid (60 cc.) at −15°. A solution of potassium nitrate (10 g., 0.098 mole) in sulfuric acid (20 cc.) was added slowly (one hour and fifteen minutes). After 18 cc. of the nitrating mixture had been added, the dark red color of the mixture faded to light yellow. The cooling bath was removed and the mixture was allowed to warm to 5°. Ice was added, the chloroform layer was separated and the aqueous layer was extracted three times with chloroform (20 cc. each time). The combined chloroform solutions were washed with water, 10% carbonate, and again with water. Evaporation of the solvent at 50–60° under diminished pressure left an oil which solidified when rubbed with a little methanol. The product was taken up in methanol (75 cc.) and allowed to crystallize slowly. The first crop of crystals weighed 10.3 g.; a second crop (0.83 g.) was obtained by concentrating the mother liquor. This material, a mixture of two nitration products, was best separated by allowing the solution in methanol to crystallize very slowly at room temperature. Crystals of one of the compounds separated first and, by watching carefully, the first crystals of the other compound could be seen. At this point the solution was decanted from the crystals; the solution then deposited the other substance. Working in this way alternate crops of the two substances could be obtained. The solubilities of these two compounds were nearly the same in all solvents tried; seeding the solutions with one or the other compound was not effective as this often caused both substances to crystallize together. When the whole mixture was allowed to crystallize very slowly, the two substances could be separated manually. The hydrocoumarin V crystallized in stubby rods which melted at 152.5–153°. The other product formed long needles of square cross section, which melted at 125–125.5°. Using the method of manual separation, the first crop of the nitration product (10.3 g.) was separated with 4.56 g. (53%) of the hydrocoumarin V and 4.66 g. (45%) of the other product.

Anal. V. Calcd. for $C_{14}H_{17}O_4N$: C, 63.87; H, 6.46; N, 5.14. Found: C, 63.97; H, 6.63; N, 5.25. *Anal.* of second nitration product. Calcd. for $C_{15}H_{20}O_6N_2$: C, 55.55; H, 6.17; N, 8.64. Found: C, 55.35; H, 6.31; N, 8.72.

B. By Nitration of the Acid I.—A solution of acid I (0.5 g.) in acetic acid (5 cc.) was dropped slowly into

(12) Microanalyses by J. W. Opie, C. O. Guss and H. H. Hoehn.

fuming nitric acid (5 cc., d. 1.6). Each drop produced a dark color, which immediately faded. The mixture was stirred for fifteen minutes and then diluted with ice. The gummy yellow material was taken up in ether, dried, and the ether was removed. The product (V) was crystallized from dilute ethanol, when it melted at 146–148° alone or when mixed with a specimen of V prepared from the ester. The yield was about 20%. Several attempts to nitrate the acid at lower temperatures without using sulfuric acid failed; only starting material was recovered.

4,4,6,7,8-Pentamethyl-5-aminohydrocoumarin, VI.—Granulated zinc (1.0 g., 20-mesh) was added to a boiling solution of the nitro compound V (1.0 g.) in acetic acid (8 cc.) and water (3 cc.). The mixture was refluxed for ten minutes; the solution was then carefully decanted from the zinc onto ice. The solid was removed and crystallized from dilute methanol. The amine (0.8 g., 90%) crystallized in long needles melting at 125–125.5°. It dissolved readily in hot dilute acids or bases; the hydrochloride and sulfate were both fairly insoluble in cold water. Several attempts were made to reduce the nitro compound V catalytically under low pressures, but the starting material was always recovered in these cases.

Anal. Calcd. for $C_{14}H_{19}O_2N$: C, 72.10; H, 8.15. Found: C, 71.88; H, 8.39.

4,4,6,7,8-Pentamethyl-5-hydroxyhydrocarbostyril, VII.—When a solution of the amine VI in dilute sodium hydroxide was acidified with hydrochloric acid or saturated with carbon dioxide, the hydrocarbostyril precipitated almost quantitatively. After crystallization from dilute ethanol it melted at 193–194°. The substance was soluble in 20% sodium hydroxide and was recovered unchanged when the solution was acidified. No color was produced when VII was subjected to the successive action of nitrous acid and β-naphthol.

Anal. Calcd. for $C_{14}H_{19}O_2N$: C, 72.10; H, 8.15. Found: C, 71.43; H, 8.19.

Acetate, VIII.—The hydrocarbostyril VII (0.1 g.) was refluxed for ten minutes in acetic anhydride (3 cc.) containing a drop of sulfuric acid. The mixture was poured into water and the solid was removed and crystallized from dilute methanol. It melted at 207–208°.

Anal. Calcd. for $C_{16}H_{21}O_3N$: C, 69.82; H, 7.64. Found: C, 69.75; H, 7.56.

4,4,6,7,8-Pentamethyl-5-iodohydrocoumarin, IX.—The amino compound VI (0.50 g.) was warmed with sulfuric acid (10%, 5 cc.). The amine dissolved and, as the solution was cooled, the sulfate separated. To the cooled (0°) suspension of the sulfate a solution of sodium nitrite (0.152 g.) in water (2 cc.) was slowly added. The amine sulfate gradually dissolved and a finely divided, foamy solid appeared at the surface of the solution. The diazonium solution was allowed to stand at 0° for thirty minutes, and then a solution of potassium iodide (1.0 g.) in water (5 cc.) was added. After standing at room temperature for an hour, the mixture was warmed on the steam-bath for thirty minutes. The solution became dark and a black solid separated. Saturated thiosulfate solution (2 cc.) was added and the heating was continued. The dark color gradually disappeared and a light yellow solid then remained suspended in the liquid. The solid was removed and crystallized from ethanol. It formed white plates (0.45 g.) which melted at 131.5–132.5°. The substance contained no nitrogen.

Anal. Calcd. for $C_{14}H_{17}O_2I$: C, 49.16; H, 5.12. Found: C, 48.83; H, 4.94.

The substance dissolved in boiling 20% potassium hydroxide, giving a crimson solution. Acidification of this solution by nitric acid produced a small amount of a solid melting at 150–180°; the aqueous solution gave a heavy precipitate of silver iodide when silver nitrate was added.

4,4,6,7,8-Pentamethyl-5-hydroxyhydrocoumarin, X.—When the diazonium solution prepared from the amine VI (0.50 g.) was refluxed with copper sulfate (saturated solution, 2 cc.) and sulfuric acid (3 cc.), a vigorous evolution of nitrogen occurred and a white solid separated. After crystallization from methanol, this substance (0.40 g.) formed square plates melting at 207–208°. The phenol dissolved readily in Claisen's alkali, giving a red solution, from which the phenol was recovered unchanged when the solution was acidified with hydrochloric acid or saturated with carbon dioxide.

Anal. Calcd. for $C_{14}H_{18}O_3$: C, 71.79; H, 7.69. Found: C, 71.38; H, 8.04.

4,4,6,7,8-Pentamethyl-5-methoxyhydrocoumarin, XI.—The phenol X (0.343 g.) was dissolved in methyl sulfate (1.66 g.) and methanol (2 cc.). To the boiling solution potassium hydroxide (0.75 g.) in methanol (3 cc.) was added slowly. The mixture was refluxed for fifteen minutes and then diluted with water. The product separated readily and after crystallization from dilute methanol it formed long, flat needles (0.340 g.), melting at 132–132.5°. The substance was soluble in dilute alkali, giving a faintly pink solution. Acidification of this solution regenerated the ether XI. Several attempts were made to methylate this compound further in order to open the hydrocoumarin ring, but repeated action of methyl sulfate and 20% potassium hydroxide was without any effect. Likewise the action of benzoyl chloride and 20% potassium hydroxide was without effect; in all cases the ether XI was recovered practically quantitatively and in a pure state.

Anal. Calcd. for $C_{15}H_{20}O_3$: C, 72.57; H, 8.06. Found: C, 72.59; H, 8.25.

Summary

1. Nitration of β-[3,4,5-trimethylphenyl]-isovaleric acid (I) results in the formation of 4,4,-6,7,8-pentamethyl-5-nitrohydrocoumarin (V). Nitration of the methyl ester of this acid produces the nitrohydrocoumarin and a second product $C_{15}H_{20}O_6N_2$ in about equal amounts. The structure of this second product has not yet been established.

2. Several transformations of the nitrohydrocoumarin V are described. In particular, the aminohydrocoumarin VI rearranges readily into the isomeric hydroxyhydrocarbostyril VII when its solution in alkali is acidified.

3. It was not possible to open the heterocyclic

rings of any of the derivatives of the hydrocoumarin or of the hydrocarbostyril.

4. The formation of the hydrocoumarin V by nitration of the ester II is paralleled by a similar reaction in connection with the tocopherols and compounds related to them. Here also the action of nitric acid is equivalent to hydroxylation of a ring at one of the stages of the reaction.

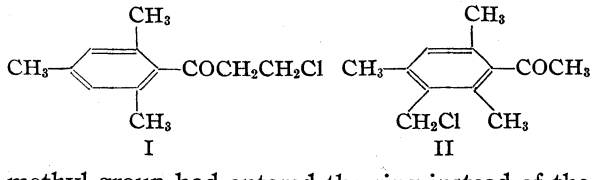
MINNEAPOLIS, MINNESOTA
RECEIVED NOVEMBER 15, 1939

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

Chloromethylation of Aryl Ketones

BY REYNOLD C. FUSON AND C. H. MCKEEVER[1]

The chloromethylation of methyl aryl ketones was undertaken in the hope of obtaining a useful synthesis of β-chloropropiophenones. The success of Colonge[2] in chloromethylating aliphatic ketones by treatment with formalin in the presence of hydrogen chloride and zinc chloride suggested that a similar procedure might prove effective in the aromatic series. We therefore attempted to adapt his method to serve our purpose. In order to minimize the amount of water present, and thus enhance the solubility of the ketones, paraformaldehyde was used in place of formalin. Preliminary experiments on acetomesitylene showed that zinc chloride was not necessary to bring about the reaction. However, the product was not the expected β-chloropropiomesitylene (I) but a chloroacetoisodurene (II). The chloromethyl group had entered the ring instead of the side-chain. In other words, we appeared to have a method for nuclear chloromethylation similar to that developed by Blanc[3] for aromatic hydrocarbons and extended by others, notably Quelet,[4] to other types of aromatic compounds.



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Experiments with other aromatic ketones have substantiated this surmise. The method appears to be general for ketones in which the aryl radical carries two or more alkyl groups. Acetophenone and benzophenone failed to react under these conditions.

The reaction provides an indirect method of methylation; this is shown by the fact that acetoisodurene and pentamethylacetophenone were obtained in 80 and 90% yields, respectively, by reducing the corresponding chloromethyl derivatives according to the method of v. Braun and Nelles.[5]

TABLE OF RESULTS

Compound	Time, hr.	Yield, %	M. p., °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Chlorine, % Calcd.	Chlorine, % Found
5-Chloromethyl-2,4-dimethylacetophenone[a]	41	50	68.5–69	67.17	67.03	6.66	6.75	18.02	17.94
3-Chloromethylacetomesitylene[b]	12	80	74.5–75.5	68.42	68.55	7.18	7.04		
3-Chloromethylacetoisodurene[b]	12	75	88.5–90	69.48	69.14	7.62	7.81		
3-Chloromethylpropiomesitylene	15	88	75–76	69.48	69.50	7.62	7.75	15.78	15.73
3-Chloromethylisobutyromesitylene[c]	36	78		70.43	70.23	8.02	8.09		
3-Chloromethylpivalylmesitylene[b,d]	15	25	54–55	71.27	71.11	8.37	8.34	14.02	14.29
3-Chloromethylbenzoylmesitylene[b]	150	35	90–91	74.85	74.87	6.28	6.20		
3-Chloromethyl-2,4,6-triethylacetophenone	60	57	57–58	71.27	71.41	8.37	8.27	14.02	14.29

[a] The reaction mixture was kept at 80°. The position of the chloromethyl group in this compound was not proved. [b] The yield here is calculated on the original amount of ketone, in all other cases on the amount of ketone that reacted. [c] This compound is a liquid, b. p. 140° (2 mm.); $n^{20}D$ 1.5395; d^{20}_{20} 1.0785. [d] Pivalylmesitylene is a new compound. It was prepared from mesitylene and pivalyl chloride by the Friedel-Crafts method; b. p. 97–97.5° (2.5 mm.); $n^{20}D$ 1.5093; d^{20}_{20} 0.9531. *Anal.* Calcd. for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.33; H, 9.83.

Procedure.—A mixture of 0.1 mole of the ketone, 0.11 mole of paraformaldehyde and 100 cc. of concentrated hydrochloric acid was shaken for fifteen to seventy-two hours at 25–85° depending upon the nature of the ketone. The solid which precipitated was removed by filtration, washed thoroughly and recrystallized from high-boiling petroleum ether or methyl alcohol.

In some cases the chloromethyl derivative did not sepa-

(1) Röhm and Haas Research Assistant.

(2) Colonge, *Bull. soc. chim.*, [5] **3**, 2116 (1936).

(3) Blanc, *ibid.*, **33**, 313 (1923).

(4) For a leading reference see Quelet and Allard, *Compt. rend.*, **205**, 238 (1937).

(5) v. Braun and Nelles, *Ber.*, **67**, 1094 (1934).

rate from the reaction mixture. It was then necessary to pour the mixture into 500 cc. of water and extract with benzene or ether. After the extracts were washed several times with water and dried over calcium chloride, the solvent was removed and the residue distilled *in vacuo*. The chloromethyl derivative was separated easily from the parent ketone by this method.

All but one of the chloromethylated ketones prepared were low-melting solids which, although very soluble in organic solvents, could be recrystallized from low-boiling petroleum ether or methyl alcohol.

Summary

A method has been developed for nuclear chloromethylation of certain types of aromatic ketones.

URBANA, ILLINOIS RECEIVED JANUARY 20, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF HARVARD UNIVERSITY]

Hexahydroacetomesitylene[1]

BY E. P. KOHLER, THOMAS L. JACOBS[2] AND H. M. SONNICHSEN[3]

In continuation of a series of investigations made in this Laboratory[4] as to the effect of hindrance on the stability of enols of aliphatic monoketones, it appeared of interest to study the behavior of hexahydroacetomesitylene and its derivatives from this same point of view. The results of such a study are presented herewith.

It was decided to undertake the preparation of hexahydroacetomesitylene by catalytic hydrogenation of the mesitylene nucleus because that method seemed likely to involve the fewest stereochemical complications, although it is probable that there are other easier routes to that substance.

Preliminary experiments showed that the carbonyl group of acetomesitylene is reduced catalytically before nuclear hydrogenation begins, and the alcohol produced is dehydrated under much less drastic conditions than are necessary for the hydrogenation of the ring; consequently it was necessary to find another derivative of mesitylene which could be hydrogenated in the nucleus and later transformed into an acetyl derivative, and for this purpose mesitylene carboxylic acid seemed the logical choice. The sodium salt of this acid was successfully hydrogenated in water solution using Raney nickel catalyst activated with ammonium chloroplatinate.

It was not possible to separate the isomeric hexahydromesitylene carboxylic acids by simple crystallization, due partly to their great solubility in common organic solvents, and sublimation also failed. The acids were therefore converted into a mixture of amides from which a pure amide melting at 230° and a mixture melting sharply at 167° were obtained. The mixture was shown to contain the 230° amide.

When the residues from the amide preparation were distilled under reduced pressure the principal product was the nitrile, 2,4,6-trimethylhexahydrobenzonitrile, and from the solid residue in the distillation flask was recovered more of the mixture of amides melting at 167°. The structure of the nitrile was proved by the fact that methyl alcoholic potassium hydroxide hydrolyzed it to the 230° amide. The failure of the nitrile to be hydrolyzed past the amide stage by heating with methyl alcoholic potassium hydroxide for several hours was our first indication of the hindered nature of these derivatives of trimethylcyclohexane.[5] The amide also resisted concentrated phosphoric acid and was remarkably inert toward nitrous acid, although by this means it was possible to obtain enough pure trimethylhexahydrobenzoic acid (m. p. 85–87°) for an analysis.

The mixture of amides melting at 167° gave an acid melting at 114–117° when partially hydrolyzed with nitrous acid, and the material remaining unattacked was a mixture of the 230° amide and the 167° mixture. A mixture of the acid

(1) Abstracted from a thesis entitled "Mesitylenic and Hexahydromesitylenic Ketones" presented by H. M. Sonnichsen to the Faculty of Arts and Sciences of Harvard University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1939. The work described herein was begun under the direction of Professor Kohler and completed after his death under the direction of Dr. Jacobs.—H. M. S.

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(4) Kohler, Tishler and Potter, THIS JOURNAL, **57**, 2517 (1935); Kohler and R. B. Thompson, *ibid.*, **59**, 887 (1937); D. T. Rogers, Harvard Ph.D. Thesis, 1938.

(5) Similar cases may be found in the following references: (a) Jacobsen, *Ber.*, **22**, 1219 (1889); (b) Küster and Stallberg, *Ann.*, **278**, 207 (1893); (c) Hantzsch and Lucas, *Ber.*, **28**, 748 (1895); (d) Sudborough, Jackson and Lloyd, *J. Chem. Soc.*, **71**, 229 (1897); (e) Sachs, *Ber.*, **35**, 3325 (1902); (f) Klages, *ibid.*, **36**, 4192 (1903); (g) Knoevenagel, *ibid.*, **37**, 4091 (1904); (h) Reich, *Bull. soc. chim.*, **21**, 222 (1917); (i) Tiemann, *Ber.*, **31**, 889 (1898).

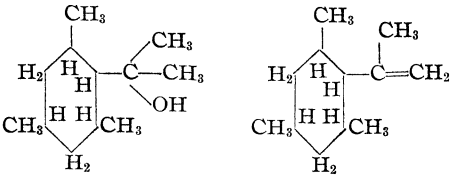
melting at 85–87° with the 114° acid melted below 80°. Carbon–hydrogen analyses showed that both had the composition of 2,4,6-trimethylhexahydrobenzoic acid. Although the troublesome separation of the amide mixture made it difficult to estimate the composition of the crude reduced acids, the fact that about 60% of the acid could be accounted for as the 230° amide in a reaction with an over-all yield not greater than 70% convinced us that the trimethylhexahydrobenzoic acid obtained by hydrogenation of mesitylene carboxylic acid was nearly all one substance, and this assumption was confirmed by the failure of any significant amount of separation of isomeric substances in subsequent reactions.

There are six possible geometric isomers of hexahydromesitylene carboxylic acid,[6] two of which are racemic mixtures separable into optical antipodes. Obviously no decisions can be made from the experimental evidence as to the configurations of the acids isolated. The rule of Skita[7] concerning the production of *cis* and *trans* isomers by hydrogenation in acid or alkaline media is of doubtful validity here because of the complicated structure of the molecule and the drastic conditions of the hydrogenation. Chavanne and Becker's observation[8] that reduction with Raney nickel favors the production of *trans*-isomers and reduction with platinum the formation of *cis*-isomers is of just as little use, not only because of the complexity of the molecule, but also because of the mixed catalyst used. Work on the configurations was not taken up because the primary object of this research was the comparison of the effect of the mesityl and the trimethylcyclohexyl radicals on the stability of enols of monoketones.

The material at hand best suited for the preparation of hexahydroacetomesitylene seemed to be the 230° amide, but when the carefully purified crystalline solid was added to a solution of methylmagnesium chloride, the main product was the nitrile obtained previously. Another possible path was the reaction of the methyl ester of hexahydrotrimethylbenzoic acid with Grignard reagent. The ester reacted slowly with methylmagnesium chloride, but the only product isolated was a small amount of 1-methyl-1-hexahydromesitylethylene (II), a hydrocarbon obtained later by the dehydration of hexahydromesityldimethylcarbinol (I).

Hexahydroacetomesitylene was finally obtained by Fuson's[9] method for preparing ketones from hindered acid chlorides. The addition of 2,4,6-trimethylhexahydrobenzoyl chloride to excess methylmagnesium chloride in benzene at the boiling point gave a mixture containing 70% hexahydroacetomesitylene, 10 or 15% hexahydromesityldimethylcarbinol (I) and 5% of the hydrocarbon obtained by dehydration of the carbinol (II). Separation by fractionation was difficult, and the chemical methods ordinarily available for the demonstration of the presence of ketone and alcohol groups failed because of hindrance. Even condensations of the ketone with aldehydes by the usual procedure failed to give more than traces of α,β-unsaturated ketone. Benzalacetohexahydromesitylene was finally prepared using sodamide as the condensing agent.

The structures of the tertiary alcohol and the hydrocarbon were more difficult to establish, for analyses do not distinguish very well between a secondary and a tertiary methyl carbinol. Of course the production of a secondary alcohol by the reaction of methylmagnesium chloride with an acid chloride seemed extremely unlikely since this reagent lacks the hydrogen in the beta-position usually associated with reductions by Grignard reagents. Reduction by metallic magnesium or magnesium–magnesium chloride mixture could be definitely ruled out, since the yield of alcohol was the same in preparations in which considerable unchanged magnesium was present and in those in which the addition of methyl chloride had been continued for several hours after the last trace of magnesium had disappeared. Nevertheless the possibility of the production of a secondary alcohol by some obscure mechanism had to be considered. The following evidence can be adduced to prove that the structures of the alcohol and the hydrocarbon are those shown below



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(6) A similar case involving a less symmetrical molecule is the hexahydropseudocumidines investigated by Skita (*Ber.*, **53**, 1792 (1920); Hennenbruch, Dissertation, Freiburg, 1920).

(7) Skita, *ibid.*, **53**, 1792 (1920); **56**, 2234 (1923); *Ann.*, **427**, 255 (1922); **431**, 1 (1923).

(8) Chavanne and Becker, *Bull. soc. chim. Belg.*, **31**, 95 (1922).

(9) Fuson, THIS JOURNAL, **59**, 1508 (1937); **60**, 2063 (1938).

The alcohol reacted rapidly with Grignard reagent in the Zerewitinoff apparatus, giving off a mole of gas in the cold. When treated with phenylisocyanate it was dehydrated and no urethan was isolated. Both acetyl chloride and acetic anhydride dehydrated the alcohol smoothly to the hydrocarbon, and when it was shaken with sodium hypobromite for a long period at room temperature the hydrocarbon was again produced in good yield. The alcohol absorbed hydrogen chloride at 0° in aqueous hydrochloric acid solution and formed an unstable chloride which boiled several degrees lower than the original alcohol. Perhaps the best evidence in favor of the tertiary alcohol structure is that when the ketone was reduced with sodium and alcohol the resulting secondary alcohol exhibited quite different properties. This might be a case of geometrical isomerism, but it is not likely.

Investigation of the hydrocarbon gave further support to the hypothesis that methylmagnesium chloride had added to the carbonyl group of hexahydroacetomesitylene. Ozonization of the hydrocarbon furnished little information, since the only product which could be detected with any certainty was formaldehyde. A trace of hexahydroacetomesitylene was detected in the ozonization products but the amount was so small that it might as reasonably be assumed to be a trace of impurity as a product of ozonolysis. No acetone could be found in the mixture, nor could any other products be isolated. Apparently ozone produced a good deal of general oxidation.

Final proof was furnished by the bromination of the unsaturated hydrocarbon, although the course of the reaction was unexpected. The hydrocarbon absorbed bromine rapidly, but almost immediately began to give off hydrogen bromide. When the product was distilled decomposition was evident, and a second distillation of the product produced further decomposition. The distillate crystallized giving a solid monobromide whose analysis, due to the introduction of the bromine, made it possible to distinguish between the various possibilities and show that the hydrocarbon resulted from dehydration of hexahydromesityldimethylcarbinol.

The above evidence shows that under the conditions of the reaction used in its synthesis hexahydroacetomesitylene adds methylmagnesium chloride to produce hexahydromesityldimethylcarbinol to the extent of about 15% of the ketone formed. Here again was an excellent opportunity to compare the hindrance of the mesityl and the trimethylcyclohexyl radicals. A large amount of 2,4,6-trimethylbenzoyl chloride was treated with methylmagnesium chloride under exactly the same conditions as had been used in the preparation of hexahydroacetomesitylene. Absolutely no evidence of any addition of Grignard reagent to the carbonyl was obtained and the yield of acetomesitylene was good enough to establish that under these conditions not more than 1 or 2% could have occurred.

The addition of Grignard reagents to hexahydroacetomesitylene was investigated further on the pure ketone. In the Zerewitinoff apparatus the hydroaromatic substance acted almost exactly the same as acetomesitylene, giving off gas slowly in the cold and requiring some heating before the reaction was complete. The hydroaromatic ketone could be recovered practically unchanged when treated with ethylmagnesium bromide in the cold, but if the ether solution was boiled for two hours 15 to 20% of by-products resulted. The treatment of the bromomagnesium enolate with acylating and alkylating agents also was undertaken but will not be reported, since the work is not complete.

Hexahydroacetomesitylene was reduced easily with sodium and alcohol to hexahydromesitylmethylcarbinol, a liquid, which was characterized by means of its phenylurethan.

Three weeks of shaking with alkaline hypobromite produced a small amount of cleavage of hexahydroacetomesitylene to hexahydromesitylene carboxylic acid. The cleavage product was found to be the geometrical isomer melting at 86–87°. The bromine-containing oil which formed the remainder of the product decomposed on distillation, and there was isolated not a tribromo but a dibromo ketone, $(CH_3)_3C_6H_8COCHBr_2$.

Benzalacetohexahydromesitylene formed a dibromide which was converted to a β-diketone by the usual treatment with alcoholic base. The liquid diketone was characterized as its copper derivative.

The preparation of the enol peroxide of β,β-diphenylpropiohexahydromesitylene was carried out according to the general method used for the preparation of peroxides of this type,[10] furnishing further evidence that di-ortho-substitution pro-

(10) R. B. Thompson, Harvard Ph.D. Thesis, 1938, p. 65, and ref. (4).

duces considerable hindrance in this derivative of cyclohexane. The isolation of this peroxide adds another to the list of hindered ketones whose enols are sufficiently stable in solution to permit their reaction with molecular oxygen. The list now includes β,β-diphenylpropiomesitylene,[11] β,β-diphenylpropiohexahydromesitylene, α,β,β-triphenylpropiophenone,[12] α,β-diphenylvalerophenone,[13] β,β-diphenylpropiotriphenylmethane,[14] 2-diphenylmethyl - 6 - benzalcyclohexanone,[15] and β,β-diphenylpropiotriphenylfuran.[16]

The first peroxide preparation gave two isomers, both of which behaved as peroxides with potassium iodide and on heating. In a second preparation only the lower melting isomer was obtained. It should be mentioned that there are a number of possibilities for isomers of this peroxide, and no decision can be made concerning either structure or configuration in this case. In addition to the usual problem of whether the peroxide is cyclic or in the hydroperoxide form, the existence of two carbon atoms bearing hydrogens in the alpha-position to the carbonyl introduces extra complications. The possibility of *cis* and *trans* isomers of a cyclic peroxide structure and of dimorphic crystalline forms should not be forgotten, and finally there is the stereoisomerism of the cyclohexane ring already mentioned, a list of possibilities so large that exploration seems futile. Thermal decomposition of the peroxide was attempted, but none of the products obtained could be identified.

Experimental

Mesitylene Carboxylic Acid.—Mesitylene carboxylic acid was prepared by carbonation of mesitylmagnesium bromide and purified by recrystallization from methanol. Acid which had been recrystallized only once was found to serve as well for the hydrogenation reaction as very carefully purified material.

Reduction of Mesitylene Carboxylic Acid.—A solution of the sodium salt of mesitylene carboxylic acid was prepared from 100 g. of the acid, 24.3 g. of sodium hydroxide, and 150 cc. of water, and shaken with 5 to 10 g. of Raney nickel catalyst and 0.2 g. of ammonium chloroplatinate at 250° under 3600 lb. (240 atm.) pressure of hydrogen for twenty-four hours. The catalyst was then filtered off and a fresh portion of Raney nickel and ammonium chloroplatinate added. During the first treatment the aromatic acid sometimes absorbed as much as half the theoretical amount of hydrogen, but in the majority of runs no hydrogen was taken up. The material was again shaken at the same temperature and pressure for forty-eight hours before the catalyst was again filtered off and a fresh batch added. The process ordinarily required three treatments, but in some cases without the use of ammonium chloroplatinate as many as six were required to obtain the complete conversion of the aromatic acid to the corresponding derivative of cyclohexane. The primary factor affecting the rate of absorption seemed to be the condition of the copper can used as a reaction vessel. After continued use the inside of the can became covered with a dark-colored deposit of metal and the hydrogenations were completed in much less time.

After the solution of the sodium salt had absorbed the theoretical amount of hydrogen it was filtered and acidified with concent ratedhydrochloric acid. Hexahydromesitylene carboxylic acid was precipitated in 95–99% yield as a thin oil which slowly solidified to a waxy mass from which the water could be decanted. The crude solid was taken up in petroleum ether and separated from the remaining water. If the hydrogenation had not been carried to completion most of the aromatic acid remaining was precipitated at this point.

Preparation of Trimethylhexahydrobenzamides.—A mixture of 7.5 cc. of thionyl chloride and 10 g. of trimethylhexahydrobenzoic acid was allowed to stand overnight, heated on the steam-bath to drive off excess thionyl chloride, and poured into 50 cc. of concentrated ammonium hydroxide cooled in an ice-bath. The precipitate after drying weighed 8.0 g. and consisted of 5.0 g. of an amide melting at 230°, some ammonium chloride, and some oily material containing a good deal of sulfur. From the ammonia solution was recovered 2.1 g. of unchanged acid. The amide was recrystallized from methyl alcohol.

Anal. Calcd. for $C_{10}H_{19}ON$: C, 70.94; H, 11.31. Found: C, 70.75; H, 11.04.

The above analysis is of a sample burned in air. Samples burned in oxygen exploded with an audible detonation. The results of analyses in oxygen agreed with the theoretical percentage of carbon but were four to six-tenths per cent. low in hydrogen.

The oily residues from several preparations of the 230° amide were distilled *in vacuo*. The main fraction boiled at 61–62° at 3 mm., but there was water in the distillate and considerable smell of methyl mercaptan. When the liquid boiling at 62° was heated for twelve hours with saturated methyl alcoholic potassium hydroxide, there was obtained in about 50% yield the same 230° amide which had been isolated earlier.

The flask residue crystallized, giving a solid which melted at 167° after recrystallization from benzene or ether. This substance when mixed with the 230° amide melted between 180 and 220°, different samples of apparently equal purity giving a different mixed melting point. In subsequent preparations the residues from a number of runs were combined and the 167° amide obtained by very tedious fractional crystallization from benzene. Hydrolysis with sodium nitrite in acetic acid showed that this substance was a mixture of the amide melting at 230° and an isomeric amide which it was not possible to isolate in pure form.

(11) Kohler, Tishler and Potter, THIS JOURNAL, **57**, 2517 (1935).
(12) Kohler and Tishler, *ibid.*, **54**, 1595 (1932).
(13) Kohler, *Am. Chem. J.*, **36**, 185 (1906).
(14) D. T. Rogers, Harvard Ph.D. Thesis, 1938, p. 61.
(15) C. E. Barnes, Harvard Ph.D. Thesis, 1935, p. 96.
(16) R. D. Cramer, unpublished work.

Anal. Calcd. for $C_{10}H_{19}ON$: C, 70.94; H, 11.31. Found: (burned in air) C, 70.75; H, 10.93.

Hydrolysis of 230° Amide.—Two grams of amide, m. p. 230°, was added to 50 cc. of glacial acetic acid. The mixture was heated until the amide dissolved, then 2 g. of solid sodium nitrite was added in small portions. The solution was heated for fifteen minutes, then neutralized with 20% sodium hydroxide and filtered. Half of the original amide was recovered. The water solution was acidified and extracted with ether. The ether solution was dried over calcium chloride, filtered and evaporated. The solid material remaining was sublimed and 0.13 g. of crystals obtained which after two more sublimations melted at 85–87°.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.57; H, 10.65. Found: C, 70.90; H, 10.43.

Hydrolysis of the 167° Amide.—The substance melting at 167° was submitted to the same procedure as above, but its solubility in water (approximately 0.1 g. per 100 cc.) made it necessary to extract the crude hydrolysis mixture with ether, and then extract the ether solution with bicarbonate. When the bicarbonate solution was acidified there was deposited in about 15% yield a solid melting at 95–105°. The ether solution deposited a mixture of the 230° amide and the 167° substance, showing that the original 167° substance was a mixture of two amides. The acid was recrystallized twice from petroleum ether (in which it was extremely soluble) and resublimed. The analytical sample sintered slightly at 100° and melted at 114–117°.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.57; H, 10.65. Found[17]: C, 70.63; H, 10.42.

Reaction of 230° Amide with CH_3MgCl; Preparation of Hexahydrotrimethylbenzonitrile.—A solution of methylmagnesium chloride was prepared from 7.2 g. (0.30 mole) of magnesium and to this was added in small portions 20 g. (0.12 mole) of the pure amide melting at 230°. The ether boiled vigorously during the addition and the amide went into solution. After all of the solid had been added the ether was almost all gone and a pasty mass was left. The product was allowed to stand overnight, boiled for one hour and poured into iced dilute hydrochloric acid. When the mixture was extracted with a large amount of ether, the ether solution extracted with sodium bicarbonate, dried with calcium chloride and evaporated it deposited 1.7 g. of unchanged amide. The residue, distilled through a short column, boiled 66–71° (3 mm.). The product gave a qualitative test for nitrogen.

Anal. Calcd. for $C_{10}H_{17}N$: C, 79.41; H, 11.33. Found: C, 80.32; H, 11.28.

When burned in oxygen the sample (14 mg.) exploded with such violence that it shattered the combustion tube. The above analysis is of a sample burned in air. The composition of the compound was made certain by treatment with strong alcoholic potassium hydroxide which produced in good yield the original 230° amide, leaving no doubt that the liquid was the corresponding nitrile.

Preparation of Trimethylhexahydrobenzoyl Chloride.—A mixture of 90 cc. of purified thionyl chloride and 180 g. of hexahydromesitylene carboxylic acid was allowed to stand for four hours, during which time hydrogen chloride was evolved rapidly. The acid chloride was then distilled *in vacuo* (20 mm.), and there was obtained:

Fraction	B. p., °C.	Weight, g.
Forerun		6.0
Fraction I	102–104	27.0
Fraction II	104	111.0
Flask residue	.....	42.0

The flask residue when hydrolyzed yielded 14.0 g. of a neutral fraction from which nothing could be obtained, 21.0 g. of mesitylene carboxylic acid and 7.0 g. of hexahydromesitylene carboxylic acid. This represents a yield of 79% and a recovery of 91%. In most preparations the amount of mesitylene carboxylic acid recovered was much smaller, representing more complete reduction of the original material. The acid chloride was a clear colorless liquid with a pungent odor, $n^{20}D$ 1.472, d^{20}_4 1.01.

Preparation of Methyl Ester of Trimethylhexahydrobenzoic Acid.—Methyl alcohol (75 cc.) was added to 51 g. of trimethylhexahydrobenzoyl chloride and heated in an all-glass apparatus on the steam-bath overnight. The ester was taken up in ether, washed with water and bicarbonate solution, dried over sodium sulfate and distilled. All of the material came over between 90 and 96° at 14 mm.; recovery 96%; $n^{20}D$ 1.452; b. p. 93° (14 mm.); d^{20}_4 0.934.

Anal. Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94. Found: C, 72.14; H, 11.22.

Reaction of Ester with Methylmagnesium Chloride.—In the Zerewitinoff machine the ester gave off gas very slowly at 100° and a white solid separated. The total amount of gas given off after heating for one and one-quarter hours at 100° was 0.25 mole. When 29.5 g. of the ester was added dropwise to a solution in boiling benzene of methylmagnesium chloride prepared from 24 g. of magnesium, heat was evolved and solid separated. The suspension was boiled for thirty-six hours, and decomposed with ice and hydrochloric acid. Fractionation through a 50-cm. column at 15 mm. pressure gave:

Fraction	B. p., °C.	Weight, g.
Fraction I	83–92.2	5.3
Fraction II (unchanged ester)	93.4–94.2	11.0
Flask residue	.....	4.4

Anal. of Fraction II. Calcd. for $C_{11}H_{20}O_2$: C, 71.69; H, 10.94. Found: C, 73.60; H, 11.25.

The low-boiling fraction was redistilled and the material boiling 84.5 to 86° was analyzed.

Anal. Calcd. for $C_{12}H_{22}$: C, 86.65; H, 13.33. Found: C, 86.26; H, 13.63.

Comparison of physical properties ($n^{20}D$ 1.444, d^{20}_4 0.831) with the hydrocarbon obtained by dehydration of the tertiary alcohol $(CH_3)_3C_6H_8C(OH)(CH_3)_2$ showed that the material was still impure.

Addition of $(CH_3)_3C_6H_8COCl$ to Methylmagnesium Chloride.—Methylmagnesium chloride was prepared from 60 g. of magnesium in one liter of ether solution in a two-liter three-necked flask. Dry benzene was added and the

(17) This analysis was performed by Mr. H. S. Wight.

solution boiled until the temperature of the vapor was 75° and the volume of the solution approximately 800 cc. Hexahydrotrimethylbenzoyl chloride (100 g.) dissolved in 200 cc. of benzene was added slowly with vigorous stirring. The resulting paste was boiled for one-half hour, then poured into iced hydrochloric acid. The mixture was extracted with ether, and the ether layer was washed with water and sodium bicarbonate. Most of the benzene was evaporated and the residue was distilled at 9 mm.

Fraction	B. p., °C.	Weight, g.
Forerun	60–86	5.0
Fraction II	86–87	46.0
Fraction III	87–95	17.0
Flask residue	...	16.8

Fraction III was redistilled along with the flask residue and there was obtained 17.0 g. more of hexahydroacetomesitylene, b. p. 86–87°, and 14.5 g. of a solid boiling at 105° at 11 mm. This represents a 5.5% yield of the low-boiling material, which was shown to be the same hydrocarbon as that obtained from the action of methylmagnesium chloride on the ester and of dehydrating agents on the alcohol, a 70% yield of hexahydroacetomesitylene and a 16% yield of the solid $(CH_3)_3C_6H_8C(OH)(CH_3)_2$; total recovery, 91% of the theoretical. The same ketone was produced when methylzinc chloride prepared by the addition of anhydrous zinc chloride to a solution of methylmagnesium chloride was treated with trimethylhexahydrobenzoyl chloride, but the yield was only 55% of the theoretical.

Hexahydroacetomesitylene, $(CH_3)_3C_6H_8COCH_3$.—The ketone was a colorless liquid, b. p. 86–87° (9 mm.), 93–94° (15 mm.), 97–98° (25 mm.), $n^{20}D$ 1.452; d^{20}_4 0.892. *MR* obsd., 50.85; calcd., 50.83; surface tension at 25°, 30.9; parachor, calcd. 445.7; found 445.

Anal. Calcd. for $C_{11}H_{20}O$: C, 78.50; H, 11.98. Found: C, 78.76; H, 12.21. Found[18]: C, 78.93; H, 12.41.

The ketone had a faint pleasant odor and was quite volatile with steam. It gave no iodoform test by Fuson's method.[19] When hexahydroacetomesitylene was treated with Grignard reagent in the Zerewitinoff apparatus it gave off gas slowly in the cold. The total amount of gas evolved was 0.84 equivalent and the total amount of reagent which added was only 0.05 equivalent.[20] When 20.0 g. of hexahydroacetomesitylene was treated with two equivalents of ethylmagnesium bromide at 0° for thirty minutes, gas was given off slowly during the addition (acetomesitylene reacts more vigorously). When distilled at 10 mm. the product of decomposition of the clear colorless Grignard solution boiled over a range of seven degrees but refractive index measurements indicated that not more than a negligible amount of addition had occurred. Boiling the ketone with ethylmagnesium bromide in ether solution for two hours produced between 12 and 25% of by-products.

Hexahydromesityldimethylcarbinol, $(CH_3)_3C_6H_8C(OH)(CH_3)_2$, was a white solid which boiled at 106° under 10 mm. pressure. It was extremely soluble in all the ordinary organic solvents, but could be recrystallized from methanol–water mixtures, forming stout needles, m. p. 67–69°.

Anal. Calcd. for $C_{12}H_{24}O$: C, 78.19; H, 13.12. Found[21]: C, 78.43, 78.66; H, 12.53, 12.58. Found[22]: C, 78.56; H, 12.91.

When treated with Grignard reagent in the Zerewitinoff apparatus,[20] the alcohol gave off 1.12 equivalents of gas rapidly in the cold. When treated with phenyl isocyanate it reacted vigorously at 120°, but the only product isolated was diphenyl urea. When treated with acetyl chloride or acetic anhydride the hydrocarbon $C_{12}H_{22}$ was produced in good yield. The sample of this hydrocarbon redistilled for analysis boiled 70.8–71.2° (10 mm.), $n^{20}D$ 1.4605, d^{20}_4 0.831, *MR* calcd. 54.97, found 54.83.

Anal. Calcd. for $C_{12}H_{22}$: C, 86.65; H, 13.33. Found[17]: C, 86.60; H, 13.43.

The same hydrocarbon was produced when 5.0 g. of the alcohol was shaken for two weeks with a mixture of 75 cc. of water, 7.5 g. of sodium hydroxide, and 7.5 g. of bromine.

When 4.0 g. of the alcohol was added to 15 cc. of concentrated hydrochloric acid at −5° and dry hydrogen chloride bubbled through the mixture, the solid disappeared and was replaced by a layer of clear liquid. This was separated from the aqueous layer, washed with water, dried over sodium carbonate and distilled through a small column. The main fraction boiled 94.6–97.1° (9 mm.) and was a clear, almost odorless liquid, $n^{20}D$ 1.472. It was allowed to stand overnight before redistillation, and this time it gave off hydrogen chloride and the sole product was the same hydrocarbon obtained in the dehydration of the alcohol. Lack of material prevented repetition of the reaction.

Determination of Structure of the Hydrocarbon $C_{12}H_{22}$.—A solution of 4.1 g. of the hydrocarbon in 30 cc. of glacial acetic acid was treated with 4% ozone at room temperature. The ozone was absorbed quantitatively at first, but after about two-thirds of the theoretical amount had been taken up absorption ceased. The ozonide was rinsed into a hydrogenation bottle with glacial acetic acid and hydrogenated with palladium catalyst. There was an induction period of nearly an hour before the catalyst began to be reduced. The solution then took up one-third of the theoretical quantity of hydrogen in about twenty minutes, after which absorption stopped. The solution, after filtering off the catalyst, gave a faint test with hypoiodite and a strong test with ammoniacal silver nitrate. When 2,4-dinitrophenylhydrazine was added to a portion of the product the dinitrophenylhydrazone of formalde-

(18) By H. S. Wight.

(19) R. C. Fuson, THIS JOURNAL, **56**, 1638 (1934).

(20) This determination performed by Mr. Richard Cramer.

(21) These analyses by the Arlington Laboratories, Arlington, Va. The sample had been distilled three times through a 3-ft. (90-cm.) column. The boiling point was constant at 105.9° (10 mm.). Unfortunately it was necessary to distil rather rapidly to prevent the product solidifying in the condenser. The freezing point of the product was 50.4°. The material was a white waxy-looking solid.

(22) This analysis was performed by H. S. Wight. The sample had been recrystallized four times from methanol–water solution and melted at 67–69°. The analyses do not distinguish very well between the tertiary alcohol and the corresponding secondary alcohol, $(CH_3)_3C_6H_8CH(OH)CH_3$ (calcd.: C, 77.58; H, 13.03). The composition of the ketone is also very close to the same figure (calcd.: C, 78.49; H, 11.98). The chemical evidence leaves no doubt about the structure.

hyde was obtained, identified by a mixed melting point with an authentic sample. No other crystalline substance was isolated. The original solution, after oxidation with ammoniacal silver nitrate, no longer gave a detectable amount of iodoform when hypoiodite was added, proving that acetone was absent.

An attempt to isolate hexahydroacetomesitylene from the product of ozonization by condensation with benzaldehyde and formation of the dibromide of the benzal compound gave such a small amount of product (identified by a mixed melting point) that it might conceivably have come from a trace of ketone present as an impurity in the hydrocarbon before ozonization, so this cannot be considered a proof of structure.

Better evidence was furnished by bromination of the unsaturated hydrocarbon: 9.5 g. of crude material in 50 cc. of carbon tetrachloride was cooled in an ice-bath and a solution of 9.0 g. of bromine in 30 cc. of carbon tetrachloride was added slowly. Hydrogen bromide was evolved almost immediately. The solution was decolorized with sodium bisulfite, filtered, and washed with sodium bicarbonate. When the carbon tetrachloride was pumped off and the remaining oil distilled under reduced pressure, it boiled 60–135° (10 mm.) with no evidence of any pure substance being present. The distillate was mixed with methyl alcohol and cooled in dry-ice until it deposited about 1.5 g. of gummy crystals which were filtered off and recrystallized from methanol to give a product melting at 41–42°. The analysis indicated that it was the unsaturated monobromohydrocarbon $(CH_3)_3C_6H_8C(CH_3)=CHBr$. It was not investigated further.

Anal. Calcd. for $C_{12}H_{21}Br$: C, 58.77; H, 8.63. Found[17]: C, 58.78; H, 8.38.

Reaction of Trimethylbenzoyl Chloride with CH_3MgCl.—Trimethylbenzoyl chloride was treated with methylmagnesium chloride under exactly the same conditions as had been used in the preparation of hexahydroacetomesitylene. From 103.0 g. of the acid chloride there was obtained 79.9 g. of acetomesitylene, $n^{20}D$ 1.517–1.519 ($n^{20}D$ of purest sample on hand 1.5190). There was also obtained 4.8 g. of forerun, refractive index 1.515, and 4.0 g. of high-boiling material. This high-boiling material was shaken with copper acetate and there was obtained 3.2 g. of the copper enolate of dimesitoylmethane. This represents a 90% yield of acetomesitylene and leaves only 1.25% of the liquid obtained unidentified. Therefore it is estimated that there could not have been more than 1 or 2% of addition to the carbonyl group under conditions where hexahydroacetomesitylene adds to the extent of 16%.

Reduction of Hexahydroacetomesitylene. Preparation of $(CH_3)_3C_6H_8CHOHCH_3$.—A solution of 10 g. of hexahydroacetomesitylene in 100 cc. *t*-amyl alcohol was heated on the steam-bath and metallic sodium (8 g.) was added in small pieces over a period of six hours. The mixture was heated six hours more, let stand overnight, then treated with methyl alcohol and water to destroy traces of sodium remaining. The resulting emulsion was poured into water, extracted with ether and the ether solution steam distilled. The steam distillate was extracted with ether, dried over sodium sulfate, and distilled at 8 mm. After 1.5 g. of forerun boiling at 76–97°, there was obtained 6.3 g. of secondary alcohol, b. p. 97.5–98.2°, $n^{20}D$ 1.470. A second distillation divided the material into three fractions boiling at 94–99.5° (8 mm.), $n^{20}D$ of all three fractions 1.4700, $n^{20}D$ of flask residue 1.4701. The fraction taken as an analytical sample boiled at 99.5°, d^{20}_4 0.905, *MR* obsd., 52.5; calcd., 52.35.

Anal. Calcd. for $C_{11}H_{22}O$: C, 77.58; H, 13.03. Found[17]: C, 77.36; H, 12.83.

Phenylurethan of Methylhexahydromesityl Carbinol.—Two cc. of the secondary alcohol was mixed with 2 cc. of phenyl isocyanate and heated in an oil-bath. Reaction began when the temperature reached 130°. The mixture was heated for one-half hour at 150° then cooled in ice, when 1.0 g. of solid material was precipitated melting around 100°. Three recrystallizations from ether–petroleum ether raised the melting point to 130–132°. Three more recrystallizations from ligroin raised the melting point slightly to 132–134°.

Anal. Calcd. for $C_{18}H_{26}O_2N$: C, 74.72; H, 9.41; N, 4.84. Found[17]: C, 74.94; H, 9.28; N, 5.24.

Alkaline Bromination of Hexahydroacetomesitylene. Preparation of $(CH_3)_3C_6H_8COCHBr_2$.—When 5 g. of hexahydroacetomesitylene was shaken for seventy-four hours with 100 cc. of a 10% solution of bromine in 10% sodium hydroxide, the organic material increased in density sufficiently to cause it to settle to the bottom of the flask. When it was distilled some decomposition was evident and on redistillation more decomposition occurred. The distillate crystallized on standing and was recrystallized three times from petroleum ether to give a substance melting at 63–65°.

Anal. Calcd. for $C_{11}H_{18}OBr_2$: Br, 49.01. Found:[21] Br, 48.90.

From the aqueous hypobromite layer was recovered a very small amount of acid which gave an amide melting at 215–225° after three recrystallizations. A mixture with the 230° amide melted at 220–228°.

Condensation of Hexahydroacetomesitylene with Benzaldehyde.—Finely ground sodamide (12 g.) was suspended in 100 cc. of benzene and 42.0 g. of hexahydroacetomesitylene was added. Benzaldehyde (30.0 g.) was added slowly to the suspension of ketone and sodamide and a vigorous reaction ensued. A gelatinous solid was produced which was allowed to stand for six hours, then extracted with ether and water. The ether layer was treated with a saturated solution of sodium bisulfite to remove excess benzaldehyde and then washed thoroughly with sodium bicarbonate solution and water. When the ether was evaporated and the residue distilled in a Claisen flask at 15 mm., 12.8 g. of unchanged ketone was recovered (30% of the starting material). The pressure was then reduced to 2.5 mm. and 43.7 g. of the unsaturated ketone distilled over as a yellow viscous oil at 160–165° (68% yield). The flask residue weighed 8.4 g. but only a trace of the dibromide of benzalacetohexahydromesitylene could be recovered from it when it was treated with bromine. Redistillation of the main fraction gave a pale yellow liquid, b. p. 148–150° (0.5 mm.). This was again distilled and an analytical sample, b. p. 148.0° (0.5 mm.), was removed, $n^{20}D$ 1.562, d^{20}_4 0.994; *MR* obsd., 83.62; calcd., 79.09. The yellow liquid crystallized in dry-ice but melted again below 0°.

Anal. Calcd. for $C_{18}H_{24}O$: C, 84.34; H, 9.44. Found: C, 84.59; H, 9.74.

Dibromide of Benzalacetohexahydromesitylene, $C_6H_5CHBrCHBrCOC_6H_8(CH_3)_3$.—When the unsaturated ketone was treated with a solution of bromine in carbon tetrachloride and the carbon tetrachloride evaporated, there remained a white solid melting near 180°. Three recrystallizations from benzene brought the melting point to 211–212° (with slight decomposition).

Anal. Calcd. for $C_{18}H_{24}OBr_2$: C, 51.95; H, 5.81. Found[17]: C, 52.50; H, 6.04.

Preparation of $C_6H_5COCH_2COC_6H_8(CH_3)_3$.—A solution of 1.8 g. of the dibromide, $C_6H_5CHBrCHBrCOC_6H_8(CH_3)_3$ in 10 cc. of methyl alcohol was heated for thirty minutes on the steam-bath with 0.75 g. of potassium hydroxide. The solution was acidified with hydrochloric acid and again heated for thirty minutes. Fifty cc. of water was added, the solution extracted with ether, and the ether layer shaken with saturated cupric acetate solution. The copper derivative of the beta-diketone was soluble in ether. When the ether layer was evaporated to dryness and the resulting solid recrystallized from ether–petroleum ether, there was obtained 1.2 g. of crystals, m. p. 195–200° (90% yield). Two more recrystallizations gave an analytical sample with m. p. 197–199°.

Anal. Calcd. for $C_{36}H_{46}O_4Cu$: C, 71.20; H, 7.65. Found[17]: C, 71.19; H, 7.81.

Hydrogenation of Unsaturated Ketone. Preparation of $C_6H_5CH_2CH_2COC_6H_8(CH_3)_3$.—When benzalacetohexahydromesitylene was hydrogenated with Adams catalyst it took up exactly one equivalent of hydrogen. The product boiled between 179 and 187°, and when redistilled for analysis boiled 180–182° (8 mm.), $n^{20}D$ 1.514, d^{20}_4 0.967; *MR* obsd., 80.4; calcd., 79.56. The analytical sample was a pale yellow liquid, indicating that the material still contained some unchanged unsaturated ketone.

Anal. Calcd. for $C_{18}H_{26}O$: C, 83.68; H, 10.15. Found[18]: C, 83.35; H, 10.34.

Reaction of Benzalacetohexahydromesitylene with Phenylmagnesium Bromide.—Five grams (0.0195 mole) of unsaturated ketone was added rapidly to a solution of phenylmagnesium bromide prepared from 1.05 g. (0.045 mole) of magnesium. The solution boiled during the addition but remained colorless and clear. It was allowed to stand for eight hours under nitrogen, then cooled in ice and decomposed by the addition of iced dilute hydrochloric acid. The mixture was allowed to stand overnight under nitrogen, then extracted with water and steam distilled to remove diphenyl and bromobenzene. The residue from the steam distillation was extracted with ether, dried over calcium chloride, evaporated, and diluted with petroleum ether. Cooling in dry-ice caused the mixture to solidify, and after allowing it to warm to room temperature 3.5 g. of an oily solid was filtered off. The remaining 2.5 g. of oil would deposit no more solid material. The solid, after three recrystallizations from petroleum ether, melted at 78–80° and a mixture with β,β-diphenylpropiomesitylene melted below 60°.

Anal. Calcd. for $C_{24}H_{30}O$: C, 86.18; H, 9.05. Found[17]: C, 86.38; H, 8.88.

Enol Peroxides of β,β-Diphenylpropiohexahydromesitylene.—A solution of phenylmagnesium bromide was prepared from 1.9 g. of magnesium, and to this was added 10 g. of $C_6H_5CH{=}CHCOC_6H_8(CH_3)_3$ dissolved in dry ether. The solution was boiled for fifteen minutes, then poured into a mixture of 500 cc. of ice, 50 cc. of concentrated hydrochloric acid, and 250 cc. of water. The mixture formed an emulsion with a clear ether layer on top. The ether layer was removed, washed three times with ice-water and diluted to 200 cc. Oxygen was passed into this solution for several hours until it had evaporated to 50 cc., then 100 cc. of petroleum ether was added and oxygen passed in until the solution had evaporated to a yellow viscous oil. The oil was allowed to stand overnight in ice, then cooled in dry-ice, when it deposited 2.0 g. of crystals melting over a wide range around 75°. Recrystallization from ether and petroleum ether gave 0.1 g. or less of material melting at 119–121° and 1.3 g. melting 83–87°. Both substances depressed the melting point of β,β-diphenylpropiohexahydromesitylene, of β,β-diphenylpropiomesitylene and its enol peroxide. Both substances liberated a small amount of iodine from acidified potassium iodide solution and both decomposed vigorously when heated slightly above the melting point. When the higher-melting substance was mixed with the lower-melting peroxide the mixture melted at the same point as the lower-melting substance alone. Both substances were soluble in ether, the higher-melting one much less than the other, and both were precipitated by petroleum ether in micro-crystalline form.

Anal. Calcd. for $C_{24}H_{30}O_3$: C, 78.65; H, 8.25. Found[17]: (87° peroxide) C, 79.51, 79.56; H, 8.83, 8.57: Found[21]: (87° peroxide) C, 79.34; H, 8.56. Found[17]. (133° peroxide) C, 78.51; H, 8.43.

There was not enough of the higher-melting peroxide to investigate further. When the preparation of the peroxide was repeated 10.8 g. of crude solid peroxide (50% yield) was obtained from 20.0 g. of benzalacetohexahydromesitylene, but this was found to be entirely the 86–87° material, and none of the higher-melting peroxide could be isolated.

Preparation of Hydroxyketone.—Both peroxides took up hydrogen very rapidly, but the amount of the higher melting substance available was so small that the quantitative results were not significant. When 0.666 g. of the 87° peroxide was dissolved in 50 cc. of absolute alcohol and hydrogenated with Adams catalyst, it took up 34.0 cc. of hydrogen (90% of the theoretical amount). When the alcohol solution was filtered and evaporated, a yellow oil was obtained which deposited 0.25 g. of white crystals melting at 81–84°. After two more recrystallizations from petroleum ether the melting point was 86–87°; mixed melting point with 87° peroxide 75–80°.

Anal. Calcd. for $C_{24}H_{30}O_2$: C, 82.23; H, 8.62. Found[17]: C, 82.00; H, 8.76.

The product is therefore a hydroxyketone, analogous to the substance $(CH_3)_3C_6H_2COCHOHCH(C_6H_5)_2$ obtained in the mesitylene series.[11]

Thermal Decomposition of the Peroxide.—When 1.5 g. of crude peroxide (m. p. 85°) was dropped into a hot test-tube it decomposed with a rush, giving off quantities of gas. When the residue was cooled and extracted with sodium bicarbonate only a trace of acidic material was ob-

tained. This was taken up in ether, dried, evaporated to dryness and treated with thionyl chloride. When the thionyl chloride solution was poured into an excess of iced ammonium hydroxide, the precipitate was barely visible and embedded in a yellow oil. When washed with ether it melted at 165–170° and lowered the melting point of the 167° amide thirty degrees. The melting point of a mixture with the 232° amide was 180–190°. Apparently the substance was not the amide of hexahydromesitylene carboxylic acid. No conclusions can be drawn from this evidence as to the structure of the peroxide, since apparently most of the material gave up its oxygen without cleavage. The remaining neutral material when treated with hydroxylamine deposited a trace of crystalline material which analysis showed to be a hydrocarbon, m. p. 200–205°.

Anal. Found[17]: C, 92.64; H, 6.83. No other crystalline material could be isolated.

Summary

The preparation and properties of one of the six possible geometric isomers of hexahydroacetomesitylene are described.

Investigation of this isomer of hexahydroacetomesitylene and some of its derivatives indicates that this particular configuration of the trimethylcyclohexane ring offers slightly less hindrance to the reactions of a ketone group adjacent to the ring than does the mesitylene nucleus.

RECEIVED DECEMBER 8, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

The Separation of the Isomeric Hexenes by Batch Fractionation

BY ARTHUR ROSE

The maximum sharpness of separation between any two components in a batch fractionation may be estimated by an extension of the reasoning of Sydney Young[1] and of Rayleigh[2] as will soon be described in detail elsewhere.[3] The present paper applies this line of reasoning to the separation of the isomeric hexenes so as to obtain a definite idea of the fractionating efficiency required and the results to be expected in attempts at such separations.

The Vapor Pressure Ratios of the Hexenes.—In order to estimate the maximum possible sharpness of separation for any pair of substances it is necessary to know the vapor pressure ratio (α) for the pair. These may be obtained for the hexenes by using the boiling points of Schmitt and Boord[4] and the boiling point correction method cited by Eaton.[5] Thus 2-ethyl-1-butene boils at 66.45° at 760 mm. while 3-hexene boils at 66.8°. At this temperature the b. p. correction would be about 0.042° per mm., so that at 66.8° the vapor pressure of 2-ethyl-1-butene must be about 768 mm. and *alpha* for this pair must be about 768/760 = 1.011.

(1) Sydney Young, "Distillation Principles and Processes," Macmillan Co., London, 1922, p. 117.

(2) Walker, Lewis, McAdams and Gilliland, "Principles of Chemical Engineering," p. 532, McGraw-Hill Book Co., New York, N. Y., 1937; also Badger and McCabe, "Elements of Chemical Engineering," McGraw-Hill Book Co., Inc., New York, N. Y., 1936, p. 336.

(3) Arthur Rose and L. M. Welshans, *Ind. Eng. Chem.*, **32**, May (1940).

(4) Schmitt and Boord, THIS JOURNAL, **54**, 751 (1932); **53**, 2427 (1931).

(5) E. S. Beale, "Science of Petroleum," Vol. II, Oxford University Press, Oxford, 1937, p. 1280, etc.

The values in Table I were obtained in a similar manner. In every case only three significant figures are retained but in dropping excess figures the value of *alpha* was increased, except for pair A, so the other pairs are actually more difficult to separate than the values of *alpha* indicate.

TABLE I

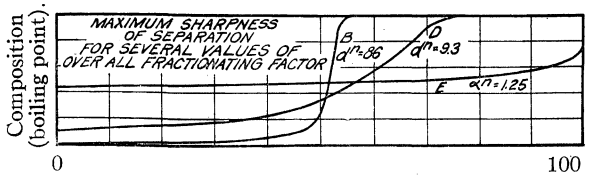
	Hexene pair	Alpha
(A)	2-Ethyl-1-butene and 3-hexene	1.01
(B_1)	2-Methyl-2-pentene and 3-methyl-2-pentene-*trans*	1.02
(B_2)	3-Hexene and 2-methyl-2-pentene	1.02
(B_3)	3-Methyl-2-pentene-*cis* and 3-ethyl-1-butene	1.02
(C)	2-Ethyl-butene-1 and 2-methyl-2-pentene	1.03
(D)	3-Methyl-2-pentene-*cis* and -*trans*	1.07

The estimates of maximum sharpness of separation to be given below assume that α is constant over the temperature range and concentrations involved in the distillations. The temperature ranges involved are so narrow that the variation in α from this source may certainly be disregarded. The conclusions of Beatty and Calingaert[6] make it reasonable to assume that none of the hexene mixtures would depart sufficiently from ideality to alter the general nature of the conclusions to be drawn in this paper.

Distillation Curves to be Expected.—It can be shown[3] that a distillation curve with a maximum sharpness of separation approximately like that

(6) H. A. Beatty and G. Calingaert, *Ind. Eng. Chem.*, **26**, 504 (1934).

of curve E in Fig. 1 would be obtained if the column employed had only a sufficient number of plates (n) so that the over-all fractionating factor (α^n) would be 1.25. Thus α^n would need to be



Per cent. distilled over.

Fig. 1.

1.25 where α is the vapor pressure ratio of the pair being separated and n is the equivalent number of plates used in the separation. The zero of the horizontal coördinates on the figure coincides approximately with the beginning of the plateau of the *lower boiling* component, and the 100 of the horizontal coördinates coincides approximately with the end of the plateau of the higher boiling component of the pair being separated. On this basis the number of plates required to obtain a separation like that indicated by curve E would be as listed in Table II.

TABLE II

Pair	Plates required for curve E
A	22
B	11
C	8
D	4

In other words the number of plates indicated would lead to no noticeable separation.[7] In Table III, from similar[3] calculations, are given the number of plates necessary to obtain the reasonable separation indicated by curve D or the sharp separation of curve B of Fig. 1.

TABLE III

Pair	α	Plates required Curve D $\alpha^n = 9.3$	Curve B $\alpha^n = 86$
A	1.01	224	450
B	1.02	112	224
C	1.03	75	150
D	1.07	33	66

Interpretation of Curves.—In studying curves B, D and E of the figure it should be recalled that the vertical coördinates have been greatly stretched and the horizontal coördinates compressed. Actually for the case of the hexenes under discussion the entire vertical scale of the figure represents only about 0.3, 0.6, 0.9, 2.0°, for pairs A, B, C and D, respectively. As stated above, the entire length of the horizontal scale of the figure corresponds approximately with the distance from the beginning of the plateau of the low boiler to the end of the plateau of the high boiler of the particular pair under discussion. Thus curve E indicates no separation at all. Curve D represents a separation in which the intermediate fraction is about 40% of the combined amount of the two components being separated, and curve B a good separation in which the intermediate fraction is only about 5% of the combined amount of the two components being separated.

Comparison with Results of Goldwasser and Taylor.—These authors[8] have recently described the separation of isomeric hexenes with a modified Podbielniak–Simons type column, and it is of interest to compare their results with those to be expected from the above calculations. The comparison must be approximate because the small scale of the distillation curves in their paper makes it difficult to interpret them accurately. One case has been worked out in some detail. In Fig. 2 of the paper by Goldwasser and Taylor there is shown the separation of a hexene boiling at 67.5° from another boiling at 67.8°. The value of α for such a pair would be approximately 1.01. The combined amount of these two components corresponds to a length of 16.8 mm. on their figure, the length of the intermediate cut is about 3 mm., so the intermediate cut is about 18% of the total amount of the two components. Assuming a 95% purity along the plateaus as stated by Goldwasser and Taylor, this would require[3] α^n to be about 70, and with α = 1.01 it would require about 425 plates to achieve this separation, if it was carried out in the absence of other components and under total reflux in a column with zero holdup. The assignment of 3 mm. to the length of the intermediate cut is rather arbitrary but even if 6 mm. were assigned the minimum plates required would be 350. The separations of hexene pairs boiling at 67.8 and 68.0°, and 67.2 and 67.5° would require a similar efficiency; in fact, all except the first four pairs shown on this figure would require in excess of 200 theoretical plates for the separations indicated. Deviations from ideality and the presence of additional components would not be expected to change the order

(7) Data obtained in this Laboratory since these calculations were made confirm these predictions; see Whitmore, *et al.*, **62**, 795 (1940).

(8) S. Goldwasser and H. S. Taylor, THIS JOURNAL, **61**, 1751 (1939).

of magnitude of the number of plates required, but consideration of the holdup and the 30 to 1 reflux ratio actually used in these distillations would certainly increase the estimates considerably.[9]

Consideration of Holdup and Reflux Ratio.—All the above computations are on the assumption that reflux was nearly total and that holdup was zero so that the conclusions are for maximum sharpness of separation and minimum plates required. No statement of the holdup in the Podbielniak–Simons–Taylor[8] column is given but it must be appreciable compared with the amount of any one component and quite large compared with the amounts of the components present in small amount so that the separations involving these would be expected to be much less sharp than the above discussion indicates.

(9) Arthur Rose, L. M. Welshans and H. H. Long, *Ind. Eng. Chem.*, **32**, May (1940).

Summary

Calculations have been made to show that a minimum of 400 or more theoretical plates are required for sharp separation of certain close boiling hexenes, and that the use of a fractionating column with a small number of theoretical plates can produce no appreciable separation in such cases even with low holdup and high reflux ratio.

STATE COLLEGE, PA. RECEIVED NOVEMBER 20, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Attempted Separation of Isomeric Hexenes by Fractional Distillation

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These laboratories have long been interested in the separation of difficult mixtures, especially of olefins, by fractional distillation. Consequently, it was hoped that the recent work by Goldwasser and Taylor[1] would point the way to separations hitherto not possible. We are indeed sorry to have to report that this hope has not been realized.

The Podbielniak–Simons–Taylor column[1] seems to be an excellent one of its type but has an efficiency of only about fifteen theoretical plates. Whereas the published results[1] seem to indicate a successful separation of six hexenes with a total boiling point spread of 2.5°, we have found it impossible to obtain separations even with two binary mixtures of pure hexenes having boiling point spreads of 1.5 and 2.7°, or with a ternary mixture having an over-all spread of 2.7°.

It is interesting to note that a calculation of the column efficiency needed to effect the indicated separation of the six hexenes[1] gives a value of at least 450 theoretical plates.[2]

Goldwasser and Taylor[1] use the boiling point and density to identify an olefin. This is at least difficult because of the conflicting values recorded for these constants.

Inconsistencies appear in the paper.[1] Thus, on pp. 1753–1754 there is a confusion of the *cis* and *trans* forms of 3-methyl-2-pentene. Agreement with the work of van Risseghem[3] is cited "to emphasize the confidence that may be placed in the fractionations obtained." As a matter of fact such agreement is lacking. The authority cited[3] obtained three fractions in the careful distillation of the hexenes from 3-methyl-3-pentanol, *viz.*: I, b. p. 65.1–65.7°; II, 67.2–67.8°; III, 69.9–70.2°. She states that I and III are stereoisomers of 3-methyl-2-pentene and that II is a mixture containing some of the methylene isomer. The boiling points given by Goldwasser and Taylor (Table 1a[1]) for the two 3-methyl-2-pentenes are 65.7–66.2° and 67.6–68.2°. These differ from those actually reported by van Risseghem,[3] which are 65.1–65.7° and 69.9–70.2°.

In certain cases where geometrical isomerism is possible, one constant used for identification[1] belongs to the *trans* form, while the other belongs to the *cis*. The literature values given for the isomers of 3-hexene are: *cis*, b. p. 70–71.2°, d^{20}_4 0.7190; *trans*, 67.3–67.5°, 0.7170. However, in the dehydration of 1-hexanol, 3-hexene was identified by the observed values, 67.5° and 0.720.

For 4-methyl-2-hexene the accepted values[4] are:

(1) Goldwasser and Taylor, THIS JOURNAL, **61**, 1751, 1762, 1766 (1939).

(1a) Submitted in partial fulfillment for the Ph.D. degree.

(2) Rose, THIS JOURNAL, **62**, 793 (1940).

(3) Van Risseghem, *Bull. soc. chim. Belg.*, **47**, 47 (1938).

(4) Egloff, "Physical Constants of Hydrocarbons," Reinhold Publishing Company, New York, 1939. Doss, "Physical Constants of Principal Hydrocarbons," The Texas Company, New York, 1939.

1 isomer, b. p. 87.1–87.6°, d^{20}_4 0.7007; 2 isomer, 85.1–85.6°, 0.6981. In reporting the presence of 4-methyl-2-hexene the literature values given by Goldwasser and Taylor[1] are 85.1–85.6° and 0.7007 and the observed values[1] are 85.1–85.2° and 0.701.

The significance of the cyclopropane mechanism suggested[1] for the formation of the suspected isomeric olefins need not be discussed.[5]

Experimental

Distillation Equipment.—Column I was of the total condensation partial take-off type.[6] It was packed with 1/8-inch inside diameter single turn glass helices.[7] The packed section was 65 × 1.5 cm., and its efficiency was about 13 theoretical plates. A calibrated thermometer gave the head temperature.

Column II was also of the total condensation partial take-off type. It was packed with 3/32-inch single turn stainless steel helices made from no. 30 wire.[8] The packed section was 100 × 1.0 cm., and its efficiency equal to at least 35–40 theoretical plates. The still was heated by an air-bath that was controlled automatically by utilizing the pressure drop through the column. A calibrated thermometer gave the head temperature.

Column III was identical with Column I, but with a packed section 45 × 0.9 cm. It had an efficiency of about 12 theoretical plates.

Column IV was built exactly as described by Goldwasser and Taylor[1] in their reported separation of the isomeric hexenes. It was a Podbielniak type column, the section within the jacket being 150 × 0.45 cm. The jacket was evacuated to below 10^{-6} mm. The head was of the total condensation partial take-off type designed by Simons.[9] Column V was made exactly like Column IV, except that the jacket was air-filled instead of being evacuated. The efficiencies of columns IV and V are given in the next section.

Determination of Theoretical Plate Values.—The theoretical plate values were determined for columns IV and V using carbon tetrachloride–benzene mixtures.[10] This method was also used to determine the efficiencies of Columns I, II, and III.

The operating conditions varied with respect to rate of refluxing at the condenser and the control of the jacket temperature. Three rates of refluxing were used, namely, a very slow rate of one drop per minute, an intermediate rate of 150 drops per minute, and a very fast rate of approximately 360 drops per minute. The last was just below flooding. The jacket temperature for the two columns was varied 1° above and 1° below the head temperature, and in the case of Column V also 5° above and 5° below the head temperature. A typical run will be described in detail.

About 100 cc. of a carbon tetrachloride–benzene mixture in a 200-cc. flask was used in making the tests. The refractive indices, $n^{20}D$, of the carbon tetrachloride and benzene were 1.4595 and 1.4999, respectively. The column was brought to equilibrium with total refluxing at a rate just below flood stage. The jacket thermometers read 1° below the head thermometer. Samples of 1 cc. were taken from the flask and from the head at the end of each specified time. The following data will illustrate the operating conditions: reflux time fifteen minutes, bath 118°, jacket 74°, head 75°, flask $n^{20}D$ 1.4960, head $n^{20}D$ 1.4820, theoretical plates 12.6. Identical theoretical plate values were obtained at 60, 90, 120, and 180 minutes. Other runs duplicated this procedure and the results are summarized in Table I.

TABLE I

Condition	Theoretical plates with air jacket (Column V)	Theoretical plates with vacuum jacket (Column IV)
Rapid rate		
Jackets 1° below head	14.0	13.4
1° above	14.0	12.6
5° above	14.6	..
5° below	14.6	..
Intermediate rate		
Jackets 1° below head	11.7	12.1
1° above	..	12.7
5° above	10.8	..
5° below	13.7	..
Very slow rate		
Jackets 1° below head	11.4	11.5
1° above	11.4	12.7
5° above	..	..
5° below	12.5	..

Thus columns IV and V are equivalent under these test conditions to approximately 13 theoretical plates regardless of the rate of operation or the use of a vacuum jacket. This is to be compared with the value of 450 theoretical plates calculated by Rose and Welshans[2] as necessary for the separations reported by Goldwasser and Taylor.[1]

The above studies on distillation Columns IV and V were made according to the analytical technique used by Goldwasser and Taylor.[1] However, they did not report any test data. In addition, a separate investigation on the efficiency of Column IV, as well as on analytical distillation columns in general, gave the results summarized in Table II. These results show that the single-turn wire helices combine at one time the four important qualities so necessary in packing for analytical fractionating columns; namely, they are efficient as shown by the low H. E. T. P. values given in Column 4, they allow a high operating throughput as shown by Column 2, they have a low holdup as shown by Column 5, and they make possible operation at low pressure drops as shown by Column 6. The data presented are representative of hundreds of tests and it is believed that the manner of presentation of the data will facilitate the work of the designer of packed fractionating columns.

Preparation of 2-Ethyl-1-butene.—2-Ethyl-1-chlorobutane, b. p. 83° at 202 mm. and $n^{20}D$ 1.4222, was prepared

(5) *Cf.* Wallis in Gilman's "Organic Chemistry," John Wiley and Sons, New York, N. Y., 1938, pp. 733–736.

(6) Whitmore and Lux, THIS JOURNAL, **54**, 3451 (1932).

(7) Wilson, Parker and Laughlin, *ibid.*, **55**, 2795 (1933).

(8) Tongberg, Lawroski and Fenske, *Ind. Eng. Chem.*, **29**, 957 (1937).

(9) Simons, *Ind. Eng. Chem., Anal. Ed.*, **10**, 29 (1938).

(10) Fenske, Tongberg and Quiggle, *Ind. Eng. Chem.*, **26**, 1169 (1934).

TABLE II

SUMMARY OF DATA ON VARIOUS PACKINGS AT NORMAL PRESSURES

Packing	(1)[c] Column dia., mm.	(2)[d] Throughput l./hr./cm.^{2}	(3)[e] No. theo. plates	(4)[f] H. E. T. P., cm.	(5)[g] Holdup cc./theo. plate	(6)[h] Press. drop mm. Hg/theo. plate
A.[a] Open tube with no. 20 gage wire spiral (Column IV)	4.5	0.3	14	10.7	0.17	0.02
		.6	15	10.0	.19	.05
		1.0	16	9.4	.29	.10
B.[a] 1/8-in. i. d. single turn glass helices	10	0.2	11	3.9	.70	..
	10	.6	11	3.9	.77	..
	12	.2	21	3.8	..	..
	12	.6	18	4.3	..	..
C.[a] 1/16-in. i. d. single turn helices of no. 34 stainless wire	8	.3	55	1.3	.16	..
	25.4	.1	65	1.6	1.2	.02
	25.4	.2	62	1.7	1.6	.07
	25.4	.6	43	2.5	3.3	.65
D.[a] 3/32-in. i. d. single turn helices of no. 30 stainless wire	8	.4	27	2.6	0.29	..
	12	.4	37	2.2	.54	..
	25.4	.1	140	1.9	1.2	.013
	25.4	.2	126	2.1	1.6	.05
	25.4	.6	88	3.0	3.4	.57
	50.8	.1	58	3.9	13.5	.009
	50.8	.2	54	4.2	16.3	.048
	50.8	.6	44	5.2	31.0	.72
E.[b] Empty tube	9.5	.2	7.2	8.5	..	..
	9.5	.3	4.0	15.3	..	..
	19	.1	3.6	17.0	..	..
	19	.2	1.2	50.9	..	..
	19	.3	1.0	61.0	..	..
	25	.1	1.7	35.9	..	..
	25	.2	1.6	38.1	..	.
F.[b] Stedman packing No. 105	9.5	.21	56.4	1.08	0.14	.07
(Max. efficiency)	9.5	.30	41	1.49	.22	.23
(Max. rate)	9.5	.32	39	1.56	.24	.30
G.[b] Stedman Packing No. 104	19	.05	50.3	1.21	.21	.01
(Max. efficiency)	19	.10	44	1.4	.28	.05
	19	.20	31.5	1.93	.76	.42
(Max. rate)	19	.23	27.8	2.19	.92	.60
H.[b] Stedman Packing No. 112	25	.03	48.4	1.25	.19	.004
(Max. efficiency)	25	.10	31.1	1.96	.77	.10
	25	.20	25	2.42	1.36	.60
(Max. rate)	25	.22	24	2.54	1.50	.74

[a] Packings A, B, C, and D were tested in this Laboratory. [b] Packings E, F, G, and H were tested by Bragg, *Ind Eng. Chem., Anal. Ed.*, **11**, 283 (1939). [c] Column (1) is the inside diameter of the test fractionating column in mm. [d] Column (2) is the liquid boilup or throughput under total reflux as liters of liquid per hour per square cm. of column cross section. [e] Column (3) is the number of theoretical plates in the packed section of the fractionating column. With packings A, B, C, and D a series of careful tests were made under total reflux using pure binary hydrocarbon mixtures such as heptane–toluene, heptane–methylcyclohexane, and methylcyclohexane–toluene. Packings E, F, G, and H were tested with benzene–ethylene dichloride mixtures. [f] Column (4) is the height of packing in cm. equivalent to one theoretical plate. [g] Column (5) is the dynamic holdup in cc. per theoretical plate (cc. of liquid per theoretical plate retained in the packed section while operating). With packings A, B, C, and D the principle described in *Ind. Eng. Chem.*, **26**, 1215 (1934), was used to obtain such dynamic holdup data. With packings E, F, G, and H the holdup was obtained by diverting the vapors and measuring the liquid draining from the packing, allowing for the static holdup. However, such holdup values are believed to be definitely low, for static holdup values for this type of packing appear to be 0.05–0.1 cc. of liquid per cc. of packing, while the values reported for packings F, G, and H are about one-fifth to one-tenth of this value. [h] Column (6) is the pressure drop as mm. of mercury per theoretical plate for the corresponding throughputs tabulated in Column (2).

from 2-ethyl-1-butanol (Carbide and Carbon), 439 g. thionyl chloride, and pyridine in 74% yield.

A 2-liter three-neck flask was attached by one neck to Column I, set for total reflux, and a mercury-seal stirrer

and dropping funnel were placed in the other two necks. In the flask were placed 647 g. (14.5 moles) of absolute ethyl alcohol and 336 g. (6 moles) of potassium hydroxide. This mixture was heated to refluxing and stirred. When solution of the potassium hydroxide was complete, 439 g. (3.6 mole) of 2-ethyl-1-chlorobutane was added at the rate of one drop per second. After the addition of the halide had begun, the reflux temperature dropped from 76 to 54°. Product was then taken off at a reflux ratio of 20:1. The distillation was continued until the distillate did not form two layers upon the addition of water. The combined upper layers were washed several times with water, dried, filtered, and distilled through Column I. There resulted 64 g., or a 21% yield, of 2-ethyl-1-butene, b. p. 63° at 728 mm. and $n^{20}D$ 1.3967.

This olefin, combined with that obtained from a later run, was redistilled through Column II at 734 mm. to give fractions: 1, 2.0 g., b. p. 59–63.3°, $n^{20}D$ 1.3948; 2, 2.2 g., 63.6°, 1.3967; 3–11, 52.9 g., 63.6°, 1.3968; residue 5.5 g.

Fractions 4–10 were distilled at 733 mm. through Column IV following exactly the technique of Goldwasser and Taylor[1] to give fractions: 12, 3.0 g., b. p. 63.7°, $n^{20}D$ 1.3967; 13–16, 26.8 g., 63.8°, 1.3968; 17, 5.0 g., 63.8°, 1.3969; residue 2.0 g.

Only fractions 13–16 were used to make the isomeric hexene mixtures for the attempted separations using Column IV. Physical constants for the 2-ethyl-1-butene used were Cottrell b. p. (50%) 63.75 ± 0.05° at 731 mm., $n^{20}D$ 1.3968 ± 0.0001, d^{20}_4 0.6992 ± 0.0002.

It should be noted that this material is the best from successive distillations through Columns I, II, and IV.

Preparation of 2-Methyl-1-pentene.—Into a one-liter flask with a one-liter dropping funnel, a mercury-seal stirrer, a thermometer, and a reflux condenser was placed 77.4 g. (0.86 mole) of redistilled 2-methyl-3-chloro-1-propene (Shell Technical), b. p. 70.2–73.0° at 732 mm. and $n^{20}D$ 1.4270. Ethylmagnesium bromide prepared from 105 g. (0.96 mole) of redistilled ethyl bromide, b. p. 37.8° at 727 mm., and 23 g. (0.96 mole) of magnesium turnings was filtered through glass wool under nitrogen pressure into the dropping funnel. The Grignard reagent was added dropwise to the halide with vigorous stirring, keeping the reaction mixture below 0° with a salt–ice-bath. The addition was completed in twelve hours, and stirring was continued for an additional ten hours. To the reaction mixture surrounded by a salt–ice-bath was added with vigorous stirring 300 cc. of ice water, which was sufficient to dissolve the magnesium chloride. The layers were then separated and the ether layer washed once with water. The combined water layers were then extracted several times with ether, and the combined ether extracts dried over anhydrous potassium carbonate. The ethereal solution was then filtered and distilled through Column III, the ether being removed with a reflux ratio of 10:1. The distillation, carried out at 731 mm., yielded fractions: 1–5, 22.8 g., b. p. 34.5–60.0°, $n^{20}D$ 1.3616–1.3903; 6–11, 28.2 g., 61.0°, 1.3923–1.3925; 12–13, 6.7 g., 61.0°, 1.3933–1.3935.

Fractions 6–11, combined with 2-methyl-1-pentene from a similar run making a total of 54.4 g., were distilled through Column II at 737 mm. to give fractions: 14–16, 6.3 g., b. p. 41–61.3°, $n^{20}D$ 1.3794–1.3919; 17–18, 8.3 g., 61.3°, 1.3925; 19, 3.9 g., 60.5–61.3°, 1.3924; 20–21, 9.6 g., 61.3°, 1.3925; 22–23, 7.1 g., 61.3°, 1.3927.

Fractions 17, 18, 20, and 21 were distilled through Column IV at 737 mm. using the technique of Goldwasser and Taylor[1] with the resulting fractions: 24, 2.0 g., b. p. 61.3°, $n^{20}D$ 1.3923; 25–26, 7.2 g., 61.3°, 1.3925; 27–28, 5.3 g., 61.3°, 1.3926–1.3927.

Only fractions 25 and 26 were used with isomeric hexenes for attempted separation through Column IV. The physical constants for the 2-methyl-1-pentene used were Cottrell b. p. (50%) 61.35 ± 0.05° at 738 mm., $n^{20}D$ 1.3925 ± 0.0001, d^{20}_4 0.6817 ± 0.0002.

Preparation of 1-Hexene.—The method of preparation was similar to that used for 2-methyl-1-pentene. *n*-Propylmagnesium bromide was prepared from 615 g. (5 moles) of *n*-propyl bromide, b. p. 70–71° at 738 mm. and $n^{20}D$ 1.4340, and 121 g. (5 moles) of magnesium. This was added to 500 g. (4.1 mole) of allyl bromide, b. p. 70–71° at 735 mm. and $n^{20}D$ 1.4653. Ether was first removed through Column I at 739 mm. using a 10:1 reflux ratio. Continued distillation yielded fractions: 1–6, 62.8 g., b. p. 53–61.2°, $n^{20}D$ 1.3720–1.3886; 7–15, 82.7 g., 61.2–63.0°, 1.3886–1.3889; 16–21, 53.5 g., 63.0°, 1.3889–1.3885; 22–30, 74.6 g., 63.0°, 1.3883–1.3880.

Fractions 7–21 were distilled through Column II at 737 mm., and there resulted fractions: 31–36, 30.4 g., b. p. 60.3–60.7°, $n^{20}D$ 1.3901–1.3889; 37–39, 15.3 g., 60.7–62.5°, 1.3890–1.3897; 40, 4.6 g., 62.5°, 1.3893; 41–48, 32.8 g., 62.5°, 1.3890; 49–52, 9.3 g., 62.5°, 1.3889–1.3883.

Fractions 41–48 were distilled through Column IV at 733 mm. using the technique of Goldwasser and Taylor[1] to give fractions: 53–54, 7.0 g., b. p. 62.5°, $n^{20}D$ 1.3892; 55–57, 16.3 g., 62.5°, 1.3891; 58, 5.6 g., 62.5°, 1.3890; 59–60, 5.8 g., 62.5°, 1.3889.

Only fractions 55–58 were used with isomeric hexenes for attempted separation with Column IV. The physical constants for the 1-hexene used were Cottrell b. p. (50%) 62.52 ± 0.05° at 737 mm., $n^{20}D$ 1.3891 ± 0.0001, d^{20}_4 0.6873 ± 0.0002.

Table III shows a comparison of our physical constants with those of Boord and his co-workers.[11,12,13]

Attempted Separation of Isomeric Hexenes.—Three mixtures for distillation were made up as follows: 1, 15 cc. of 1-hexene (fractions 55–58) and 15 cc. of 2-ethyl-1-butene (fractions 13–16); 2, 11.6 cc. of 2-ethyl-1-butene (fractions 13–16) and 9.0 cc. of 2-methyl-1-pentene (fractions 25–26); 3, the distillates from the above two distillations were combined to give a mixture containing 50% 2-ethyl-1-butene, 26% 2-methyl-1-pentene, and 24% 1-hexene. The latter figures are weight %, and were calculated from refractive index–composition curves.

The procedure followed was exactly that used by Goldwasser and Taylor,[1] even to the extent of requiring one-half hour after the heat was applied for the material to boil. The rate of reflux was just below the flood stage, or approximately 360 drops per minute. The rate of

(11) Hull and Boord, Ohio State Univ., Abstr. Doctor's Dissertation, No. 18, 191, 1936.

(12) Schmitt and Boord, THIS JOURNAL, **53**, 2427 (1931); **54**, 754 (1932).

(13) Rudel, Thesis, Ohio State Univ., Sept., 1938.

TABLE III

Hexene	B. p., °C. Expt.	B. p., °C. Lit.	$n^{20}D$ Expt.	$n^{20}D$ Lit.	d^{20}_4 Expt.	d^{20}_4 Lit.
1-Hexene	63.4	63.4–63.7	1.3891[a]	1.3870	0.6873[a]	0.6732
2-Ethyl-1-butene	64.9	64.9–65.1	1.3968	1.3970	.6892	.6899
2-Methyl-1-pentene	62.2	61.5–62.0	1.3925	1.3921	.6827	.6817 .6831

[a] The higher values obtained were probably due to impurities of hexadiene not removable by distillation. Since our 1-hexene was a constant boiling constant index material during three distillations through efficient columns, it was suitable for checking Column IV.

take-off was 1 drop every five seconds. Jackets were kept within 0.1° of the reflux temperature. The reflux temperature was noted for every 0.2 cc. of product obtained and a curve plotted while the distillation was in progress. At the end of each horizontal part of the resulting curve the column was put at total reflux for five minutes. In case the reflux temperature dropped to the preceding value and the horizontal continued for another 1 cc., total reflux was again used for five minutes. The care with which this technique was followed is illustrated by the exaggerated distillation curve in Fig. 1. One-cc. fractions were collected in a 1-cc. receiver calibrated to 0.01 cc.

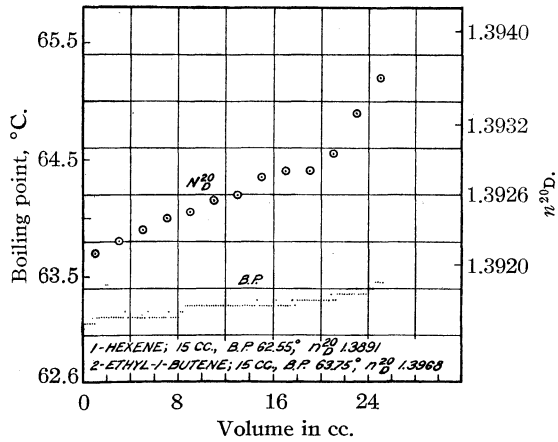


Fig. 1.—Fractionation of 2-ethyl-1-butene and 1-hexene through column IV.

Figures 2, 3, and 4 illustrate three attempts to separate isomeric hexene mixtures. Each distillation was followed by both the boiling point and index of refraction. The continuous lines in the accompanying figures are the theoretical distillation curves assuming perfect separation, while the experimental points are shown by dots.

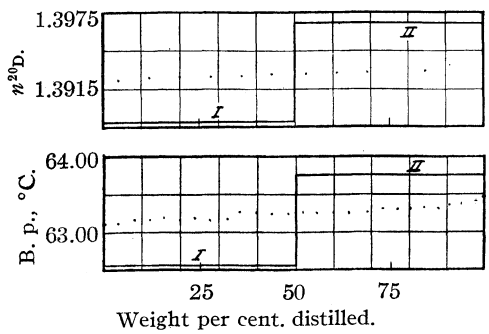


Fig. 2.—I, 50%, 1-hexene; II, 50%, 2-ethyl-1-butene.

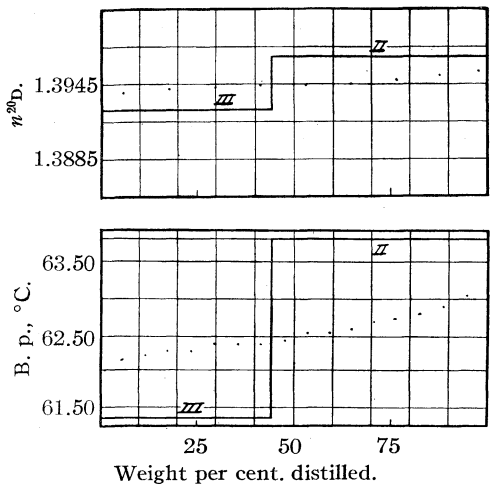


Fig. 3.—II, 56%, 2-ethyl-1-butene; III, 44%, 2-methyl-1-pentene.

It will be seen that the over-all temperature spreads produced in the course of these fractionations are much less than the temperature differences stated to exist between the boiling points of the pairs of substances in question. This obviously means that little separation occurred in the course of the fractionations. The same is true for indices of refraction. Density values further substantiate the data on temperature and refractive index, namely, that little if any separation resulted.

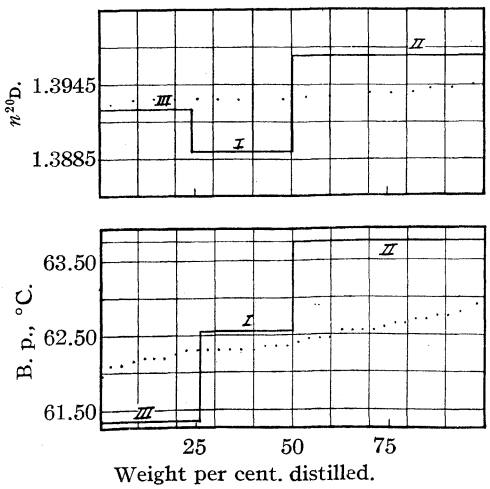


Fig. 4.—I, 24%, 1-hexene; II, 50%, 2-ethyl-1-butene; III, 26%, 2-methyl-1-pentene.

Acknowledgment is made to the following members of the Petroleum Refining Laboratory for help in connection with the data compiled in Table IV: J. P. Haimovicz, G. Herbolsheimer, J. H. Jones, R. H. McCormick, A. E. Schubert, and K. A. Steel.

Summary

1. The identification of olefins as reported by Goldwasser and Taylor in their dehydration of certain alcohols is questioned.

2. The Podbielniak–Simons–Taylor column has an efficiency of about fifteen theoretical plates.

3. Fruitless efforts were made to separate by distillation through the Podbielniak–Simons–Taylor column two binary mixtures having boiling point spreads of 2.7 and 1.5°, and a ternary mixture having an over-all boiling point spread of 2.7°. Our failure is in sharp contrast to the reported separation and identification of six hexenes with an over-all boiling point spread of 2.5°.

4. The Podbielniak–Simons–Taylor column is compared in Table IV with other types of fractional distillation columns.

STATE COLLEGE, PENNSYLVANIA
RECEIVED DECEMBER 18, 1939

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

Ionic Character and Dipole Moments

BY FREDERICK T. WALL

In discussing the nature of the chemical bond in hydrogen halides, Pauling[1] has found it convenient to regard the normal states of those molecules as superpositions of ionic and covalent states. As a measure of the fraction of ionic character in the molecules he took the values of μ/er where μ is the dipole moment and r the internuclear separation. In this paper the notion is extended somewhat, and a theory of dipole moments for the normal and first excited states is developed.

In a previous paper[2] the author considered the problem by supposing that the wave function (unnormalized) for the molecule can be taken as

$$\psi = \psi_c + a\psi_i$$

where ψ_c is a purely covalent function and ψ_i a purely ionic function, and a is a parameter. To get the best energy value from that function, the energy expression was minimized with respect to a. If W represents that minimized value and W_c and W_i the covalent and ionic energies, then it was shown that

$$a^2 = \frac{W - W_c}{W - W_i} \qquad (1)$$

By use of equation (1) estimates of values for a^2 were obtained for the different hydrogen halides at their equilibrium internuclear separations and the results roughly correlated with dipole moment values.

A more precise relationship between dipole moment and ionic character will now be developed and some conclusions drawn from it. Using the function $\psi = \psi_c + a\psi_i$ in which ψ_c and ψ_i are each normalized to unity, then the general expression for the dipole moment becomes

$$\mu = \frac{\mu_{cc} + 2a\mu_{ci} + a^2\mu_{ii}}{1 + 2a\Delta + a^2} \qquad (2)$$

where μ_{cc} is the moment of the covalent structure, μ_{ii} that of the ionic structure and μ_{ci} the corresponding integral of the moment expression over the states ψ_i and ψ_c. That is

$$\mu_{ci} = \int \psi_c^* \mu \psi_i d\tau = \int \psi_i^* \mu \psi_c d\tau$$

Also

$$\Delta = \int \psi_c^* \psi_i d\tau = \int \psi_i^* \psi_c d\tau$$

Now the moment of the covalent structure can be taken as zero and that of the ionic structure as er. It remains then to find the value of μ_{ci}.

In order to get an idea as to the nature of μ_{ic}, consider the hypothetical case of resonance between HH and H^+H^-. (For the actual hydrogen molecule, the structure H^-H^+ is equally as important as H^+H^-,[3] but it will not be considered here in order that the results can be used for the hydrogen halides for which only the structures HX and H^+X^- are important.) Setting up a purely covalent function of the Heitler–London[4] type for HH and a simple ionic function such as was used by Weinbaum[3] for H^+H^-, the integral μ_{ic} readily can be evaluated. In this case it turns out that

(1) Linus Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1939, II-8.

(2) F. T. Wall, THIS JOURNAL, **61**, 1051 (1939).

(3) S. Weinbaum, *J. Chem. Phys.*, **1**, 593 (1933).

(4) W. Heitler and F. London, *Z. Physik*, **44**, 455 (1927).

$$\mu_{ic} = \frac{\mu_{cc} + \mu_{ii}}{2}\Delta \qquad (3)$$

where $\mu_{cc} = 0$ and $\mu_{ii} = er$.

The result expressed by equation (3) is a simple one which seems quite plausible. It will be assumed that (3) also holds for the hydrogen halides. Combining (3) with (2) there is obtained

$$\mu = \frac{\mu_{cc}(1 + a\Delta) + \mu_{ii}(a\Delta + a^2)}{1 + 2a\Delta + a^2} \qquad (4)$$

Letting $\mu_{cc} = 0$ and $\mu_{ii} = er$, equation (4) becomes

$$\mu = \frac{a\Delta + a^2}{1 + 2a\Delta + a^2} er \qquad (5)$$

Equations (4) and (5) can be demonstrated to be satisfactory in several ways. Obviously they have the correct characteristics for the two limiting cases when $a \longrightarrow 0$ (covalent) and when $a \longrightarrow \pm\infty$ (ionic). They are also highly satisfactory for the intermediate cases when $a = \pm 1$. If $a = \pm 1$, then

$$\mu = \frac{\mu_{cc} + \mu_{ii}}{2} \text{ from (4)}$$

or

$$\mu = {}^1/_2 er \text{ from (5)}$$

In other words, when the ionic and covalent states contribute equally, the moment is just the mean of the moments (or half the ionic moment).

It is also seen from (5) that whenever $-1 < a < 1$, then $0 < \mu < 1/2(er)$. This situation can be realized for the normal state of a molecule whenever the covalent state is more stable than the ionic state. The fact that hydrogen chloride, hydrogen bromide and hydrogen iodide all have dipole moments less than $1/2(er)$ is in agreement with this result and their assumed energy curves.

On the other hand, when $1 < a < \infty$ or $-1 > a > \infty$ then $\mu > 1/2(er)$. This state of affairs should exist for normal hydrogen fluoride according to Pauling's energy curves, because the ionic curve cuts below the covalent one. We should expect then that the dipole moment of hydrogen fluoride would be greater than $1/2(er)$.

Another interesting result can be derived as follows. The energy W for a system with a wave function $\psi_c + a\psi_i$ is given by

$$W = \frac{H_{cc} + 2aH_{ic} + a^2H_{ii}}{1 + 2a\Delta + a^2} \qquad (6)$$

Letting $\partial W/\partial a$ equal zero and combining that result with equation (6), there is obtained a quadratic equation in a, the two roots of which are subject to the relations

$$a_1a_2 = \frac{\Delta H_{cc} - H_{ic}}{H_{ic} - \Delta H_{ii}}$$
$$a_1 + a_2 = \frac{H_{ii} - H_{cc}}{H_{ic} - \Delta H_{ii}} \qquad (7)$$

One of the roots (say a_1) corresponds to dissociation into neutral atoms and the other (a_2) to dissociation into ions. Each of the two resultant states has a dipole moment given by (4) or (5) by putting into those equations a_1 and a_2. But from (7) it can be shown that

$$1 + (a_1 + a_2)\Delta + a_1a_2 = 0 \qquad (8)$$

which is precisely the condition for orthogonality of $\psi_c + a_1\psi_i$ and $\psi_c + a_2\psi_i$. But

$$\mu_1 + \mu_2 = \frac{\mu_{cc}(1 + a_1\Delta) + \mu_{ii}(a_1\Delta + a_1^2)}{1 + 2a_1\Delta + a_1^2} + \frac{\mu_{cc}(1 + a_2\Delta) + \mu_{ii}(a_2\Delta + a_2^2)}{1 + 2a_2\Delta + a_2^2} \qquad (9)$$

Simplifying this expression and making use of (8), we find that

$$\mu_1 + \mu_2 = \mu_{cc} + \mu_{ii} \qquad (10)$$

or if $\mu_{cc} = 0$ and $\mu_{ii} = er$

$$\mu_1 + \mu_2 = er \qquad (11)$$

Equations (10) and (11) express the simple result that the total dipole moment of the two resultant states is equal to the sum of the moments of the interacting states. For that reason, the quantity μ/er is an excellent measure of ionic character even though it is not simply related to the quantity a.

The qualitative features of the relationship between dipole moments and energy curves are shown in Figs. 1 and 2. In these figures the dotted energy curves apply to the purely covalent and ionic states, whereas the solid curves represent the energies of the states resulting from the resonance. Immediately below are given dipole moment curves. In each case, for large internuclear separations the ionic moments approach the line $\mu = er$ asymptotically and the covalent moments approach zero.

In Fig. 1, the purely covalent energy is everywhere less than the ionic energy so that the moment associated with the normal state is everywhere less than $1/2(er)$ and the other moment greater than $1/2(er)$. In Fig. 2, the purely ionic curve cuts below the covalent curve, so that the moment of the normal molecule is greater than $1/2(er)$ for a certain range of r. The two moment curves cross with the value $1/2(er)$ at the same internuclear separation where the idealized energy curves cross. The case exhibited by Fig. 2 is to be expected for hydrogen fluoride.

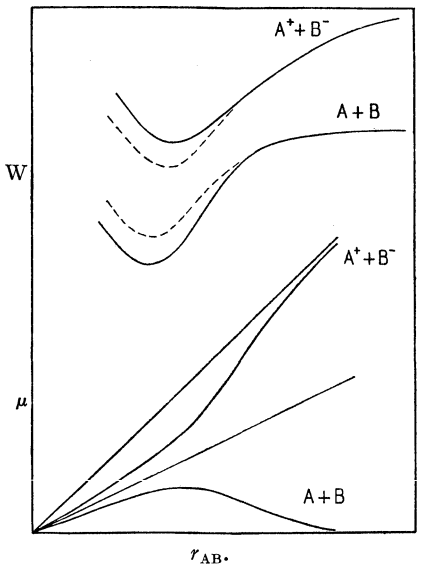


Fig. 1.—Energy and dipole moment curves with covalent state everywhere more stable than ionic state.

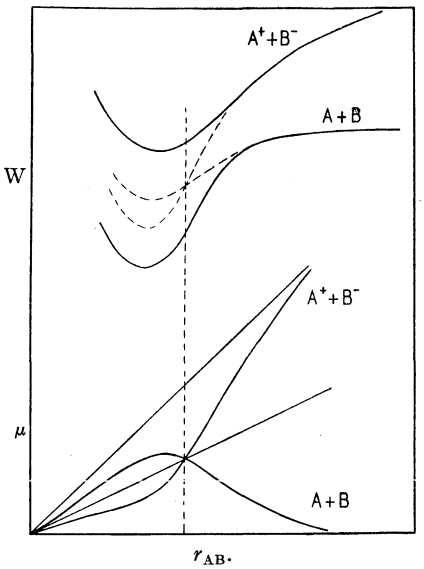


Fig. 2.—Energy and dipole moment curves with ionic state more stable than covalent state for certain range of internuclear separations.

The behavior of the moment curves for small internuclear separations is not certain, though it seems reasonable to suppose that the slopes are both different from zero for $r = 0$. At any place, of course, the sum of the slopes equals e by reason of equation (11). The two curves for the moments of the normal molecules were drawn to resemble those proposed by Mulliken.[5]

Since $0 \leqslant |\Delta| \leqslant 1$, it follows from equation (5) that a must lie in the range

$$\sqrt{\frac{\mu}{er - \mu}} \text{ to } \frac{\mu}{er - \mu}$$

From a knowledge of μ/er, one can then calculate upper and lower limits for $|a|$ for the normal molecules. The results of such calculations are given in Table I. Values of $|a|$ could of course be obtained for any value of Δ by use of equation (5). Such values have been calculated taking $\Delta = 0.3$, since it is likely that Δ is nearer 0 than it is to 1.

TABLE I

Molecule	μ/er	a values $\Delta = 0$	$\Delta = 0.3$	$\Delta = 1$	From energy data[2]
HF	0.60[a]	1.22	1.30	1.50	
HCl	.170	0.45	0.35	0.20	0.39
HBr	.114	.36	.25	.13	.35
HI	.049	.23	.13	.052	.26

[a] Value estimated by Pauling.[1]

In a previous paper,[2] values for a^2 were computed by means of energy data using equation (1). The corresponding values of $|a|$ except for hydrogen fluoride are shown in the last column of Table I. The energy curves used in those calculations were not very reliable, especially in the case of hydrogen fluoride, in which case they were way off. However, it is seen that the values for hydrogen chloride and hydrogen bromide calculated by the use of those energy curves lie between the upper and lower limits specified by dipole moment data. The value from energy curves for hydrogen iodide is a little higher than the upper limit from dipole moment data.

Since $a^2/(1 + a^2)$ might well be adopted as a measure of ionic character, values for that quantity are given in Table II for $\Delta = 0$, $\Delta = 0.3$ and $\Delta = 1$, as well as those values obtained from energy data. It should be noted that if $\Delta = 0$, then $a^2/(1 + a^2)$ is just μ/er. It is clear from the results in the tables that with increasing atomic number, a and $a^2/(1 + a^2)$ become increasingly sensitive to variations in Δ. It might well be that for hydrogen bromide and hydrogen iodide, Δ is nearer zero than 0.3.

TABLE II

Molecule	$a^2/(1 + a^2)$ $\Delta = 0$	$\Delta = 0.3$	$\Delta = 1$	From energy data[2]
HF	0.60	0.63	0.69	
HCl	.170	.11	.040	0.134
HBr	.114	.061	.016	.107
HI	.049	.016	.0026	.064

Summary

A theory of dipole moments of diatomic mole-

(5) R. S. Mulliken, *J. Chem. Phys.*, **2**, 400 (1934).

cules is developed and it is shown that the sum of the dipole moments of two states resulting from resonance is the same as the sum of the dipole moments of the original states. Assuming a wave function $\psi = \psi_c + a\psi_i$ for a system resonating between covalent and ionic states, upper and lower limits to $|a|$ are calculated using dipole moment data, and the results compared to calculations of $|a|$ based on energy values.

URBANA, ILLINOIS RECEIVED JANUARY 15, 1940

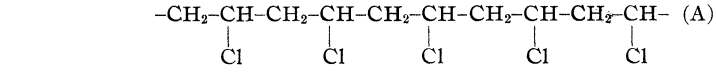
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

Removal of Substituents from Vinyl Polymers

BY FREDERICK T. WALL

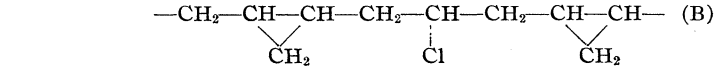
Experimental studies by Marvel and coworkers[1] have shown that chlorine can be partly removed from vinyl chloride polymers by means of zinc. The removal of chlorine is not quantitative, however, owing to the fact that some of the chlorides become isolated. A given chlorine atom is considered isolated when its nearest neighbor is so far away that it and that neighbor can no longer be removed as a pair by means of zinc.

This notion can be illustrated as follows. Suppose the polymer has all its substituents in 1–3 relationship with respect to their nearest neighbors. Then a portion of the polymer would look as follows



(A)

If this portion of the polymer were attacked by zinc, some of the chlorides might be removed in any of several ways. If, say, zinc removed the first and last pairs, there would result



(B)

in which the middle chloride is now isolated and hence incapable of removal.

Assuming that zinc removes chlorides in a perfectly random way, the problem of what fraction of the chlorides becomes isolated is simply a question of probability. This problem has been solved by Flory[2] for the cases where all of the substituents are the same. His results show that if the polymer has all of its chlorides in 1–3 relationship, then the portion $1/e^2$ (or 13.53%) of the original chlorides will become isolated, a result for which there is experimental support.[1] This was derived after making the reasonable assumption that no two chlorides separated by more than three carbons can be removed as a pair.

Flory also considered the case where the polymer is not necessarily 1–3 throughout, but is made up of vinyl units oriented at random. Since a given vinyl unit can be oriented in either of two ways along the line of the polymer chain, 1–2, 1–3 and 1–4 relationships will exist between substituents. Assuming that 1–2 and 1–3 substituents can be removed with equal ease but that 1–4 or more widely separated substituents cannot be removed, he showed that the portion $1/2e$ (or 18.40%) of the original substituents could be expected to remain after reaction.

More recently, Marvel and Mastin[3] have studied the removal of chlorine from mixed vinyl chloride vinyl acetate polymers. In such a case, the acetates will divide up the long polymer into isolated groups of chlorides. Assuming that the acetates are interspersed at random in the polymer, one is confronted with a more general statistical problem in attempting to calculate the fraction of the original chlorides which can be expected to remain after treatment with zinc. In this paper, the solution to that problem is given for the two cases when the linkages are all 1–3 and when the orientations are random.

Statistical Treatment.—In attacking both cases of this problem, it is first to be noted that any two chlorides which have one or more acetates between them as substituents along the chain cannot be removed as pairs by means of zinc. The problem then resolves itself first into finding the number of groups of chlorides of given lengths formed by interspersing acetates, and, second, into summing up those numbers multiplied by the chloride expectancy per group. The chloride expectancy per group depends upon whether or

(1) C. S. Marvel, J. H. Sample and Max F. Roy, THIS JOURNAL, **61**, 3241 (1939).

(2) P. J. Flory, *ibid.*, **61**, 1518 (1939).

(3) Private communication.

not the linkages are all 1–3 or are random. The number of groups of specified lengths, however, does not depend upon the presence or absence of link orientation restrictions, as far as probability alone is concerned.

We shall accordingly first turn to the problem of group distribution. Let N_X equal the total number of X's (chlorides) and N_Y the total number of Y's (acetates) in the long polymer. In the following treatment it will be assumed that these N's are very large numbers. Then if p_i equals the number of groups of X's containing i members, it follows that

$$N_X = \sum_i i p_i \tag{1}$$

and

$$N_Y = \sum_i p_i \tag{2}$$

In order for (2) to be valid, it is necessary that we include values for $i = 0$. Regarding the Y's as spacers, two adjacent Y's surround a group of X's zero members long. Each group of X's has one Y as a spacer; hence the equality (2).

Now the number of complexions in the statistical state represented by $p_0, p_1, p_2, \ldots$ is given by

$$W = \frac{N_Y!}{p_0!p_1!p_2!\ldots} \tag{3}$$

The most probable distribution corresponds to the maximum value for W. Using Stirling's approximation for ln W and setting the variation of it equal to zero, we have[4]

$$\delta \ln W = -\sum_i \ln p_i \, \delta p_i = 0 \tag{4}$$

This equation is subject to two additional equations obtained by taking variations of (1) and (2).

$$\delta N_X = \sum_i i \, \delta p_i = 0 \tag{5}$$

$$\delta N_Y = \sum_i \delta p_i = 0 \tag{6}$$

Introducing Lagrangian multipliers and combining in the usual way, we find that

$$p_i = e^{-\lambda - \mu i} \tag{7}$$

To determine μ and λ, equation (7) is combined with equation (1) and with equation (2), giving

$$N_X = \sum_i i e^{-\lambda-\mu i} = e^{-\lambda-\mu}\{1 + 2e^{-\mu} + 3e^{-2\mu} + \ldots\} = \frac{e^{-\lambda}e^{-\mu}}{(1 - e^{-\mu})^2} \tag{8}$$

(4) This treatment is similar to that employed in deriving the Maxwell–Boltzmann distribution law; see for example, Tolman, "Statistical Mechanics," Oxford University Press, 1938.

and

$$N_Y = \sum_i e^{-\lambda-\mu i} = e^{-\lambda}\{1 + e^{-\mu} + e^{-2\mu} + \ldots\} = \frac{e^{-\lambda}}{1 - e^{-\mu}} \tag{9}$$

From (8) and (9) it is found that

$$e^{-\mu} = \frac{N_X}{N_X + N_Y} \tag{10}$$

and

$$e^{-\lambda} = \frac{N_Y^2}{N_X + N_Y} \tag{11}$$

Substituting (10) and (11) into (7), we find

$$p_i = \frac{N_Y^2}{N_X + N_Y}\left(\frac{N_X}{N_X + N_Y}\right)^i \tag{12}$$

Define

$$x = \frac{N_X}{N_X + N_Y} \tag{13}$$

Then

$$p_i = N_X(1 - x)^2 x^{i-1} \tag{14}$$

Equation (14) tells us the number of groups of X's containing i members in terms of the mole fraction of substituents which are of the X variety and the total number N_X.

If the average number of X's (chlorides) remaining after treatment with zinc is S_i for a group originally containing i members, then the total number N_r of X's remaining in the infinite polymer is

$$N_r = \sum_i S_i p_i \tag{15}$$

and the fraction, f, of the original number is

$$f = \frac{N_r}{N_X} = \sum_i S_i(1 - x)^2 x^{i-1} \tag{16}$$

Expanding and rearranging

$$f = \sum_i S_i(x^{i-1} - 2x^i + x^{i+1}) = \sum_i (S_{i+1} - 2S_i + S_{i-1})x^i \tag{17}$$

Defining $\Delta_n = S_n - S_{n-1}$ we see that

$$f = \sum_i (\Delta_{i+1} - \Delta_i)x^i \tag{18}$$

Case 1: 1–3 Coupling Throughout.—If all of the substituents are 1–3 with respect to each other, then $\Delta_{i+1} - \Delta_i$ is subject to a relationship derived by Flory,[2] namely

$$\Delta_{i+1} - \Delta_i = (-2)^i/i! \tag{19}$$

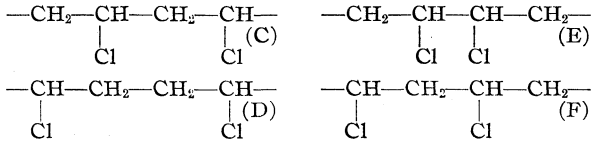
Substituting into (18)

$$f = \sum_i \frac{(-2)^i}{i!}x^i = e^{-2x} \tag{20}$$

Equation (20) gives a very simple expression for the fraction of chlorine remaining after

treatment with zinc. If $x = 1$, which would be the case when all of the substituents are chlorides, $f = 1/e^2$ in agreement with Flory's result for that special case. On the other hand, it is seen that the smaller the value of x, the greater will be the fraction of original chlorides remaining at the end. This follows because of the tendency of acetates to isolate many chlorides. Preliminary experimental evidence obtained by Marvel and Mastin[5] supports the validity of the result $f = e^{-2x}$.

Case 2: Random Coupling Throughout.— In the event that the vinyl links join together in a random way, the chloride expectancy per group will not be the same as for the case where all the linkages are 1–3, assuming that 1–4 or more widely separated pairs cannot be removed by zinc. Consider, for example, the situation possible for a group containing two vinyl units. Four possibilities will exist, namely



Of the four possibilities, C, E and F will have no chlorides remaining after treatment with zinc, whereas D will have two remaining. If each possibility is equally probable, then the average number of chlorides remaining from randomly built up groups of two vinyl units will be 2/4 or 1/2 per group. This value, which we will denote by S_2', is different from the S_2 value for 1–3 orientation, which equals zero.

The problem in case 2 is precisely the same as that of case 1 up through equation (18). That is

$$f' = \sum_i (\Delta'_{i+1} - \Delta'_i)x^i \qquad (18')$$

the primes serving to distinguish case 2 from case 1.

Consider once more the situation for $n = 2$. By the use of + and − signs, where a plus sign denotes a vinyl unit with its substituent on the right-hand side and a minus sign denotes a vinyl unit with its substituent on the left-hand side, the array CDEF can be abbreviated as follows.

$$\begin{array}{ll} + + & \text{(C)} \\ -|+ & \text{(D)} \\ + - & \text{(E)} \\ - - & \text{(F)} \end{array}$$

(5) Private communication. Their results will be published soon.

For n greater than 2, similar arrays of 2^n members could be set up. Whenever a minus sign is followed by a plus sign, the member is divided into two smaller groups (indicated by the vertical line in D above). For $n = 3$ we would have the array

$$\begin{array}{ll} + + + & + + - \\ -|+ + & -|+ - \\ + -|+ & + - - \\ - -|+ & - - - \end{array} \qquad \text{(G)}$$

where four of the members are broken up by minus signs followed by plus signs. Direct counting would then tell us that $S_3' = 1$.

Let us now consider the case of a general array each of whose 2^n members will be considered equally probable. For a particular value of n, let r_i equal the number of groups i members long ending with + signs on the right and let s_i equal the number of groups i members long ending with − signs in the extreme right-hand column. Also let l_i equal the number of groups (ending with − signs) without their terminal symbol in the extreme right-hand column. It follows then, that

$$2^n S_n' = (r_1 + s_1 + l_1)S_1 + (r_2 + s_2 + l_2)S_2 + \ldots + (r_n + s_n + l_n)S_n \qquad (21)$$

assuming 1–2 and 1–3 removals are equally probable.

Now in going from the array of 2^n members to the next higher array, one need only add + signs to all members of the n array and then − signs to all members of the n array to arrive at the 2^{n+1} members of the $n + 1$ array. The effect of adding + or − signs upon the classes of groups defined in the previous paragraph is apparent. We see that

$$2^{n+1}S'_{n+1} = (2^{n-1} + s_1 + 2l_1)S_1 + (2r_1 + s_1 + s_2 + 2l_2)S_2 + (2r_2 + s_2 + s_3 + 2l_3)S_3 + \ldots + (2r_n + s_n)S_{n+1} \qquad (22)$$

where the r_i's, s_i's and l_i's refer back to the case of n members. Combining (21) and (22)

$$2^{n+1}(S'_{n+1} - S'_n) = (2^{n-1} - 2r_1 - s_1)S_1 + (2r_1 + s_1 - 2r_2 - s_2)S_2 + (2r_2 + s_2 - 2r_3 - s_3)S_3 + \ldots + (2r_n + s_n)S_{n+1} \qquad (23)$$

Rearranging (23)

$$2^{n+1}\Delta'_{n+1} = 2^{n-1}S_1 + (2r_1 + s_1)\Delta_2 + (2r_2 + s_2)\Delta_3 + \ldots + (2r_{n-1} + s_{n-1})\Delta_n + (2r_n + s_n)\Delta_{n+1} \qquad (24)$$

But by an inductive method for the various arrays, it can be shown that

$$r_j = 2^{n-j-1} \text{ and } s_j = 2^{n-j-1}(j-1) \text{ for } j < n \quad \text{and } r_j = 1 \quad \text{and } s_j = n \quad \text{for } j = n \qquad (25)$$

Combining the results expressed by (25) with equation (24) there is obtained

$$\Delta'_{n+1} = \frac{S_1}{2^2} + \frac{2\Delta_2}{2^3} + \frac{3\Delta_3}{2^4} + \cdots + \frac{n\Delta_n}{2^{n+1}} + \frac{(n+2)\Delta_{n+1}}{2^{n+1}} \quad (26)$$

Also

$$\Delta'_n = \frac{S_1}{2^2} + \frac{2\Delta_2}{2^3} + \frac{3\Delta_3}{2^4} + \cdots + \frac{(n+1)\Delta_n}{2^n} \quad (27)$$

Subtracting (27) from (26) we see that

$$\Delta'_{n+1} - \Delta'_n = \frac{n+2}{2^{n+1}}(\Delta_{n+1} - \Delta_n) \quad (28)$$

But

$$\Delta_{n+1} - \Delta_n = \frac{(-2)^n}{n!} \quad (19)$$

Hence

$$\Delta'_{n+1} - \Delta'_n = \frac{(2+n)(-1)^n}{2n!} \quad (29)$$

Substituting (29) into (18′) there results

$$f' = \sum_i \frac{(2+i)(-1)^i}{2i!}x^i$$
$$= \sum_i \frac{(-x)^i}{i!} - \frac{x}{2}\sum_i \frac{(-x)^{i-1}}{(i-1)!}$$
$$= e^{-x} - \frac{x}{2}e^{-x} = e^{-x}\left(1 - \frac{x}{2}\right) \quad (30)$$

The result expressed by equation (30) is also a simple result, yet substantially different from that applying to case 1, namely, $f = e^{-2x}$. It should be noted that if $x = 1$, equation (30) gives $f' = 1/2e$ in agreement with Flory's result for that special case.

Discussion

A certain amount of evidence as to the nature of the vinyl polymers can be obtained by seeing which of the two formulas e^{-2x} or $e^{-x}(1 - x/2)$ best predicts the fraction of chlorine isolated in the mixed polymers. Preliminary evidence obtained by Marvel and Mastin[5] indicates that the former expression is the better of the two. This alone would not prove the 1–3 hypothesis, since the same result could be obtained with the random distribution, if 1–2, 1–3 and 1–4 pairs could be drawn off with equal ease and 1–5 or higher pairs not removed at all. However, agreement with the formula e^{-2x} would substantiate other evidence[1] for the 1–3 hypothesis.

The author is indebted to Professor Marvel and Mr. Mastin for bringing this problem to his attention.

Summary

By statistical methods, formulas are developed to predict the fraction of chlorine remaining in mixed vinyl chloride–vinyl acetate polymers upon treatment with zinc, assuming the acetates to be distributed in a random manner. Two cases are considered: first, 1–3 coupling throughout with the assumption that only 1–3 pairs of chlorides can be removed; second, random coupling with only 1–2 and 1–3 pairs of chlorides capable of removal by zinc, it being assumed that 1–2 and 1–3 removals are equally probable. These two cases yield the results $f = e^{-2x}$ and $f' = e^{-x}\cdot(1 - x/2)$ for the two respective cases where x is the chlorine mole fraction of the substituents.

URBANA, ILLINOIS RECEIVED JANUARY 26, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF HARVARD UNIVERSITY]

The Vapor Pressures of Certain Unsaturated Hydrocarbons

BY ARTHUR B. LAMB AND EDWIN E. ROPER

In connection with a study of the adsorption of the vapors of certain unsaturated hydrocarbons upon charcoal and other adsorbents, more accurate and extensive information as to the vapor pressures of these hydrocarbons was required than was available in the literature. The measurements of vapor pressure here presented were therefore made over a considerable range of temperature and, since our samples of hydrocarbons were of exceptional purity, with particular care.

Materials.—The hydrocarbons studied by us (Tables II–IV) were those used by Professor Kistiakowsky and his collaborators in their studies of the heats of hydrogenation, etc., and were prepared in part by them and in part by them and ourselves jointly. We wish to express our appreciation of this generous arrangement. A description of the methods of preparation has already been published.[1]

The high purity of these hydrocarbons has been demonstrated by the close concordance of the heats of hydrogenation, boiling points, freezing points and other physical properties of different distillation fractions of the same samples

(1) (a) Kistiakowsky, Romeyn, Ruhoff, Smith and Vaughan, THIS JOURNAL, **57**, 65 (1935); (b) Kistiakowsky, Ruhoff, Smith and Vaughan, *ibid.*, **57**, 876 (1935); (c) **58**, 137 and (d) 146 (1936).

and of samples of the same hydrocarbons prepared by different methods. Further evidence of their high purity also has been obtained in our own work by the close concordance of the vapor pressures of successive fractions obtained in a further isothermal distillation of our samples at 0°, as will be explained later. No deterioration of these samples over the period of our measurements has been detected except in the case of 2-methylpropene which in the liquid phase was found to undergo a slow change, its vapor pressure at 0° decreasing at the rate of about 1 mm. per day. Definitive measurements of this substance were therefore made only upon freshly distilled samples.

Apparatus and Procedure

A static method of measurement was adopted as affording the greatest promise of accuracy. A cryostat to maintain a constant, known temperature over a considerable period of time and over the temperature range of −130 to 25° was therefore required; also, a carefully standardized platinum resistance thermometer and an accurately legible manometer.

Cryostat.—This (see Fig. 1) was of the type developed by Scott and Brickwedde[2] in which the bath liquid contained in an inner cylindrical Dewar flask (E) is circulated through and around a submerged vertical tube of bakelite (J) about which the heating element (H) is wound. Refrigerant (liquid air) in an outer Dewar flask surrounds the inner Dewar flask and by adjusting the pressure in its jacket the rate of cooling of the cryostat bath can be controlled. The intermittent, regulated current in the heating element is superposed upon a continuous one. The thermoregulator is of a type of which many designs have been published[2,3] which comprises a Mueller thermometer bridge, a galvanometer, a photocell, a 3-stage amplifier and a relay. The sensitivity of the regulator is such that the total, cyclical fluctuation of temperature in the center of the cryostat is 0.003°. The stirrer and gear shafts are of Monel metal and the bearings of a lead–tin alloy, high in lead; two bearings and one set of gears are immersed in the bath liquid. About one gram of finely divided graphite added to the bath liquid aids materially in lubrication at the lower temperatures. The non-inflammable bath liquid is a five-component mixture (No. 39) as recommended by Kanolt.[4] To compensate for the slow sinking of the liquid air level in the outer container during an experiment, an automatic modulator was installed which slowly increases the continuous energy input during the time that the intermittent heater is on and slowly decreases it during the time that the intermittent heat input is off.[5] For the measurements on the vapor pressure of the crystals and on the triple point of propadiene, an aneroid cryostat was utilized, which has been described in another connection.[6]

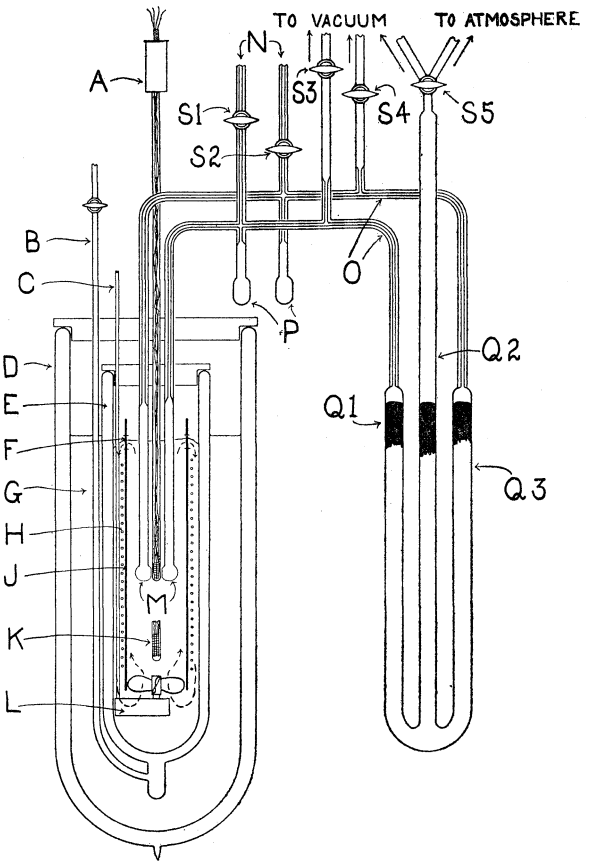


Fig. 1.—Double vapor pressure apparatus: A, measuring thermometer; B, connection for exhausting jacket of E; C, stirrer shaft; D, outer Dewar tube; E, inner Dewar tube; F, ports in J for circulating liquid; G, refrigerant; H, heating coil on J; J, bakelite tube; K, control thermometer; L, stirrer gearing; M, vapor pressure bulbs; N, gas admitted or withdrawn here; O, to manometers; P, condensing bulbs; Q, double manometer; S, stopcocks.

The Platinum Resistance Thermometer.—This had a resistance of 25 ohms and was of the coiled filament type.[7] It has shown a high stability over a long period. Its resistance was measured on a calibrated Mueller type Wheatstone bridge in an oil thermostat at 25.0 ± 0.1° to 0.0001 ohm, which corresponds to about 0.001° and produces a galvanometer deflection of 1.8 mm. with a measuring current in the thermometer of 1.3 ma. This thermometer assembly already has been described elsewhere.[6,8]

To obtain the constants in the quadratic calibration equation[9] of this thermometer for

(2) Scott and Brickwedde, *Bur. Standards J. Research*, **6**, 40 (1931).
(3) Southard and Andrews, *J. Franklin Inst.*, **207**, 323 (1929).
(4) Kanolt, Bur. Standards Sci. Paper No. 520, March, 1926.
(5) Roper, *Ind. Eng. Chem., Anal. Ed.*, **12**, 113 (1940).
(6) Roper, THIS JOURNAL, **60**, 1693 (1938).
(7) Meyers, *Bur. Standards J. Research*, **9**, 807 (1932).
(8) Roper, THIS JOURNAL, **60**, 866 (1938).
(9) Burgess, *Bur. Standards J. Research*, **1**, 635 (1928).

temperatures above 0°, observations were made at three primary points: the sulfur b. p.,[9,10] the steam point[9,11] and the ice-point.[8] The thermodynamic temperature of the last was taken as 273.16°K.[12] To obtain the two additional constants of the biquadratic equation[13] for temperatures below 0°, one additional primary point, the vapor pressure of oxygen,[14a] and one secondary point, the vapor pressure of crystalline carbon dioxide,[14a] were also observed. As a check upon the accuracy of our temperature scale, three other secondary points were observed, namely, the b. p. of naphthalene,[9,15] the transition point of sodium sulfate decahydrate[9,16] and the f. p. of mercury,[9,14b] these observations indicating that the absolute accuracy was of the order of 0.01°, while the relative precision was of the order of 0.002°. In all cases more than one standardizing run was performed, bracketed in each instance with a determination of the ice-point, using material for standardization from different sources, purified by different methods. For the fixed point temperatures above 0° we took the values as defined by the International Temperature Scale[9]; for those below 0°C., the values determined by Heuse and Otto.[14b,c]

Vapor Pressure Apparatus.—This was a double apparatus permitting the simultaneous measurement of the vapor pressure of two samples at a given temperature-setting of the cryostat. This proved convenient, since eight of the nine hydrocarbons studied-formed well-defined pairs with boiling points close together. The bulbs (M) to contain the liquid samples were small (volume about 0.5 cc.) with thin walls and were placed close to the sensitive part of the thermometer (A). The thermometer and twin bulb assembly was wound with thin aluminum foil to facilitate thermal equilibration. The manometer was of 18, and the connecting tube (0) of 3 mm., bore (to minimize the effect of changes in room temperature). The height of the mercury was read to ±0.04 mm. with an accurate cathetometer, a correction for the meniscus being applied always and the pressures converted to millimeters of mercury at 0° and g = 980.665 cm./sec.[2,9] In most cases the final value for the pressure was rounded off to the nearest 0.1 mm. All stopcocks were of the type having a bulb sealed onto the base of the barrel for evacuation, giving a seating force of one atmosphere on the plug at all times. For pressures greater than 900 mm. (the length of the cathetometer scale), manometer Q2 with stopcock S5 turned to the atmosphere was utilized in conjunction with a barometric manometer read with the same cathetometer. High vacuum technique was followed in all operations.

Procedure.—The compounds, after being freed from all water[17] and air, were stored in 5-liter Pyrex glass reservoirs connected to cocks S1, S2 (Fig. 1). The vapor was condensed into the bulbs (P) from the storage reservoirs by the use of refrigerants. The vapor pressure bulbs (M) were not visible during a measurement, but it was easy to ascertain from the pressure changes during distillation from P to M whether liquid phase was present in them. The cryostat was then adjusted to the desired temperature and after equilibrium had been established as shown by no change for ten minutes, the pressure and the temperature were read, the latter observations bracketing the former.

The measurements on propadiene were made with the aneroid cryostat and McLeod gage (except the one at 188.17°). This gage was carefully standardized and comparison of it with the U-type manometer at 2 mm. showed satisfactory correspondence. The hydrocarbon was purified by pumping for a half-hour on the liquid phase at −136° and this purging was continued until no further change in vapor pressure could by detected at this temperature. Nine separate determinations of the triple point in three different cryostats gave 136.94 ± 0.02°K. (pressure 0.1448 mm.).

For the six highest-boiling hydrocarbons studied, a test was made for the presence of impurities. For this purpose the bulbs (P) were surrounded with cracked ice in an unsilvered Dewar tube. The ice-bath was brought to 0.000 ± 0.001° by a modified White washing technique,[8] the vapor pressure of the condensed sample determined, slow isothermal vaporization

TABLE I

VARIATIONS OBSERVED IN THE VAPOR PRESSURE AT 0.000°

Substance	Pressure, mm. Maximum	Pressure, mm. Minimum	Change Mm.	observed °K.
2-Methylpropene	989.00	987.78	1.22	0.035
1-Butene	965.12	963.10	2.02	.057
t-2-Butene	733.98	733.25	0.73	.026
c-2-Butene	661.50	658.31	3.19	.121
1,4-Pentadiene	275.02	273.78	1.24	.103
2-Methyl-2-butene	165.21	164.14	1.07	.140
Average			1.63	.084

(10) Mueller and Burgess, *Bull. Bur. Standards*, **15**, 163 (1919).
(11) Mueller and Sligh, *J. Optical Soc. Am.*, **6**, 958 (1922).
(12) Heuse and Otto, *Ann. Physik*, **2**, 1012 (1929).
(13) Van Dusen, THIS JOURNAL, **47**, 326 (1925).
(14) (a) Loomis and Walters, *ibid.*, **48**, 3101 (1926); (b) Heuse and Otto, *Ann. Physik*, **9**, 486 (1931); (c) *ibid.*, **14**, 185 (1932).
(15) Finck and Wilhelm, THIS JOURNAL, **47**, 1577 (1925).
(16) Dickinson and Mueller, *Bull. Bur. Standards*, **3**, 641 (1907).
(17) Ethene was dried by a simple bulb-to-bulb distillation; the remaining eight hydrocarbons by a physical method: Roper, *Ind. Eng. Chem., Anal. Ed.*, **9**, 414 (1937).

TABLE II

VAPOR PRESSURE OF ETHENE, PROPENE AND THE FOUR BUTENES

T, °K.	p, mm.	(Diff., calcd. − obsd.) Mm.	°K.	T, °K.	p, mm.	(Diff., calcd. − obsd.) Mm.	°K.
	Ethene				*trans*-2-Butene		
147.89	174.0	−0.4	−0.03	204.76	18.46	+0.12	+0.09
154.92	296.2	+1.3	+ .06	219.95	53.45	− .44	− .01
163.13	523.4	−3.2	− .10	225.67	75.78	− .30	− .07
168.31	714.4	+0.8	+ .02	230.11	97.94	− .03	− .01
170.17	794.7	+2.4	+ .05	239.51	163.7	+ .01	+ .00
173.25	948.8	−0.9	− .02	250.93	287.4	+ .3	+ .02
	Propene			258.50	403.1	+1.6	+ .09
151.72	3.87	0.00	0.00	259.37	419.9	−0.6	− .03
185.08	75.75	− .10	− .02	266.20	559.5	+ .03	+ .01
198.47	183.4	+ .32	+ .03	273.16	733.4	+ .8	+ .03
212.51	404.6	− .7	− .03	273.16	734.0	+ .2	+ .01
222.52	662.8	+1.7	+ .05	276.03	820.2	−2.6	− .09
227.58	834.2	−0.2	− .01	282.76	1047.9	−7.1	− .20
235.43	1164.2	−1.2	− .03				
	2-Methylpropene				*cis*-2-Butene		
216.41	65.44	+0.03	+0.01	186.26	3.71	−0.03	−0.09
247.86	357.8	−2.1	− .13	219.95	45.44	− .42	− .16
252.28	431.0	+2.2	+ .12	225.67	64.73	+ .36	+ .07
265.69	748.5	+1.4	+ .05	230.11	83.79	+ .58	+ .13
272.49	966.0	−1.0	− .03	239.51	141.2	+ .2	+ .03
273.16	987.8	+0.6	+ .02	258.50	361.2	−5.4	− .33
273.16	989.0	− .3	− .02	259.37	373.7	−3.7	− .22
	1-Butene			273.16	658.3	+3.1	+ .12
216.41	64.12	−0.01	−0.00	273.16	658.9	+2.5	+ .09
247.86	340.7	− .3	− .02	276.03	749.7	−8.9	− .32
250.25	378.3	+ .9	+ .05	282.76	951.5	+5.1	+ .15
262.56	641.4	− .7	− .03				
265.69	727.5	−1.6	− .05				
272.49	941.7	0.0	.00				
273.16	963.1	+2.3	+ .06				
273.16	965.1	+0.7	+ .02				

at 0° carried out until only about one-twentieth of the original sample remained in the bulbs, and the vapor pressure then re-determined. The decrease in the vapor pressure under such treatment is a partial measure of the purity of the sample.[18] Table I gives the results, and also the temperature changes corresponding to the observed decrease in vapor pressure computed from the temperature coefficient at 0°.

These slight changes between the beginning and end of the fractionation indicate that the liquids were quite pure.

However, since in the actual vapor pressure measurements during the transfer of hydrocarbon from the reservoirs to the vapor pressure bulbs and when the temperature of the cryostat was raised much of the liquid vaporized from the vapor pressure bulb, similar though perhaps not so drastic fractionation may have taken place. If this occurred, deviations similar to those in Table I, namely, of about 0.08°, would be expected. Actually the average of the apparently random deviations of our observed boiling points from those computed from our empirical vapor pressure formulas derived by least squares was about ±0.06°. This shows that our fractionation and vapor pressure data are in accord and indicates that the random deviations of our vapor pressure measurements are probably due to the presence of these slight impurities, rather than to thermometric errors.

The Observed Vapor Pressures and Empirical Formulas.—Tables II, III and IV contain the results of our measurements.[19]

(18) Shepherd, *Bur. Standards J. Research*, **12**, 185 (1934).

(19) One earlier set of measurements on the liquid phase of propadiene using the Scott–Brickwedde type of cryostat where the purging was done on the solid phase gave slightly higher vapor pressures than those obtained later and listed in Table IV. We suspected inadequate purging and perhaps adsorption on the crystalline material and have not included them in our table although they agreed with certain earlier measurements recorded in the literature.[20] All measured values will, however, be found in "An Experimental Study of Various Manifestations of Van der Waals Forces in Certain Hydrocarbons," by Edwin E. Roper, a thesis submitted to the Faculty of Harvard University, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(20) Livingston and Heisig, THIS JOURNAL, **52**, 2409 (1930).

TABLE III

VAPOR PRESSURE OF 1,4-PENTADIENE AND OF 2-METHYL-2-BUTENE

	1,4-Pentadiene			2-Methyl-2-butene		
T, °K.	p, mm. obsd.	Diff.: calcd. − obsd. Mm.	°K.	p, mm. obsd.	Diff.: calcd. − obsd. Mm.	°K.
194.31	1.60	0.00	0.00	0.73	0.00	0.00
218.38	12.08	− .01	− .01	6.08	+ .01	+ .02
235.18	37.80	− .14	− .06	20.22	− .05	− .00
243.32	61.27	− .12	− .03	33.88	− .16	− .08
252.10	99.67	− .17	− .03	56.53	− .26	− .08
260.45	152.0	+ .3	+ .04	88.26	+ .05	+ .01
269.18	299.2	+ .6	+ .06	136.8	− .2	− .03
273.16	273.7	+ .6	+ .05	164.4	+ .6	+ .08
273.16	275.0	− .7	− .06	165.2	− .2	− .03
275.60	304.5	+ .3	+ .02	184.7	− .1	− .01
277.67	332.3	+ .5	+ .04	202.7	− .1	− .01
289.47	533.1	− .1	− .00	335.9	−1.0	− .08
291.23	572.7	−3.2	− .15	359.1	+0.3	+ .02

TABLE IV

VAPOR PRESSURE OF PROPADIENE

T, °K.	p, mm. Obsd.	Calcd.
Crystalline Phase Equilibria		
127.0	0.0218	0.0210
129.5	.0356	.0351
131.2	.0496[a]	.0496
131.3	.0486	.0501
132.1	.0573	.0585
132.1	.0585	.0585
132.3	.0602	.0615
132.8	.0667	.0666
134.2	.0873	.0873
Supercooled Liquid Phase Equilibria		
134.87	0.1043	0.1050
135.71	.1196	.1198
136.64	.1380	.1383
Liquid Phase Equilibria		
137.92	0.1670	0.1680
141.17	.2702	.2707
144.56	.4390	.4347
145.59	.5015	.4997
147.02	.6086	.6041
150.82	.9832	.9820
157.65	2.210	2.208
188.17	37.86	38.05

[a] Utilized in conjunction with the triple point coördinates, 136.94°K. and 0.1448 mm., to evaluate the constants in the vapor pressure equation for the crystalline phase.

A preliminary examination showed that the vapor pressures could be represented within the accuracy of our measurements by a three-constant equation of the form $\log p = A/T + BT + C$, equations with four and more constants affording very little improvement. Equations of this form were therefore derived for all of our data on each hydrocarbon by the method of least squares. In the case of certain of the more complex hydrocarbons (with the exception of propadiene) this disclosed a very few erratic values[19]; these were discarded and a new set of constants evaluated. The resulting constants and the temperature range covered are given in Table V.

TABLE V

CONSTANTS IN THE VAPOR PRESSURE EQUATION

$$\log_{10} p_{mm} = -A/T - BT + C$$

Hydrocarbon	A	B	C	Temp. range °K.
Liquid Phase Equilibria				
Ethene	907.768	0.0063661	9.31934	148 to 173
Propene	1195.712	.0038733	9.05678	152 to 235
Propadiene	1318.091	.0039204	9.32289	137 to 188
2-Methylpropene	1503.866	.0046649	9.77465	195 to 274
1-Butene	1330.977	.0017607	8.33816	195 to 274
trans-2-Butene	1532.745	.0040597	9.58593	171 to 282
cis-2-Butene	1375.857	.0011167	8.16234	171 to 282
1,4-Pentadiene	1717.300	.0040279	9.82523	194 to 291
2-Methyl-2-butene	1773.506	.0035747	9.68640	194 to 291
Crystalline Phase Equilibrium				
Propadiene	1464.40	0.000	9.8545	118 to 137

The deviations of our experimental results from these empirical equations are given in columns three, four, seven and eight of Table II and columns three, four, six and seven of Table III, expressed both in mm. and in °C., the latter being obtained from the differential of the equations together with the pressure deviations. In general the over-all accuracy of the measurements is governed at the lower temperatures by the accuracy of the pressure measurements, and at the higher temperatures by the accuracy of the temperature measurements.

The constants of the empirical equation for the crystalline phase of propadiene were derived by drawing the best line through the data. Those for the liquid were derived by least squares, as usual.

Boiling Points, Temperature Coefficients of Vapor Pressure and Heats of Vaporization.—The boiling points and the temperature coefficients of the vapor pressures were computed from the empirical equations for the vapor pressure and from these in turn the molecular heats of vaporization were computed using the Clausius–Clapeyron equation in the form

$$\Delta H^{p}_{vap} = \frac{RT_b^2}{p}\frac{dp}{dT} = 0.0026147T_b^2\left[\frac{dp}{dT}\right]_{T_b}$$

which neglects the volume of the liquid phase and assumes the saturated vapor to behave as a perfect gas. These values are listed in Table VI.

It can be seen from this table that, as would be expected, isomers exhibit very similar properties. However, it is surprising that 1-butene and 2-methylpropene are more nearly identical than are *cis*- and *trans*-2-butene.

TABLE VI

VALUES CALCULATED FROM THE VAPOR PRESSURE EQUATIONS

$T_0 = 273.16°K.$ $R = 1.9877$ cal./mole/deg.

Hydrocarbon	Normal boiling point, °C. L. and R.	Prior values		dp/dT at T_b mm./deg.	ΔH^v_{vap} at T_b cal./mole
Ethene	−103.81	−103.70[21]	−104.1[1a]	44.25	3320
Propene	− 47.66	− 47.75[22]	− 47.76[1b]	34.37	4570
Propadiene	− 33.64	− 34.28[1d]	− 35.0[20]	33.35	5000
2-Methylpropene	− 7.12	− 6.6[23]	− 7.02[1b]	29.02	5370
1-Butene	− 6.30	− 6.1[24]	− 6.46[1b]	29.62	5520
trans-2-Butene	+ 0.91	+ 0.96[1b]		28.60	5620
cis-2-Butene	3.53	3.73[1b]		29.50	5900
1,4-Pentadiene	26.06	26.0[25]	26.01[1d]	26.52	6210
2-Methyl-2-butene	38.43	38.42[26,27]	38.60[1c]	25.71	6520

TABLE VII

RAMSAY–YOUNG RULE

Alkenes (this research)	T_{100}/T_{760} obsd.	Linear equation Δ % calcd. − obsd.	Alkanes (ref. no.)	T_{100}/T_{760}	Linear equation Δ % calcd. − obsd.
			Methane[29]	(0.8207)	(−1.16)
Ethene	0.8351	0.00	Ethane[30]	.8319	+0.05
Propene	.8384	− .01	Propane[31]	.8374	− .15
Propadiene	.8425	(− .76)			
2-Methylpropene	.8394	+ .14	*i*-Butane[32]	.8366	+ .30
1-Butene	.8391	+ .18	*n*-Butane[33]	.8422	− .33
trans-2-Butene	.8410	.00			
cis-2-Butene	.8425	− .15			
1,4-Pentadiene	.8428	− .05	*n*-Pentane[32]	.8407	+ .11
2-Methyl-2-butene	.8436	.06	*i*-Pentane[32]	.8416	+ .08
Means (all)	.8405	.15	Means (omitting methane)	.8384	.17
	± .27%			± .37%	
Mean (omitting propadiene)	.8402	.07	*n*-Hexane[32]	.8450	.00
	± .21%		*n*-Heptane[32]	.8479	− .07
			n-Octane[32]	.8497	.00
			Mean of all	.8394	.22%
				± .74%	

In order to appraise the reliability of our values for the vapor pressures and boiling points of these hydrocarbons more rigorously, we have tested them by the rules of Ramsay–Young and of Dühring and by an equation giving the slopes of the vapor pressure curves at the boiling point as a function of the absolute boiling point.

The Ramsay–Young Rule.—This may be expressed[28] as $T_A/T_B = T'_A/T'_B$ where T_A and T_B are the temperatures of the saturated vapors of substances A and B at one, and T'_A and T'_B those at another pressure. Values for the ratio T_{100}/T_{760} for the hydrocarbons studied, corresponding to a 7.6-fold change in pressure, are given in the second column of Table VII.

It can be seen that the ratios for these alkenes are indeed very constant, the average deviation from the mean being only ±0.27%. There is a a slight tendency for the ratios to increase with increasing boiling point. If allowance is made for this by expressing the ratio as a linear function of the absolute boiling point, *i. e.*, $T_{100}/T_{760} = 0.8225 + 5.66 \times 10^{-5} T_{760}$, the agreement becomes even better, the average deviation, Δ, of the calculated from the observed ratio being only 0.15%. Omitting the values for propadiene, a still better correspondence (0.07) is noted (see third column, Table VII).

A similar tabulation has been made for the corresponding saturated hydrocarbons using values calculated from the vapor pressure equations in

(21) Egan and Kemp, THIS JOURNAL, **59**, 1264 (1937).
(22) Powell and Giauque, *ibid.*, **61**, 2366 (1939).
(23) Coffin and Maass, *Trans. Roy. Soc.* [*Can.*], **21**, 33 (1927).
(24) Coffin and Maass, THIS JOURNAL, **50**, 1427 (1928).
(25) Kogerman, *ibid.*, **52**, 5060 (1930).
(26) Norris and Reuter, *ibid.*, **49**, see p. 2633 (1927).
(27) Carr and Walter, *J. Chem. Phys.*, **4**, 756 (1936).
(28) Perry and Smith, *Ind. Eng. Chem.*, **25**, 195 (1933).
(29) Henning and Stock, *Z. Physik*, **4**, 226 (1921).
(30) (a) Burrell and Robertson, THIS JOURNAL, **37**, 1893 (1915); (b) Loomis and Walters, *ibid.*, **48**, 2051 (1926).
(31) Kemp and Egan, *ibid.*, **60**, 1521 (1938).
(32) Roper, submitted to *Ind. Eng. Chem.*
(33) Dana, Jenkins, Burdick and Timm, *Refrig. Eng.*, **12**, 387 (1926).

TABLE VIII

DÜHRING RULE

Constants in Quadratic Equation for Dühring Lines

$T_B = B_1 + B_2T_A + B_3 \times 10^{-5}T_A^2$

where T_A is for the reference (propene)

Hydrocarbon and reference no.	B_1	B_2	B_3	Deviation, °K. Average	Deviation, °K. maximum
Propene[34] (standard)	0.00	1.00000	0.00	(0.00)	(0.00)
Ethene[21]	3.53	0.6918	19.24	.05	− .17
Ethene[34]	3.56	.6991	16.08	.02	+ .08
Propene[22]	0.40	.9954	0.96	.003	− .01
1-Butene[34]	− 9.10	1.27364	− 22.29	.07	− .23
2-Methylpropene[34]	6.96	1.12660	10.09	.08	+ .24
Propadiene[34]	0.97	1.08451	− 11.82	.01	− .02
Propane[31]	4.70	0.96897	15.25	.05	− .18
trans-2-Butene[34]	5.24	1.18827	1.82	.03	+ .08
cis-2-Butene[34]	−47.09	1.76480	−145.15	.69	+1.56
1,4-Pentadiene[34]	6.67	1.30848	− 4.79	.06	+0.16
2-Methyl-2-butene[34]	4.17	1.39734	− 14.98	.06	+ .13
n-Heptane[32]	− 3.51	1.72956	− 43.21	.02	+ .05
n-Butane[32]	− 6.41	1.29613	− 26.36	.02	− .08
			Average	.089	.23°K.
Discarding the *cis*-2-butene value:			Average	.039	.12°K.

the literature. The results are given in the fifth column of the above table. The mean value of the ratios of comparable hydrocarbons is 0.8384 and the average deviation from the mean is ±0.37%, close to the value for the unsaturated hydrocarbons. A similar variation with the absolute boiling point is also evident here. Using the linear equation $T_{100}/T_{760} = 0.8176 + 8 \times 10^{-5}T_{760}$, values of the ratios are obtained whose percentage deviations, Δ, from the observed values average only 0.17 (omitting methane).

Summarizing, it appears that these hydrocarbons in general obey the Ramsay–Young rule closely, particularly if the rule is slightly modified. Among the hydrocarbons studied by us only propadiene shows more than the usual minimum discrepancy, suggesting that our vapor pressure data for this substance are relatively less accurate.

Dühring Rule.—This may be expressed[28] as $T_B = b_1 + b_2T_A$ where T_A and T_B have the same significance as above and b_1 and b_2 are constants characteristic of substances B. To test our results by this rule we have computed from our empirical vapor pressure equations the temperatures of the saturated vapor corresponding to nine round pressures over the range 1 mm. to 1000 mm. Taking the values for propene as standard (T_A) we find for the nine hydrocarbons we have studied and for four additional hydrocarbons for which sufficiently reliable data are available in the literature, that the temperatures of the saturated vapor can be represented by these linear equations (Dühring lines) over the whole range with an average deviation of only ±5% corresponding to about ±1.5° (omitting the discordant values for *cis*-2-butene).

While these lines appear almost linear, examination shows some curvature. Addition of a quadratic term giving the equation $T_B = B_1 + B_2T_A + B_3T_A^2$ suffices to reproduce them with great fidelity, as can be seen from the values in the last columns of Table VIII, where the average deviations and the average maximum deviations are only ±0.04 and 0.12°, respectively, again omitting the discordant values for *cis*-2-butene.

This agreement with the Dühring rule also encourages us to think that our vapor pressure data are reliable except perhaps in the case of *cis*-2-butene where the presence of some slight impurity is to be inferred. It should be remarked, however, that the values for propadiene which appeared to be in some doubt from the point of view of the Ramsay–Young rule show no irregularity here.

The Temperature Differential of the Vapor Pressure.—It follows from the Clausius–Clapeyron equation, assuming the gas to be perfect and the heat of vaporization ΔH_{vap} to be independent of the temperature, that $dp/dT = p\Delta H_{vap}/RT^2$. Combining this with Trouton's rule gives

$$\left[\frac{dp}{dT}\right]_{T_b} = \frac{760 \times 20.85}{RT_b} = \frac{7975}{T_b}$$

(34) Data of this research.

TABLE IX

THE TEMPERATURE DIFFERENTIAL OF THE VAPOR PRESSURE

Hydrocarbon	T_b, °K.	$\frac{dp/dT}{\frac{mm.}{deg.}}$ obs.	$\frac{dp}{dT}$, 100 $\frac{calcd. - obsd.}{obsd.}$, % Trouton	Nernst	Gen.	Spec.	Ref.
			n-Alkanes, $a_s = 3409$; $b_s = -1.28$				
Methane	111.73	61.28	+16.5	+4.3	−3.5	−0.1	29
Ethane	184.47	40.95	+ 5.6	+2.4	−0.5	− .9	30
Propane	231.04	33.50	+ 3.0	+3.0	+0.4	+ .3	31
Butane	272.48	29.29	− 0.1	+1.7	−0.5	− .3	33
Pentane	309.26	25.75	+ 0.2	+3.9	+1.4	+1.6	32
Hexane	341.90	23.78	− 1.9	+2.0	+0.4	+0.8	32
Heptane	371.53	22.36	− 4.0	+0.4	−0.8	−0.3	32
Octane	398.82	20.73	− 3.5	+1.4	+0.8	+1.1	32
Means			4.4	2.4	1.0	0.7	
			Branched Chain Alkanes, $a_s = 3372$; $b_s = -1.56$				
2-Methylpropane	261.06	29.69	+ 2.9	+4.1	+2.0	−0.1	32
2,2-Dimethylpropane	282.62	27.58	+ 2.3	+4.6	+2.4	+ .4	36
2-Methylbutane	301.11	26.31	+ 0.7	+3.5	+1.6	− .4	32
2,3-Dimethylbutane	331.15	24.12	− 0.2	+0.8	+1.9	− .1	32
2,2,4-Trimethylpentane	372.39	21.50	− 0.4	+4.2	+2.9	+1.0	37
2,5-Dimethylhexane	382.36	21.48	− 2.9	+1.5	+0.6	−1.3	32
2,6-Dimethyloctane	431.70	19.18	− 3.7	+1.7	+ .9	−0.8	32
Means			1.9	2.9	1.8	.6	
			n-Alkenes, $a_s = 3634$; $b_s = -3.38$				
Ethene	169.35	44.25	+ 6.4	+0.7	−1.1	+0.4	34
Propene	225.50	34.37	+ 2.9	+2.5	−0.1	+ .5	34
1-Butene	266.86	29.62	+ 0.9	+2.5	+ .3	+ .1	34
trans-2-Butene	274.07	28.60	+ 1.8	+3.7	+1.5	+1.2	34
cis-2-Butene	276.69	29.50	− 2.3	−0.4	−2.4	−2.7	34
1-Heptene	366.94	21.77	− 0.1	+4.4	+3.0	+1.2	32
Means			2.4	2.4	1.4	1.0	
			Branched Chain Alkenes, $a_s = 3634$; $b_s = -3.38$				
2-Methylpropene	266.04	29.02	+ 3.3	+4.9	+2.6	+2.5	34
2-Methyl-2-butene	311.59	25.71	− 0.5	+2.7	+0.9	−0.0	34
Means			1.9	3.8	1.8	1.2	
			Dienes, $a_s = 3895$; $b_s = -5.50$				
Propadiene	239.52	33.35	− 0.2	+0.2	−0.8	−0.5	34
1,3-Butadiene	268.65	29.42	+ .9	+2.6	+ .4	+1.0	32
1,4-Pentadiene	299.22	26.63	+ .1	+2.9	+ .9	−0.4	34
2-Methyl-1,3-butadiene	307.24	26.18	− .8	+2.1	+ .3	+ .6	38
Means			.5	2.0	.6	.6	
			n-Alkynes, $a_s = 4125$; $b_s = -6.77$				
Ethyne	187.94	43.58	− 2.6	−5.2	−8.0	−1.0	39
Propyne	249.95	33.50	− 4.7	−3.9	−6.2	−2.1	32
1-Butyne	282.21	27.97	+ 1.0	−3.2	+1.1	+3.9	32
2-Butyne	300.27	27.55	− 3.6	−0.9	−2.8	−1.0	40
Means			3.0	3.3	4.5	2.0	
			Miscellaneous				
1-Buten-3-yne	278.27	29.58	− 3.1	−1.2	−3.2	...	32
1,3-Butadiyne	282.95	28.52	− 1.2	+1.0	−1.0	...	32
Cyclohexane	353.90	22.81	− 1.2	+3.0	+1.5	...	41
1,5-Hexadien-3-yne	356.66	22.97	− 2.7	+1.5	+0.1	...	32
Means			2.0	1.7	1.4		
Means of values for all hydrocarbons listed			2.5	2.5	1.7	0.9	

(36) Aston and Messerly, THIS JOURNAL, **58**, 2354 (1936).

(37) Smith and Matheson, *J. Research Natl. Bur. Standards*, **20**, 641 (1928).

(38) Bekkedahl, Wood and Wojciechowski, *ibid.*, **17**, 883 (1936).

(39) "International Critical Tables," Vol. III, 208, 230 (1928).

(40) Heisig and Davis, THIS JOURNAL, **57**, 339 (1935).

(41) Scatchard, Wood and Mochel, *ibid.*, **61**, 3206 (1939).

where 20.85 is the Trouton constant (the mean value for the 35 hydrocarbons listed in Table IX) and T_b the absolute boiling point at 760 mm. pressure. Values of $[dp/dT]_{T_b}$ computed from our measurements and for some 26 additional hydrocarbons for which accurate vapor pressure data are available are in good agreement with this equation, the average deviation being 2.5%. Trouton's rule often can be replaced advantageously by the equation of Nernst[35] $\Delta H_{vap} = 9.5 \log T_b - 0.007 T_b$. Our equation then becomes

$$\left[\frac{dp}{dT}\right]_{T_b} = \frac{3634 \log_{10} T_b}{T_b} - 2.68$$

The differences between the values of $[dp/dT]_{T_b}$ computed from this equation and from the empirical equations (observed values) are listed in the fifth column of Table IX. The average percentage deviation is, however, still 2.5%.

Since the deviations were in general positive, we have altered the constants in the above equation slightly to obtain the general equation

$$\left[\frac{dp}{dT}\right]_{T_b} = 3461 \frac{\log T_b}{T_b} - 1.77$$

Using this equation we find the deviations listed in the sixth column of the above table, averaging 1.7%.

Finally, since a constitutive influence is evident we have framed special equations of the general type

$$\left[\frac{dp}{dT}\right]_{T_b} = a_s \frac{\log_{10} T_b}{T_b} + b_s$$

for each group of hydrocarbons and the resulting deviations are listed in the seventh column of the table. It can be seen that an even better agreement is attained, particularly with the alkanes and alkenes, the deviations averaging on the whole 0.9%.

Here again we find that the values of *cis*-2-butene show a considerably greater discrepancy than any of the other alkenes or alkanes, which confirms our previous inference that our data for this substance are less reliable than our other data.

(35) Nernst, "Theoretical Chemistry," Eng. ed. transl. by Tizard, Macmillan and Co., Ltd., London, 1916, p. 295.

Summary

1. Measurements have been made of the vapor pressures of very pure samples of liquid ethene, propene, 2-methylpropene, 1-butene, *cis*-2-butene, *trans*-2-butene, 1,4-pentadiene and 2-methyl-2-butene over the approximate range 10 to 1000 mm. by the static method. Equations with three constants have been derived by the method of least squares from the results of these measurements expressing the vapor pressure as a function of the temperature. The vapor pressure of liquid and of crystalline propadiene its triple point temperature and pressure also have been ascertained.

2. From the least square equations the normal boiling points and the slopes of the vapor pressure curves at these points as well as the heats of vaporization of these substances as perfect gases have been computed.

3. Our vapor pressures, with one or two exceptions, have been found to agree excellently with the Ramsay–Young and the Dühring rules, particularly when in each rule an additional constant is introduced. A general equation has been derived expressing the temperature differential of the vapor pressure at the absolute boiling point as a function of the absolute boiling point. With this equation, too, our data are found to be in excellent agreement.

CAMBRIDGE, MASS. RECEIVED JANUARY 30, 1940

[CONTRIBUTION FROM THE BUREAU OF AGRICULTURAL CHEMISTRY AND ENGINEERING, U. S. DEPARTMENT OF AGRICULTURE, WASHINGTON, D. C.]

The Solubility of Carbon Dioxide in Water at Various Temperatures from 12 to 40° and at Pressures to 500 Atmospheres. Critical Phenomena*

BY R. WIEBE AND V. L. GADDY

The present paper extends previous work on the solubility of carbon dioxide in water. The apparatus and procedure are essentially the same as described.[1]

Aside from the particular interest in the solubility data themselves, we were also interested in investigating a phenomenon we had noticed in our previous work but had not reported. It was found that during saturation at pressures exceeding 700 atm. there was some pressure above which the solubility of water in the gas phase increased tremendously. This was shown by the appearance of large amounts of water in the expanded gas. We had apparently reached the critical solution pressure for the carbon dioxide–water system.

Discussion of Results

The results on the solubility are given in Table I and are expressed as the number of cc. of carbon dioxide (S. T. P.) contained in 1 g. of water.

TABLE I

SOLUBILITY OF CARBON DIOXIDE IN WATER

(cc. S. T. P. PER G. OF H_2O)

Total pressure in atm.	Temperatures, °C. 12	18	25	31.04	35	40
25		19.51		14.18	12.95	11.62
50	35.54	32.03	27.23	24.15	22.21	20.35
75	36.33	33.85	31.17	29.33	27.84	25.81
100	36.77	33.98	31.75	30.17	29.13	27.81
125						28.71
150	38.39	35.75		31.59	30.52	29.39
200	39.77	37.17		32.78	31.83	31.74
300	41.07	39.31				
400			38.62	36.78	35.73	34.87
500				38.67	37.99	36.73

In Fig. 1 the solubility is plotted *versus* temperature, our previous data having been included. For the most part the curves resemble those obtained for hydrogen, nitrogen, and helium[2] except that the minimum solubility occurs at higher temperatures, but there are decided differences in the low temperature range. The principal reason for this is undoubtedly the fact that we are dealing here with two liquid systems but other factors are also influential and will be discussed presently.

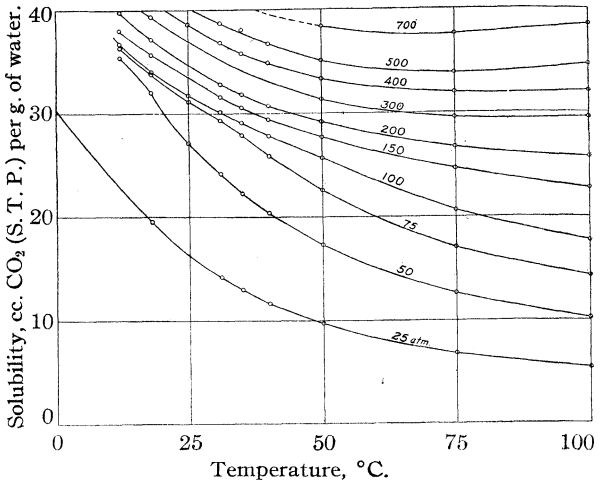


Fig. 1.

Although several attempts were made to get data at 10° above 50 atm. total pressure, only one series of measurements, at 150 atm., was obtained. When proceeding to check these values, a solid, presumably carbon dioxide hexahydrate, formed and the freezing of the liquid in the connecting lines made further measurements impossible. The fact that one series was obtained is very typical of the mode of formation of these gas hydrates.[3] A special technique, *e. g.*, sudden expansion, must often be used to initiate the formation of the hydrate, although once started it will form readily. At 12° we were able to get measurements up to 300 atm. but above this pressure, aside from solid formation, another difficulty was encountered, the disappearance of one phase, indicating complete miscibility. The compositions of the gas and liquid phases at 12° and 600 atm. were identical. We believe this to be true also for 500 atm. at the same temperature. At 18° similar conditions prevail.

In Fig. 2 we have attempted to portray qualitatively the probable course of the critical curve. With our present set-up it was not possible to determine accurately the change of the critical

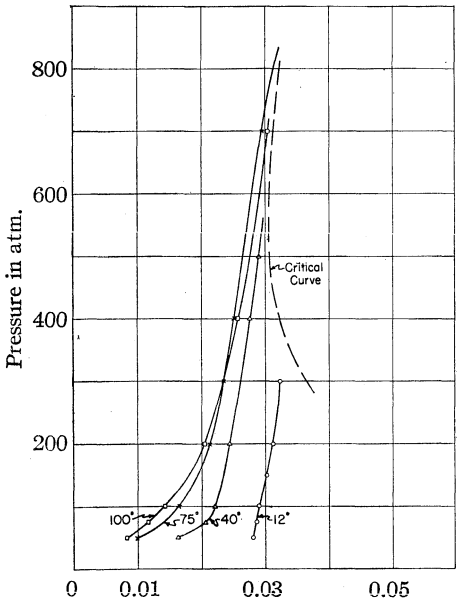
(*) Not copyrighted.

(1) Wiebe and Gaddy, THIS JOURNAL, **61**, 315 (1939).

(2) Wiebe, Gaddy and Heins, *ibid.*, **55**, 947 (1933); Wiebe and Gaddy, *ibid.*, **56**, 76 (1934); **57**, 847 (1935).

(3) For a summary on gas hydrates with references, see W. Schroeder, *Sammlung Chem. und Chem. tech. Vorträge*, **29**, 1 (1927).

solution pressure with either temperature or composition. It will be seen that apparently there is a pressure maximum at about 75° and that both the 100 and 40° solubility curves will end at lower pressures than the 75° isotherm. It must be emphasized that we are basing our discussion on qualitative evidence only.



Mole fraction of CO_2 in water at various temperatures.

Fig. 2.

The dissociation pressure curve of the system hydrate–vapor–water saturated with carbon dioxide is shown in the lower left-hand corner of Fig. 3.[4] This curve ends in the critical decomposition point at 10° and 44.3 atm., the latter being practically the vapor pressure of pure carbon dioxide at that temperature. The critical decomposition point represents the invariant system consisting of hydrate, vapor, carbon dioxide saturated with water, and water saturated with carbon dioxide. When increasing the pressure the vapor phase disappears and the univariant system, hydrate, carbon dioxide saturated with water, and water saturated with carbon dioxide will continue to exist under certain temperature and pressure conditions.

We found evidence of this univariant system at 10 and 12°, *i. e.*, increase of pressure raises the temperature of coexistence of the three phases. At the point of complete miscibility (possibly 500 atm.), even at 12° no solid was detected, though the possibility of its existence is not ex-

(4) Data taken from "I. C. T.," Vol. VIII, p. 244.

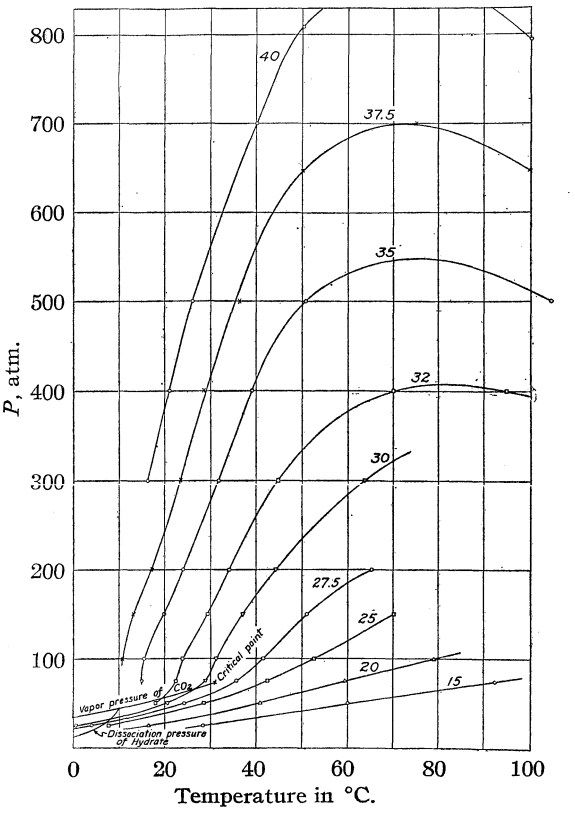


Fig. 3.—Composition expressed as cc. of CO_2 (S. T. P.) per g. of water.

cluded. We believe that the curve bounding the region of complete miscibility roughly follows the course of the curves of constant composition, at least in the low temperature range (see data in Table II). Our deduction is based on the fact that we encounter complete miscibility when-

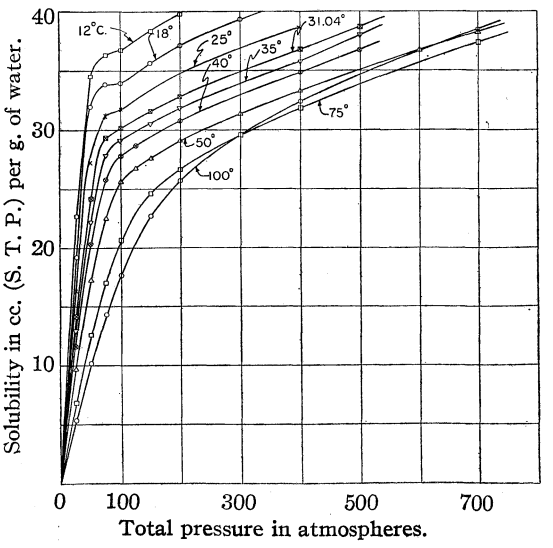


Fig. 4.—Solubility of carbon dioxide in water.

TABLE II

TEMPERATURES AT CONSTANT COMPOSITION EXPRESSED IN CC. OF CO_2 (S. T. P.) PER G. OF WATER

Total press. in atm.	Composition (cc. of CO_2 (S. T. P.) per g. of water)									
	10	15	20	25	27.5	30	32	35	37.5	40
25	48.1	28.4	16.5	7.7	4	0.6				
50	102.4	60.0	40.9	28.6	24.3	20.6	18.0			
75		92.5	59.4	42.5	35.8	29.0	22.5			
100			79.2	52.6	41.6	31.3	24.0		10.8	
150				70.2	51.0	37.1	29.5		13.1	
200					65.3	44.2	34.1		17.1	11.6
300						63.7	44.7	16.2	23.5	16.2
400							72, 95	21.0	28.5	21
500								50.7,		
								104	36.3	26
646									50, 100	
700									75	40
789										100
818										50

ever we try to obtain values higher than about 40 cc. of carbon dioxide (S. T. P.) per gram of water. We have mentioned the likelihood of a possible pressure maximum at 75° in connection with the discussion of Fig. 2.

Figure 4 shows solubility isotherms that illustrate particularly the change of state of carbon dioxide from gas to liquid. At the lower temperatures this amounts to almost a discontinuity. In Table III we have made a few additional calculations by means of the approximate formula derived previously[1]

$$\mathrm{d} \ln N_1 = \frac{\overline{V}_1^1 - \overline{V}_1}{RT} \mathrm{d}P$$

where $\overline{V}_1^1$ and $\overline{V}_1$ are the partial molal volumes of carbon dioxide in the vapor and liquid phases, respectively; and N_1 the mole fraction of carbon dioxide in the liquid phase. The agreement between calculated and observed values is good and only breaks down at about 400 and 700 atm. at 40° and 50°, respectively.

TABLE III

MOLE FRACTION OF CARBON DIOXIDE IN WATER

Pressure of CO_2 atm.	40°		50°	
	Exp.	Calcd.	Exp.	Calcd.
50	0.0162	0.0159	0.0138	0.0136
75	.0205	.0202	.0179	.0177
100	.0220	.0221	.0203	.0198
125	.0227	.0228	.0212	.0207
150	.0232	.0234	.0219	.0214
200	.0243	.0246	.0230	.0226
300		.0266	.0247	.0247
400	.0275	.0285	.0262	.0266
500	.0289	.0304		.0284
700		.0338	.0301	.0318

Summary

The solubility of carbon dioxide in water has been determined at 12, 18, 25, 31.04, and 40° and at pressures to 500 atmospheres.

Evidence of complete miscibility was found particularly in the low temperature range and an attempt was made to portray qualitatively the course of the critical curve.

Solid carbon dioxide hexahydrate was discovered at 10° at all pressures above 50 atm. and at 12° between 300 and 500 atm.

RECEIVED JANUARY 18, 1940

[CONTRIBUTION FROM THE METALLURGICAL FUNDAMENTALS SECTION, METALLURGICAL DIVISION, BUREAU OF MINES, UNITED STATES DEPARTMENT OF THE INTERIOR]

The Specific Heats at Low Temperatures of Tantalum Oxide and Tantalum Carbide[1]

BY K. K. KELLEY[2]

The measurement of specific heats, at low temperatures, of metallurgically important substances has been one of the programs of study of the Metallurgical Division of the Bureau of Mines for the past several years. This paper presents results for tantalum oxide and tantalum carbide for which no low-temperature specific heat or entropy data have been available heretofore. The results for tantalum carbide may be of special interest in that they are the first adequate set of low-temperature true specific-heat measurements to be obtained for a metal carbide, the only other pertinent data being those of Nernst and Schwers[3] and Günther[4] for silicon carbide in the temperature range 22 to 97°K.

Materials

The tantalum oxide was a product of the Fansteel Products Co., purchased several years ago. It was stated to be of virtually atomic weight purity. Because of its low apparent density, it was compressed into pellets and the pellets broken into sizes below 2 mm. for filling the calorimeter. A 210.5-g. sample was used.

The tantalum carbide was loaned for this work by the Fansteel Metallurgical Co. through the courtesy of Mr. J. H. Harper and Mr. F. L. Hunter. This material was in powder form and according to the manufacturers contained 4.26% carbon compared with 4.23%, the theoretical figure for TaC. Impurities other than the excess carbon were stated to be of the order of 0.02%. It required 803.5 g. to fill the calorimeter.

Results

Specific Heats.—The method and apparatus have been described previously.[5]

The results, expressed in defined calories (1 calorie = 4.1833 int. joules), are given in Table I and shown graphically in Fig. 1. The values for tantalum carbide have been corrected for the 0.03% excess carbon on the assumption that it is present as graphite. The correction increases with the temperature and ranges from 0.02 to 0.09%.

The tantalum oxide results appear normal and require no discussion. There are, however, two items of interest to be mentioned concerning the measurements for tantalum carbide. Comparison of the results for this substance with those for pure tantalum[6] shows that at temperatures below 125°K. the former has the lower specific heat per gram formula mass, the difference at 54°K. being 0.59 calorie. Also, if C_p for tantalum carbide is plotted against log T, an inflection point in the neighborhood of 100–110°K. is readily apparent. This is caused by the carbon skeleton, the vibrations of which contribute only a very minor portion of the specific heat at the lowest temperatures studied, beginning to take up vibrational energy. Such an inflection is not usual in low temperature specific-heat curves but has been observed in other instances in which the constituent atoms differ widely in atomic mass, as, for example, hydrogen chloride.[7]

The results for tantalum oxide may be adequately represented throughout the entire temperature range studied by the function combination

TABLE I

SPECIFIC HEAT OF Ta_2O_5 (441.76 G.)

T, °K.	C_p	T, °K.	C_p	T, °K.	C_p
53.4	5.872	115.7	16.19	214.2	26.88
57.6	6.623	124.9	17.49	224.5	27.71
62.1	7.480	134.9	18.86	234.7	28.54
66.6	8.353	145.0	20.10	245.2	29.34
70.9	9.142	154.7	21.23	255.8	30.15
75.4	9.971	165.0	22.33	265.8	30.63
81.5	10.93	174.6	23.34	275.5	31.14
86.2	11.70	184.4	24.29	285.0	31.76
95.6	13.12	194.5	25.20	294.2	32.10
105.3	14.70	203.4	26.04		

SPECIFIC HEAT OF TaC (192.89)

54.6	2.275	104.3	4.583	214.6	7.292
58.1	2.505	114.7	4.876	224.5	7.514
62.1	2.759	124.8	5.149	234.5	7.713
66.5	3.032	134.8	5.415	244.7	7.912
71.1	3.298	144.8	5.661	255.1	8.109
75.6	3.525	154.5	5.900	265.3	8.280
80.2	3.735	164.6	6.141	275.1	8.424
80.6	3.752	174.2	6.377	284.6	8.559
84.4	3.903	184.5	6.614	293.9	8.741
84.9	3.924	194.3	6.843	294.5	8.764
94.5	4.271	204.5	7.078		

(1) Published by permission of the Director, Bureau of Mines, U. S. Department of the Interior. (Not copyrighted.)

(2) Chemist, Metallurgical Division, Bureau of Mines, U. S. Department of the Interior.

(3) Nernst and Schwers, *Sitzber. Kgl. Preuss. Akad. Wiss.*, 355 (1914).

(4) Günther, *Ann. Physik*, [4] **51**, 828 (1916).

(5) Millar, THIS JOURNAL, **50**, 1875 (1928); Anderson, *ibid.*, **52**, 2296 (1930).

(6) Kelley, unpublished data.

(7) Giauque and Wiebe, THIS JOURNAL, **50**, 101 (1928).

$$D\left(\frac{170}{T}\right) + 2E\left(\frac{265}{T}\right) + 2E\left(\frac{528}{T}\right) + 2E\left(\frac{880}{T}\right)$$

In the case of tantalum carbide

$$D\left(\frac{268}{T}\right) + E\left(\frac{861}{T}\right)$$

represents the data adequately except in the region near the inflection point, where the function sum is somewhat low (at worst 0.1 calorie). Below 72°K., however, the Debye function alone is adequate.

Entropy Calculations.—The entropies at 298.1°K. were calculated in the usual manner. The extrapolated portions below 53.1°K. were obtained from the functions given above. Only the Debye function and first pair of Einstein functions for tantalum oxide need be considered at 53.1°K. while for tantalum carbide only the Debye function is significant at this temperature. The results are given in Table II.

There are no other values for these substances with which to compare the present results. It may be of interest to note, however, that the figure for tantalum carbide is only 0.2 unit higher than the entropy at 298.1°K. of pure tantalum.[6]

Related Thermal Data.—The heat of formation of tantalum carbide never has been determined. Several values exist for tantalum oxide: −498,400, Moose and Parr[8]; −480,500, Sieverts, Gotta and Halberstadt[9]; −486,000 ± 500, Becker and Roth[10]; and −499,900 ± 1000, Neumann, Kröger and Kunz.[11]

TABLE II

ENTROPIES AT 298.1°K.

	Ta_2O_5	TaC
0–53.1°K. (extrapolation)	2.83	0.95
53.1–298.1°K. (graphical)	31.36	9.16
$S_{298.1}$	34.2±0.4	10.1±0.1

The spread in these values probably may be attributed to the presence of different amounts of hydrogen in the samples of metal burned to oxide. For the present purpose the result of Becker and Roth is adopted. From this value and the entropies of the oxide, metal (9.9 ± 0.1)[6] and oxygen (49.03)[12] there is computed $\Delta F^0_{298.1} = -453{,}700$ as the free energy of formation of tantalum oxide from the elements.

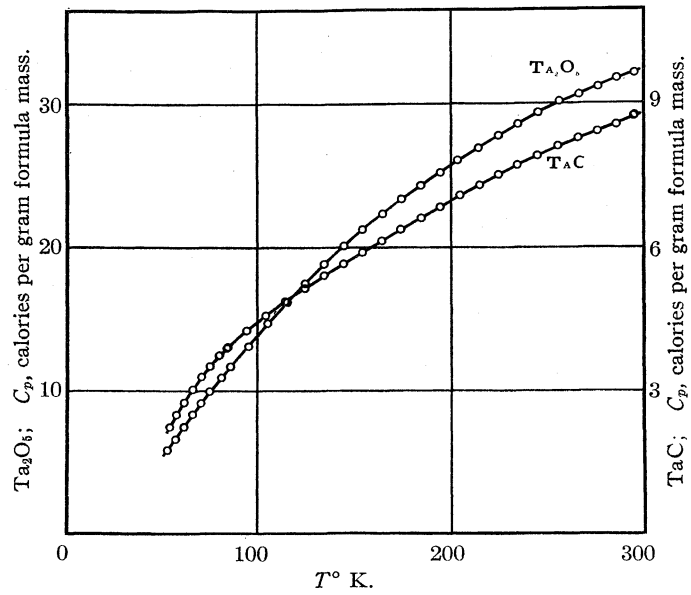


Fig. 1.—Specific heats of Ta_2O_5 and TaC.

Summary

Specific heat measurements of tantalum oxide and tantalum carbide were made in the temperature range 53 to 298.1°K.

The entropies are $S_{298.1} = 34.2 \pm 0.4$ for tantalum oxide and $S_{298.1} = 10.1 \pm 0.1$ for tantalum carbide.

The free energy of formation of tantalum oxide from the elements has been computed as $\Delta F^0_{298.1}$ −453,700.

RECEIVED JANUARY 8, 1940

(8) Landolt–Börnstein, "Physikalisch-chemische Tabellen," Julius Springer, Berlin, 1st Suppl., 1927, p. 838.

(9) *Ibid.*, 2nd Suppl., Vol. 2, 1931, p. 1515.

(10) Becker and Roth, *Z. physik. Chem.*, **A167**, 16 (1933).

(11) Neumann, Kröger and Kunz, *Z. anorg. Chem.*, **218**, 395 (1934).

(12) Giauque and Johnston, THIS JOURNAL, **51**, 2300 (1929).

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

The Stereochemistry of Complex Inorganic Compounds. VII.[1] The Mechanism of the Walden Inversion in Some Reactions Leading to the Formation of the Carbonato-diethylenediamine Cobaltic Ion

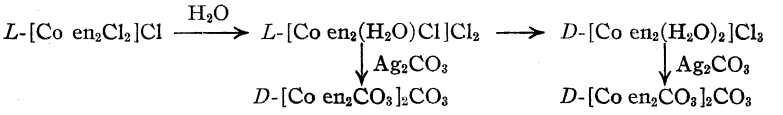
BY JOHN C. BAILAR, JR., AND DONALD F. PEPPARD[2]

It has been shown recently[1e] that the carbonato-di-levopropylenediamine cobaltic ion exists in two diastereoisomeric forms. One of these is less stable than the other, and is readily converted into it by warming. Both of them can be prepared from the one known form of the corresponding dichloro salt. The more stable (and, hence, the non-inverted) isomer, evidently is formed through an intermediate aquo complex, for it is obtained only under conditions in which such an intermediate is known to form. The less stable form, on the other hand, is obtained under conditions which would minimize the formation of aquo complexes. This gives a clue to the mechanism of the Walden inversion which takes place in the formation of the carbonato-diethylenediamine cobaltic ion from the corresponding dichloro ion,[1a,b] and has led us to study the mechanism of this and some related reactions.

It is indicated that the change of *L*-dichloro-diethylenediamine cobaltic ion to the *D*-carbonato ion probably proceeds through the formation of the *L*-chloro-aquo ion. Since this takes place under the same conditions which produce the non-inverted carbonato complex in the propylenediamine series,[1e] it is probable that the *L*-dichloro-diethylenediamine salt and the *D*-carbonato salt have the same configuration. Mathieu has come to the same conclusion, but from very different evidence.[3]

That aquation plays an important part in the reaction of dichloro-diethylenediamine cobaltic ion and silver carbonate is shown by the fact that the rotation of the carbonato complex obtained depends upon how long the solution of the dichloro salt is allowed to stand before the silver carbonate is added (Table I).

Mathieu[4] has shown that *L*-dichloro-diethylenediamine cobaltic chloride aquates to give both the *L*-chloro-aquo complex and the *D*-diaquo complex. The latter is formed only in small amounts, however, and the equilibrium between the two, when disturbed, is restored very slowly. It thus appears that the chloro-aquo complex is the important intermediate in the reaction under investigation. The diaquo complex may take part to some extent; upon treatment with silver carbonate it also gives the *dextro* carbonato complex. It seems probable that none of the reactions shown in the following scheme involves change of configuration



Mathieu[3] has come to the same conclusion from studies of circular dichroism. From this and the data of Table I it follows that the conversion of *L*-[Co en$_2$Cl$_2$]Cl to *L*-[Co en$_2$CO$_3$]$_2$CO$_3$ does not go through an intermediate and involves a change of configuration. These hypotheses completely explain the results of the experiments previously reported.[1a,b,c] The addition of potassium carbonate, or the slow addition of silver carbonate, to solutions of the dichloro salt allows aquation to take place before the carbonate group is introduced into the complex; direct entrance of the

TABLE I

EFFECT OF AGING A 4% SOLUTION OF *L*-[Co en$_2$Cl$_2$]Cl BEFORE TREATING WITH A TEN-FOLD EXCESS OF SILVER CARBONATE

"*t*" represents the time of aging, in minutes, and "[α]D" represents the specific rotation of the resultant carbonato salt, in degrees.

t	[α]D	*t*	[α]D
0	−212	75	+684
1	−183	120	+635
3	− 96	170	+587
6	− 19	186	+539
10	+ 87	235	+520
20	+250	260	+520
40	+501	296	+462
50	+530	360	+433
60	+578	1080	+147

(1) Previous articles in this series have appeared in THIS JOURNAL: (a) **56**, 774 (1934); (b) **58**, 2224 (1936); (c) **58**, 2226 (1936); (d) **61**, 2402 (1939); (e) **61**, 3199 (1939); (f) **62**, 105 (1940).

(2) From a portion of the doctorate thesis of Donald F. Peppard, 1939.

(3) Mathieu, *Bull. soc. chim.*, [5] **3**, 476–500 (1936).

(4) Mathieu, *ibid.*, [5] **4**, 687–700 (1937).

carbonate group is effected only when an *excess* of silver carbonate is ground with the dichloro salt as soon as it is put in solution, or when a large excess of dry potassium carbonate is ground with the dry complex before solution takes place.[1e]

The dichloro complex reacts rapidly with potassium carbonate; it also aquates rapidly in the presence of potassium carbonate, due to the basicity of the solution. When a fresh solution of the dichloro salt is mixed with a solution of potassium carbonate, a mixture of *D* and *L* carbonato salts is formed, with the *D* in preponderance.[5] If the solution is allowed to age until aquation is essentially complete (about sixty-five minutes for a 4% solution) before the carbonate is added, a nearly pure *D* carbonato salt may be obtained.

The reactions of the chloro-bromo and dibromo-diethylenediamine cobaltic complexes with carbonates also have been studied. These behave just as the dichloro complex does, and their reactions give inversions under the same conditions. They evidently aquate in the same way, and the chloro-bromo, at least, at about the same rate. The data of Table II are strictly comparable to those of Table I.

TABLE II

EFFECT OF AGING A 4% SOLUTION OF *L*-[Co en$_2$ClBr]Cl

t	[α]D
1	−190
10	+ 90
20	+220
65	+510

Experiments with [Co en$_2$ClBr]Cl showed conclusively that the relative amounts of complex and silver carbonate used are of little significance compared to the time the solution is allowed to stand before the reagent is added. In one series of experiments, the reactants were ground together before the water was added. The amount of silver carbonate used varied from the calculated amount to a ten-fold excess, but the rotation of the resultant carbonato salt varied only slightly, [α]D −160 to −200°. In another series, the cobalt complex stood in a 4% solution for sixty-five minutes before the reagent was added. The same amounts of silver carbonate were used as before; [α]D +470 to +500°.

If the hypothesis here suggested is correct, conversion of the chloro-aquo complex to the carbonato complex should proceed under all conditions without inversion. This has been found to be the case: *L*-chloro-aquo-diethylenediamine cobaltic bromide was treated with potassium carbonate and silver carbonate under a wide variety of conditions, and always gave a dextro-rotatory product. The positive rotation was somewhat lower when potassium carbonate was used, but this is evidently due to racemization, rather than to any tendency to form the levo-rotatory product.

These experiments naturally suggest a reinvestigation of the reactions of potassium and silver oxalates with *L*-dichloro-diethylenediamine cobaltic chloride, which have previously been shown[1a] to give a dextro-oxalato complex under all conditions. The formation of the oxalato complex takes place somewhat more slowly than that of the carbonato complex, which suggests that aquation may always take place before the oxalate group enters the complex. A comparison of Table III with Table I shows how differently the silver oxalate and silver carbonate react.

TABLE III

EFFECT OF AGING A 4% SOLUTION OF *L*-[Co en$_2$Cl$_2$]Cl BEFORE TREATING WITH A TEN-FOLD EXCESS OF SILVER OXALATE

"*t*" represents the time of aging, in minutes, and "[α]D" represents the specific rotation of the resultant oxalato salt, in degrees.

t	[α]D
0	+357
1	+357
25	+293
60	+266
100	+238
150	+202
270	+147

It is possible that silver oxalate cannot react directly with the *L*-dichloro complex, but only with the *L*-chloro-aquo complex which is formed by aquation. This ion has been shown to react with silver oxalate to give the dextro-oxalato ion. On the other hand, it is possible that the oxalate and carbonate reactions are entirely different in character.

One entirely new reaction was studied in the course of this investigation, the change of the chloro-aquo complex to the dichloro complex. This is effected by allowing the complex to stand in a large excess of thionyl chloride for about one hundred hours. The reaction evidently proceeds without inversion.

(5) Werner and McCutcheon, *Ber.*, **45**, 3284 (1912).

Experimental

L-[Co en$_2$Cl$_2$]Cl was prepared and resolved as previously described.[1a]

L-[Co en$_2$(H$_2$O)Cl]Br$_2$ was prepared according to the directions of Werner and Tschernoff[6] and was resolved following Werner and Schwyzer's[7] description of Fischlin's method.[8] The hydrobromic acid used in the last step of the procedure may be replaced by hydrochloric, thus giving the levo-chloro-aquo chloride.

A more convenient method of preparing the active chloro-aquo salts was devised using racemic *cis* dichloro diethylenediamine cobaltic chloride as the starting material.

Ten grams of *cis* [Co en$_2$Cl$_2$]Cl and 40 cc. of water are shaken with glass beads for twelve hours. The beads and any small amount of residue are removed by filtration and the solution allowed to stand in a stoppered flask for sixty hours. It is then cooled to 20°, 6 g. of ammonium dextro-α-bromocamphor-π-sulfonate added, and the mixture stirred by a mechanical stirrer at 18–20° for ten minutes. The solution is filtered from the green crystalline precipitate, 6 g. more of the resolving agent is added, and the stirring continued. Precipitation of the pink levo-chloro-aquo diethylenediamine cobaltic dextro-α-bromocamphor-π-sulfonate begins after some time. The filtrate from this precipitate (about 35 cc.) is treated with 20 cc. of cold aqueous hydrobromic acid (density, 1.4) and cooled in ice–salt mixture with occasional stirring. In from fifteen to twenty-five minutes precipitation of *D*-[Co en$_2$Cl(H$_2$O)]Br$_2$ begins. After fifteen minutes, this is filtered and washed with absolute alcohol and ether. For purification it is dissolved in water at 33° (5 cc. of water per g. of salt), filtered quickly, treated with one-third its volume of hydrobromic acid (density, 1.4), and cooled in an ice–salt mixture. The salt precipitates almost at once on scraping the sides of the beaker. The yield is 0.7–1.0 g. of purified salt. For a 0.1% solution $[\alpha]_D$ −220°.

The precipitated levo-chloro-aquo diethylenediamine cobaltic dextro-α-bromocamphor-π-sulfonate is washed on the filter with 5 cc. of ice water, followed by alcohol and ether. The dry salt is ground in a cold mortar with 6 cc. of cold hydrobromic acid for one minute. The *L*-[Co en$_2$Cl(H$_2$O)]Br$_2$ is filtered and washed with alcohol and ether. It is purified in the same manner as the dextro isomer. The yield is 0.9 to 1.3 g. of purified salt. For a 0.1% solution, $[\alpha]_D$ is +220°.

Usually one purification is sufficient to give a maximum optical activity for either isomer.

In order to obtain the levo-chloro-aquo chloride the precipitate of levo-chloro-aquo dextro-α-bromocamphor-π-sulfonate obtained from 10 g. of racemic dichloro diethylenediamine cobaltic chloride is ground in a cold mortar with 5 cc. of cold concentrated hydrochloric acid for thirty seconds. Fifteen cubic centimeters of cold alcohol–ether mixture (1:1) is added with grinding. At the end of about two minutes the red crystals are filtered and washed with alcohol and ether. For a 0.1% solution, $[\alpha]_D$ is +200°.

(6) Werner and Tschernoff, *Ber.*, **45**, 3296 (1912).
(7) Werner and Schwyzer, *Helv. Chim. Acta*, **4**, 117 (1921).
(8) Fischlin, Dissertation, Zürich, 1919.

[Co en$_2$ClBr]Br was prepared and resolved according to the directions of Werner and Tschernoff.[6]

trans-[Co en$_2$Br$_2$]Br was prepared by the method of Werner, Gerb, Lorie and Rapiport.[9] A modification of their method was used, however, in converting this to the *cis* form. Fifteen grams of *trans*-[Co en$_2$Br$_2$]Br (heated at 110° for eight hours to remove traces of acid) is heated on the steam-bath in 80 cc. of water for twenty minutes. It is then allowed to stand at room temperature in an acid-free atmosphere for twenty-four hours. Thirty cubic centimeters of water is added, and the mixture is well ground. After standing for a day the gray-violet powder, which is essentially *cis*-[Co en$_2$Br$_2$]Br, is filtered. A further quantity of the salt is obtained by allowing the filtrate to evaporate. It is purified by extracting the admixed *trans*-dibromo- and *cis*-bromo-aquo complexes with water.[9]

The resolution of the salt, which has not been previously described, was carried out as follows. Six grams of finely ground racemic [Co en$_2$Br$_2$]Br is added to 500 cc. of water at 20° and stirred rapidly for three minutes. The small amount of residue is removed by filtration and 14 g. of ammonium dextro-α-bromocamphor-π-sulfonate added to the filtrate. The mixture is cooled to about 5° and stirred for fifty minutes. (Precipitation begins in about four minutes.) The precipitate is washed with alcohol and ether. Approximately 1.5 g. of a gray-violet crystal powder is obtained. This is ground in a cold mortar with 8 cc. of ice cold hydrobromic acid (density 1.4). Thirty cubic centimeters of cold alcohol–ether mixture (1:1) is added and the grinding continued. The gray-violet powder is filtered and washed with absolute alcohol and ether. Sometimes it has a pronounced greenish color, probably due to the presence of a small amount of the *trans* dibromo salt. The product always has a slight greenish cast.

For a 0.025% solution at 29°, $[\alpha]_D$ is +520°. The rotation was observed exactly two minutes after adding water to the solid salt.

Werner and McCutcheon's method[5] of preparing the *D*-[Co en$_2$CO$_3$]$^+$ ion gives a product of low activity, so the following modification was developed. Twenty-five grams of *L*-[Co en$_2$Cl$_2$]Cl is dissolved in 500 cc. of water at about 25° and kept at approximately this temperature for eighty-five minutes. Forty-five grams of silver carbonate is then added and the mixture stirred mechanically for two hours. The silver salts are removed and the filtrate is evaporated by blowing a current of air across the surface. For a 0.1% solution at 29°, $[\alpha]_D$ is +740°.

Active [Co en$_2$BrH$_2$O]Br$_2$·$^1/_2$H$_2$O.—Five grams of *D*-[Co en$_2$CO$_3$]$_2$CO$_3$·3H$_2$O is ground with 20 cc. of hydrobromic acid for forty minutes. After cooling to 0°, the red-purple salt is removed by filtration and washed with alcohol and ether. Approximately 4.5 g. of salt is obtained. For purification it is dissolved in water at 30° (5 cc. of water per gram of salt), filtered, and treated with one-third its volume of hydrobromic acid. The solution is cooled rapidly in a salt–ice mixture and the walls of the beaker scraped with a glass rod; yield: about 1 g. For a 0.05% solution at 29°, $[\alpha]_D$ is +260°. For analysis the salt was dried over potassium hydroxide.

(9) Werner, Gerb, Lorie and Rapiport, *Ann.*, **386**, 111–112 (1912).

Anal. Calcd. for $[Co\,en_2(H_2O)Br]Br_2 \cdot {}^1/_2H_2O$: Br, 53.81. Found Br, 53.93. Werner[10] reports the air dried racemic product to be the monohydrate.

The reactions of *L*-$[Co\,en_2Cl_2]Cl$, *L*-$[Co\,en_2ClBr]Cl$, and *L*-$[Co\,en_2Br_2]Br$ with silver carbonate were all carried out in essentially the same way. If the complex (say, 0.1 g.) is ground with a large excess of silver carbonate (say 1 g.) in a small amount (5–10 cc.) of water, the *L*-carbonato carbonate is formed. This may be isolated by pouring the solution into a large volume of a 1:1:1 mixture of alcohol, ether and acetone or may be precipitated as the bromide by the addition of solid potassium bromide (about 0.1 g.). In a typical experiment, the bromide showed $[\alpha]_D$ −650° for a 0.1% solution.

Anal. of the carbonate. Calcd. for $[Co\,en_2CO_3]_2CO_3 \cdot 2H_2O$: C, 22.98; H, 6.27. Found: C, 23.20; H, 6.27. *Anal.* of the bromide. Calcd. for $[Co\,en_2CO_3]Br$: Br, 25.05. Found: Br, 25.22, 24.96.

In experiments with aged solutions, 0.2–0.4 g. of the complex was dissolved in 10 cc. of water and, after a definite length of time, was ground with an excess of silver carbonate. Complete reaction can be obtained only by grinding for half an hour. The solution was evaporated at room temperature, and the salt isolated as before. In one typical experiment, a 4% solution was aged for sixty-five minutes. The product was isolated as the bromide, $[\alpha]_D$ +1040, for a 0.1% solution.

Anal. Calcd. for $[Co\,en_2CO_3]Br$: Br, 25.05. Found: Br, 25.11.

The reactions with potassium carbonate were carried out as follows. About 0.1 g. of the complex, 0.04 g. of potassium carbonate, and 0.4 cc. of water were warmed to 80° for a minute. The solution was diluted to 100 cc., and the rotation taken at the sodium D line. The rotations were always positive.

L-$[Co\,en_2(H_2O)Cl]Br_2$ and *L*-$[Co\,en_2(H_2O)Br]Br_2 \cdot {}^1/_2H_2O$ were treated with silver carbonate in the same ways as the di-halo complexes, and the products were isolated as before. The rotatory power of the product was always positive, and varied between +700 and +850°. The carbonate from a typical run gave the following analysis. Calcd. for $[Co\,en_2CO_3]_2CO_3 \cdot 2H_2O$: C, 22.98; H, 6.27. Found: C, 23.41; H, 6.10.

Potassium carbonate was allowed to react with the aquo complexes in the same manner as with the di-halo complexes. The solutions obtained all showed strong positive rotations.

The reactions of *L*-$[Co\,en_2Cl_2]Cl$, *L*-$[Co\,en_2Br_2]Br$, *L*-$[Co\,en_2(H_2O)Cl]Br_2$ and *L*-$[Co\,en_2(H_2O)Br]Br_2$ with silver oxalate were carried out under the same conditions as those with silver carbonate, except that the grinding was continued for an hour and a half. The oxalato complexes were not isolated; the solutions were simply diluted to give a 0.1% concentration of the complex. In every case, a positive rotation was obtained.

The conversion of *L*-$[Co\,en_2(H_2O)Cl]Cl_2$ to *L*-$[Co\,en_2Cl_2]Cl$ was carried out by suspending 0.2 g. of the thoroughly dried aquo complex in 8 cc. of thionyl chloride. After one hundred hours, with occasional shaking, the violet salt was removed by filtration and washed with alcohol and ether. That the conversion to dichloro salt was essentially complete was shown by the change in color (purple to violet) and by the fact that the product reacted with silver carbonate to give the levo-rotatory carbonato salt. The chloro-aquo compound, under similar conditions, gives a dextro-rotatory product. In one experiment, a sample of the chloro-aquo salt having $[\alpha]_D$ +160° gave a dichloro salt having $[\alpha]_D$ +260°, both readings being made on a 0.05% solution.

(10) Werner, *Ann.*, **386**, 128 (1912).

Summary

It has previously been suggested that the conversion of levo-dichloro-diethylenediamine cobaltic chloride to the dextro-carbonato salt proceeds through the formation of an aquated intermediate, while conversion to the levo-carbonato salt proceeds directly. Evidence is now advanced to support this hypothesis.

The conversions of dibromo- and chloro-bromo-diethylenediamine cobaltic complexes to the carbonato complex are strictly analogous to the corresponding reaction of the dichloro salt.

Application of these views to the reaction of oxalates with levo-dichloro-diethylenediamine cobaltic chloride has failed to give a product of inverted configuration. Whether this is due to the lower rate of reaction, or to a more fundamental difference, is not known.

Chloro-aquo-diethylenediamine cobaltic carbonate has been changed to the *cis*-dichloro salt by suspending it in thionyl chloride. This reagent, which evidently has not been used before in such reactions, presents several advantages over alcoholic hydrogen chloride.

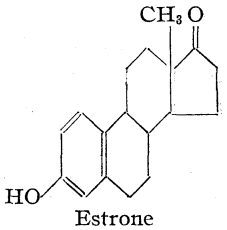
URBANA, ILLINOIS RECEIVED NOVEMBER 24, 1939

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE UNIVERSITY OF MICHIGAN]

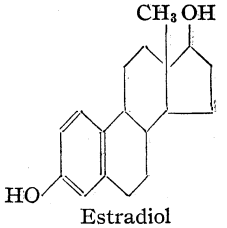
The Total Synthesis of the Sex Hormone Equilenin and Its Stereoisomers

BY W. E. BACHMANN, WAYNE COLE[1] AND A. L. WILDS[1]

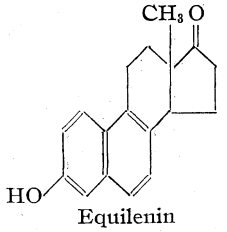
The estrogenic hormone estrone was the first sex hormone to be isolated.[2] Its isolation from pregnancy urine was reported in 1929 by Doisy, Veler and Thayer and by Butenandt. In 1932 Butenandt was able to propose a formula for estrone, which was proved to be correct in all respects by Cook and his associates. The true ovarian hormone appears to be a dihydro derivative of estrone, estradiol, which can be prepared in the laboratory by reduction of estrone. Another estrogenic hormone, equilenin, was isolated by Girard and co-workers[3] in 1932 from the urine of pregnant mares, and the structure which was proposed for it was definitely established by Cook.



Estrone



Estradiol



Equilenin

The synthesis of sex hormones and closely related compounds has engaged the attention of chemists ever since the structures of the natural products were established. One of the features of these compounds, which has been an obstacle in the synthetic path, is the presence of an angular methyl group between the C and D rings. Robinson has devised many ingenious methods for obtaining compounds which may prove useful intermediates for further synthesis. Recently he[4] succeeded in synthesizing a compound possessing the structure of equilenin except for the angular methyl group. Dane[5] has obtained an isomer of estrone by means of the Diels–Alder reaction, although the structure of the compound has not yet been established. Other important advances in the direction of the total synthesis of the sex hormones and related compounds have been made by Bardhan, Chuang, Cook, Hewett, Haberland, Kon, Linstead, Weidlich and others.[6] We have reported the synthesis of 3′-keto-1,2-cyclopentenophenanthrene and of compounds possessing a partially reduced cyclopentenophenanthrene structure.[7]

For some time we have centered our attention on a possible synthesis of equilenin. From the practical standpoint, the synthesis of this hormone possessed the advantage that equilenin contains a naphthalene nucleus and only two asymmetric carbon atoms (four stereoisomers) in contrast to the four asymmetric carbon atoms (sixteen stereoisomers) of estrone. Moreover, since Marker[8] has reported that equilenin can be reduced to estrone and to estradiol, a synthesis of equilenin would represent the synthesis of the other two hormones as well. We have succeeded in accomplishing the total synthesis of the hormone, *d*-equilenin, and also of its three stereoisomers, the antipode, *l*-equilenin, and the diastereoisomers, *d*-isoequilenin and *l*-isoequilenin. A preliminary account of the synthesis of the hormone was reported in a Communication in THIS JOURNAL.[9]

For the synthesis of these compounds we turned to the cyclic ketone, 7-methoxy-1-keto-1,2,3,4-tetrahydrophenanthrene (I), which was first prepared by Butenandt and Schramm[10] from the readily available 1-naphthylamine-6-sulfonic acid (Cleve's acid). We likewise started with the latter compound, but employed some of the procedures of Cohen, Cook, Hewett and Girard[11]

(1) Du Pont Post-doctorate Fellow.

(2) For an excellent review of the sex hormones including an account of the investigations leading toward their synthesis, see Fieser's monograph, "The Chemistry of Natural Products Related to Phenanthrene," Reinhold Publishing Corp., New York, N. Y., 1937, 2nd ed. This book gives references to the original articles up to 1937.

(3) Girard, Sandulesco, Fridenson and Rutgers, *Compt. rend.*, **195**, 981 (1932).

(4) Koebner and Robinson, *J. Chem. Soc.*, 1994 (1938).

(5) Dane and Schmitt, *Ann.*, **536**, 196 (1938); **537**, 246 (1939).

(6) Chuang, Ma, Tien and Huang, *Ber.*, **72**, 949 (1939); Haberland, *ibid.*, **72**, 1215 (1939); Kon, Linstead and Simons, *J. Chem. Soc.*, 814 (1937); Linstead and Millidge, *ibid.*, 478 (1936); Weidlich and Meyer-Delius, *Ber.*, **72** 1941 (1939).

(7) Bachmann and Kloetzel, THIS JOURNAL, **59**, 2207 (1937); **60**, 2204 (1938).

(8) Marker, *ibid.*, **60**, 1997 (1938).

(9) Bachmann, Cole and Wilds, *ibid.*, **61**, 974 (1939).

(10) Butenandt and Schramm, *Ber.*, **68**, 2083 (1935).

(11) Cohen, Cook, Hewett and Girard, *J. Chem. Soc.*, 653 (1934); 445 (1935).

and introduced some modifications of our own in order to obtain the cyclic ketone. We found that the best yields in the final step were obtained by cyclizing the acid chloride of the intermediate γ-(6-methoxy-1-naphthyl)-butyric acid by short treatment with stannic chloride; by this procedure the cyclic ketone was obtained in an average yield of 91%.

From the cyclic ketone it was planned to prepare the 2-methyl-2-carbomethoxy derivative (IV) by the method used to prepare 2-methyl-2-carbethoxycyclohexanone from cyclohexanone,[12] which consisted in forming the glyoxalate of the ketone, converting it to the carbethoxy derivative by pyrolysis and introducing a methyl group between the carbonyl group and ester group by sodium alkoxide and methyl iodide. The prospect of eliminating carbon monoxide successfully from the glyoxalate (II) of 7-methoxy-1-keto-1,2,3,4-tetrahydrophenanthrene did not appear promising in view of Haworth's experience with the corresponding derivative of 1-keto-1,2,3,4-tetrahydrophenanthrene. Eight years ago, Haworth[13] prepared the glyoxalate IIa, but he was unable to eliminate carbon monoxide from the compound to give the 2-carbethoxy derivative; continued heating resulted in extensive decomposition of the glyoxalate.[14] In spite of this result, we ventured to try the reaction on the glyoxalate of the methoxy ketone.

Condensation of 7-methoxy-1-keto-1,2,3,4-tetrahydrophenanthrene with methyl oxalate by means of sodium methoxide in an atmosphere of nitrogen gave the glyoxalate II in 96% yield. When the reaction was carried out in air, the yield was decreased slightly, presumably through oxidation of the sodio derivative of the glyoxalate Like Haworth, we encountered difficulty in eliminating carbon monoxide from the glyoxalate. We were not entirely unsuccessful, for some samples of the compound underwent the reaction and the keto ester was obtained, but the results were erratic. We found, however, that by the simple expedient of adding powdered soft glass to the glyoxalate the latter smoothly lost carbon monoxide at 180°, and the keto ester III was isolated in yields of 90 to 94%.

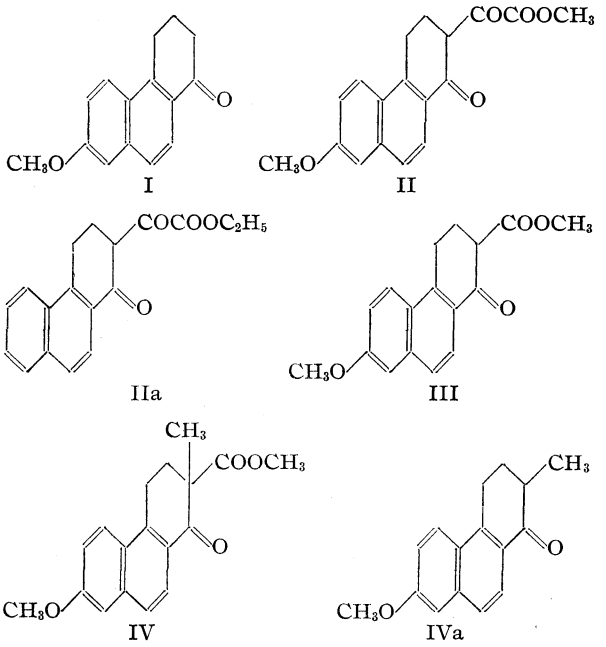
(12) Kötz and Michels, *Ann.*, **350**, 212 (1906).

(13) Haworth, *J. Chem. Soc.*, 1130 (1932).

(14) Robinson and Walker [*ibid.*, 61 (1937)] had a similar experience with a related compound, the 2-glyoxalate of 1-keto-7-methoxy-1,2,3,4,9,10-hexahydrophenanthrene. They state that the carbethoxy group cannot be introduced into this unsaturated ketone by way of the glyoxalate.

This procedure will undoubtedly prove useful with other glyoxalates. We have employed it successfully on the two glyoxalates (of 1-keto- and of 4-keto-1,2,3,4-tetrahydrophenanthrene) from which Haworth was unable to obtain the carboxy derivatives. The procedure can be used to advantage even in those cases where the glyoxalate reacts normally, for in the presence of powdered glass the reaction generally proceeds at a lower temperature and in a shorter time with less resultant decomposition. For example, this has proved to be the case with the glyoxalate of α-tetralone, the yield of carbomethoxy compound (94%) being considerably greater than has been reported previously.[15]

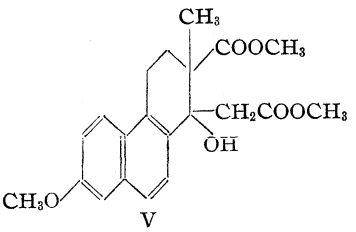
By treatment of the sodio derivative of the 7-methoxy-keto ester III with methyl iodide, 7-methoxy-2-methyl-2-carbomethoxy-1-keto-1,2,-3,4-tetrahydrophenanthrene (IV) was obtained in excellent yield.



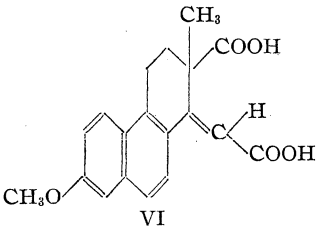
In order to build up the five-membered ring containing the carbonyl group, we proposed to introduce a propionic acid group in the 1-position, and then cyclize the dimethyl ester of the dicarboxylic acid by the Dieckmann method. First of all, conditions were determined so that a Reformatsky reaction on the keto ester IV using methyl bromoacetate gave the dimethyl ester of 7-methoxy-2-methyl-2-carboxy-1-hydroxy-1,2,3,4-tetrahydrophenanthrene-1-acetic acid (V) in 85

(15) These results will be published in future communications.

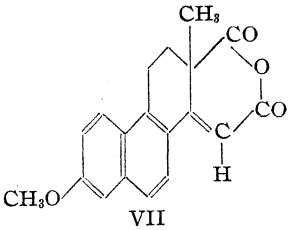
to 90% yields. This compound is susceptible to cleavage by alkali; thus, treatment with hot, concentrated aqueous potassium hydroxide stripped the molecule of its carbomethoxy and acetic ester groups and gave a good yield of 7-methoxy-2-methyl-1-keto-1,2,3,4-tetrahydrophenanthrene (IVa).[16] The same compound resulted by cleavage of IV by alkali. Accordingly dehydration was carried out on the Reformatsky ester (V), itself. This was accomplished by the indirect method, consisting in the replacement of the hydroxyl group by chlorine by means of thionyl chloride, followed by removal of the elements of hydrogen chloride by treatment with alcoholic potassium hydroxide; in this process the two ester groups also were hydrolyzed. Acidification of the alkaline solution yielded a mixture of two compounds: an unsaturated acid and an unsaturated acid anhydride. We consider the free acid and the acid corresponding to the anhydride to be geometrical isomers; to the free acid is assigned the configuration VI (in which the carboxyl group attached to the double bond extends away from the tertiary carboxyl group) and to the anhydride the structure VII.



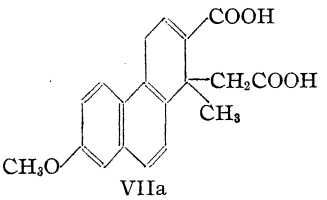
V



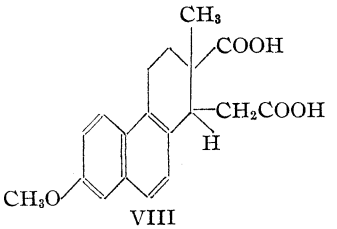
VI



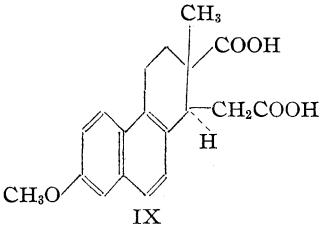
VII



VIIa



VIII



IX

In harmony with the behavior of β-aryl-α,β-unsaturated acids (cinnamic acid type), the potassium salts of the unsaturated acids from VI and VII were rapidly reduced by dilute sodium amalgam and water, and both yielded a mixture of the same two reduced acids, *cis-* (VIII) and *trans*-7-methoxy-2-methyl-2-carboxy-1,2,3,4-tetrahydrophenanthrene-1-acetic acid (IX). These facts are proof that in the process of dehydration of the Reformatsky ester (V) no rearrangement took place, involving the migration of the methyl group to the 1-position, to form a compound having the formula VIIa, for such a compound could not give rise to an acid and anhydride of an isomeric acid which would yield a mixture of the identical reduced acids. Chuang, Tien and Huang[17] applied the Reformatsky reaction to 2-methyl-2-carbethoxycyclohexanone and converted the product by dehydration and catalytic reduction of the unsaturated compound to 2-methyl-2-carboxycyclohexane-1-acetic acid; it is of interest that they obtained only a single reduced acid.

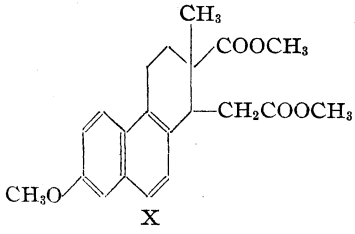
The two isomeric reduced acids, which are actually racemic mixtures, were readily separated and were found to be present in nearly equal amounts. The formation of both acids on reduction was a fortunate circumstance, for it enabled us to synthesize all four stereoisomers possessing the structure of equilenin. Each of the acids was carried through the remaining series of reactions separately, the one eventually yielding racemic equilenin, the other racemic isoequilenin. Since the configuration of the C/D ring fusion of equilenin and the other steroids is still a moot point,[18] although the *trans* arrangement appears to be favored, no definite configuration is assigned to the two acids at this time, and we withdraw the prefixes *cis-* and *trans-* which were given to the two acids in our preliminary communication.[9] Until the configurations are definitely established, the acid from which isoequilenin was finally obtained is designated as the α-acid (m. p. 231–232°), and the one yielding equilenin is called the β-acid (m. p. 213–214°).

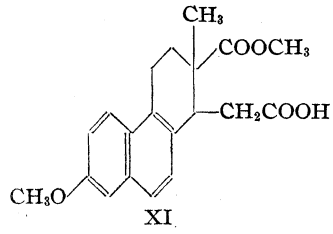
(16) Robinson and Walker [*J. Chem. Soc.*, 183 (1938)] submitted the product of the Reformatsky reaction on 7-methoxy-2-methyl-2-carbethoxy-1-keto-octahydrophenanthrene to hydrolysis with hot, concentrated potassium hydroxide. The acidic portion consisted of an intractable oily mixture which showed evidence of containing the desired acid. The principal product (67%) was the 2-methyl-1-keto compound. It occurs to us that this may have been formed by alkaline cleavage of the Reformatsky ester rather than from unreacted starting material.

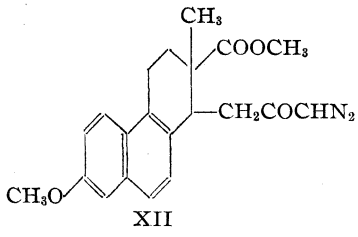
(17) Chuang, Tien and Huang, *Ber.*, **68**, 866 (1935).

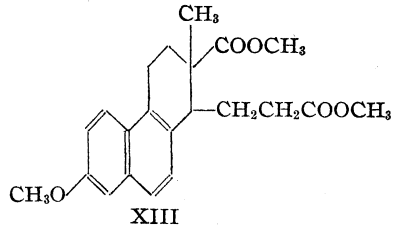
(18) Peak, *Nature*, **140**, 280 (1937); Ruzicka, Furter and Goldberg, *Helv. Chim. Acta*, **21**, 507 (1938), footnote 2.

d- **and** *l*-**Equilenin.**—In order to lengthen the acetic acid side chain to a propionic acid group, we employed the reaction of Arndt and Eistert.[19] The β-acid was converted to its dimethyl ester (X), which was hydrolyzed readily to the acid ester XI. Under the conditions employed, which consisted in the use of one equivalent of sodium hydroxide in the form of a 1% solution in methanol, only the methyl group attached to the acetic acid portion was removed, the ester group of the hindered tertiary carboxyl group being unaffected. Similar instances of partial hydrolysis of esters have been observed by others. The acid chloride, formed by interaction of the acid ester and thionyl chloride, reacted with diazomethane to yield the crystalline diazo ketone XII. When the latter compound was warmed with methanol in the presence of silver oxide, the crystalline dimethyl ester of 7-methoxy-2-methyl-2-carboxy-1,2,3,4-tetrahydrophenanthrene-1-propionic acid (XIII) was obtained in 80–84% yields.[20]

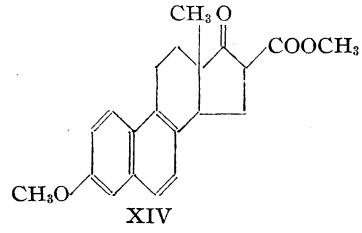

X

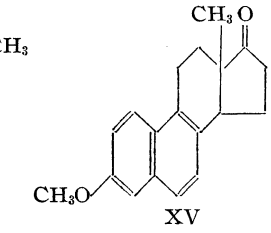

XI

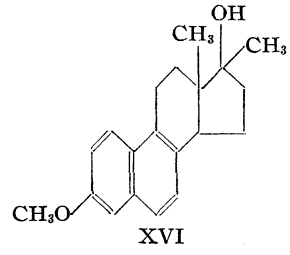

XII

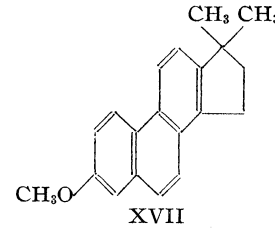

XIII

In order to effect the cyclization of the dimethyl ester XIII to XIV, we tried the action of sodium on a benzene solution of the ester containing a trace of methanol. The results by this method proved to be erratic. The powdered sodium became coated with a thin crust which effectively prevented complete reaction. Addition of methanol served to remove the coating, and all of the ester reacted, but the yield of cyclic product was only 40–50%. A thorough investigation of the reaction revealed that sodium methoxide could be used for the cyclization, and, furthermore, that the low yields of product were caused by oxidation of the substance by oxygen of the air. By running the reaction in an atmosphere of nitrogen, it was possible to prepare the methyl ether of 16-carbomethoxy-*dl*-equilenin (XIV) in 95–98% yields. By heating this compound with hydrochloric acid, the ester group was hydrolyzed and the resulting acid was decarboxylated to give the methyl ether of *dl*-equilenin (XV). When a mixture of acetic acid and hydrochloric acid was employed, it was found that even under these mild conditions the ether linkage also was cleaved and the product was *dl*-equilenin. The racemic equilenin melted at 276–278° (natural *d*-equilenin, 250–251°) and like the hormone it gave a deep red liquid when melted in air.


XIV


XV


XVI


XVII

The results of the brilliant investigations of Cook and co-workers[11] on the structures of estrone and equilenin were invaluable to us at this point, for we were enabled to confirm the structure of our racemic equilenin prior to resolution. By treatment with methylmagnesium iodide, the methyl ether of the racemic equilenin was converted to the carbinol XVI, which was dehydrated with migration of the angular methyl group and the dehydration product was dehydrogenated to 3′,3′-dimethyl-7-methoxy-1,2-cyclopentenophenanthrene (XVII), identical with the com-

(19) Arndt and Eistert, *Ber.*, **68**, 200 (1935); Eistert, *ibid.*, **69**, 1074 (1936).

(20) While this work was in progress, Litvan and Robinson [*J. Chem. Soc.*, 1997 (1938)] applied the Arndt-Eistert reaction to a closely related compound, which they obtained by degradation of estrone. They were able to isolate the pure, crystalline propionic acid derivative in about 1% yield.

pound obtained in the same manner from natural equilenin.

The *dl*-equilenin was resolved by converting it to the *l*-menthoxyacetic esters by reaction with *l*-menthoxyacetyl chloride. From the mixture of diastereoisomeric esters was isolated the ester (m. p. 174–174.5°) which on hydrolysis yielded *d*-equilenin.

l-Equilenin, the optical antipode of the natural hormone, was isolated by employing the action of *d*-menthoxyacetyl chloride on the racemic equilenin, or on the mixture obtained after some of the *d*-equilenin had been removed. It possesses the same melting point and specific rotation (opposite in sign) as the natural hormone. Its estrogenic activity is presented in Table III.

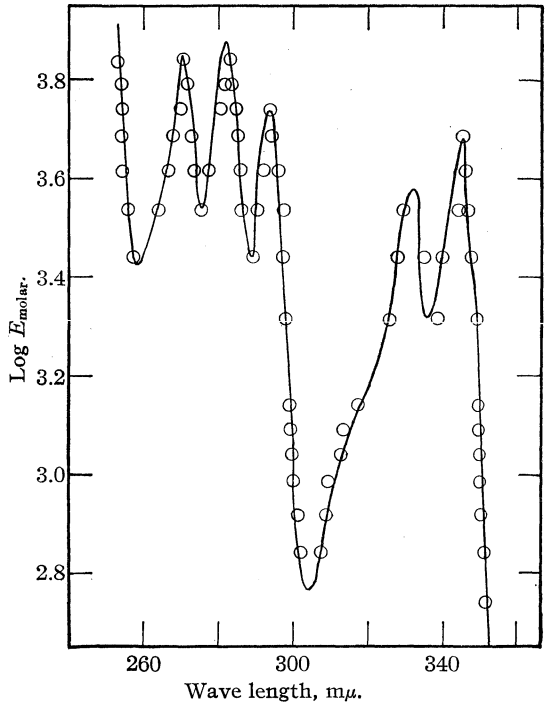


Fig. 1.—Ultraviolet absorption curve of equilenin, showing the logarithm of the extinction coefficient at various wave lengths. The solid line represents the curve for natural equilenin, the circles the values for synthetic *d*-equilenin.

Comparison of Synthetic *d*-Equilenin with the Hormone Equilenin.—The synthetic *d*-equilenin proved to be identical with the natural hormone in all respects. The identity of the two compounds was established by a determination of the melting points and mixed melting points of the hormone and a number of derivatives, by a comparison of the optical rotation, estrogenic activity, absorption spectrum and crystallographic properties. A comparison of the melting points and mixed melting points of the synthetic and natural equilenin and six derivatives is given in Table I.

TABLE I

COMPARISON OF MELTING POINTS[a]

Compound	Melting points, °C. Synthetic	Natural	Mixed
d-Equilenin	250–251	250–251	250–251
Benzoate	222.5–223	222.5–223.5	222.5–223.5
Acetate	156–157	156–156.5	156–157
l-Menthoxyacetic ester	174–174.5	173–173.5	173.5–174.5
Methyl ether	193.5–194	194–194.5	194–194.5
Trinitrobenzene complex	205.5–207	206.5–207.5	206–207
Methyl carbinol of methyl ether (XVI)	132.5–133.5	132–134.5	132.5–134.5

[a] M. p. (uncor.) determined in vacuum. The melting points of equilenin and its derivatives are in general unsatisfactory when determined in open capillary tubes because of the oxidation of the compounds to red products. By determining the melting points in sealed, evacuated (0.2 mm.) tubes, the melts remained colorless; on being cooled, the melts quickly solidified and when heated the solids showed the same melting points as before.

The specific rotation of the synthetic equilenin, $[\alpha]^{30}D$ + 84° (dioxane) agreed with the value reported for natural equilenin, $[\alpha]^{16}D$ + 87° (dioxane).[3] In estrogenic activity the synthetic hormone was indistinguishable from the natural product. In each case a dose of 30 γ produced estrus in 50% of the rats tested (Dr. Bradbury).

A comparison of the ultraviolet absorption spectrum of the synthetic and natural hormones was kindly made by Mr. Nelson V. Seeger. From Fig. 1 and the values for the maxima given in Table II, it can be seen that agreement is satisfactory throughout. This curve for the absorption spectrum in ether agrees with that of natural equilenin in alcohol given by Dirscherl and Hanusch[21] and supplemented by Wintersteiner, *et al.*,[22] in the location of the bands. However, the value of log *E* for the maximum at 282 mμ. was somewhat smaller and that for the maximum at 294 mμ. was somewhat larger than those pre-

TABLE II

COMPARISON OF POSITIONS AND INTENSITIES OF ABSORPTION SPECTRUM MAXIMA

Natural equilenin Wave length, mμ.	Log E_{molar}	Synthetic *d*-equilenin Wave length, mμ.	Log E_{molar}
270	3.85	270	3.84
282	3.87	283	3.84
294	3.74	294	3.74
332	3.58	329	3.54
345	3.68	345	3.68

(21) Dirscherl and Hanusch, *Z. physiol. Chem.*, **233**, 13 (1935).

(22) Wintersteiner, Schwenk, Hirschmann and Whitman, THIS JOURNAL, **58**, 2652 (1936).

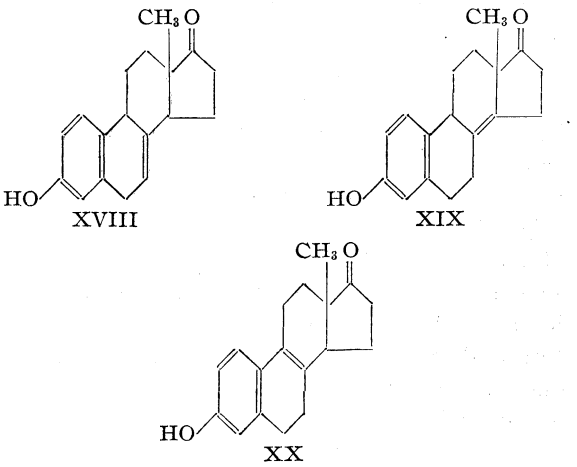
viously reported, while the minima were uniformly lower.

We are indebted to Dr. Chester B. Slawson of the Mineralogy Department for making a comparison of the crystals of the two compounds. He reports that the natural and synthetic equilenin have identical crystallographic properties. When crystallized from dilute alcohol, both formed elongated needles (probably orthorhombic) which are flattened in one direction. In both cases the crystals possessed the following optical properties: biaxial negative; $r > v$; α_D, 1.509 ($\pm$0.001); β_D, 1.718 ($\pm$0.001); γ_D, 1.800 ($\pm$0.010).[23] β may be measured parallel to the elongation and α across the flattened needles. β and γ show very strong dispersion nearly exactly equivalent to that of methylene iodide.

From all of these comparisons it is apparent that there is an exact agreement between the synthetic and natural hormone in all respects. The synthesis completely establishes the correctness of the structural formula which has been proposed for equilenin.

d- and *l*-**Isoequilenin.**—The α-acid (VIII or IX), when carried through the same series of reactions used on the isomeric acid, yielded *dl*-isoequilenin, which has the same structural formula as equilenin but a different spatial configuration. The *dl*-isoequilenin exists in two forms, one melting at 206–206.5°, the other 223–224°. Like the corresponding equilenin derivative, the methyl ether of isoequilenin could be converted to 3′,3′-dimethyl-7-methoxy-1,2-cyclopentenophenanthrene (XVII), although the yield of the product was poor. Attempts to resolve *dl*-isoequilenin by means of *l*-menthoxyacetyl chloride and certain other active compounds were unsuccessful, but resolution of the α-acid was accomplished readily. By reaction of the acid chloride of the α-acid ester (XI) with *l*-menthol, two diastereoisomeric methyl-*l*-menthyl esters were obtained, from which a pure ester was isolated. The pure active *l*-methyl-*l*-menthyl ester was hydrolyzed to the active α-acid, which was then carried through the series of reactions previously described, to yield *d*-isoequilenin. The mixture of methyl-*l*-menthyl esters remaining after removal of the pure individual was hydrolyzed to the dicarboxylic acids and the latter converted to the dimethyl esters (X). It was found possible at this stage to separate nearly completely the *d*-dimethyl ester from the *dl*-dimethyl ester which was present by taking advantage of the great difference in solubility and crystalline forms of the compounds. From the *d*-dimethyl ester was prepared *l*-isoequilenin. Both active forms of isoequilenin melted at the same temperature (257–258°) and possessed equal but opposite specific rotations (Table III).

Recently, Hirschmann and Wintersteiner[24] have converted the hormone equilin (XVIII) to an isomer of equilenin which they called 14-*epi*-equilenin. The transformation was accomplished by isomerizing equilin to isoequilin A (XX) by hydrogen chloride in boiling acetic acid. While dehydrogenation of equilin gives equilenin, dehydrogenation of isoequilin A gives the isomer of equilenin, 14-*epi*-equilenin. In the process of isomerization, epimerization at C_{14} takes place, presumably through an intermediate such as XIX. Inasmuch as equilenin can have only one dextrorotatory diastereoisomer, it follows that their 14-*epi*-equilenin (which is dextrorotatory) must be identical with our *d*-isoequilenin. A comparison of the two compounds and their acetates, which was kindly carried out by Dr. Wintersteiner, left little doubt about the identity of the samples of isoequilenin and 14-*epi*-equilenin.



As Hirschmann and Wintersteiner have pointed out, the configuration of the *d*-isoequilenin at C_{13} is the same as that of natural *d*-equilenin. It follows that the configurations of all of the stereoisomers of the natural hormone, which we have prepared, are established with reference to it.

In Table III are summarized some of the chief

(23) Gaudefroy, *Compt. rend.* **195**, 983 (1932), reports the following values for the refractive indices of natural equilenin: α, 1.51; β, 1.718.

(24) Hirschmann and Wintersteiner, *J. Biol. Chem.*, **126**, 747 (1938).

properties of the four stereoisomers and the two racemic compounds which we have prepared; included is a comparison of the estrogenic activities of the optically active compounds. These values are taken from the results of Dr. James T. Bradbury of the Department of Obstetrics and Gynecology.

TABLE III

PROPERTIES OF THE SYNTHETIC COMPOUNDS

Compound	M. p. (vac.), °C.	$[\alpha]_D$ dioxane	Estrogenic activity,[a] γ
d-Equilenin	250–251	+ 84	30
l-Equilenin	250–251	− 85	400
dl-Equilenin	276–278[b]	0	..
d-Isoequilenin	257–258[c]	+147	>500[e]
l-Isoequilenin	257–258[c]	−147	>500[e]
dl-Isoequilenin	223–224[d]	0	..

[a] Amount required to produce estrus in more than 50% of the rats tested. [b] Another form, m. p. 287–288°. [c] Another form, m. p. 272–273°. [d] Another form, m. p. 206–206.5°. [e] A dose of 500 γ produced only pro-estrus in about 25% of the rats, the rest being negative. Larger doses are being tested.

From the table it is apparent that the natural *d*-equilenin is more than thirteen times as active as its antipode, *l*-equilenin, and that both forms of isoequilenin are less potent than the forms of equilenin. It is of interest that here, as in the case of the four known forms of androsterone, the isomer with the greatest physiological activity is the one which occurs naturally.

In this investigation we usually endeavored to determine the conditions for obtaining maximum yields of the intermediates. Frequently this necessitated running a reaction twenty to thirty times under varying conditions before the optimum conditions were discovered. In this way it was sometimes possible to double the yield originally obtained and in nearly all cases we were able to raise the yields to about 90%. As a consequence of this, although numerous steps were involved, ten grams of 7-methoxy-1-keto-1,2,3,4-tetrahydrophenanthrene(I) yielded about two and one-half grams of *dl*-equilenin and the same amount of *dl*-isoequilenin.

Having successfully worked out the experimental conditions for the reactions in this investigation, it appeared of interest to determine whether they could be applied to similar reactions leading to the synthesis of other steroids, such as estrone, vitamin D and related compounds. As a matter of fact, the procedures have already proved successful in the synthesis of desoxyequilenin and desoxyisoequilenin. Moreover, the structural isomer of equilenin with the hydroxyl group in the 6-position has been prepared in both *cis* and *trans* forms by Mr. David W. Holmes in this Laboratory. It has proved a simple matter to introduce other alkyl groups in the position occupied by the angular methyl group, as well as to build up a six-membered D ring. In addition simple analogs of the sex hormones have been synthesized. These compounds should furnish interesting information in regard to the relation between structure and estrogenic activity.

We are extremely grateful to Dr. Oliver Kamm of Parke, Davis and Company for his generosity in supplying us with natural equilenin for purposes of comparison.

Experimental

The melting points of a number of compounds that were found to oxidize in air were determined in sealed, evacuated (0.2 mm.), capillary tubes; these values are indicated by (vac.).

β-(6-Methoxy-1-naphthyl)-ethyl Bromide.—1-Naphthylamine-6-sulfonic acid (Cleve's acid) was fused with alkali and the resulting aminonaphthol was acetylated and methylated according to the procedure of Butenandt and Schramm.[10] Hydrolysis of the 6-methoxy-1-acetylaminonaphthalene was accomplished by refluxing a mixture of 200 g. of the compound, 200 cc. of water and 250 cc. of concentrated hydrochloric acid for fifteen to twenty minutes. All of the compound went into solution and then the hydrochloride of 6-methoxy-1-naphthylamine began to precipitate. The hydrochloride which was filtered from the cooled solution was sufficiently pure for diazotization and conversion to 6-methoxy-1-iodonaphthalene, which was carried out according to the directions of Cohen, Cook, Hewett and Girard.[11]

A solution of 57 g. of 1-iodo-6-methoxynaphthalene and 21 g. of ethyl bromide in 150 cc. of benzene was added in six portions to 9.8 g. of powdered magnesium and 100 cc. of ether in a 1-liter flask. Refluxing was continued for five hours after all of the reagent had been added. The Grignard reagent was diluted with 200 cc. of dry benzene, the solution cooled to 5° and ethylene oxide gas after passing through a tube containing potassium hydroxide was led to within an inch of the surface of the solution. During the addition of 24 g. of ethylene oxide the solution was swirled every few minutes. After standing at room temperature for eight hours, the mixture was warmed to 50–80° for one hour. The mixture was hydrolyzed with ammonium chloride solution and cold 5% hydrochloric acid (about 30 cc.) was added until the emulsion broke. After being washed and dried, the organic layer was distilled; the product boiling at 140–185° at 1 mm. was found to be suitable for conversion to the bromide, although it contained some nerolin; yield, 31–34 g. (76–84%). This method is patterned after that of Cohen, Cook and Hewett.[11]

An ice-cold solution of 40.4 g. of β-(6-methoxy-1-naphthyl)-ethyl alcohol in 125 cc. of dry benzene was treated with a solution of 40 g. of phosphorus tribromide in 50 cc.

of benzene with swirling; the mixture was then kept at 60–75° for three hours. The cooled mixture was poured onto ice and water and worked up according to the procedure of Cohen, Cook and Hewett.[11] The total yield of bromide boiling at 160–175° at 0.6 mm. was 40–42 g. (75–79%).

γ-(6-Methoxy-1-naphthyl)-butyric Acid.—Ten grams of sodium (thin slices) in 25 cc. of benzene was treated with absolute alcohol (about 30 cc.) in portions until all of the sodium had reacted. One hundred grams of malonic ester was introduced and the mixture was warmed with swirling until a clear solution resulted. To the cooled solution was added 79.5 g. of β-(6-methoxy-1-naphthyl)-ethyl bromide in 100 cc. of benzene. After being warmed at 70–80° in a water-bath for eight hours, the mixture was refluxed on a steam-bath for four hours.

The warm solution was poured cautiously into a hot solution of 112 g. of potassium hydroxide in 150 cc. of water and 50 cc. of alcohol (2-l. flask); hydrolysis proceeds rapidly as the solutions mix. The benzene and much of the alcohol were removed in a current of air, more water was added and the turbid solution was heated for two hours on a steam-bath, then cooled and extracted with benzene. The clear aqueous solution was poured with stirring into 275 cc. of concentrated hydrochloric acid. The colorless plates of the substituted malonic acid were filtered from the chilled solution and dried. The product obtained by decarboxylation at 200° was poured while still hot into acetic acid, and the solution diluted with water. The yield of γ-(6-methoxy-1-naphthyl)-butyric acid melting at 149–150° was 55–65 g. (75–89%) depending on the purity of the bromide. Cohen, Cook and Hewett[25] prepared this acid (m. p. 150–151°) by means of potassiomalonic ester in boiling toluene.

7 - Methoxy - 1 - keto - 1,2,3,4 - tetrahydrophenanthrene (I).—Five grams of powdered γ-(6-methoxy-1-naphthyl)-butyric acid was added to a cold solution of 25 cc. of anhydrous ether, 2.4 cc. of thionyl chloride and 2 drops of pyridine. The mixture was allowed to stand at room temperature with occasional swirling until all of the solid had disappeared (about three hours). The mixture was warmed to 35° for ten minutes and the solvent removed under reduced pressure (water pump). Two cc. of benzene was added and then removed by means of a water pump and finally by means of an oil pump in order to remove completely the unreacted thionyl chloride, the acid chloride being warmed finally to 35°. A solution of the acid chloride in 100 cc. of benzene was cooled in a freezing mixture until the benzene began to crystallize, then removed from the cooling bath and treated rapidly with a solution of 5.5 g. of stannic chloride in 20 cc. of benzene, the mixture being swirled until a homogeneous, yellow slurry was obtained. After being kept cold for one minute, the mixture was poured onto ice and 30 cc. of concentrated hydrochloric acid and 30 cc. of ether. When all of the yellow solid had disappeared, more ether was added and the two layers were separated. The ether–benzene solution was washed three times with cold 10% hydrochloric acid, once with water, twice with 10% sodium hydroxide and several times with water. Evaporation of the solvents and the addition of methanol to the residue gave 3.8–4.0 g. of colorless prisms of the cyclic ketone (m. p. 98–100°).[10] From the mother liquors an additional quantity of only slightly less pure ketone was isolated and a further small amount was obtained by sublimation of the remainder at 200° at 0.5 mm. The total yield of ketone was 4.2–4.4 g. (90–95%). The yield was somewhat smaller when larger amounts were cyclized.

Methyl 7 - Methoxy - 1 - keto - 1,2,3,4 - tetrahydrophenanthrene - 2 - glyoxalate (II).—A solution of sodium methoxide prepared from 0.46 g. of sodium and 5 cc. of anhydrous methanol was evaporated to dryness at 100° under reduced pressure. The solid cake was broken up somewhat, 2.36 g. of dimethyl oxalate was added and the flask and condenser were evacuated and then filled with dry nitrogen. Ten cc. of dry, thiophene-free benzene was added and the mixture was refluxed for ten minutes in order to dissolve most of the solid. To the cooled solution was added a solution of 2.26 g. of the aforementioned cyclic ketone in 15 cc. of benzene and the mixture was swirled at room temperature. Within two minutes a clear, light-yellow solution resulted, which soon deposited a light-yellow precipitate of the sodio derivative of the glyoxalate. After four hours at room temperature, the mixture was hydrolyzed with cooling, and a small amount of sodium hydroxide solution was added in order to give two clear layers. After drawing off the aqueous layer, the benzene solution was extracted twice with 2% sodium hydroxide solution and the combined aqueous solution was acidified with cold, dilute hydrochloric acid. The light-yellow crystalline glyoxalate was filtered off and the dried product was digested with a warm mixture of acetone–methanol and cooled. By filtration, 2.95 g. of the glyoxalate (m. p. 133–135°) was obtained; this with an additional 0.06 g. isolated from the filtrate corresponded to a yield of 96%. When the condensation reaction was carried out in an atmosphere of air, using sodium methoxide prepared in benzene with the theoretical amount of methanol, the product was accompanied by varying amounts of a green oxidation product, and the yield of glyoxalate dropped to 88–92%.

The glyoxalate crystallized from methanol–acetone in clusters of long, thin, light-yellow prisms; these melted at 134–135° but the solid formed on cooling the melt showed a melting point of 139–140° with gas. In a Pyrex tube the crystals melted at 138–140°; the solid formed on cooling remelted at 130°; addition of powdered glass to the melt raised the melting point to 138–140° with gas. The glyoxalate gives an intense red-brown color instantly with an alcoholic solution of ferric chloride; it gives a red-brown color with concentrated sulfuric acid.

Anal. Calcd. for $C_{18}H_{16}O_5$: C, 69.2; H, 5.2. Found: C, 69.5; H, 5.0.

Methyl Ester of 7-Methoxy-1-keto-1,2,3,4-tetrahydro-2-phenanthroic Acid (III).—The first attempts to prepare this ester by heating the glyoxalate at 180–200° gave low and variable yields of an impure product. Frequently the reaction required more than two hours of heating before the evolution of carbon monoxide ceased. Excellent yields of the product were obtained when powdered glass was added to the glyoxalate, and on small runs the reaction was complete within ten minutes.

Ten grams of the glyoxalate was melted in an 8″ (22-cm.) test-tube in an oil-bath (140–150°); 5 g. of finely powdered soft glass was stirred into the melt with a glass rod and the

(25) Cohen, Cook and Hewett, *J. Chem. Soc.*, 52 (1936).

mixture heated to 180°. A vigorous evolution of carbon monoxide took place, all of the gas being evolved in one-half hour. After being cooled, the light-brown semi-solid product was dissolved in benzene and the solution was decanted from the glass. After decolorization with Norite, the solution was evaporated and the residue stirred with methanol, whereupon crystallization took place. The first crop of cream-colored crystals of the keto ester weighed 8.0 g. (m. p. 108–110° with solidification and remelting at 118–120°); the second crop (0.2–0.6 g.) of only slightly less pure product brought the yield to 90–94%. The product so obtained is sufficiently pure to be used in the next step.

A sample of the methyl ester of 7-methoxy-1-keto-1,2,3,4-tetrahydro-2-phenanthroic acid, after sublimation at 220° (0.5 mm.) and recrystallization from acetone–methanol and then from benzene–methanol, was obtained as clusters of colorless prisms. The crystals melted nearly completely at 110–111°; the melt solidified and the solid remelted at 125–126.5°. The keto ester is soluble in benzene and in hot acetone, but is only slightly soluble in methanol. It gives a light orange-yellow color with concentrated sulfuric acid, and slowly develops a deep blue-green color with alcoholic ferric chloride solution (two to ten minutes).

Anal. Calcd. for $C_{17}H_{16}O_4$: C, 71.8; H, 5.7. Found: C, 71.6; H, 5.7.

7 - Methoxy - 2 - methyl - 2 - carbomethoxy - 1 - keto-1,2,3,4-tetrahydrophenanthrene (IV).—To 2.3 g. of sodium dissolved in 45 cc. of anhydrous methanol was added 5.68 g. of the aforementioned keto ester (crude) as a finely divided solid, followed by 25 cc. of dry benzene. As the mixture was refluxed, the solid partially dissolved and then reappeared as the fine, powdery sodio-derivative, which ultimately nearly filled the solution; any lumps which formed were broken up. After thirty minutes of refluxing, the mixture was cooled and treated with 7 cc. of methyl iodide. After forty-five minutes at room temperature, during which time the mixture was swirled occasionally, much of the solid had dissolved. An additional 7 cc. of methyl iodide was added and within thirty minutes all of the solid had reacted. The clear yellow solution was refluxed for forty-five minutes, cooled and neutralized with acetic acid. After being evaporated nearly to dryness, the mixture was treated with benzene and water, and the benzene solution after separating was washed with 5% sodium hydroxide, again with water and dried over sodium sulfate. The solution was decolorized with Norite and evaporated. The residue crystallized from methanol in colorless crystals; yield 5.3–5.5 g. (89–92%); m. p. 84–86°.

After sublimation at 230° (0.2 mm.) and two recrystallizations from methanol, a sample of the 7-methoxy-2-methyl - 2 - carbomethoxy - 1 - keto - 1,2,3,4 - tetrahydrophenanthrene was obtained as colorless, hexagonal plates; m. p. 84.5–85°. The compound gives a light-yellow color with concentrated sulfuric acid, but neither the pure nor the unrecrystallized product gives a color with ferric chloride solution.

Anal. Calcd. for $C_{18}H_{18}O_4$: C, 72.5; H, 6.1. Found: C, 72.3; H, 5.8.

Cleavage of the Keto Methyl Ester (IV) by Alkali.—A mixture of 0.3 g. of the above ester, 3 cc. of 45% aqueous potassium hydroxide and 10 cc. of methanol was refluxed on a steam-bath for two hours, diluted with water and cooled. The resulting crystals were filtered off and recrystallized from methanol; from the solution 0.23 g. (96%) of 7-methoxy-2-methyl-1-keto-1,2,3,4-tetrahydrophenanthrene (IVa) crystallized in thin, colorless plates; m. p. 109–110° (Haberland and Blanke,[26] 108°).

7 - Hydroxy - 2 - methyl - 1 - keto - 1,2,3,4 - tetrahydrophenanthrene was obtained by refluxing 0.2 g. of the methyl ether (IVa) in 12 cc. of 42% aqueous hydrobromic acid for three hours. The residue obtained after removal of the liquids by distillation under reduced pressure was dissolved in aqueous potassium hydroxide, the solution filtered and acidified. The precipitated phenolic ketone (0.17 g.) after sublimation at 180° at 0.01 mm. crystallized from methanol in colorless plates; m. p. 195.5–197.5° (vac.); after cooling the product remelted sharply at 197–197.5° (vac.). In an open tube the compound melted at 193–196° to a brown melt. Haberland and Blanke[26] failed to report the melting point of the compound.

Dimethyl Ester of 7-Methoxy-2-methyl-2-carboxy-1-hydroxy - 1,2,3,4 - tetrahydrophenanthrene - 1 - acetic Acid (V).—To 2.5 g. of granulated zinc (20-mesh, previously washed with dilute hydrochloric acid, water, acetone and dried) and 0.07 g. of iodine in 25 cc. of dry benzene (thiophene-free) and 25 cc. of anhydrous ether was added 1.5 g. of the keto ester IV and 0.75 cc. of methyl bromoacetate. As the mixture was refluxed on a water-bath, the iodine color faded and the solution became cloudy. After five to ten minutes a colorless addition product was deposited. Five additions of 2.5 g. of zinc and a trace of iodine were made at forty-five minute intervals and an additional 0.75 cc. of methyl bromoacetate was introduced after one and one-half hours. The mixture was refluxed for a total of four hours. Frequently the mixture was shaken vigorously in order to free the zinc from the adhering mass of crystals.

The addition product was dissolved by adding a little acetic acid and methanol and the solution was decanted from the zinc into water and the mixture acidified with acetic acid. The ether–benzene layer was separated, the aqueous solution was extracted with benzene and the combined extracts were washed with water and then dilute ammonium hydroxide until no more color was removed. The residue obtained by evaporation of the ether–benzene solution crystallized readily from methanol; yield 1.5–1.6 g. of colorless crystals (m. p. 123–126°). Additional product from the filtrate brought the total yield up to 85–90%. Should the yield fall below this, retreatment of the material in the filtrates with zinc and methyl bromoacetate will give additional product.

The hydroxy ester crystallizes from methanol containing a few drops of acetone in colorless leaflets; m. p. 125–125.5°. With concentrated sulfuric acid the compound gives a blue color which soon changes to a red-brown color and then fades to yellow.

Anal. Calcd. for $C_{21}H_{24}O_6$: C, 67.8; H, 6.5. Found: C, 67.8; H, 6.6.

The zinc which is recovered from the reaction may be used over again after being cleaned with acid, washed with water, acetone and dried.

(26) Haberland and Blanke, *Ber.*, **70**, 169 (1937).

Cleavage of the Reformatsky Ester (V) by Alkali.—A mixture of 100 mg. of the ester and 3 cc. of 45% aqueous potassium hydroxide was heated on a steam-bath for forty-five minutes. The solid melted to an oil which later solidified in the hot mixture. The colorless crystals (55 mg. or 85%) of 7-methoxy-1-keto-2-methyl-1,2,3,4-tetrahydrophenanthrene (IVa) which were filtered off melted at 105–107°; when mixed with authentic ketone (m. p. 109–110°), the melting point was 107–109°. Only a trace of acidic material precipitated when the alkaline filtrate was acidified.

Conversion of the Reformatsky Ester (V) to the Unsaturated Acids.—To a cold mixture of 2 cc. of benzene and 0.6 cc. of pyridine was added 1.2 cc. of pure thionyl chloride. The solution was chilled and 1.65 g. of powdered Reformatsky ester was added. An immediate reaction ensued, and after a few minutes a clear yellow solution resulted. After standing at 25° for one-half hour, the mixture was evaporated under reduced pressure at room temperature and finally at 40°. The crystalline chloride was dissolved in 5 cc. of benzene and decanted from the insoluble pyridine hydrochloride; the latter was digested several times with small portions of benzene and the extracts were added to the main portion. (Alternately, the mixture of ester, thionyl chloride and pyridine in 10 cc. of benzene was allowed to stand at 25° for one-half hour, then chilled and shaken with ice and water; the benzene solution was then separated from the aqueous layer.) To the chilled benzene solution was added a solution of 1.6 g. of potassium hydroxide in 22 cc. of methanol and the mixture was refluxed for fifteen minutes. Four and one-half cc. of 45% aqueous potassium hydroxide was added to the cooled solution and refluxing was continued. After three-quarters of an hour, a large amount of precipitate was present. Sufficient water (20 cc.) was added to dissolve the solid, some of the methanol and benzene were removed in a current of air, and refluxing was continued for four hours.

The excess of alkali was carefully neutralized with 5% hydrochloric acid, and the solution was boiled with Norite and filtered. Acidification of the filtrate precipitated a mixture of unsaturated acid and acid anhydride. The dried product was boiled with 100 cc. of acetone and the insoluble acid anhydride (VII) was filtered from the solution, which contained all of the unsaturated acid (VI) and a small amount of anhydride. The **anhydride of *syn*-7-methoxy-2-methyl-2-carboxy-1,2,3,4-tetrahydrophenanthrylidene-1-acetic acid** (VII) crystallized from acetic acid–xylene in the form of colorless plates; yield, 0.71 g.; m. p. 233–234°. It dissolves only slowly in hot aqueous sodium hydroxide solution.

Anal. Calcd. for $C_{19}H_{16}O_4$: C, 74.0; H, 5.2. Found: C, 73.9; H, 5.2.

The acetone solution was evaporated to dryness and the residue was warmed with a 5% solution of sodium bicarbonate. The solution was filtered from 0.06 g. of the anhydride. Acidification of the aqueous filtrate gave 0.26 g. of the unsaturated acid. From benzene the ***anti*-7-methoxy-2-methyl-2-carboxy-1,2,3,4-tetrahydrophenanthrylidene-1-acetic acid (VI)** crystallized in broad, colorless needles; m. p. 216–217° with evolution of gas. When the acid is dissolved in sodium bicarbonate and the solution is acidified, the same acid and no anhydride is precipitated.

Anal. Calcd. for $C_{19}H_{18}O_5$: C, 69.9; H, 5.6. Found: C, 70.2; H, 5.8.

The unsaturated acid reacted immediately with an ether solution of diazomethane while the acid anhydride remained unaffected under the same conditions. The **methyl ester** of the unsaturated acid crystallized from methanol in thin, colorless, nacreous leaflets which melted at 86–87°. The second crop of crystals consisted of stout plates which melted about twenty-five degrees higher. This represented a second form of the ester; when the low-melting product was recrystallized from methanol–petroleum ether and the solution seeded with the high-melting form, stout, colorless plates of the methyl ester were formed; m. p. 113.5–114°.

Anal. Calcd. for $C_{21}H_{22}O_5$: C, 71.2; H, 6.3. Found: C, 70.9; H, 6.2.

Reduction of the Unsaturated Acid (VI).—A warm solution of 120 mg. of the unsaturated acid in 0.12 cc. of 45% potassium hydroxide and 2.4 cc. of water was shaken vigorously with 5 g. of 2% sodium amalgam for fifteen minutes. Acidification of the clarified solution precipitated a mixture of the reduced acids. The dried product was dissolved in a hot mixture of 0.48 cc. of acetic acid and 0.72 cc. of xylene and the solution without filtering was allowed to cool; 55 mg. (45%) of colorless crystals melting at 227–229° precipitated. From xylene–acetic acid the **α-7-methoxy-2-methyl-2-carboxy-1,2,3,4-tetrahydrophenanthrene-1-acetic acid (VIII or IX)** crystallized in colorless rhombic prisms; m. p. 231–232°.

Anal. Calcd. for $C_{19}H_{20}O_5$: C, 69.5; H, 6.1. Found: C, 69.7; H, 5.8.

The filtrate was evaporated to dryness and the residue was dissolved in a small volume of hot benzene. On cooling, the solution deposited colorless plates (65 mg.). The compound melted slightly at 145°, the melt solidified and the solid melted at 208–210°. It melted completely with bubbling when put into a bath at 150°. It appears that the acid crystallizes with benzene of crystallization. A sample of the pure acid was prepared by hydrolysis of the pure acid ester (XI). From acetone–petroleum ether the **β-7-methoxy-2-methyl-2-carboxy-1,2,3,4-tetrahydrophenanthrene-1-acetic acid (VIII or IX)** crystallized in colorless prisms; m. p. 213–214°.

Anal. Calcd. for $C_{19}H_{20}O_5$: C, 69.5; H, 6.1. Found: C, 69.6; H, 6.2.

Reduction of the Acid from the Unsaturated Anhydride (VII).—A mixture of 300 mg. of the acid anhydride, 100 mg. of potassium hydroxide and 10 cc. of methanol was refluxed for one-half hour. The methanol was removed in a current of air and the potassium salt of the unsaturated acid was dissolved in a small amount of water. After being shaken with 12 g. of 2% sodium amalgam for fifteen minutes the solution was acidified and the mixture of reduced acids was separated in the manner already described into 100 mg. (33%) of the α-acid and 130 mg. (43%) of the β-acid. The acids and their methyl esters were identical with the corresponding compounds obtained by reduction of the unsaturated acid.

Direct Preparation of the Reduced Acids, α and β.—Inasmuch as the unsaturated acid and the acid anhydride yielded the same two reduced acids on reduction, it was un-

necessary to isolate the unsaturated compounds. Usually 7.44 g. (0.02 mole) of the Reformatsky ester was converted to the potassium salts of the unsaturated acids as described. The aqueous solution of the salts was then transferred to a strong 500-cc. bottle and shaken vigorously for one-half hour with 150 g. of 2% sodium amalgam; in this process the yellow solution became practically colorless. The dried mixture of reduced acids (6.3–6.4 g.) was dissolved in a hot mixture of 20 cc. of acetic acid and 30 cc. of xylene. Without filtering, the solution is allowed to cool; 3.0–3.1 g. of the α acid crystallized (m. p. 222–225°). By evaporation of the solution and recrystallization of the residue from benzene, the β-acid was obtained; the weight of the latter varied from 2.8–3.5 g., depending on whether benzene of crystallization was present. The yields of the acids formed in the reaction were best obtained from the amount of dimethyl ester produced on treatment with diazomethane. Numerous runs showed that the yield of the α-acid was 44–47%, that of the β-acid 40–43% (total, about 87%) of the theoretical amount based on the Reformatsky ester.

Synthesis of *d*- and *l*-Equilenin

Dimethyl Ester of β-7-Methoxy-2-methyl-2-carboxy-1,2,3,4-tetrahydrophenanthrene-1-acetic Acid (X).—The ester was prepared from the β-acid by means of diazomethane and recrystallized from acetone–methanol. The yield of the ester varied with the purity of the acid. In a typical run, 0.69 g. of the acid as it was obtained in the reduction process yielded 0.62 g. of the ester melting at 107–109°; this product was found to be sufficiently pure for conversion to the acid ester (XI). Since the acid ester can be obtained more readily in a high state of purity, a pure sample of the dimethyl ester was prepared by reaction of the acid ester with diazomethane. The pure dimethyl ester crystallized from ether in thin, colorless plates; m. p. 114–115.5°.

Anal. Calcd. for $C_{21}H_{24}O_5$: C, 70.8; H, 6.8. Found: C, 70.6; H, 6.7.

β-7-Methoxy-2-methyl-2-carbomethoxy-1,2,3,4-tetrahydrophenanthrene-1-acetic Acid (XI).—A mixture of the aforementioned dimethyl ester (0.62 g., m. p. 107–109°), 10 cc. of methanol and 1.8 cc. of *N* sodium hydroxide was refluxed for two hours; the solution was clear after a few minutes. After evaporation of the methanol in a current of air, the residue was dissolved in a few cc. of water. About 2 cc. of ethyl acetate was added and the solution was acidified with hydrochloric acid; the precipitated acid went into solution in the ethyl acetate and then reprecipitated in the form of crystals. In the absence of the solvent, the acid usually precipitated in extremely fine crystals which were difficult to filter. The ethyl acetate was removed in a current of air, and the crystals were filtered off; yield, 0.58 g. (97%); m. p. 208–210°. Runs up to 10 g. were carried out in the same manner; two hours was found to be sufficient time for hydrolysis of the one ester group. Ethyl acetate can be used for recrystallization. For 7.2 g. of the acid ester about 400 cc. of boiling ethyl acetate was required to effect solution; the ethyl acetate was then concentrated by distillation until crystals of the acid ester appeared in the hot solution. The pure acid ester crystallizes from ethyl acetate in colorless plates; m. p. 211–212°.

Anal. Calcd. for $C_{20}H_{22}O_5$: C, 70.2; H, 6.5; neut. equiv., 342. Found: C, 70.1; H, 6.4; neut. equiv. 339.

A sample of the acid ester (0.15 g.) was hydrolyzed completely to the dicarboxylic acid by heating it with 1.5 cc. of 45% aqueous potassium hydroxide and 3 cc. of methanol for one hour.

Arndt–Eistert Reaction on the β-Acid Ester.—To 4 cc. of ice-cold dry benzene in a 125-cc. suction flask fitted with a drying tube was added 2 drops of pyridine and then 1.5 cc. of pure thionyl chloride. To the cold solution was added 1.71 g. of the aforementioned acid ester (unrecrystallized, m. p. 208–210°) in powdered form. After standing at room temperature for one-half hour, the mixture was warmed to about 40° for ten minutes. The orange-yellow solution containing some pyridine hydrochloride in suspension was evaporated under reduced pressure (water pump); 2 cc. of benzene was added and the solution again evaporated in order to remove traces of thionyl chloride from the crystalline acid chloride. The acid chloride was dissolved in 16 cc. of warm benzene, the solution was cooled somewhat and decanted carefully (through a small plug of cotton in the side-arm of the flask) drop by drop into a cold (5°) solution of diazomethane in ether; during the addition the diazomethane solution was swirled constantly.

Since the acid chloride being used was aliphatic in nature, it was felt desirable to employ a solution of diazomethane which was as free from alcohol as possible; hence, the diazomethane was prepared in *n*-propyl alcohol and ether free from alcohol was used. A solution of 2.8 g. of powdered potassium hydroxide (85%) in 10 cc. of warm *n*-propyl alcohol was prepared in a 125-cc. Claisen flask; 60 cc. of anhydrous ether was added to the solution and the flask was attached to a dry condenser which was attached to a receiver (a suction flask fitted with a drying tube) containing about 10 cc. of pure ether. Through a dropping funnel a solution of 4.5 cc. of nitrosomethylurethan in 10 cc. of anhydrous ether was dropped into the alkaline mixture; the diazomethane was distilled from the mixture as it was formed. The diazomethane solution was poured into a 200-cc. round-bottomed flask which had a ground-glass connection for a reflux condenser. The addition of the acid chloride resulted in the evolution of gas. After fifteen to thirty minutes, the ether and excess of diazomethane were removed under reduced pressure (water pump) at room temperature. The diazo ketone (XII) usually crystallized in the form of cream-colored, elongated, hexagonal plates.

To the diazo ketone was added 35 cc. of dry methanol and to the warm (50°) mixture was added one-half of the finely divided silver oxide obtained from 3.6 cc. of 10% silver nitrate solution (precipitating with alkali, washing well with water, filtering, washing with water and finally methanol, breaking up the silver oxide into a slurry with 1 cc. of methanol). The mixture was warmed on a water-bath at about 60° with frequent swirling of the contents. Nitrogen was evolved and after fifteen to twenty minutes the rather insoluble diazo ketone had gone into solution. At this time a small amount of silver oxide was added and heating was continued; further additions of silver oxide were made every five minutes; after six additions all of the silver oxide had been added. Then the mixture was refluxed for fifteen minutes.

The solution was boiled with Norite, filtered and concentrated to a small volume; on cooling, the product crystallized. Two crops of crystals (1.4–1.48 g.) were isolated; by sublimation of the material in the mother liquor at 240° (0.5 mm.), an additional 0.08 g. of the compound was obtained, making a total yield of 80–84%. The product (m. p. 97–101°) was sufficiently pure for cyclization. Should the crystals darken on exposure to light, the presence of traces of silver compounds is indicated; this impurity can be removed readily by passage of a benzene solution of the ester through a short column of anhydrous alumina. The pure **dimethyl ester of β-7-methoxy-2-methyl-2-carbomethoxy-1,2,3,4-tetrahydrophenanthrene-1-propionic acid (XIII)** crystallizes from methanol in glistening, colorless plates; m. p. 101–102°. It is readily soluble in acetone and in benzene, but is little soluble in methanol.

Anal. Calcd. for $C_{22}H_{26}O_6$: C, 71.3; H, 7.1. Found: C, 71.1; H, 6.9.

Cyclization to the Methyl Ether of 16-Carbomethoxy-*dl*-equilenin (XIV).—In the theoretical part mention was made of the difficulty encountered in trying to cyclize the aforementioned ester by the action of sodium on the ester in benzene containing a trace of methanol. Addition of methanol caused the ester to react completely but during the process the mixture became red and a considerable amount of acidic material (extractable by sodium bicarbonate solution) accompanied the cyclic keto ester; as a result the latter was obtained in only 40–50% yields. The observation that the acidic material on esterification did not give back the original ester suggested that oxidation was taking place during the cyclization, and this was found to be the case. By running the reaction in nitrogen and using two moles of sodium methoxide as the condensing agent, the cyclic keto ester was obtained in yields as high as 98%.

A solution of sodium methoxide was prepared from 0.3 g. of clean sodium and 5 cc. of anhydrous methanol; as soon as the reaction was complete, the excess methanol was removed on a steam-bath under reduced pressure. To the solid sodium methoxide, after breaking up the cake, was added 2.0 g. of the ester (XIII) (m. p. 97–101°), and the flask, which was fitted with a condenser, was evacuated and then filled with pure, dry nitrogen. Through the top of the condenser was added 20 cc. of dry benzene and the mixture was refluxed on a water-bath for two hours. The solution was cooled in nitrogen and acidified with acetic acid, and then water containing a little hydrochloric acid. The organic layer was washed with sodium bicarbonate solution to remove a trace of acidic product, the benzene solution was clarified with anhydrous calcium chloride, filtered and evaporated in a current of air. On addition of methanol the product crystallized in colorless plates; yield, 1.77 g. (97%); m. p. 175–180°. By recrystallization from acetone–methanol the methyl ether of 16-carbomethoxy-*dl*-equilenin was obtained in thin, elongated rectangular plates; m. p. 181–182° (vac.) with slight previous softening. It is desirable to recrystallize the compound before converting it to racemic equilenin. The compound gave no color with alcoholic ferric chloride solution.

Anal. Calcd. for $C_{21}H_{22}O_4$: C, 74.5; H, 6.6. Found: C, 75.1; H, 6.5.

***dl*-Equilenin.**—In view of our experiences with oxidation of the cyclic keto ester, subsequent operations were generally carried out in an inert atmosphere. A mixture of 1.56 g. of the methyl ether of 16-carbomethoxy-*dl*-equilenin, 75 cc. of acetic acid, 37 cc. of concentrated hydrochloric acid and 7 cc. of water was refluxed in a nitrogen or carbon dioxide atmosphere. A lively evolution of carbon dioxide took place during the first twenty minutes, corresponding to the formation of the methyl ether of *dl*-equilenin. When the evolution of gas had ceased, a slow stream of nitrogen (or carbon dioxide) was passed through a stopcock attached to the tube leading from the top of the condenser to a mercury trap; in this manner bumping of the boiling solution was prevented. After ten hours of refluxing all of the methyl ether was hydrolyzed, but if heating was discontinued before this time some of the methyl ether of *dl*-equilenin was present. Thus, after eight hours of refluxing, the solution was cooled in order to allow most of the product to precipitate (1.06 g.; m. p. 268–270°); by removal of the solvents under reduced pressure and treatment of the solid residue with sodium bicarbonate solution, an additional 0.11 g. was obtained. In order to separate the racemic equilenin from its methyl ether, the product was heated with 160 cc. of a 2.5% aqueous solution of potassium hydroxide and filtered; there remained 0.06 g. of the methyl ether. After sublimation at 180° (0.01 mm.), the **methyl ether of *dl*-equilenin (XV)** crystallized from acetone–methanol in colorless plates; m. p. 185–186.5° (vac.). The same methyl ether was obtained when the *dl*-equilenin was treated with methyl sulfate in alkaline solution.

Anal. Calcd. for $C_{19}H_{20}O_2$: C, 81.4; H, 7.2. Found: C, 81.7; H, 7.0.

The *dl*-equilenin obtained by acidification of the alkaline solution was dried and recrystallized from acetone–ethanol. The compound was obtained in at least two forms. In one run the product obtained by one crystallization formed colorless leaflets which melted at 287–288° (vac.). Usually, the racemic equilenin melted at 276–278° (vac.), although sometimes a melting point of 265° was observed; in the latter case the solid formed on cooling remelted at 276–278° (vac.). The yield of purified *dl*-equilenin varied between 90–95%. The *dl*-equilenin crystallized well from benzene, but the crystals were found to contain solvent of crystallization; they melted at about 180° with loss of solvent.

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.2; H, 6.8. Found: C, 81.2; H, 6.8.

The **benzoate** of *dl*-equilenin, prepared by means of benzoyl chloride and pyridine, crystallizes from methanol–ethyl acetate in thin, colorless plates; m. p. 248.5–249.5° (vac.).

Anal. Calcd. for $C_{25}H_{22}O_3$: C, 81.1; H, 6.0. Found: C, 80.7; H, 5.8.

The **acetate** of *dl*-equilenin, prepared by the method described for the active product, crystallizes from methanol in broad, colorless needles, which melted at 153–154° (vac.), solidified and remelted at 159.5–160° (vac.).

Anal. Calcd. for $C_{20}H_{20}O_3$: C, 77.9; H, 6.5. Found: C, 77.8; H, 6.5.

Conversion of the Methyl Ether of Equilenin to 3',3'-Dimethyl - 7 - methoxy - 1,2 - cyclopentenophenanthrene (XVII).—Following the procedure of Cohen, Cook and Hewett,[11] 26 mg. of the methyl ether of *dl*-equilenin was converted to the methylcarbinol by means of methylmagnesium iodide. The product (23 mg., m. p. 119–135°) was heated with 100 mg. of powdered potassium acid sulfate (freshly fused) at 160–170° for one hour. The product was extracted with acetone, the solution decolorized with Norite and evaporated, and the residue crystallized from methanol. The thin, colorless plates (5 mg.) proved to be 3',3'-dimethyl-7-methoxy-1,2-cyclopentenophenanthrene rather than the dihydro compound, indicating that dehydrogenation occurred during the process of dehydration. No other products were found in the filtrate. The same action was observed when the carbinol from the natural equilenin was treated in the same manner. The product melted at 162–163.5° (Cohen, Cook and Hewett,[11] 165–165.5°) alone and when mixed with the compound (m. p. 160.5–161.5°) prepared from natural equilenin. Likewise, the trinitrobenzene complexes of the compounds obtained from the two sources melted at 170–171.5° (Cohen, Cook and Hewett, 174–175°) alone and when mixed with each other.

Resolution of *dl*-Equilenin

***d*-Equilenin-*l*-menthoxyacetate.**—Two hundred mg. of *dl*-equilenin was dissolved in 1.5 cc. of dry dioxane and 1 cc. of pyridine by warming. The solution was cooled, the air displaced by nitrogen, and 0.5 cc. of *l*-menthoxyacetyl chloride was added.[27] The flask was stoppered and the mixture was allowed to stand for five hours at room temperature with occasional swirling. The colorless, mobile solution, which may contain crystals of pyridine hydrochloride, was hydrolyzed, the product taken up in benzene and the benzene extract was washed with dilute hydrochloric acid, water, sodium bicarbonate solution and dried with sodium sulfate. The product obtained by evaporation of the benzene crystallized readily from petroleum ether containing a few drops of acetone. Sometimes the crystals consisted nearly entirely of one ester [100 mg., m. p. 160–171° (vac.)]; at other times both esters crystallized out [200 mg., m. p. 135–138° (vac.)]. After two to five recrystallizations from petroleum ether–acetone and finally from acetone alone, pure *d*-equilenin-*l*-menthoxyacetate was obtained as thin, colorless plates; m. p. 174–174.5° (vac.); yield, 85–96 mg. (49–55%). The melting point was 173.5–174.5° when the compound was mixed with the same ester (m. p. 173–173.5°) prepared from natural (*d*-) equilenin.

Anal. Calcd. for $C_{30}H_{38}O_4$: C, 77.9; H, 8.3. Found: C, 77.6; H, 8.4. *Rotation.* 30.4 mg. made up to 2 cc. in benzene gave a rotation of +0.27° at 30°; *l*, 1; $[\alpha]^{30}D$ +18°.

The remaining crystalline material (about 180 mg.; m. p. 135–140°), which could not be separated further by recrystallization, was hydrolyzed, and the product was used for the isolation of the ester of *l*-equilenin; this is described under the preparation of that compound.

***d*-Equilenin.**—A mixture of 115 mg. of *d*-equilenin-*l*-menthoxyacetate, 2.5 cc. of acetic acid, 1.5 cc. of concentrated hydrochloric acid and 0.3 cc. of water was refluxed in an atmosphere of carbon dioxide (mercury trap) for one hour. The light yellow solution was diluted with water and cooled; from the solution nearly colorless *d*-equilenin precipitated; yield, 57–62 mg. (86–94%); m. p. 246.5–249° (vac.). By recrystallization from dilute alcohol, using Norite, the synthetic hormone was obtained as colorless needles; m. p. 250–251° (vac.); 258–259° (vac., cor.). Mixed with natural equilenin (m. p. 250–251°), the melting point was unchanged. Effective purification also can be obtained by sublimation at 170–180° at 0.01 mm.

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.2; H, 6.8. Found: C, 81.3; H, 6.7. *Rotation.* 12.8 mg. made up to 1.8 cc. in dioxane gave a rotation of +0.60° at 30°; *l*, 1; $[\alpha]^{30}D$ +84°. Girard, *et al.*[3] report 258–259° (cor.) for the melting point and $[\alpha]^{16}D$ +87° (dioxane) for the specific rotation of natural equilenin.

The acetate was prepared by mixing 5 mg. of *d*-equilenin, 2 drops of acetic acid, 1 drop of pyridine and 1 drop of acetyl chloride and allowing the mixture to stand at room temperature for fourteen hours. The product (4 mg.) which was isolated crystallized from methanol in broad, colorless needles; m. p. 156–157° alone, and when mixed with the acetate (m. p. 156–156.5°) of natural equilenin.[3]

The benzoate of *d*-equilenin crystallized from acetone–alcohol in colorless plates; m. p. 222.5–223° (vac.); the mixed melting point with the benzoate (222.5–223.5°) of natural equilenin[3] was 222.5–223.5° (vac.).

The methyl ether was prepared by treating a solution of 10 mg. of *d*-equilenin in 2 cc. of *N* sodium hydroxide and 3 cc. of water with 2 drops of methyl sulfate; the mixture was swirled while being heated on a steam-bath. More methyl sulfate (6 drops) was added until no further precipitate formed, the solution being kept alkaline throughout. By recrystallization from methanol, the methyl ether (6 mg.) was obtained in the form of long, narrow, colorless plates; m. p. 193.5–194° (vac.). Mixed with the methyl ether (m. p. 194–194.5°) of natural equilenin,[28] the melting point was 194–194.5° (vac.).

The **trinitrobenzene complex** of equilenin, which was made because it is more stable than the picrate, was prepared by dissolving 5 mg. of each component in hot absolute ethanol; the first crop of broad, yellow needles melted at 205–207.5° (vac.) and after recrystallization from absolute ethanol melted at 205.5–207° (vac.). When mixed with the same complex (m. p. 206.5–207.5°) of natural equilenin, the melting point was 206–207° (vac.).

Anal. Calcd. for $C_{24}H_{21}O_8N_3$: N, 8.8. Found: N, 9.1.

The methyl carbinol (XVI), prepared from the methyl ether of *d*-equilenin and methylmagnesium iodide according to the procedure of Cohen, Cook and Hewett,[11] crystallized from cyclohexane in colorless needles; m. p. 132.5–133.5° (vac.). The mixed melting point with the same derivative (m. p. 132.0–134.5°) of natural equilenin was 132.5–134.5° (vac.).

***l*-Equilenin.**—*dl*-Menthol[29] was resolved and the *d*-menthol was converted to *d*-menthoxyacetic acid according

(27) Frankland and O'Sullivan, *J. Chem. Soc.*, **99**, 2329 (1911); Read and Grubb, *J. Soc. Chem. Ind.*, **51**, 330T (1932).

(28) Sandulesco, Tchung and Girard, *Compt. rend.*, **196**, 137 (1933).

(29) *dl*-Menthol (Menthol-Y) was purchased from the New York Quinine and Chemical Works, Inc., New York City.

to the procedure of Read and Grubb.[27] Treatment of the *dl*-equilenin or the mixture of *dl*- and *l*-equilenin recovered after removal of some of the *d*-isomer with *d*-menthoxyacetyl chloride yielded a mixture of esters from which the **l-equilenin-d-menthoxyacetate** was isolated in pure form by recrystallization as was done for the antipode. From acetone, the ester was obtained in thin, colorless plates; m. p. 174.5–175° (vac.). A mixture of equal parts of this ester and its antipode (m. p. 174–174.5°) melted at 151–152° (vac.).

Anal. Calcd. for $C_{30}H_{38}O_4$: C, 77.9; H, 8.3. Found: C, 77.5; H, 8.4. *Rotation.* 30.6 mg. made up to 2 cc. in benzene gave a rotation of −0.25° at 30°; *l*, 1; $[\alpha]^{30}D$ −16°.

Hydrolysis of the aforementioned ester gave *l*-equilenin, which formed colorless needles from acetone–methanol; m. p. 250–251° (vac.), 258–259° (vac., cor.).

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.2; H, 6.8. Found: C, 81.0; H, 7.1. *Rotation.* 20.8 mg. made up to 2 cc. in dioxane gave a rotation of −0.88° at 30°; *l*, 1; $[\alpha]^{30}D$ −85°.

Synthesis of *d*- and *l*-Isoequilenin

Dimethyl Ester of α-7-Methoxy-2-carboxy-1,2,3,4-tetrahydrophenanthrene-1-acetic Acid (X).—The α-acid as obtained by separation from its isomer was converted to its dimethyl ester by means of ethereal diazomethane; during the process benzene or acetone was added to dissolve the ester. After decolorization and filtration the solution was concentrated to a small volume and methanol added. From the solution the ester crystallized in large, colorless plates or prisms; yield, practically quantitative. The first time this compound was prepared it was obtained as broad, colorless needles melting at 86–89°; these gradually changed over to the plates which melted at 126–126.5°. In all subsequent runs the higher melting form was always obtained.

Anal. Calcd. for $C_{21}H_{24}O_5$: C, 70.8; H, 6.8. Found: C, 70.7; H, 6.7.

α-7-Methoxy-2-methyl-2-carbomethoxy-1,2,3,4-tetrahydrophenanthrene-1-acetic Acid (XI).—A mixture of 10.3 g. of the aforementioned dimethyl ester (powdered), 29.0 cc. of *N* sodium hydroxide and 150 cc. of methanol was refluxed for three hours. After removal of the methanol in a current of air, the residue was digested with 50 cc. of hot water; all but 0.21 g. of unchanged dimethyl ester dissolved. From the filtered solution 9.65 g. (99%, based on the ester used) of the acid ester was obtained on cautious acidification with hydrochloric acid; this product was sufficiently pure for the next step. When recrystallized from acetone–ligroin, it was obtained in fine, colorless needles; these melted at about 110–112° with bubbling; after long standing the melt solidified and the solid then melted at 137–138°. For analysis a sample was fused under reduced pressure.

Anal. Calcd. for $C_{20}H_{22}O_5$: C, 70.2; H, 6.5. Found: C, 69.7; H, 6.5.

Arndt–Eistert Reaction on the α-Acid Ester.—The reaction was carried out in essentially the same manner as for the β-acid ester except that anhydrous ether was used in place of benzene in the preparation of the acid chloride. The acid chloride from 1.71 g. of the acid ester was dissolved in 10 cc. of ether and the solution decanted into the ethereal solution of diazomethane. Evaporation of the resulting solution yielded broad, cream-colored needles of the diazo ketone. The latter was warmed with methanol and silver oxide in the manner described for the diazo ketone from the β-acid, and after the reaction was complete, the hot methanol solution was passed through a small column of alumina to remove colloidal silver from the solution. After treatment with Norite and concentration to a small volume, the chilled solution deposited 1.27 g. of the dimethyl ester of **α-7-methoxy-2-methyl-2-carboxy-1,2,3,4-tetrahydrophenanthrene-1-propionic acid** (XIII). In the filtrate an additional 0.10 g. (determined by cyclization to the cyclic keto ester) of the ester was present, making a total yield of 74%. The compound crystallizes from acetone–methanol in colorless plates; m. p. 89–89.5°.

Anal. Calcd. for $C_{22}H_{26}O_5$: C, 71.3; H, 7.1. Found: C, 70.9; H, 7.0.

***dl*-Isoequilenin.**—Cyclization of the aforementioned ester was carried out in nitrogen in the manner described for the isomer. A solution of 1.4 g. of the ester in 14 cc. of benzene refluxed with the dry sodium methoxide from 0.16 g. of sodium for one hour gave 1.115 g. (87%) of the **methyl ether of 16-carbomethoxy-*dl*-isoequilenin.** The compound crystallized from acetone–methanol in colorless plates; m. p. 149–149.5° in an open tube and 152.5–153.5° in a sealed, evacuated tube. The keto ester develops a deep blue-green color with alcoholic ferric chloride solution.

Anal. Calcd. for $C_{21}H_{22}O_4$: C, 74.5; H, 6.6. Found: C, 75.1; H, 6.6.

A mixture of 1.92 g. of the aforementioned cyclic keto ester, 40 cc. of acetic acid, 25 cc. of concentrated hydrochloric acid and 5 cc. of water was refluxed in an atmosphere of nitrogen for ten hours. The product obtained by evaporation of the solution under reduced pressure was digested with 200 cc. of a 2.5% aqueous solution of potassium hydroxide and the solution was filtered from 60 mg. (4%) of the **methyl ether of *dl*-isoequilenin.** After sublimation at 160–180° at 0.01 mm., the methyl ether crystallized from acetone–methanol in colorless prisms; m. p. 127–127.5° (vac.) with solidification and remelting at 130–130.5° (vac.).

Anal. Calcd. for $C_{19}H_{20}O_2$: C, 81.4; H, 7.2. Found: C, 81.4; H, 7.2.

Acidification of the alkaline solution precipitated the *dl*-isoequilenin (1.42 g., 93%). Recrystallization from acetone–ethanol gave nearly colorless plates (1.27 g.) of ***dl*-isoequilenin;** these melted at 206–206.5°, the melt solidified and the solid remelted at 221–222°. Further recrystallization from benzene–acetone and then from acetic acid containing some water raised the melting point to 223–224° (vac.). Frequently the high-melting form crystallized directly from the solution. By sublimation in a high vacuum (0.01 mm.) the product can be obtained perfectly colorless.

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.2; H, 6.8. Found: C, 81.0; H, 6.8.

The **acetate** of the *dl*-isoequilenin crystallized from acetone–methanol in colorless prisms; m. p. 159–160° (vac.).

Anal. Calcd. for $C_{20}H_{20}O_3$: C, 77.9; H, 6.5. Found: C, 77.8; H, 6.7.

The **trinitrobenzene complex** crystallized from absolute ethanol in clumps of long, fine, yellow needles; m. p. 186–187° (vac.).

Anal. Calcd. for $C_{24}H_{21}O_8N_3$: N, 8.8. Found: N, 8.8.

Conversion of *dl*-Isoequilenin to 3′,3′-Dimethyl-7-methoxy-1,2-cyclopentenophenanthrene.—The methyl ether of the racemic isoequilenin (80 mg.) was treated with methylmagnesium iodide to give the corresponding methyl carbinol (63 mg., m. p. 88–92°), which was heated with potassium acid sulfate and worked up in the manner described for the *dl*-equilenin derivative. The product was treated with palladium-charcoal at 360° for one hour, then sublimed and crystallized from methanol. Unlike that from *dl*-equilenin methyl ether, the product was a mixture from which only a small amount (3%) of 3′,3′-dimethyl-7-methoxy-1,2-cyclopentenophenanthrene could be isolated as the trinitrobenzene complex; m. p. 170–171° alone and when mixed with an authentic sample prepared from natural equilenin.

Resolution of α-7-Methoxy-2-methyl-2-carbomethoxy-1,2,3,4-tetrahydrophenanthrene-1-acetic Acid.—To an ice-cold mixture of 4 cc. of anhydrous ether, 2 drops of pyridine and 2.2 cc. of thionyl chloride was added 3.38 g. of the acid ester of the α-acid. After forty-five minutes at room temperature, the solution was evaporated under reduced pressure; the acid chloride was dissolved in 2 cc. of benzene and the mixture was again evaporated. To the solution of the acid chloride in 4 cc. of ether 2 g. of *l*-menthol was added. After twenty-four hours at room temperature, the mixture of esters which had precipitated in solid form was filtered off and recrystallized from petroleum ether (60–75°), yielding 1.43 g. of methyl-*l*-menthyl ester melting at 135–138°; from the original filtrate an additional 0.09 g. of the same ester was isolated. The product (1.52 g.) crystallized from acetone–methanol in colorless needles (1.4 g.) which melted at 139–139.5°; this product is sufficiently pure for the next step. In the experiment just described practically only one of the esters came out; if both crystallize, the mixture of esters must be recrystallized several times in order to effect a separation. Further recrystallization of a sample of the ***l*-methyl-*l*-menthyl ester of α-7-methoxy-2-methyl-2-carboxy-1,2,3,4-tetrahydrophenanthrene-1-acetic acid** raised the melting point to 139.3–139.8°.

Anal. Calcd. for $C_{30}H_{40}O_5$: C, 75.0; H, 8.4. Found: C, 75.2; H, 8.4. *Rotation.* 30.6 mg. made up to 2 cc. in benzene gave a rotation of −2.31° at 30°; *l*, 1; $[\alpha]^{30}D$ −152°.

***d*-Isoequilenin.**—The aforementioned ester was rather resistant to hydrolysis. A suspension of 1.2 g. of the active ester in a solution of 16 g. of potassium hydroxide (85%) in 40 cc. of methanol was heated on a steam-bath for seven hours. The methanol was removed in a current of air, and the residue was dissolved in water. After the menthol had been extracted by means of benzene, the solution was acidified with hydrochloric acid. The dicarboxylic acid (m. p. 220–224° unrecrystallized) was filtered off, dried and converted to the dimethyl ester by reaction with diazomethane. By recrystallization from methanol 0.82 g. (92%) of the ***l*-dimethyl ester** of the α-acid was obtained in the form of thin, colorless plates; m. p. 110–110.3°.

Anal. Calcd. for $C_{21}H_{24}O_5$: C, 70.8; H, 6.8. Found: C, 70.7; H, 6.7. *Rotation.* 30.2 mg. made up to 2 cc. in benzene gave a rotation of −2.28°; *l*, 1; temp. 30°; $[\alpha]^{30}D$ −151°.

The dimethyl ester was hydrolyzed to the acid ester in the same manner employed for the racemic ester. From acetone–petroleum ether the active acid ester crystallized in colorless needles; the crystals melt when put into a bath at 130°, the melt solidifies and the solid remelts at 159–160°. The high melting point is observed when the tube is placed into the bath at 90°. The acid ester (0.7 g.) was converted to the propionic acid derivative through the Arndt–Eistert reaction, yielding 0.56 g. in the first crop, which melted at 102–103.5°. From acetone–methanol the ***l*-dimethyl ester of α-7-methoxy-2-methyl-2-carboxy-1,2,3,4-tetrahydrophenanthrene-1-propionic acid** crystallized in broad, colorless needles; m. p. 103–103.5°.

Anal. Calcd. for $C_{22}H_{26}O_5$: C, 71.3; H, 7.1. Found: C, 71.1; H, 6.9. *Rotation.* 12.7 mg. made up to 1.8 cc. in benzene gave a rotation of −0.87° at 28°; *l*, 1; $[\alpha]^{28}D$ −123°.

Cyclization in the manner described for the *dl*-ester gave the active **methyl ether of 16-carbomethoxy-isoequilenin** (0.44 g. from 0.56 g.; after recrystallization, 0.39 g.; m. p. 147–150°); hydrolysis of the latter by refluxing with a mixture of 12 cc. of acetic acid, 8 cc. of concentrated hydrochloric acid and 1.5 cc. of water for ten hours yielded the *d*-isoequilenin, which was isolated in the same manner as the racemic compound. The product dissolved completely in 80 cc. of boiling 1% sodium hydroxide; acidification of the filtered solution precipitated the ***d*-isoequilenin** (0.29 g.). It was recrystallized by dissolving it in acetone, boiling the solution with Norite, filtering, adding alcohol and then concentrating the solution on a steam-bath until crystallization set in. The colorless plates (0.26 g.) melted at 272–273° (vac.). When the compound was recrystallized again, this time by dissolving it in 8 cc. of boiling acetic acid and adding a small amount of water to the solution, colorless leaflets or plates of a second form were obtained; m. p. 257–258° (vac.); 265–266° (vac., cor.).

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.2; H, 6.8. Found: C, 80.9; H, 6.7. *Rotation.* 30 mg. made up to 2 cc. in dioxane gave a rotation of +2.20° at 29°; *l*, 1; $[\alpha]^{29}D$ +147°. In absolute alcohol a specific rotation of +173° was observed with a solution of 8.1 mg. in 2 cc. of solution. In view of the higher concentration possible in dioxane, we consider the dioxane value to be the more accurate. Hirschmann and Wintersteiner reported $[\alpha]^{30}D$ +160° (0.4% in ethanol) for the specific rotation of their 14-*epi*-equilenin.[24]

The **methyl ether** of the *d*-isoequilenin, prepared by the action of methyl sulfate on an aqueous solution of the sodium salt, was obtained as thin colorless plates after two recrystallizations from methanol; m. p. 118.5–119.5°.

The **acetate** of *d*-isoequilenin, prepared by means of a mixture of acetic acid, acetyl chloride and pyridine, crystallized from methanol in long, colorless prisms; m. p. 146–147° (vac.).

Anal. Calcd. for $C_{20}H_{20}O_3$: C, 77.9; H, 6.5. Found: C, 77.9; H, 6.6.

Comparison of Synthetic *d*-Isoequilenin with 14-*epi*-Equilenin.—Dr. O. Wintersteiner kindly made a comparison of our *d*-isoequilenin and its acetate with his 14-*epi*-equilenin,[24] prepared from equilin, and its acetate. The melting points of the isoequilenin and 14-*epi*-equilenin were taken in capillary tubes evacuated to approximately 0.1 mm. He reported the following melting points: *d*-isoequilenin, 263–264°; 14-*epi*-equilenin, 262–263°; mixed sample 261–264°; all melting points are corrected. In all cases there was previous softening before the melting point was reached.

The acetate of 14-*epi*-equilenin, prepared by Dr. Wintersteiner with acetic anhydride in pyridine at room temperature, had a melting point of 126–127.5°; later it melted fairly sharply at 148–149° (after another recrystallization, 148.5–149.5°) with slight softening around 126°. The higher melting point was observed after the sample had been dried at 100° for analysis (Calcd. for $C_{20}H_{20}O_3$: C, 77.88; H, 6.54. Found: C, 77.63; H, 6.73). Our recrystallized *d*-isoequilenin acetate melted at 149–149.5° with slight softening at 148°. A mixture of the two acetates melted at 149.5° after softening at 148°; the sample resolidified after some time and the solid now melted at 127–128°. From this it is clear that the acetate exists in two forms. The compounds possessed the following specific rotations: 14-*epi*-equilenin acetate, $[\alpha]^{24}D$ +137±7° (0.635% in absolute alcohol); *d*-isoequilenin acetate, $[\alpha]^{22}D$ +129.4° (0.307% in absolute alcohol). The margin of error is probably smaller in the latter case because the readings, which were determined using a 2 dcm. tube, were sharper.

***l*-Isoequilenin.**—The mixture of methyl-*l*-menthyl esters of the α-acid (2.35 g.) which remained after removal of the *l*-methyl-*l*-menthyl ester was hydrolyzed to the dicarboxylic acids by heating with a solution of 24 g. of potassium hydroxide (85%) in 60 cc. of methanol for three hours. After removal of the methanol in a current of air, the product was dissolved in water and the menthol was extracted with benzene. The acid (1.58 g.) which precipitated on acidification of the aqueous solution was converted to the dimethyl ester by means of diazomethane. A benzene solution of the ester was boiled with Norite, the solution was filtered and concentrated to a small volume and the residue was dissolved in hot methanol. On cooling the solution deposited fairly large prisms of the racemic dimethyl ester of the α-acid (0.73 g., m. p. 125.5–126°). With luck these can be filtered from the solution by suction before the active (*d*-) dimethyl ester precipitates. Ordinarily it is safer to decant the clear solution from the heavy crystals. The active ester crystallizes in fine colorless plates which dissolve more rapidly and are more soluble than the coarse prisms of the racemic ester. Even when both crystallize out at the same time, one can effect a separation by warming the mixture to dissolve the fine crystals and decant the solution from the coarse prisms. Still another method, which works well after the bulk of the racemic ester has been removed, is to allow the crystallizing solution to stand for ten hours or longer so that the prisms can grow larger; the latter can then be separated by picking them out of the fine crystals by hand. **The *d*-dimethyl ester of α-7-methoxy-2-methyl-2-carboxy-1,2,3,4-tetrahydrophenanthrene-1-acetic acid** (0.8 g.) melted at 108–109°, and it was obtained sometimes as high as 110–110.5°. The lower melting point is probably due to a small amount of the racemic ester, but the product is sufficiently pure for the steps which follow. A mixture of equal parts of the *d*-ester (m. p. 110–110.5°) and the *l*-ester (m. p. 110–110.3°) was recrystallized from acetone–methanol; from the solution was obtained prisms of the racemic ester which melted at 126–126.5°, alone and when mixed with the original racemic ester.

The *d*-dimethyl ester was carried through the remaining steps in the manner described for its antipode, the yields of the products being about the same. The product of the Arndt–Eistert reaction, **d-dimethyl ester of α-7-methoxy-2-methyl-2-carboxy-1,2,3,4-tetrahydrophenanthrene-1-propionic acid,** was quite free from its antipode, for it possessed a melting point of 103–103.5° and a specific rotation $[\alpha]^{29}D$ +122° (antipode, m. p. 103–103.5°, $[\alpha]^{28}D$ −123°). A mixture of equal parts of the antipodes recrystallized from methanol yielded crystals of the racemic ester; m. p. 89–89.5°, alone and when mixed with the racemic ester. Cyclization, followed by hydrolysis of the product, yielded the ***l*-isoequilenin.** The latter melted at 272–273° (vac.) when first obtained from its sodium salt by acidification, but after two recrystallizations from acetone–alcohol it formed large colorless plates, which melted at 257–258° (vac.). A mixture of equal parts of the *d*- and *l*-isoequilenin recrystallized from acetic acid yielded the racemic isoequilenin; m. p. 223–224°, alone and when mixed with the original racemic compound.

Anal. Calcd. for $C_{18}H_{18}O_2$: C, 81.2; H, 6.8. Found: C, 81.1; H, 6.9. *Rotation.* 30.7 mg. made up to 2 cc. in dioxane gave a rotation of −2.26°; *l*, 1; $[\alpha]^{28}D$ −147°. In absolute ethanol (7.9 mg. made up to 2 cc.) a specific rotation $[\alpha]^{28}D$ −162° was observed.

Summary

The total synthesis of the sex hormone equilenin and its three stereoisomers is described.

ANN ARBOR, MICHIGAN RECEIVED FEBRUARY 5, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY, CASE SCHOOL OF APPLIED SCIENCE]

The Halogenation of Unsymmetrical Diphenylethane[1]

BY F. E. SHEIBLEY AND C. F. PRUTTON

When 1,1-diphenylethane at 100° in sunlight is treated with chlorine, hydrogen chloride is evolved and a yellow colored, liquid product results. From this material, on distillation, there was isolated unchanged diphenylethane, stilbene, and 1,1-diphenyl-2,2-dichloroethylene. The failure of the product to undergo any appreciable hydrolysis with caustic alkalies, and the absence in it of detectable amounts of 1,1-diphenylethylene and 1,1-diphenyl-2-chloroethylene, indicate that the over-all reaction is a result of stepwise additions of chlorine to intermediate unsaturates produced by the loss of hydrogen chloride.

$$(C_6H_5)_2CHCH_3 \xrightarrow{Cl_2} (C_6H_5)_2CClCH_3 \xrightarrow{-HCl}$$
I II

$$(C_6H_5)_2C{=}CH_2 \xrightarrow{Cl_2} (C_6H_5)_2CClCH_2Cl \xrightarrow{-HCl}$$
III

$$(C_6H_5)_2C{=}CHCl \xrightarrow{Cl_2} (C_6H_5)_2CClCHCl_2 \xrightarrow{-HCl}$$
IV

$$(C_6H_5)_2C{=}CCl_2$$
V

The chloride (II), prepared from the corresponding carbinol, has been described[2] as an uncrystallizable oil which slowly reverts to 1,1-diphenylethylene (III) at ordinary temperatures. The ethylene (III) was observed by Hepp[3] to react vigorously with chlorine at low temperatures giving a product which yielded 1,1-diphenyl-2,2-dichloroethylene (V) on distillation. The initial chlorination, I → II, is, therefore, the slowest reaction and constitutes the rate determining step.

Bromination mixtures, similarly prepared and distilled, gave only small amounts of 1,1,4,4-tetraphenylbutadiene-1,3 and stilbene.

The presence of stilbene in the halogenation mixtures from 1,1-diphenylethane parallels the experience of Kharasch and Clapp[4] who obtained this substance in excellent yields by heating 2,2-diphenylethanol with phosphorus pentoxide, and recognized the change as another case of the Wagner rearrangement. 1,1-Diphenyl-2-chloroethane is known[5] to give stilbene on distillation, and a similar observation has been recorded for 1,1-diphenyl-2-chloroethylene[6] (IV).

1,1-Diphenyl-2,2-dichloroethylene (V) is a remarkably stable substance and requires the action of alcoholic potassium hydroxide at 150° in order to effect its complete hydrolysis. The product, diphenylacetic acid, was similarly prepared by Fritsch and Feldmann,[7] who employed alcoholic sodium ethylate in a sealed tube and describe the removal of unreacted dichloro compound. A diphenoxy derivative was obtained by using sodium phenate in phenol at 225°. The composition of this product, m. p. 111.5°, indicates that hydration of the double bond has occurred to give the diphenylacetal of benzilic aldehyde,[8] since the alternative structure, $(C_6H_5)_2CHC(OH)(OC_6H_5)_2$, might be expected to lose phenol and give the phenyl ester of diphenylacetic acid.[9]

The pyrolysis of 1,1-diphenylethane in a silica tube at 700° gave benzene, toluene, and styrene in small amounts. Goldschmiedt[10] effected this pyrolysis in a pumice-filled tube and reported stilbene as a product, most of the diphenylethane being unchanged.

Experimental Part

1,1-Diphenyl-2,2-dichloroethylene.—Fifty grams of 1,1-diphenylethane[11] in a quartz flask at 100–150° was treated with a slow stream of chlorine during ten hours, the mixture being exposed to sunlight and finally to the light of an electric lamp. The increase in weight was 16 g. The product on distillation evolved abundant fumes of hydrogen chloride and yielded, at 277–308°, 50.8 g. of distillate which soon turned yellow. On adding solid calcium chloride, 1,1-diphenyl-2,2-dichloroethylene crystallized. The mixed solids were collected, freed of adhering oil by suction and pressing, washed with alcohol, and suspended in water. The undissolved material, 13.1 g., was crystallized from alcohol yielding 11.0 g. of 1,1-diphenyl-2,2-dichloroethylene, m. p. 78–79.5°.

The dark yellow oil, 29 cc., remaining from the crystallization with calcium chloride, was rectified at 1 mm. At

(1) Abstracted from a thesis presented by F. E. Sheibley to Case School of Applied Science in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) Schoepfle and Ryan, THIS JOURNAL, **52**, 4027 (1930).

(3) Hepp, *Ber.*, **7**, 1411 (1874).

(4) Kharasch and Clapp, *J. Org. Chem.*, **3**, 357 (1938).

(5) Hepp, *Ber.*, **6**, 1439 (1873); Anschütz, *Ann.*, **235** 229 (1886).

(6) Buttenberg, *ibid.*, **279**, 326 (1894).

(7) Fritsch and Feldmann, *ibid.*, **306**, 79 (1899).

(8) Scheibler and Depner, *Ber.*, **68**, 2155 (1935), report a melting point of 103° for this compound.

(9) *Cf. ibid.*, **68**, 2137, 2139, 2144, 2151 (1935).

(10) Goldschmiedt, *ibid.*, **6**, 1503 (1873).

(11) The 1,1-diphenylethane, b. p. 273–274° cor. at 744 mm., used in these experiments was obtained from the Dow Chemical Company. It has an odor remindful of mushrooms.

88° 14.6 cc. of colorless 1,1-diphenylethane, saturated toward bromine water, was recovered. At 113° 3.4 cc. of material passed over and partially crystallized; the crystals, recrystallized from a large volume of boiling alcohol, formed white, glistening plates, m. p. 121–123°, identified as stilbene by comparison with an authentic specimen and by conversion to the dibromide. The residue in the still consisted of crude diphenyldichloroethylene and solidified on cooling.

Bromination of 1,1-Diphenylethane. Stilbene.—To 25 cc. of 1,1-diphenylethane at 100° in a quartz flask suspended in the light from an electric lamp, 18 cc. of bromine was added slowly during three hours. The brown reaction mixture yielded copious fumes of hydrogen bromide on distillation and, at 290–310°, 15 cc. of distillate which crystallized on standing. The crystals were sucked free of oil and recrystallized from alcohol to give 0.4 g. of large plates, m. p. 122–124° alone and when mixed with a known sample of stilbene.

1,1,4,4-Tetraphenylbutadiene-1,3.—1,1-Diphenylethane 25 cc., was brominated as described above but only 10 cc. of bromine was used. Distillation of the product gave a fraction, 277–325°, which slowly crystallized. The crystals, sucked free of oil and recrystallized from acetone–alcohol, gave long, white, flat, glistening needles exhibiting a pale violet fluorescence in diffused daylight, m. p. 204–205° cor. An identical product was obtained from a bromination conducted at 65–70°.

Anal. Calcd. for $C_{28}H_{22}$: C, 93.81; H, 6.19; mol. wt., 358.5. Found: C, 93.45; H, 6.52; mol. wt. (Rast), 364, 361.

The melting point was not changed when the product was mixed with an authentic specimen of 1,1,4,4-tetraphenylbutadiene-1,3.[12]

1,1-Diphenyl-2,2-dichloroethylene crystallizes readily from alcohol in long, white, glistening needles, m. p. 79–80° cor. Melting point depression measurements, using naphthalene and *p*-dibromobenzene as solutes, gave for the cryoscopic constant of the compound respective values of 10.0° and 10.2° (mole/kg.), corresponding to a heat of fusion of 24.7 cal. per g.

Anal. Calcd. for $C_{14}H_{10}Cl_2$: C, 67.49; H, 4.05; mol. wt., 249. Found: C, 68.04; H, 4.51; mol. wt. (Rast), 271.

Diphenylacetic Acid.—Hydrolysis of 1,1-diphenyl-2,2-dichloroethylene was not effected by twenty-four-hour periods of treatment with alcoholic sodium hydroxide at 100° or aqueous sodium hydroxide at 150°. One gram of diphenyldichloroethylene, 3 g. of potassium hydroxide, and 17 cc. of alcohol were heated in a 38-cc. stainless steel bomb at 150° during twenty-four hours. The reaction mixture was diluted with water, boiled to remove alcohol, and extracted with ether. Acidification of the aqueous portion gave a precipitate of diphenylacetic acid, 0.62 g. (73%), m. p. 144.5–145°; crystallization from 325 cc. of boiling water yielded 0.56 g., m. p. 145–145.5°; recrystallized, m. p. 147–148° cor. The presence of phenol in a methyl alcoholic reaction mixture did not alter the product of hydrolysis.

Anal. Calcd. for $C_{14}H_{12}O_2$: C, 79.22; H, 5.70. Found: C, 78.97, 79.24; H, 5.64, 5.62.

Benzilic Aldehyde Diphenylacetal.—Three-tenths gram of sodium dissolved in 6 g. of warm phenol, and 0.7 g. of diphenyldichloroethylene were heated at 225° during twenty-four hours. The cold reaction mixture, treated with dilute sodium hydroxide solution, left a yellow gummy mass which was washed with water, air-dried, and crystallized from alcohol, yielding 0.09 g. of a brown-tinted mass of small, opaque, chlorine-free prisms, m. p. 111.5–112° cor. The compound is insoluble in hot aqueous sodium hydroxide or hot concentrated hydrochloric acid.

Anal. Calcd. for $C_{26}H_{22}O_3$: C, 81.65; H, 5.80. Found: C, 82.34, 81.97; H, 5.60, 5.51.

Pyrolysis of 1,1-Diphenylethane.—The hydrocarbon, 340 cc., was slowly fed into an electrically heated, baffled silica tube at 676–702° during one hour and forty-five minutes. Carbon dioxide, 1.25 cubic feet (35.4 liters) was introduced with the charge, and 2.02 cubic feet (57.2 liters) of mixed gas, containing unsaturated material, resulted. The less volatile products amounted to 308 cc., 311 g., of dark colored oil and on distillation gave, at 71–153°, 64 cc. of a mixture consisting principally of benzene, toluene, and styrene. The viscous black residue, b. p. 258–300°, contained much unchanged diphenylethane and, possibly, some 1,1-diphenylethylene. The benzene–toluene–styrene mixture was cooled and treated with bromine until absorption ceased. The product yielded on distillation 52 cc. of distillate and a black residue which crystallized on cooling. Analysis of the distillate in a column still indicated approximately 42% benzene and 58% toluene. The black residue, freed from oil by suction and pressing, was crystallized from alcohol to give glistening plates, m. p. 71.5–72.5° alone or mixed with an authentic specimen of styrene dibromide.

(12) Valeur, *Bull. soc. chim.*, (3) **29**, 685 (1903).

Summary

The photochemical chlorination of 1,1-diphenylethane at 100°, followed by distillation of the product, gives 1,1-diphenyl-2,2-dichloroethylene and small amounts of stilbene.

The analogous bromination of 1,1-diphenylethane yields stilbene and 1,1,4,4-tetraphenylbutadiene-1,3 in small amounts.

The hydrolysis of 1,1-diphenyl-2,2-dichloroethylene to diphenylacetic acid requires the action of hot alcoholic caustic alkali under pressure.

The pyrolysis of 1,1-diphenylethane yields benzene, toluene, and styrene.

CLEVELAND, OHIO RECEIVED OCTOBER 16, 1939

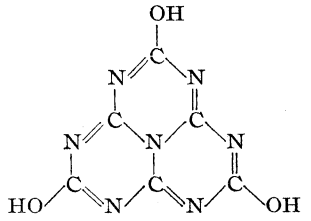
[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, PASADENA, CALIFORNIA, NO. 748]

Some Derivatives of Cyameluric Acid and Probable Structures of Melam, Melem and Melon

BY C. E. REDEMANN AND H. J. LUCAS

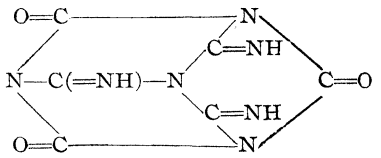
Since it has been shown recently that the structure proposed by Pauling and Sturdivant for the cyameluric acid nucleus,[1] I, accounts more satisfactorily for the acidic strength and for the products of hydrolysis[2] than any other proposed structure, and because of the prediction made by these authors[1] that there should be a group of cyameluric compounds analogous to the cyanuric compounds, attempts have been made to prepare some of these analogs.

Cyameluric acid forms a blue-lavender cupric ammonium salt, $CuNH_4(C_6N_7O_3)NH_3$, entirely analogous to that of cyanuric acid,[3] $CuNH_4(C_3N_3O_3).NH_3$. The insoluble cupric ammonium cyamelurate is useful in purifying cyameluric acid since the acid is readily regenerated from the salt by suspending it in water and acidifying with hydrochloric acid.



Pauling and Sturdivant

I



Franklin

II

In the case of the mercuric salts the parallelism is not so satisfactory. While Hantzsch[4] reported two different mercuric cyanurates with the formula $Hg_3(C_3N_3O_3)_2$, one called an oxygen salt, the other a nitrogen salt, specimens of mercuric cyamelurate, $Hg_3(C_6N_7O_3)_2$, obtained under conditions shown by Hantzsch to give different salts with the former gave only a single salt with the latter. This salt gave an immediate precipitate of yellow mercuric oxide with aqueous sodium hydroxide, hence it would be called the oxygen salt from the Hantzsch point of view. Although in this case the analogy with cyanuric acid is not complete, nevertheless the behavior of the mercury salt favors structure I rather than structure II, for of the latter only a nitrogen salt is possible. This argument is, however, open to criticism, for if the N–Hg bond has sufficient ionic character the salt would be expected to react with sodium hydroxide.

Cyanuryl trichloride, $C_3N_3Cl_3$, and cyameluryl trichloride, $C_6N_7Cl_3$, are completely analogous. Hydrolysis of the two chlorides is similar except that cyameluryl chloride hydrolyzes more rapidly, as might be expected since it is the acid chloride of the stronger acid.[2] When heated with acetic acid each acid chloride yields the respective acid and acetyl chloride; upon alcoholysis each yields the respective acid and an alkyl chloride.

Esters of cyameluric acid are more difficult to prepare than are those of cyanuric acid. Two series of esters are known for the latter: the oxygen esters, and the nitrogen esters. Potassium cyamelurate does not react readily with alkyl halides at room temperature. After standing with methyl iodide for nineteen months, only a small amount of iodide ion was formed and no ester could be isolated. Likewise, cyameluryl trichloride with sodium methoxide (or benzoxide) failed to give the ester. Potassium cyamelurate and allyl bromide gave an allyl derivative at 100° which was not obtained pure. A tribenzyl ester was obtained from benzyl chloride and potassium cyamelurate at 156°. This ester is a nitrogen ester since it gave benzylamine and no benzyl alcohol upon hydrolysis. Cyanuric acid[5] also forms the nitrogen ester at elevated temperatures.

From cyameluric acid and diazomethane was obtained a mixture of monomethyl esters with the nitrogen ester predominant, and also a trimethyl ester which was entirely a nitrogen ester.

(1) Pauling and Sturdivant, *Proc. Natl. Acad. Sci.*, **23**, 615 (1937).

(2) Redemann and Lucas, THIS JOURNAL, **61**, 3420 (1939).

(3) (a) Benrath and Meckenstock, *Z. anorg. allgem. Chem.*, **151**, 35 (1926); (b) Claus and Putensen, *J. prakt. Chem.*, [2] **38**, 216 (1888).

(4) Hantzsch, (a) *Ber.*, **35**, 2717 (1902); (b) *ibid.*, **39**, 139 (1906); (c) *Z. anorg. allgem. Chem.*, **209**, 219 (1932).

(5) Hantzsch and Bauer, *Ber.*, **38**, 1009 (1905).

Cyanuryl chloride and cyameluryl chloride both react with ammonia, the former to produce a monochlordiamide and a triamide, melamine, and the latter to produce a diamide and apparently some triamide, although not pure.

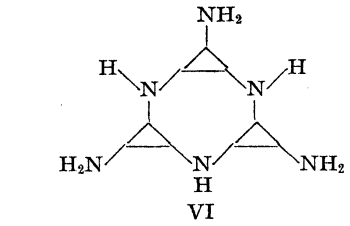
The resemblance of the derivatives of cyameluric acid to the corresponding derivatives of cyanuric acid indicates that cyameluric acid contains hydroxyl groups and suggests that formula I, or $C_6H_7(OH)_3$, is the one which most closely resembles $C_3N_3(OH)_3$.

On the basis that cyameluric acid is represented by I, satisfactory structures can be assigned to melam, melem and melon. Melam,[6] empirical formula $C_6H_9N_{11}$, is probably tetraaminodicyanurimide,[7] III. This structure accounts for the feebly basic property of melam, and is supported by the behavior of melam with 30% aqueous ammonia[8] at elevated temperatures to yield melamine and ammeline; also by Liebig's[6] observation that when boiled with nitric acid melam yields cyanuric acid and ammonium nitrate.

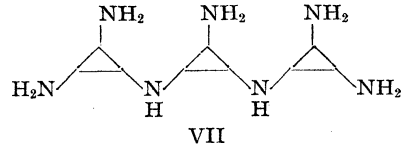
Melem,[6] empirical formula $C_6H_6N_{10}$, is probably cyameluryl triamide, IV. This structure satisfactorily accounts for the formation of large quantities of ammelide upon hydrolysis, and for the fact that melem is more resistant to hydrolysis than melam. Structures III and IV account satisfactorily for the observation that melam is a stronger base than melem, for the latter is derived from much the stronger acid.

$[3.5\text{-}(NH_2)_2C_3N_3]_2NH$	$C_6N_7(NH_2)_3$	$(HN{=}C_3H_3)_2NH$
Melam	Melem	Melon; Franklin
III	IV	V

Melon, with empirical formula $C_6H_3N_9$,[9,10] was assigned structure V by Franklin.[7b] But since melon gives good yields of cyameluric acid upon alkaline hydrolysis[11] a satisfactory structure for melon must involve the planar nucleus characteristic of cyameluric acid, I. Such a structure results from melem, IV, by the loss of ammonia from two or more molecules. One possibility is that shown by structure VI, where three molecules of ammonia have been split out from three molecules of cyameluric triamide. This compound, the molecule of which has three cyameluric nuclei, has the formula $C_{18}H_9N_{27}$, three times $C_6H_3N_9$, the accepted formula for melon. Here the side chains are $-NH_2$ groups, the =NH group forming part of a new ring. Larger molecules of the compact type, where the maximum number of ring closures had taken place would have a higher carbon, lower hydrogen and lower nitrogen content. In such a molecule hydrogen is found only along the periphery. The symmetrical triangular molecule with six cyameluric nuclei is $C_{36}H_{12}N_{52}$ or more simply $C_6H_2N_{8^2/_3}$. As condensations extend indefinitely the empirical formula approaches asymptotically the limit C_3N_4, Franklin's carbonic nitride. Another type of condensation product, in which the cyameluric nuclei, except for the two terminal ones, are joined to only two other nuclei (structure VII), would approach $C_6H_3N_9$ if extended indefinitely.



VI



VII

Melon[12]

On this basis it is possible to account for the lack of constancy of composition of melon observed by Liebig, Franklin and others. The hydrogen content of Franklin's preparations varied from 1.1 to 2.0%, while for the accepted formula, $C_6H_3N_9$, the hydrogen content is 1.5%. By taking extreme precautions to dry mercuric thiocyanate at 150° in the vacuum of a mercury vapor pump before decomposing it to melon, Franklin was able to obtain a product with a hydrogen content of only 0.6%. This corresponds closely to a compact condensation product, triangular in form, with twenty-one nuclei, and molecular formula $C_{126}H_{21}N_{175}$ or more simply $C_6HN_{8^1/_3}$ with a hydrogen content of 0.5%. Franklin's material was probably composed of both larger and smaller units, giving an average value corresponding to the above figures. It is probably incorrect to assign any one structure to melon, for it is more than likely a mixture of

(6) Liebig, *Ann.*, **10**, 10 (1834).

(7) (a) Klason, *J. prakt. Chem.*, [2] **33**, 287 (1886); (b) Franklin, THIS JOURNAL, **44**, 507 (1922).

(8) Rathke, *Ber.*, **23**, 1675 (1890).

(9) Laurent and Gerhardt, *Ann. chem.*, [3] **19**, 85 (1847).

(10) Vockel, *Pogg. Ann.*, **58**, 151 (1834).

(11) Volhard, *J. prakt. Chem.*, [2] **9**, 30 (1874).

(12) In VI and VII, each triangle represents C_6H_7, the cyameluric nucleus.

molecules of different sizes and shapes. This gives rise to its amorphous character.

It is seen that there is a formal resemblance between melon and graphite, in that the molecules are infinitely large and planar. The formal resemblance becomes even more pronounced if in the molecule of melon the void between the three cyameluric nuclei is filled by writing in three atoms of carbon and one of nitrogen. Taking the density of graphite as 2.25 and neglecting the hydrogen, we can predict a density for melon of less than 1.7. An observed value is 1.40 at 25°, which value may differ considerably with different preparations. Anhydrous cyameluric acid, which is not predicted to have large void spaces in its structure corresponding to those in melon, is found to have a density of 1.75 at 25°. The high stability of melon, like that of graphite, may be explained in terms of the enormous number of resonating forms contributing to the structure of the compound.

Experimental

Cupric Ammonium Cyamelurate.—To a solution of 2 g. of cyameluric acid trihydrate in 200 ml. of hot 0.5 *N* ammonium hydroxide, there was added an excess of cupric ammonium sulfate solution. After cooling, the resulting lavender precipitate was filtered off, washed and air dried. The color changed to a very blue shade of lavender upon drying, probably due to the loss of either ammonia to form a less amminated compound, or to the loss of water of crystallization.

Anal. Calcd. for $CuNH_4(C_6H_7O_3)\cdot NH_3$: Cu, 20.08. Found: Cu (iodometrically), 19.84, 20.13.

This salt is much less soluble than the one obtained from cyanuric acid under the same conditions.

Mercuric Cyamelurate.—Two samples of mercuric cyamelurate were prepared under conditions which Hantzsch[4] found to yield two different types of salts in the case of cyanuric acid. (A) To a solution of 2 g. of pure potassium cyamelurate in 50 ml. of boiling water was added a slight excess of a boiling solution of mercuric chloride. The white flocculent precipitate of the mercury salt which separated immediately was well washed with water and dried.

Anal. Calcd. for $(C_6N_7O_3)_2Hg_3$: Hg, 57.99. Found: Hg, 58.31, 58.33. The high values for mercury probably are due to adsorption of mercury by the semi-gelatinous precipitate.

(B) The same procedure was followed except that mercuric chloride was replaced by mercuric acetate, and the solutions were ice-cold. Both salts looked alike and gave immediate precipitates of yellow mercuric oxide when treated with a cold 1 *N* sodium hydroxide. Upon standing overnight, nearly colorless crystals of trisodium cyamelurate separated in each case.

Cyameluryl Trichloride.—(A) From tripotassium cyamelurate. Thirty grams of the salt dried at 150° for forty-eight hours and 60 g. of phosphorus pentachloride were ground to a fine mixture in a mortar. This was sealed in a large bomb-tube and heated in a boiling water-bath for seven hours. The tube was opened to relieve the pressure, then after resealing heated for an additional nine hours at 139° (*m*-xylene vapor-bath). After phosphorus oxychloride had been removed by letting stand in a desiccator over flake sodium hydroxide in a thin layer, the residue was crushed into a coarse powder and slowly sprinkled into and well stirred with an ice–water mixture to remove potassium chloride and any remaining phosphorus compounds. The light yellow solid was filtered off and dried in a vacuum desiccator over concentrated sulfuric acid. The yield of light yellow crystalline powder, which under the microscope was seen to consist of thin pale yellow platelets, was 23 g. (93%).

Cyameluryl trichloride is highly insoluble in all organic solvents tested, which included chloroform, anisole, nitrobenzene, acetonitrile, *o*-dichlorobenzene and glacial acetic acid (with which it reacted giving acetyl chloride and cyameluric acid). The compound was shown to be essentially free from inorganic salts by ignition upon platinum foil where no ash remained. No melting was observed, but the compound gradually disappeared by a combination of oxidation and perhaps sublimation. Attempts to secure purification by sublimation at atmospheric pressure and under high vacuum were unsuccessful. Analyses were finally run on the dry material without further purification.

Anal. Calcd. for $C_6N_7Cl_3$: N, 35.44; Cl, 38.49. Found: N (Kjeldahl), 35.76, 35.32; Cl (Carius), 32.83, 37.4, 37.4.

Results of the analysis indicate that the compound was slightly impure cyameluric trichloride. When completely decomposed by digesting with nitric acid, the solution gave but a faint test for phosphorus with ammonium molybdate.

(B) From cyameluric acid. Two grams of the acid which had been dried for several days at 150° and six grams of phosphorus pentachloride were ground and intimately mixed. The mixture was sealed in a heavy walled bomb-tube and heated to 218° (naphthalene vapor-bath) for thirty-six hours. The tube was opened periodically to relieve the pressure. The contents of the tube were worked up, as in A. The yield was 2.3 g. (92%) of product closely resembling that prepared from tripotassium cyamelurate.

N-Tribenzyl Cyamelurate.—A mixture of 5 g. of anhydrous trisodium cyamelurate and 17 ml. of freshly distilled benzyl chloride in a sealed bomb-tube was heated for twenty-three hours in a boiling water-bath. As little reaction appeared to take place at this temperature, heating was continued for an additional twelve hours in a vapor-bath at 156° (boiling bromobenzene). The contents were transferred to a Soxhlet extractor and extracted for four hours with boiling benzene. Following removal of volatile compounds by distillation under 18 mm. pressure, the residue was crystallized from boiling benzene; 4.2 g. (36%). After two additional recrystallizations from ethyl alcohol very small white needles melting at 283–284° (cor.) were obtained.

Anal. Calcd. for $C_{27}H_{21}N_7O_3$: mol. wt., 491; N, 19.96;

C, 65.96; H, 4.31. Found: mol. wt. (Rast camphor), 497; N (Kjeldahl), 19.54, 19.57; C, 65.46; H, 4.46.

Saponification of 0.2 g. of tribenzyl cyamelurate by refluxing for one hour with 10 ml. of aqueous 6 *N* potassium hydroxide, followed by distillation of the reaction mixture, gave a faintly cloudy distillate with an odor suggestive of ammonia. Extraction of this with ethyl ether following acidification with hydrochloric acid gave no trace of benzyl alcohol. However, extraction of the aqueous solution with ether after the addition of an excess of sodium hydroxide gave a few drops of a viscous residue which reacted readily with benzoyl chloride. The resulting solid after crystallization from aqueous ethyl alcohol melted at 105.5–106.0°, and melted at the same temperature when mixed with an authentic sample of N-benzylbenzamide, m. p. 105°. This shows that benzylamine but not benzyl alcohol is formed when tribenzyl cyamelurate is saponified and that the tribenzyl compound is a nitrogen, not an oxygen ester.

Action of Cyameluryl Trichloride on Benzyl Alcohol.—A mixture of 1.0 g. of cyameluryl trichloride and 1.5 g. of dry benzyl alcohol reacted spontaneously. The mixture became very hot and the yellow color of the cyameluryl trichloride changed to a pure white. The mixture was then boiled for one minute, cooled and 2 ml. of benzene added. The solid was removed by filtration and the filtrate was fractionally distilled. The fraction boiling between 170–190° had an unmistakable odor of benzyl chloride. This was confirmed by converting into the *p*-bromobenzenesulfon-*p'*-anisidide, m. p. 169.5–170.0° (uncor.), after recrystallizing from ethanol. The melting point was 170.0–0.5 when mixed with a known sample, m. p. 170–171°.[13]

The white residue was shown to be cyameluric acid by its solubility in sodium bicarbonate solution, from which the trisodium salt was precipitated in characteristic colorless needles upon adding an excess of strong sodium hydroxide solution.

Methyl Cyamelurate from Cyameluric Acid and Diazomethane.—An excess of an ethereal solution of diazomethane was added to 1.7 g. of very finely powdered cyameluric acid. The evolution of gas, vigorous at first, soon became rather slow. A strong yellow color from excess diazomethane was still present after standing for three days in the refrigerator, although the evolution of gas had become quite slow. The solid was filtered off and dried over concentrated sulfuric acid. The dry pale yellow solid thus obtained weighed 1.8 g. No melting was observed in a capillary tube; no solvent was found from which the material could be purified without some decomposition.

Anal. Calcd. for $C_6H_2N_7O_3(CH_3)$: C, 35.7; H, 2.12; CH_3, 6.38. Found: C, 35.4, 35.1; H, 3.22, 3.05; CH_3 (methoxyl), 0.58, 0.62; CH_3 (methylimide) 6.95, 6.48.

Analysis indicates slightly more than one methyl group per nucleus and some methylation of the hydroxyl groups.

The partially methylated product from the above experiment after fine pulverization was treated again with an excess of diazomethane at room temperature for four days. Since all apparent reaction had ceased, the solid was filtered off, dried over concentrated sulfuric acid, and analyzed.

Anal. Calcd. for $C_6N_7O_3(CH_3)_3 \cdot 1^1/_2H_2O$: C, 36.72; H, 4.12; H_2O, 9.18; CH_3, 15.3. Found: C, 36.22; H, 4.14; H_2O, 9.13; CH_3 (methoxyl), 0.060, 0.062.

When heated on platinum foil the anhydrous compound melted. In a capillary tube no melting was observed up to 290°, but instead extensive charring.

Attempts to Prepare Cyameluric Triamide.—(1) On adding 25 ml. of 15 *N* ammonium hydroxide to 1.19 g. of cyameluryl chloride, a very vigorous reaction took place immediately. The light yellow color of the cyameluryl chloride disappeared and a white flocculent precipitate took its place. After standing for one hour this was filtered off, washed well with cold water and dried in the oven at 75°; weight 0.88 g. As no solvent was found from which this material could be recrystallized, the sample was analyzed without further purification.

Anal. Calcd. for $C_6N_7(NH_2)_3$: N, 64.2; for $C_6N_7(NH_2)_2Cl$: N, 53.1; Cl, 14.93; for $C_6N_7(NH_2)_2OH$: N, 57.6. Found: N (Kjeldahl), 54.28, 54.17; Cl (Carius), 3.32, 3.50.

The analytical data indicate an impure mixture largely composed of one or both diamides, cyameluryl monochlorodiamide, and cyameluryl diamide.

(2) Two grams of cyameluryl chloride was suspended in 100 ml. of anhydrous ethyl ether into which was passed gaseous ammonia until the solution was saturated. It was then allowed to stand for two hours and again saturated with ammonia gas and allowed to stand overnight. Twenty-five ml. of water was then added and the mixture was vigorously shaken. The precipitate was separated by filtration, washed with concentrated ammonium hydroxide, and air dried. It was then crushed and digested with 100 ml. of warm 1 *N* ammonium hydroxide for thirty minutes, filtered, and dried at 100° for one hour. *Anal.* Found: N, 59.88, 60.01.

Since this analytical result agreed most nearly with a possible monohydrate of the triamide or the ammonium salt of the acid diamide the compound was dried for twenty-six hours at 150°. A loss in weight of 4.52% took place, with but little change in the analysis, but the material still appeared to be impure. *Anal.* Found: N, 60.20, 61.96.

(3) Two grams of cyameluryl chloride was sealed in a bomb-tube with anhydrous liquid ammonia and left for twenty hours at room temperature. The tube was opened and the ammonia allowed to evaporate. The residue was extracted with cold water to remove the ammonium chloride. The flocculent solid was collected upon a filter and dried at 100° for four hours. *Anal.* Found: N, 60.34, 60.01.

None of these preparations has a nitrogen content as high as that for the triamide (64.2%), but the purification is hampered because no satisfactory solvent has been found from which the compound can be crystallized.

Summary

1. Cyameluric acid has been shown to form a group of compounds entirely analogous to those of cyanuric acid. The analogy is complete for

(13) Gillespie, THIS JOURNAL, **56**, 2740 (1934), gives 167.5°, which is too low.

the cupric ammonium salts, the trichlorides, and the nitrogen esters formed by the reaction of benzyl chloride with the respective alkali salts at elevated temperature. The analogy is less exact for the diamides, the mercuric salts and the oxygen esters.

2. The existence of a trichloride and of an oxygen ester indicates that hydroxyl groups are present in the molecule of cyameluric acid.

3. The analogy with cyanuric compounds and the presence of hydroxyl groups substantiate the planar ring structure for cyameluric acid proposed by Pauling and Sturdivant.

4. Melam is probably dicyanurylimide and melem, cyameluryl triamide.

5. It is proposed that melon is a condensation product of cyameluryl triamide, and that the resulting very large molecules consist of planar cyameluryl rings joined through nitrogen atoms.

PASADENA, CALIF. RECEIVED NOVEMBER 6, 1939

[CONTRIBUTION FROM THE STERLING CHEMISTRY LABORATORY OF YALE UNIVERSITY]

The Ionization Constants of Weak Acids at 25° from Conductance Measurements. A Method of Extrapolating the Data[1]

BY BLAIR SAXTON[2] AND LAWRENCE S. DARKEN[3]

A large number of investigations[4-14] have been conducted in recent years on the determination of ionization constants of weak acids by the conductance method. At the lower concentrations the degree of ionization is determined accurately from conductance data alone by use of the additive law that the specific conductance of the weak acid is equal to the specific conductance of the hydrogen ion and the acid ion as determined from the conductance of the sodium or the potassium salt of the acid, sodium or potassium chloride and hydrochloric acid at the corresponding ionic concentration. The salts and hydrochloric acid are considered completely ionized. The degree of dissociation of the weak acid is set equal to Λ/Λ_ϵ where Λ_ϵ is the equivalent conductance of the theoretical completely dissociated acid at the same ionic concentration. Values of Λ/Λ_ϵ are obtained by a method of successive approximations from the above-mentioned data. From the degree of dissociation of the acid a so-called mass law ionization constant is determined directly according to the relation

$$k = \alpha^2 c/(1 - \alpha) = c_i^2/c_u$$

where α is the degree of dissociation, c is the stoichiometric concentration of the weak acid, c_i is the ionic concentration, and c_u is the concentration of undissociated weak acid. At finite concentrations

$$K = y_\pm^2 k$$

where K is the thermodynamic ionization constant as usually written, and $y_\pm$ is the mean ionic activity coefficient. Several investigators[4-14] have shown that at extremely low concentrations the variation of k with concentration is in good agreement with that predicted by the Debye–Hückel[15] theory of interionic attraction which at low ionic concentrations reduces to this relation

$$\log y_\pm = -A\sqrt{c_i}$$

which combined with the previous equation gives

$$\log K = \log k - 2A\sqrt{c_i}$$

Unfortunately, the range over which this equation holds within an experimental error of one part in a thousand (to give a constant value of log K) is below an ionic concentration of about 0.003 (depending on the acid). Hence, extrapolating to obtain the limiting value of log K from a plot of log k *versus* $\sqrt{c_i}$ is not a convenient method in that it demands high accuracy at low concentrations. It will be shown that the true thermodynamic ionization constant may be determined

(1) This paper contains material which represents part of the dissertation submitted by Lawrence S. Darken to the Graduate School of Yale University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1933. Original manuscript received July 20, 1939.

(2) The experimental work and calculations herein reported were completed before the death of Professor Saxton.

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(4) MacInnes and Shedlovsky, THIS JOURNAL, **54**, 1429 (1932).

(5) Davies, *ibid.*, **54**, 1698 (1932).

(6) Saxton and Langer, *ibid.*, **55**, 3638 (1933).

(7) MacInnes, Shedlovsky, and Longsworth, *Chem. Rev.*, **13**, 29 (1933).

(8) Ives, *J. Chem. Soc.*, 731 (1933).

(9) Brockman and Kilpatrick, THIS JOURNAL, **56** 1483 (1934).

(10) Saxton and Meier, *ibid.*, **56**, 1918 (1934).

(11) Banks and Davies, *J. Chem. Soc.*, 73 (1938).

(12) Saxton and Waters, THIS JOURNAL, **59**, 1048 (1937).

(13) Martin and Tartar, *ibid.*, **59**, 2972 (1937).

(14) Belcher, *ibid.*, **60**, 2744 (1938).

(15) Debye and Hückel, *Physik. Z.*, **24**, 185 (1923).

conveniently and accurately by extrapolating to infinite dilution a plot of log $k - 2A\sqrt{c_i}$ *versus* c_u. Such a plot has been found to be linear up to a concentration of almost one molal.

Experimental

The conductance measurements were made with the apparatus and technique used in our earlier work[6,10] and the ionization constants were calculated by the method there described. Jena glass cells and a silica cell were used. The cell constants were determined by use of both 0.01 and 0.1 demal potassium chloride solutions and all conductivities here reported are based on Jones and Bradshaw's[16] determination of the conductivities of these solutions. In the case of formic acid, half of the measurements were made with bright electrodes while the remainder were made with platinized electrodes. In the latter case, special care was taken to remove carbon dioxide and oxygen by bubbling nitrogen through the solutions. These measurements were made a year apart on samples of acid which had been independently purified and analyzed.

Kahlbaum cyanoacetic acid was recrystallized several times from conductivity water. The results checked those obtained with acid recrystallized from an ether–chloroform mixture and then twice from conductivity water. Formic acid was freshly distilled and standardized just before each run. Eastman *n*-butyric acid was purified by partially crystallizing three times and discarding the unfrozen liquid. The stock solution of each acid was analyzed by titrating with sodium hydroxide solution which had been standardized with potassium acid phthalate certified by the Bureau of Standards. In each analysis the titration was finished with standard base one-tenth the concentration of that used for the major part of the titration. The results usually showed deviations of about 0.01% from the average.

Sodium salt solutions were made by adding the calculated quantity of pure sodium carbonate to the acid solution. Carbon dioxide was removed by treating with nitrogen. The potassium butyrate stock solution was prepared by neutralizing a butyric acid solution with the theoretical amount of potassium hydroxide solution (the same potassium hydroxide solution which had previously been used for conductance measurements and with which the titer of the acid was determined). To suppress hydrolysis about 0.25% excess acid was added. The cell concentration was based on the amount of alkali used.

Densities were determined with a pyknometer. The following equations express the results over the concentration range covered

Formic acid: $d = 0.99704 + 0.012089c - 0.000690c^{3/2}$
Cyanoacetic acid: $d = 0.99704 + 0.023m$
Sodium cyanoacetate: $d = 0.99704 + 0.057m$
Butyric acid: $d = 0.99704 + 0.00362m$
Potassium butyrate: $d = 0.99704 + 0.0496m$

Densities for sodium formate solutions were taken from the "International Critical Tables" (m = gram moles per kilogram; c = gram moles per 1000 cc.).

The equivalent conductances of the salts follow Shedlovsky's[17] extension of Onsager's[18] equation and are given by

$Na^+ + CNCH_2COO^-$:
$$\Lambda = 91.91 - 80.79\sqrt{c_i} + 76c_i(1 - 0.2276\sqrt{c_i})$$
$Na^+ + HCOO^-$:
$$\Lambda = 104.69 - 83.69\sqrt{c_i} + 86c_i(1 - 0.2276\sqrt{c_i})$$
$K^+ + C_3H_7COO^-$:
$$\Lambda = 105.39 - 83.76\sqrt{c_i} + 110c_i(1 - 0.2276\sqrt{c_i})$$

The experimental data are given in Table I. Combining these equations with the equation for $\Lambda_{(H^+)} - \Lambda_{(Na^+)}$ given in an earlier paper,[6] the equations for the sums of the equivalent conductances of the ions of the weak acids as functions of their ionic concentrations, c_i, become

$H^+ + CNCH_2COO^-$:
$$\Lambda_e = 391.71 - 148.98\sqrt{c_i} + 151c_i(1 - 0.2276\sqrt{c_i})$$
$H^+ + HCOO^-$:
$$\Lambda_e 404.50 - 151.88\sqrt{c_i} + 161c_i(1 - 0.2276\sqrt{c_i})$$
$H^+ + C_3H_7COO^-$:
$$\Lambda_e = 381.69 - 146.57\sqrt{c_i} + 180c_i(1 - 0.2276\sqrt{c_i})$$

The measured equivalent conductances of the acids and the thermodynamic ionization constants calculated with the aid of these equations are given in Table II.

TABLE I

$c \times 10^2$	Λ calculated	Λ observed
Potassium Butyrate		
0.114958	102.68	102.64
.19572	101.90	101.89
.21807	101.72	101.67
.34349	100.85	100.85
.39483	100.55	100.56
.51451	99.94	99.95
.62395	99.45	99.49
.72295	99.05	99.06
.86320	98.54	98.58
1.00045	98.07	98.09
1.2454	97.38	97.41
1.32332	97.17	97.17
1.5759	96.45	96.58
2.0437	95.59	95.45
2.3749	95.00	94.96
Sodium Formate		
$c \times 10^3$		
0.19505	103.52	103.43
.58885	102.72	102.63
1.2449	101.84	101.85
2.8045	100.50	100.50
4.1483	99.65	99.64
5.4916	98.95	98.96
6.5543	98.47	98.46
7.2663	98.17	98.17
8.9550	97.53	97.53
10.6180	96.96	96.96
Sodium Cyanoacetate		
0.010933	91.65	91.52
.033500	91.44	91.39
.19512	90.87	90.78
.30547	90.52	90.56
.41970	90.30	90.28
.52728	90.10	90.06
.60357	89.97	89.95
1.0364	89.39	89.39
1.9170	88.52	88.53
3.1400	87.61	87.59
4.6500	86.74	86.73
6.3959	85.92	85.92

(16) Jones and Bradshaw, THIS JOURNAL, **55**, 1780 (1933).

(17) Shedlovsky, *ibid*, **54**, 1405 (1932).

(18) Onsager, *Physik. Z.*, **27**, 388 (1926); **28**, 277 (1927); *Trans. Faraday Soc.*, **23**, 341 (1927); *J. Phys. Chem.*, **36**, 2689 (1932).

TABLE II

CYANOACETIC ACID

$\times 10^3$	Λ	$K \times 10^3$	Series
0.3943	352.32	3.287	III
.9931	316.76	3.396	II
1.0169	314.82	3.340	I
1.1848	307.09	3.349	III
2.3848	266.74	3.356	III
2.9100	254.23	3.356	II
3.0217	251.82	3.356	I
3.8022	237.06	3.356	III
5.6930	210.97	3.352	III
5.7374	210.50	3.353	I
5.7749	210.08	3.352	II
7.6346	192.39	3.349	III
8.6832	184.42	3.347	II
8.7186	184.16	3.346	I
10.3136	173.96	3.342	III
12.1816	164.18	3.341	II
12.827	161.09	3.333	III
13.017	160.33	3.337	I
16.378	147.48	3.330	II
16.531	146.98	3.330	III
18.994	139.56	3.325	I

Formic Acid

$c \times 10^3$	Λ	$K \times 10^4$	Series
1.0739	137.52	1.831	V
6.8918	62.165	1.829	V
10.937	50.347	1.827	V
13.207	46.127	1.824	I
16.663	41.392	1.821	V
22.416	36.025	1.818	III
25.023	34.242	1.821	V
28.865	32.027	1.821	VI
31.738	30.605	1.818	III
35.982	28.868	1.820	V
36.929	28.500	1.817	III
41.611	26.946	1.818	II
45.085	25.939	1.817	III
48.852	24.957	1.814	V
67.463	21.445	1.818	VI
86.662	19.035	1.815	I
98.860	17.863	1.811	II
185.30	13.223	1.801	I
200.14	12.739	1.799	VI
207.15	12.528	1.797	II
361.80	9.5671	1.778	I
396.76	9.1487	1.774	VI
463.43	8.4756	1.763	II
546.81	7.8172	1.753	I
655.63	7.1437	1.738	II
734.04	6.7551	1.728	I
975.35	5.8535	1.695	VI
1141.50	5.3983	1.672	II
1227.2	5.1998	1.660	VI
1713.1	4.3530	1.590	VI
2015.9	3.9751	1.545	IV
2119.2	3.8670	1.532	VI
2549.3	3.4551	1.455	IV
3010.6	3.1335	1.399	IV
3694.0	2.7254	1.285	IV
4618.7	2.3257	1.157	IV
5690.5	1.9642	1.010	IV
6973.0	1.6194	0.8374	IV
8488.0	1.2949	.6552	IV
9555.0	1.1087	.5435	IV

Butyric Acid

$c \times 10^3$	Λ	$K \times 10^5$	Series[a]
0.3344	73.806	1.5320	I
.67024	53.581	1.5307	II
1.4000	38.084	1.5204	I
2.6510	28.768	1.5204	II
3.5224	24.471	1.5111	I
5.9664	18.975	1.5104	I
6.2922	18.940	1.5141	II
8.8766	15.638	1.5082	I
14.412	12.335	1.5030	I
14.721	12.491	1.5040	II
20.740	10.305	1.4966	I
21.060	10.475	1.5003	II
30.612	8.4910	1.4865	I
32.012	8.4924	1.4843	II
44.014	7.0759	1.4727	I
48.041	6.9232	1.4678	II
60.446	6.0226	1.4556	I
67.480	5.6899	1.4470	II
78.623	5.2610	1.4369	I
93.044	4.8178	1.4212	II
99.738	4.6475	1.4157	I
116.72	4.2721	1.3956	III
123.53	4.1498	1.3919	I
125.54	4.1126	1.3889	II
160.79	3.5976	1.3545	II
161.89	3.5824	1.3492	III
200.32	3.1846	1.3166	II
241.70	2.8625	1.2786	II
253.84	2.7836	1.2666	III
399.15	2.1158	1.1413	III
518.69	1.78146	1.0473	III
605.69	1.59898	0.98268	III
735.98	1.38433	.89334	III
861.82	1.22183	.81362	III
1006.4	1.07096	.72937	III
1070.0	1.01352	.69443	III
1220.6	0.89517	.61786	III

[a] In run II the silica cell (cell constant 0.9776) was employed. Jena glass cells were used in runs I and III (cell constants 3.7265 and 4.5760, respectively).

Discussion

The values of the mass law constant, k, follow the theoretical slope of the limiting Debye–Hückel law up to an ionic concentration of approximately 0.003 demal. This concordance has been demonstrated conclusively by earlier investigations.[4–14] The increase of the experimental error at these lower concentrations where the limiting law of Debye and Hückel holds is quite pronounced; hence it would be highly de-

sirable to employ a method of extrapolation which would make use of measured conductances at the higher concentrations where the error is much smaller. With this in view various methods of extrapolating were tried and it was found that the various extensions of the limiting law of Debye and Hückel did not account satisfactorily for the observed departures. These departures of K from constancy are such that log K is linear with the concentration of undissociated acid. It is also true that the plot of log K is essentially linear with the total concentration. It was hoped that the data on cyanoacetic acid, which is the most highly dissociated of the acids considered here, would show clearly whether log K is linear with c_u or with c. Although in the case of this acid the difference between c_u and c is pronounced, neither plot shows decided departure from linearity, but slight evidence is offered in favor of the plot against c_u. The extrapolation is shorter in the case log K *versus* c_u than in the case log K *versus* c. These plots are shown in Fig. 1.

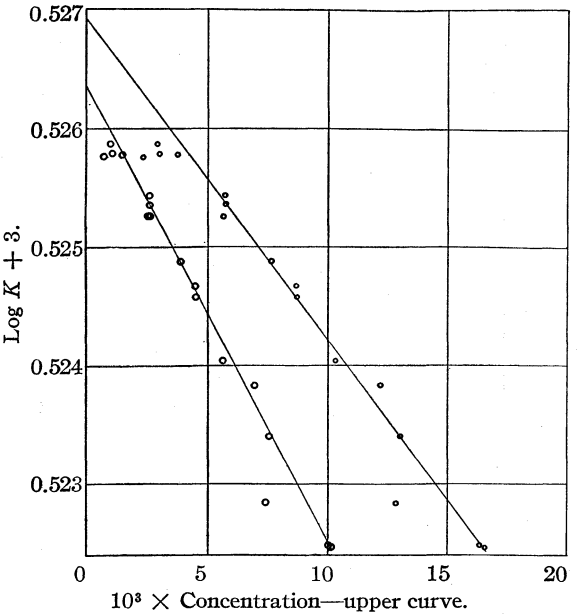


Fig. 1.—Log K *versus* c (upper curve) and c_u (lower curve) for cyanoacetic acid at 25°.

The data on formic acid were extended up to the region of the constant boiling mixture of this acid with water in order to determine the upper limit to which the linearity of log K *versus* c_u prevails. Although at the higher concentrations the ionic concentrations and hence k and K calculated by this method are meaningless, they are included in Table II as formal functions resulting from the application of the method. The linearity persists up to a concentration of about 0.7 demal; the deviation amounting to less than 0.5% in the demal solution. The data on formic acid up to 1.2 demal are represented by the top curve in Fig. 3, the scale being such that the deviations mentioned above are not perceptible. The first set of experiments on formic acid in which bright electrodes were employed yielded a value of the ionization constant (1.825×10^{-4}) which differed considerably from that obtained by Harned and Embree[19] from e. m. f. measurements of cells with buffered solutions (1.767×10^{-4}) (a figure obtained by multiplying their published value by the density of water to convert from molality to demality). As their results check the previous results of Harned and Owen[20] obtained similarly with unbuffered solutions, it was deemed advisable to repeat the work. This was done about a year later using lightly platinized electrodes and taking care to exclude oxygen. The agreement with the previous year's results is satisfactory. The discrepancy between our value and that resulting from e. m. f. measurements seems inexplicable. Previous work on acetic[4] and chloroacetic[6] acids has shown satisfactory agreement between the two methods.

Our value for the ionization constant of butyric acid agrees well with that obtained from e. m. f. measurements by Harned and Sutherland.[21] The agreement with Belcher's[14] measurements by essentially the same method is not as good as might be anticipated, as may be seen from Fig. 2, where Belcher's experimental points would appear as a cluster near log $K = -5.177$–8 and $c_u = 0.000 - 0.005$. The 0.7% discrepancy in K_0 (the extrapolated value of K) is due in part (0.3%) to differences in the measured conductances of the acid, and in part (0.4%) to differences in the measured conductances of the salt, which are reflected in Λ_0 for butyric acid. The disparity in the results of the three investigators is shown in the following table

	Saxton and Darken	Belcher[14]	Harned and Sutherland[21] Measured	Harned and Sutherland[21] From smoothed curve
$K_0 \times 10^5$ (25°C.)	1.518	1.508	1.510	1.518
Λ_0	381.69	382.40		

(19) Harned and Embree, THIS JOURNAL, **56**, 1042 (1934).

(20) Harned and Owen, *ibid.*, **52**, 5079 (1930).

(21) Harned and Sutherland, *ibid.*, **56**, 2039 (1934).

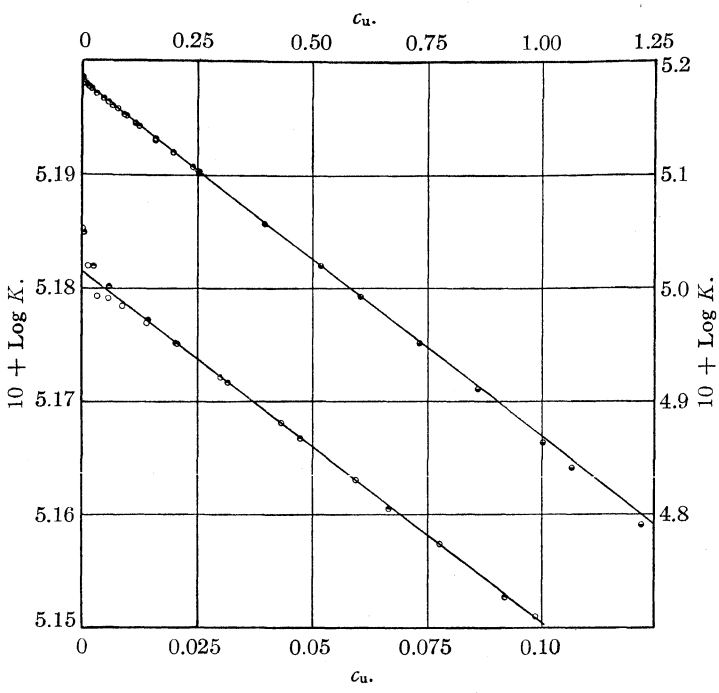


Fig. 2.—Log K *versus* c_u for butyric acid at 25°: concentration ranges, 0–0.1 (lower curve) and 0–1.25 (upper curve).

The extrapolated values from the log K *versus* c_u plots shown in Figs. 1 and 2 and the top curve of Fig. 3 correspond to 3.360×10^{-3}, 1.825×10^{-4}, and 1.518×10^{-5} for the ionization constants of cyanoacetic, formic and butyric acids, respectively.

Plots of log K *versus* c_u are shown in Fig. 3. The results of all available precise conductance measurements on aqueous solutions of weak acids (at 25°) are here shown in such a manner that the proper relative slopes of the lines are maintained, although the coördinate scales vary by large factors. From top to bottom the acids represented are: formic, acetic,[4] propionic,[14] monochloroacetic,[6] cyanoacetic, lactic,[13] and benzoic.[10] In order to avoid confusion, points corresponding to extremely low concentrations have been omitted.

Interpretation of the linearity of the plot of log K against c_u is complicated by the number of assumptions made in the evaluation of log K. In the series of equations

$$\log K_0 = \frac{-\Delta F^\circ}{2.3026\ RT} = \log \frac{a_\pm^2}{a_u} = \log \frac{c_i^2}{c_u}\frac{\gamma_\pm^2}{\gamma_u} = \log k + 2A\sqrt{c_i} + Bc_u = \log K + Bc_u$$

the first three equalities result from definition, ΔF° being the free energy of formation of one mole of undissociated acid (HA) from one mole of positive ion (H^+) and one mole of negative ion (A^-) at infinite dilution in pure water. It will be noted that the use of the third equality requires a method of measuring c_i and c_u. In the construction of Table II it is assumed that c_i and c_u can be obtained validly from conductance data. The fourth equality involves definition of k, introduction of the Debye–Hückel limiting law and statement of the linear c_u effect, while the fifth is merely another definition. The constant "A" is calculated on the assumption that the dielectric constant of the solution is that of pure water.

The reasons that log K varies with the concentration may be grouped in three classes:

1. Improper interpretation of the conductance data. In the calculation of Λ_ϵ the effect of the presence of undissociated acid on the equivalent conductance of the dissociated portion of the acid, due to changes in viscosity and dielectric constant, has been neglected. Reliable measurements of the viscosity and dielectric constant of weak acid–water solutions are at present unavailable.

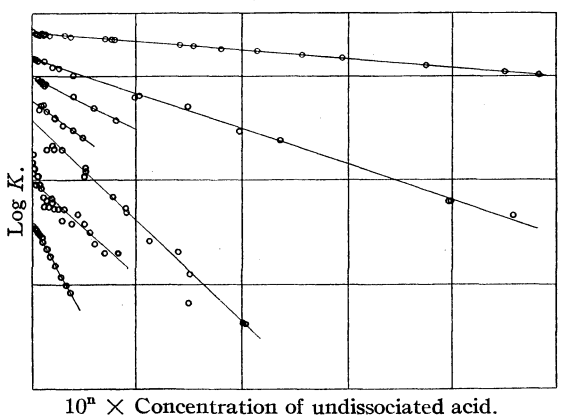


Fig. 3.—Log K *versus* c_u for aqueous solutions at 25° of: formic acid, acetic acid, propionic acid, chloroacetic acid, cyanoacetic acid, lactic acid, benzoic acid.

2. Errors introduced by use of the simplified form of the Debye–Hückel expression for the ionic activity coefficient. The authors have found that inclusion of extended terms in the Debye–Hückel relation does not improve the constancy of "K" but rather makes the deviations appear more complex. The error in the constant "A"

(caused by the assumption that the ion solvent is pure water, whereas it is really an aqueous solution of undissociated acid) is undoubtedly small.

3. Deviation of the activity coefficient of undissociated acid (γ_u) from unity. The determination of the activity coefficient of the undissociated portions of weak acids in a binary system, weak acid–water, according to the various possible experimental methods has not been investigated to any great extent. The activity coefficients of acetic acid from freezing-point lowerings show a rather pronounced maximum about 0.1 molal at 0°.[22,23] The effect in this region is complicated by the presence of a relatively large concentration of ions. Since the conductance data of MacInnes and Shedlovsky[4] on acetic acid (Fig. 3, second curve from top, covering the range up to 0.23 demal) show no such abnormality, it would seem either that conditions at 25° are significantly different from those at 0°, or that the interpretation of the freezing point measurements is erroneous, or that there is some compensating factor involved in the conductance data so that the maximum does not appear. Above 0.5 molal, freezing point data indicate an almost linear relationship between the activity coefficient of the undissociated portion of the acid and the molality (or any other common concentration function) for formic, acetic, propionic, and butyric acids.[21,22] Values of d log γ_u/dm at one molal obtained from freezing point measurements are compared in Table III with values of d log K/dc_u from conductance measurements at 25°, as shown in Fig. 3. Activity coefficients of weak acids in water from distribution experiments are not available at the present time, since the activity coefficients of these acids in solvents other than water are not known. The seemingly direct determination of activity coefficients from vapor pressure measurements is complicated by the polymerization of vapor acid molecules. In the case of acetic acid the extent of this polymerization has been investigated and the activity coefficients of undissociated acid in the aqueous phase, corrections being made for dimerization in the vapor phase, are tabulated in Landolt–Börnstein.[24] A plot of the log of these activity coefficients against the molality has a slope of about −0.12 at 1 molal. This compares favorably with d log K/dc_u read from the curve for acetic acid in Fig. 3 (−0.14). Similar data for formic acid are not available except at 80°, at which temperature the data in Landolt–Börnstein[24] yield a value for d log γ_u/dm of −0.007, which is considerably lower than d log K/dc_u read from the curve for formic acid in Fig. 3 (−0.035).

TABLE III

Acid	$-d \log \gamma_u/dm^{19}$ (freezing point)	$-\Delta \log \gamma_u/dm^{20}$ (freezing point, m = 0.2–0.5)	$-d \log \gamma_u/dm$ (vapor pressure)	$-d \log K/d c_u$ (conductance) 25°C.
Formic	0.01	..	0.007 (at 80°)	0.035
Acetic	.029	0.12	0.12 (at 25°)	.14
Propionic	.051	..	..	.20
Butyric	.094	..	..	.31

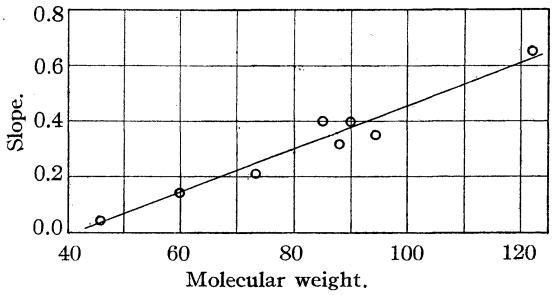


Fig. 4.—Slopes of (log K *versus* c_u) *versus* molecular weights of acids.

Hildebrand[25] has presented an equation relating the activity coefficient of one component of a "regular" binary solution to the mole fraction. At lower concentrations it reduces to the simple expression log $\gamma_2 = \alpha N_2$, in which the constant "α" is a function of the partial molal volumes and energies of vaporization of the two components. Since the ion concentrations are quite small at the higher concentrations of acids treated in this paper, the variation of activity coefficient of undissociated acid with concentration might be determined approximately from Hildebrand's equation by considering the solution to consist of two non-electrolytes, water and undissociated acid, forming "regular" solution. Unfortunately, "α" cannot be evaluated in the cases under consideration because of the polymerization of water and other departures from "regularity" as well as the uncertainty of the data available. However, it is interesting to observe that "α" and "B" have the same sign, and that, since the partial molal volumes are roughly in inverse order

(22) Van Rysselberghe, *J. Phys. Chem.*, **39**, 415 (1935).

(23) Parks and Huffman, "Free Energies of Some Organic Compounds." Chemical Catalog Co., New York, N. Y., 1932.

(24) Landolt–Börnstein, "Physikalisch-chemische Tabellen," Erg. III, Springer, Berlin, 1936.

(25) Hildebrand, "Solubility," Reinhold Publishing Corp., 330 West 42nd St., New York, N. Y., 1936.

of molecular weight for the acids considered, it would be expected on the basis of Hildebrand's equation that the "B"'s would be in the order of the molecular weights. This is in accordance with experimental finding, shown graphically in Fig. 4.

Summary

A method of extrapolating ionization constants determined by the conductance method has been suggested. The method consists of plotting the logarithm of the ionization constant, which includes the ion activity coefficient calculated by the Debye–Hückel limiting law, against the concentration of undissociated electrolyte. The validity of the method is based mainly on empirical evidence which indicates the linearity of such a plot up to high concentrations in the case of the organic acids considered.

The thermodynamic ionization constants of cyanoacetic, formic, and butyric acids in aqueous solution at 25° have been measured by the conductance method and found to be

Cyanoacetic acid	3.360×10^{-3}
Formic acid	1.825×10^{-4}
Butyric acid	1.518×10^{-5}

RECEIVED FEBRUARY 1, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA, AND THE SCHOOL OF CHEMISTRY, UNIVERSITY OF MINNESOTA]

Polarographic Study of the Reduction of Chromate Ion at the Dropping Mercury Electrode

BY JAMES J. LINGANE AND I. M. KOLTHOFF

The purpose of this study was to investigate the reduction of chromate ions at the dropping mercury electrode by means of the polarographic technique.[1] The only previous study of the reduction of chromate at the dropping electrode is found in a recent paper of Thanheiser and Willems,[2] which appeared after the present investigation was begun. These authors studied the reduction of chromate only in sodium hydroxide medium, with particular reference to the polarographic determination of chromium in steel. We have investigated the reduction of chromate in unbuffered solutions and in the presence of buffers, as well as in strongly alkaline medium, and have discovered several new and interesting phenomena.

Experimental

The current–voltage curves (polarograms) were obtained and photographically recorded by means of a standard Heyrovsky polarograph.[1] Most of the polarograms were obtained by using an external saturated calomel electrode as anode, rather than the customary stationary pool of mercury on the bottom of the cell, in order to minimize contact of the chromate solutions with mercury. The H-cell and dropping electrode arrangement described by Lingane and Laitinen[3] was used. The cell was kept in a water thermostat at 25 ± 0.1°, and air was displaced from the solutions with nitrogen. Reagent grade chemicals and conductivity water were used in preparing all solutions.

In most of the experiments the pressure on the dropping mercury, hereinafter designated by h, was maintained at 72.0 ± 0.2 cm. of mercury. The amount of mercury flowing from the dropping electrode per sec. under a pressure of 72 cm. designated by m, was determined by the method already described.[1,4] Two different capillaries were used, for which the values of m were, respectively, 1.54 and 1.58 mg. sec.$^{-1}$ at h = 72 cm.

The drop time, in dilute potassium chloride solution with the dropping electrode disconnected from the polarizing e. m. f., was 4.2 ± 0.1 sec. The drop time occasionally became erratic, especially in neutral or slightly acid chromate solutions. This probably was caused by the wetting of the interior of the capillary by the chromate solution when the mercury thread retracts momentarily into the lumen after each mercury drop falls. This erratic behavior was eliminated by dipping the tip of the capillary into concentrated nitric acid, and then washing with water, while the mercury was issuing from the tip. The erratic dropping also could be eliminated by simply polarizing the dropping electrode cathodically for a few seconds at a potential of about −1.5 v.

The current-recording galvanometer of the polarograph was calibrated carefully by the method already described.[4]

Reduction of Chromate in Alkaline Medium.—In unbuffered solutions of potassium chromate, with potassium chloride as the supporting electrolyte, the c. v. curve of chromate consists of several waves as shown by curve 1 in Fig. 1.

(1) For a review of the polarographic method, see I. M. Kolthoff and J. J. Lingane, *Chem. Rev.*, **24**, 1–94 (1939).

(2) G. Thanheiser and J. Willems, *Mitt. Kaiser Wilhelm Inst. Eisenforsch. (Düsseldorf)*, **21**, 65 (1939).

(3) J. J. Lingane and H. A. Laitinen, *Ind. Eng. Chem., Anal., Ed.*, **11**, 504 (1939).

(4) J. J. Lingane and I. M. Kolthoff, THIS JOURNAL, **61**, 825 (1939).

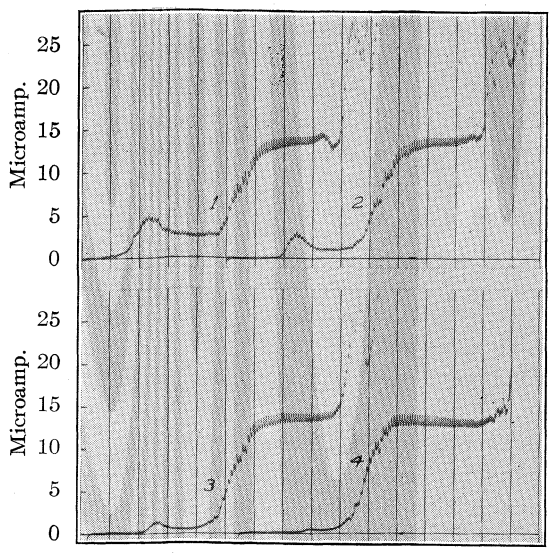


Fig. 1.—Current–voltage curves of 1.42×10^{-3} M potassium chromate in 0.1 N potassium chloride with various concentrations of sodium hydroxide: (1) no NaOH, (2) 0.002 N NaOH, (3) 0.013 N NaOH, (4) 0.2 N NaOH.

(In this and following polarograms, $E_{d.e.}$ signifies the potential of the dropping electrode against the saturated calomel electrode.) Addition of small amounts of sodium hydroxide to the solution decreases the first wave at −0.3 v., and it finally disappears when the concentration of sodium hydroxide is greater than about 0.2 N.

It will be noted that the height of the second wave at −1.0 v. is unaffected by the addition of sodium hydroxide, but the third ill-defined wave at −1.8 v. is, like the first wave, eliminated in 0.2 N sodium hydroxide.

C. v. curves of various concentrations of potassium chromate in 1 N sodium hydroxide as supporting electrolyte are shown in Fig. 2, and the corresponding values of the diffusion currents are given in Table I. The diffusion currents recorded in Table I have been corrected for the residual current that was obtained with the 1 N sodium hydroxide solution alone[1,4] (curve 1 in Fig. 2).

It will be noted that only one wave is obtained in 1 N sodium hydroxide solution, whose half-wave potential is at −0.85 v. *vs.* the S. C. E. The half-wave potential is practically constant and independent of the chromate concentration. The diffusion current is directly proportional to the concentration of chromate ions, as shown by the

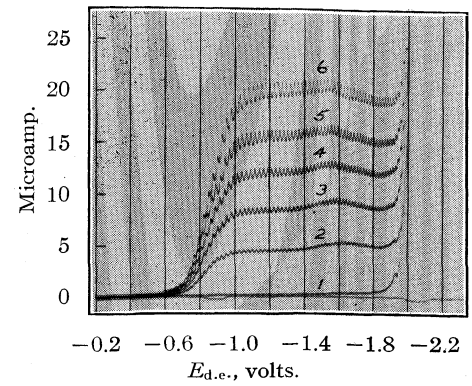


Fig. 2.—Various concentrations of potassium chromate in 1 N sodium hydroxide (see Table I).

TABLE I

RELATION BETWEEN THE DIFFUSION CURRENT AND THE CONCENTRATION OF CHROMATE IONS IN 1 N SODIUM HYDROXIDE

Diffusion currents measured at $E_{d.e.} = -1.2$ to -1.4 v. (see Fig. 2). $h = 72.1$ cm.; $m = 1.54$ mg. sec.$^{-1}$; $t = 3.36$ sec.; and $m^{2/3}t^{1/6} = 1.63$ mg.$^{2/3}$ sec.$^{-1/2}$ at $E_{d.e.} = -1.2$ v.

K_2CrO_4, millimoles per liter	i_d,[a] microamp.	i_d/C, microamp. per m mole per liter
0.473	4.35	9.20
0.901	8.40	9.33
1.298	12.00	9.25
1.667	15.52	9.32
2.100	20.08	9.55
		Av. 9.33 ± 0.09
Calcd. for $n = 3$ (Eq. 3)		9.66

[a] Corrected for the residual current.

satisfactory constancy of the ratio i_d/C given in the last column of Table I.

According to the Ilkovic equation the diffusion current should be given by [1,4]

$$i_d = 605nCD^{1/2}m^{2/3}t^{1/6} \text{ (microamperes)} \qquad (1)$$

where n is the number of faradays of electricity required per mole for the reduction, C is the concentration of the reducible substance in millimoles per liter, t is the drop time in sec., and D is the diffusion coefficient of the reducible substance in the units cm.^{2} sec.$^{-1}$. The general validity of this equation has been demonstrated in previous papers,[1,4] and it has also been shown that the effective diffusion coefficient of a reducible ion in the presence of an excess of supporting electrolyte can be calculated with satisfactory accuracy from the relation

$$D = \frac{RT\lambda_i^0}{zF_y^2} = 2.67 \times 10^{-7}\frac{\lambda_i^0}{z} \text{ (cm.}^2 \text{ sec.}^{-1}\text{)} \qquad (2)$$

where R, T, and F_y are, respectively, the molar gas constant, the absolute temperature, and the

faraday, λ_i^0 is the equivalent conductance of the reducible ion at infinite dilution and z is its valence. The equivalent conductance of the chromate ion at infinite dilution is 80.0 ohm^{-1} $cm.^2$, and hence from Eq. 2 its diffusion coefficient is 1.07×10^{-5} $cm.^2$ $sec.^{-1}$ at 25°.

Since the value of the product $m^{2/3}t^{1/6}$ for the capillary used to obtain the data in Table I was 1.63 $mg.^{2/3}$ $sec.^{-1/2}$ we find from Eq. 1 that the ratio i_d/C with this capillary should be a function of n according to

$$i_d/C = 3.22\ n \qquad (3)$$

The observed value of i_d/C from the data in Table I is 9.33 microamp. per millimole per liter, corresponding to $n = 3$. Hence in alkaline medium the reduction of $CrO_4^=$ ions at the dropping electrode takes place according to

$$CrO_4^= + 4H_2O + 3e \longrightarrow Cr(OH)_3 + 5OH^- \qquad (4a)$$

or

$$CrO_4^= + 2H_2O + 3e \longrightarrow CrO_2^- + 4OH^- \qquad (4b)$$

the latter reaction predominating in strongly alkaline medium in which the solubility of $Cr(OH)_3$ is appreciable.[5]

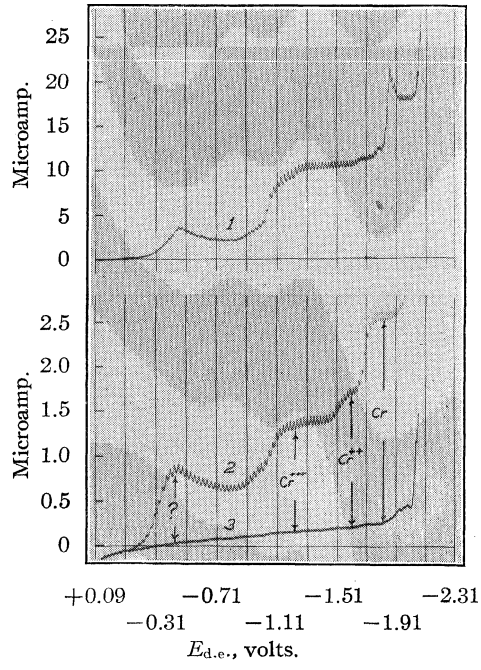


Fig. 3.—Increase of the relative height of the first wave with decreasing concentration of chromate in neutral unbuffered medium: (1) 1.10×10^{-3} M K_2CrO_4 in 0.1 N potassium chloride; (2) 1.19×10^{-4} M K_2CrO_4 in 0.1 N KCl; (3) residual current of 0.1 N KCl alone (see Table II).

(5) R. Fricke and O. Windhausen, *Z. anorg. allgem. chem.*, **132**, 273 (1924).

From the free energy data listed by Latimer[6] the reversible potentials for reactions 4a and 4b are, respectively, −0.37 v. and −0.42 v. in 1 N sodium hydroxide against the saturated calomel electrode. From the curves in Fig. 2 it is seen that the observed reduction potential is several tenths of a volt more negative than the reversible potentials, and hence the reduction of $CrO_4^=$ ions at the dropping electrode is irreversible and requires a considerable overvoltage in strongly alkaline medium.

Reduction of $CrO_4^=$ does not proceed farther than the +3 oxidation state in strongly alkaline medium apparently because the potential actually required for $CrO_2^- \longrightarrow Cr^{+2}$, or $CrO_2^- \longrightarrow Cr^0$, is more negative than the potential at which sodium ions are discharged.

Reduction of Chromate in Unbuffered Solutions.—It was thought at first that the first wave at −0.3 v. in unbuffered solutions of potassium chloride as supporting electrolyte might be due to the reduction of $CrO_4^=$ ions to some oxidation state between +6 and +3. However, this hypothesis is invalidated by the fact that *the relative height of the first wave in unbuffered medium increases markedly with decreasing concentration of chromate.* This is demonstrated by the polarograms in Fig. 3, and the diffusion current data in Table II.

TABLE II

DIFFUSION CURRENTS OF THE THREE WAVES OF CHROMATE IN UNBUFFERED 0.1 N POTASSIUM CHLORIDE SOLUTION AS A FUNCTION OF THE CHROMATE CONCENTRATION

The three diffusion currents were measured at potentials of −0.8 v., −1.4 v., and −1.9 v., respectively (see Fig. 3). h = 72.0 cm., m = 1.58 mg. $sec.^{-1}$, and $m^{2/3}t^{1/6}$ was equal to 1.71, 1.66, and 1.60 $mg.^{2/3}t^{-1/2}$ at the foregoing three potentials.

K_2CrO_4, millimoles per liter	i_d, microamp.[a] at voltages			i_d/C, microamp. per m mole. per liter at voltages		
	−0.8	−1.4	−1.9	−0.8	−1.4	−1.9
0.016	0.11	0.15	0.32	6.9	9.4	20.0
.047	.28	.47	.91	6.0	10.0	19.4
.119	.55	1.23	2.32	4.6	10.3	19.5
.236	.88	2.36	4.34	3.7	10.0	18.4
.439	1.30	4.48	8.07	3.0	10.2	18.4
.736	1.68	7.40	[b]	2.3	10.1	
1.10	2.06	10.45	[b]	1.9	9.5	
1.42	2.40	13.35	[b]	1.7	9.4	
			Av.	...	9.86	19.2
	Calcd. for n = 3				9.90	
	Calcd. for n = 6					19.0

[a] Corrected for the residual current.

[b] Maxima present and diffusion current not well defined.

(6) W. M. Latimer, "The Oxidation States of the Elements and their Potentials in Aqueous Solutions," Prentice-Hall, Inc., New York, 1938.

With concentrations of chromate smaller than 0.001 molar the last wave at −1.8 v. becomes well-defined (compare curve 1 of Fig. 1 with curve 2 of Fig. 3). It will be shown later that this last wave is due to the complete reduction of chromate ions to metallic chromium.

With concentrations of chromate less than about 2×10^{-4} M a fourth wave appears at −1.5 v. (curve 2, Fig. 3). The total diffusion current at −1.6 v. is very close to 4/3 the diffusion current at −1.3 v., and hence it corresponds to the reduction of chromate ion to chromous hydroxide according to

$$CrO_4^{=} + 4e + 4H_2O \longrightarrow Cr(OH)_2 + 6OH^- \qquad (5)$$

This same conclusion follows by application of the Ilkovic equation. The value of m for the capillary used to obtain the curves of Fig. 3 was 1.58 mg. sec.$^{-1}$ and t was equal to 3.00 sec. at $E_{d.e.} = -1.6$ v. Hence the product $m^{2/3}t^{1/6}$ was 1.63 mg.$^{2/3}$sec.$^{-1/2}$, and from Equations (1), (2) and (3) the calculated ratio of i_d/C for $n = 4$ is 12.9 microamp. The concentration of chromate used to obtain curve 2 of Fig. 3 was 0.119 mmoles per liter and the observed (corrected) diffusion current was 1.50 microamp. Hence the observed ratio of i_d/C is 1.50/0.119 = 12.6 microamp., in good agreement with the calculated value for $n = 4$.

In Table II are listed the data obtained for the diffusion currents, corresponding to the three waves at −0.3 v., −1.0 v., and −1.8 v., of various concentrations of potassium chromate in unbuffered 0.1 N potassium chloride solution. The diffusion currents have been corrected for the residual current obtained with the 0.1 N potassium chloride solution alone.[1,4] The observed ratios of i_d/C for each of the three waves are listed in the last three columns, and the values of this ratio calculated from Eq. 1 for $n = 3$ and $n = 6$, respectively, are given at the bottom of the last two columns.

It will be noted that the diffusion currents of the second and last waves are directly proportional to the concentration of chromate, and the average values of i_d/C correspond very closely to values for n of 3 and 6, respectively. Hence the second wave is due to the reduction $CrO_4^{=} \longrightarrow Cr(OH)_3$, as in alkaline medium (Eq. 4), and the last wave corresponds to the complete reduction of $CrO_4^{=}$ ions to metallic chromium, according to the equation

$$CrO_4^{=} + 6e + 4H_2O \longrightarrow Cr^0 + 8OH^- \qquad (6)$$

It will be noted that the ratio of i_d/C for the first wave was not constant, but increased with decreasing concentration of chromate. It should also be mentioned that the peculiar rounded maximum shown by the first wave was neither suppressed by methyl red nor by gelatin. It is evident, from this fact, that the maximum is not a typical "adsorption" maximum,[1] but is due to some other cause.

In 1 N potassium chloride solution the first wave is well defined and does not show a maximum. However, just as in 0.1 N potassium chloride solution, the relative height of the first wave increases markedly with decreasing concentration of chromate.

When a relatively small concentration of a magnesium salt is added to a chromate solution in 0.1 N potassium chloride, the c. v. curve shows only a single wave starting at about −0.3 v., but the diffusion current is not well defined and it increases continuously with increasing applied e. m. f. This peculiar effect of magnesium ions is demonstrated in Fig. 4.

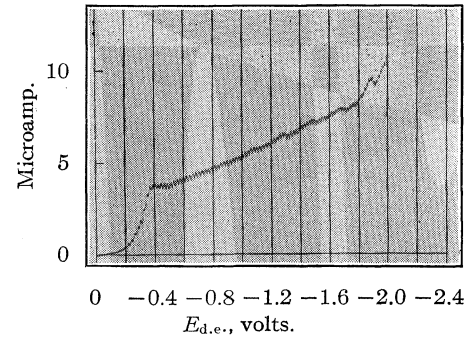


Fig. 4.—Influence of magnesium ions on the c. v. curve of chromate: 1.10×10^{-3} M K_2CrO_4 in 0.1 N KCl plus 0.01 M $MgCl_2$.

Reduction of Chromate in Buffered Solutions.—Typical c. v. curves of chromate reduction in two ammonia–ammonium chloride buffers of the same pH (8.7) but of different buffer capacity are shown in Fig. 5. Curve 1 was obtained with a 0.005 N and curve 2 with a 0.05 N buffer, and an excess of potassium chloride (0.1 N) was present in both cases. The most pronounced effect of the buffer was that it caused the first and second waves to coalesce into a single wave at −0.2 v. In the more concentrated buffer, the height of this wave corresponds to an n-value of 3 and hence reduction of chromate to chromic ions. The last wave at −1.6 v.

corresponds to the reduction of chromate ions to metallic chromium, as shown by the fact that the diffusion current corresponds to the value calculated from the Ilkovic equation for $n = 6$.

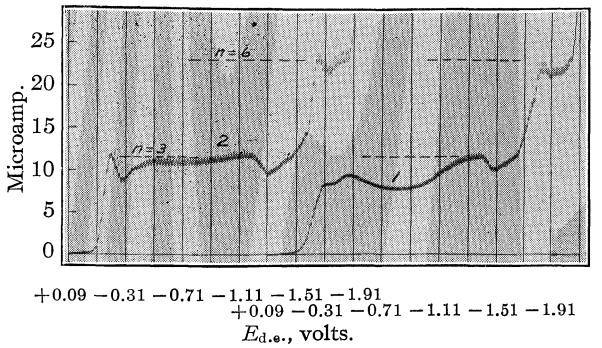


Fig. 5.—1.21 × 10^{-3} M K_2CrO_4 in 0.1 N KCl plus (1) 0.005 N NH_4Cl–NH_4OH buffer of pH 8.7, (2) 0.05 N NH_4Cl–NH_4OH buffer of pH 8.7. The short horizontal dotted lines indicate the diffusion currents calculated from the Ilkovic equation for values of n of 3 and 6, respectively.

From Eq. 4 it is evident that the concentration of hydroxyl ions formed at the electrode surface by the reduction will be between four and five times larger than the chromate ion concentration, depending on whether CrO_2^- or $Cr(OH)_3$ is formed. Hence in the reduction of the 1.21 × 10^{-3} M chromate solution, the concentration of hydroxyl ions liberated at the electrode surface was between about 0.005 and 0.006 N, when the diffusion current was reached. With the most dilute ammonium chloride–ammonia buffer (0.005 N, curve 1) the buffer capacity was not great enough to prevent a considerable change in the pH at the electrode surface, and this accounts for the fact that curve 1 has a shape intermediate between that of a c. v. curve in a completely unbuffered potassium chloride solution (compare Fig. 3) and that in a well-buffered ammonium chloride–ammonia solution. There was no significant change in the shape of the c. v. curve with increasing concentration of the ammonium chloride–ammonia buffer between 0.05 and 1 N.

The characteristics of the c. v. curve were also practically the same in various ammonia–ammonium chloride buffers of constant ammonium chloride concentration (0.1 N) but of different pH values between about 7.5 and 10. The reduction potential of the first wave was only shifted by a few hundredths of a volt, from −0.10 to −0.17 v., when the pH of a 0.1 N ammonium chloride–ammonia buffer was varied from 8 to 10. C. v. curves of 0.001 molar potassium chromate in 0.1 N ammonium chloride as supporting electrolyte (pH about 5) were similar to curve 2 in Fig. 5, except, as was to be expected, the reduction began at a more positive potential (+0.1 v.) and the slope of the first wave was smaller. The smaller slope was undoubtedly due to the poor buffer capacity of the pure ammonium chloride solution, and the consequent change in pH at the electrode surface with increasing current.

We also investigated the effect of diethylammonium chloride–diethylammonium hydroxide buffers of various pH values. Since the dissociation constant of diethylamine, 1.3 × 10^{-3}, is about one hundred times larger than that of ammonia it was possible to study the c. v. curves in these buffers up to a pH of about 12, and compare the characteristics of the curves with those obtained in dilute (*ca.* 0.01 N) sodium hydroxide solutions of about the same pH. The characteristics of the c. v. curve of chromate in a 0.1 M diethylammonium chloride–diethylammonium hydroxide buffer at a pH of about 10 are practically the same as those in an ammonium chloride–ammonia buffer of the same pH. At a pH of 10 only two waves were obtained at −0.35 v. and −1.8 v., as shown in Fig. 6. However, as the

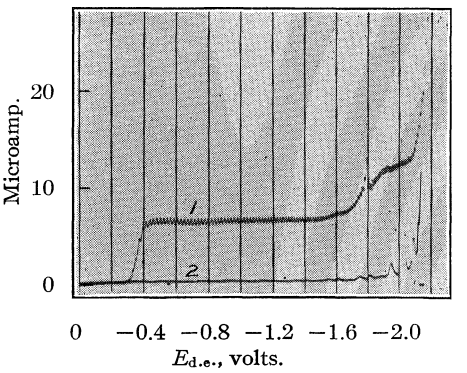


Fig. 6.—(1) 7 × 10^{-4} M potassium chromate in 0.1 M diethylammonium chloride–diethylamine buffer of pH 10.2. (2) Residual current of buffer alone.

pH was shifted from 10 to 12 the reduction potential of the first wave ($CrO_4^= \longrightarrow Cr^{+++}$) was shifted markedly from −0.35 v. to −1.1 v., and the second wave at −1.8 v. ($CrO_4^= \longrightarrow Cr$) disappeared at a pH of 12. At a pH of 12 in a diethylammonium chloride–diethylamine buffer the c. v. curve showed only a single wave which closely resembled the single wave in dilute solutions of sodium hydroxide, both in the magnitude

of the diffusion current and the value of the reduction potential. There was also a slight indication of a "pre-wave" in the diethylammonium chloride–diethylamine buffers of *p*H 11 and 12, just as in the dilute sodium hydroxide solutions.

In a 0.1 *N* solution of borax in 0.1 *N* potassium chloride (*p*H about 9) only a single well-defined wave was obtained at −0.3 v., and the diffusion current corresponded to $CrO_4^{=} \longrightarrow Cr^{+++}$. There was some indication of a second wave at −1.8 v., about twice as large as the first wave, but it was not well defined.

Discussion

The most interesting phenomenon observed in the reduction of chromate at the dropping electrode is the first wave at −0.3 v. in unbuffered solutions (Fig. 1 and Fig. 3). The most logical explanation of this wave appears to be that it is due to the reduction of $CrO_4^{=}$ ions, but that its height does not correspond to $n = 3$ because of the formation of a film of either chromic hydroxide, or basic chromic chromate, at the electrode surface which interferes with the further reduction.

The formation of basic chromic chromate at solid cathodes, presumably as a stable film impervious to chromate ions, is the usual explanation given to account for the low current efficiency in technical chromium plating.[7] According to Müller and Ekwall[8] the formula of the chromic chromate precipitated at a platinum or carbon cathode is $Cr_2(OH)_4CrO_4$, or $Cr(OH)_3 \cdot CrOH\text{-}CrO_4$. A variety of different "chromic chromates" probably can be formed depending on the experimental conditions, particularly the *p*H at the electrode surface.

Quantitative interpretation of the first wave in the present experiments, and the effect of *p*H on the reduction potential, is not possible at the present time because the detailed mechanism of the reduction is unknown. In this connection it should be emphasized that Equations 4a and 4b are intended to represent merely the *net* reaction, and not the actual mechanism of the reduction.

Qualitatively, however, the observed effects indicate that the formation of a film on the surface of the mercury drops increases the overvoltage necessary to obtain complete reduction of $CrO_4^{=}$ to Cr^{+3}. In neutral unbuffered solutions complete reduction to the +3 state does not start until a potential of about −1.0 v. is reached. When sodium hydroxide is added to the solution the first wave is decreased and shifted to a more negative value, but the second wave ($CrO_4^{=} \longrightarrow Cr^{+3}$) is shifted to a more positive value, and in 1 *N* sodium hydroxide solution it starts at about −0.7 v. (Fig. 1 and Fig. 2). Apparently the film of basic salt is not formed in strongly alkaline solution, because the chromic chromium remains in solution as chromite ion (CrO_2^{-}).

There seems to be a critical range of hydroxyl ion concentration in which the film formation occurs, which is to be expected from the amphoteric nature of the chromic ion. Apparently the film does not form in buffer solutions of *p*H less than 10 or 10.5, since in such solutions the height of the wave corresponds to $n = 3$. Under the present experimental conditions, the film appears to be stable only over a *p*H range from about 10.5 to 13 or 13.5.

In alkaline buffers the reduction potential shifts to more negative values with increasing *p*H, but the interpretation of the shift is complicated by the fact that it depends on the kind of buffer used as well as on the *p*H.

Summary

The reduction of chromate at the dropping electrode has been investigated in neutral unbuffered solutions, in buffer solutions of *p*H between 8 and 12, and in strongly alkaline medium.

With 1 *N* sodium hydroxide as supporting electrolyte the current–voltage curve consists of only a single well-defined wave, with a half wave potential of −0.85 v. *vs.* the saturated calomel electrode which is independent of the concentration of chromate. The height of the wave, which is directly proportional to the chromate concentration, corresponds to the reduction of $CrO_4^{=}$ to the +3 oxidation state (CrO_2^{-} in strongly alkaline medium).

In unbuffered solutions of potassium chloride the c. v. curve consists of four distinct waves at −0.3 v., − 1.0 v., −1.55 v., and −1.8 v., *vs.* the S. C. E. It was shown that the last three waves correspond, respectively, to $CrO_4^{=} \longrightarrow Cr^{+3}$, $CrO_4^{=} \longrightarrow Cr^{+2}$, and $CrO_4^{=} \longrightarrow Cr$. From the fact that the *relative* height of the first wave at −0.3 v. increased markedly with decreasing concentration of chromate, it was concluded that this wave was not due to the reduction of

(7) S. Glasstone and A. Hickling, "Electrolytic Oxidation and Reduction," D. Van Nostrand Co., Inc., New York, 1936, p. 120.

(8) E. Müller and P. Ekwall, *Z. Elektrochem.*, **35**, 84 (1929).

$CrO_4^=$ to some oxidation state between +6 and +3, but that the limiting current is governed by the formation of a film of chromic hydroxide, or basic chromic chromate, at the electrode surface, which interfered with the further reduction. When the solution was well-buffered at a *p*H between 8 and 10 the diffusion current at −0.3 to −0.4 v. corresponded to the reduction $CrO_4^= \longrightarrow Cr(OH)_3$. Apparently the film of basic salt is only stable under the conditions of the present experiments over a *p*H range from about 10.5 to 13.5.

From an analytical viewpoint, 1 *N* sodium hydroxide is the most suitable supporting electrolyte for the polarographic determination of chromate.

BERKELEY, CALIFORNIA
MINNEAPOLIS, MINNESOTA RECEIVED JANUARY 10, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF NEW YORK UNIVERSITY]

Ternary Systems. XXIV. Some Further Solid Solutions of Alums, at 25°[1]

BY ARTHUR E. HILL, NORMAN O. SMITH AND JOHN E. RICCI

This is a report of experiments continuing an investigation, conducted in this Laboratory, of ternary systems involving the formation of solid solutions between isomorphous double salts in equilibrium with aqueous solution. The general purpose of the investigation is the accumulation of reliable data on which to base, ultimately, speculations on the formation of solid solutions between such salts. In this respect it has been of interest especially to study the distribution of the two salts between the conjugate liquid and solid solutions, and to attempt to relate this distribution with the aqueous solubilities of the individual salts. On the basis of results, already published, on the formation of such solid solutions in a series of picromerites, studied as ternary systems of pairs of double salts with water,[2a] and in a number of alum pairs,[2b] an empirical equation has already been suggested[2a] for the relation between the mole fraction of a component in the liquid phase and its mole fraction in the solid phase; the degree of success toward a theoretical interpretation of the observed relation will be presented in a forthcoming publication from this Laboratory, making use of the present and additional data collected on this type of system.

Alums crystallize as regular octahedra and provided the lattice dimensions be not greatly different they would be expected to form solid solutions with one another. Early work with alums had been done by Hollmann[3] with the alum pairs $KFe(SO_4)_2$–$KAl(SO_4)_2$ and $KCr(SO_4)_2$–$KAl(SO_4)_2$, and by Fock[4] with the pair $KAl(SO_4)_2$–$TlAl(SO_4)_2$. In addition Hill and Kaplan[2] have studied the pairs $NH_4Al(SO_4)_2$–$KAl(SO_4)_2$, $NH_4Fe(SO_4)_2$–$NH_4Al(SO_4)_2$ and $NH_4Al(SO_4)_2$–$NaAl(SO_4)_2$. Complete miscibility between the alums was found in all these pairs studied, with the exception of the last mentioned, the sodium alum–ammonium alum pair, which formed no solid solution at all at the temperature of the measurements, 25°. The present paper describes similar measurements for the following pairs of alums in equilibrium with aqueous solutions at 25°: $TlAl(SO_4)_2$–$NH_4Al(SO_4)_2$, $TlAl(SO_4)_2$–$KAl(SO_4)_2$, $NH_4Cr(SO_4)_2$–$KCr(SO_4)_2$ and (partially) the pair $NH_4Fe(SO_4)_2$–$KAl(SO_4)_2$; complete miscibility was found to prevail for all these pairs at the temperature studied. Included also in this report is the ternary system for the formation of thallium alum from its component salts and water at 25°. This was desirable in view of the fact that thallium alum was to be prepared for use in solid solutions with other alums.

As has been emphasized in the preceding papers of this series, the present measurements are distinguished by the fact that special attention has been given to the question of attainment of equilibrium, inasmuch as the uncertainty about equilibrium generally vitiates the older results on the solubilities of such mixed salts. The procedure followed, for this purpose, already has been described,[2] the essential point being that

(1) This paper is being published, following the death of Professor Hill, by his collaborators. The material of the article is taken from a thesis presented for the degree of Doctor of Philosophy at New York University, June, 1939, by N. O. Smith, whose present address is the University of Manitoba, St. Vital, Manitoba, Canada.

(2) (a) Hill and Taylor, THIS JOURNAL, **60**, 1099 (1938); (b) Hill and Kaplan, *ibid.*, **60**, 550 (1938).

(3) Hollmann, *Z. physik. Chem.*, **37**, 193 (1901).

(4) Fock, *Z. Krist.*, **28**, 337 (1897).

TABLE I

Tl_2SO_4–$Al_2(SO_4)_3$–H_2O AT 25°

Original complex, wt. % Tl_2SO_4	Original complex, wt. % $Al_2(SO_4)_3$	Liquid solution, wt. % Tl_2SO_4	Liquid solution, wt. % $Al_2(SO_4)_3$	Solid phase
0.00	....	0.00	27.83 (U)	$Al_2(SO_4)_3 \cdot n\ H_2O$[a]
			27.83 (S)	$Al_2(SO_4)_3 \cdot n\ H_2O$[a]
2.012	29.93	.118	27.63	$Al_2(SO_4)_3 \cdot n\ H_2O$ + Tl Alum
3.984	29.97	.114	27.64	$Al_2(SO_4)_3 \cdot n\ H_2O$ + Tl Alum
3.987	21.02	.391	20.37	Tl Alum
4.008	11.02	1.341	9.82	Tl Alum
5.996	4.98	3.502	3.343	Tl Alum
6.797	3.91	4.743	2.460	Tl Alum
15.70	6.30	5.774	2.044	Tl Alum + Tl_2SO_4
8.47	2.48	5.764	2.040	Tl Alum + Tl_2SO_4
7.96	1.257	5.590	1.294	Tl_2SO_4
....	0.00	5.208 (U)	0.00	Tl_2SO_4
		5.218 (S)		

[a] n is probably 17.

equilibrium is approached, for every solubility determination, from opposite sides as follows. Complexes are made up in duplicate from weighed amounts of the two alums and water in 50-ml. glass-stoppered solubility tubes and brought to equilibrium by rotation in a thermostat at 25 ± 0.02°; each solubility tube also contained two glass marbles which by their rolling motion kept the solid phases well ground. Following the usual procedure the duplicates differed only in the order of addition of the components, so that in one tube one of the two alums was dissolved completely and the second then added in solid form; in the duplicate tube the order of addition of the salts was reversed. Agreement between the duplicates upon analysis of the liquid and solid phases after rotation is proof that the measurements represent equilibrium, a factor of prime importance for our ultimate purpose.

Thallium Alum at 25°.—Complexes were made up from weighed amounts of recrystallized Eimer and Amend thallous sulfate, Merck hydrated aluminum sulfate and water. The thallous sulfate was found to be 99.61% pure by precipitation as the chromate. The composition of the aluminum salt, as a result of efflorescence, did not correspond exactly to that of a single hydrate, being always somewhat less hydrated than the usually accepted formula $Al_2(SO_4)_3 \cdot 18H_2O$; the analytically determined composition was therefore always used in calculating the compositions of the complexes. We may point out that similar observations on the low hydration of aluminum sulfate (low compared to the formula $Al_2(SO_4)_3 \cdot 18H_2O$) were being made at the same time by Horan and Skarulis,[5] who in fact offer serious evidence for doubting the usually accepted value for the hydration, and suggest the possibility of the formula $Al_2(SO_4)_3 \cdot 17H_2O$ for the hydrate in equilibrium with solution at 0°. Although it seems likely, on the basis of the work of Horan and Skarulis and of further investigations now being conducted by one of us (Dr. N. O. Smith), that the formula may be $Al_2(SO_4)_3 \cdot 17H_2O$, we are temporarily not assigning any definite formula to this hydrate in the present paper. Similar uncertainty exists for the degree of hydration of the corresponding chromic sulfate, for which the hepta-decahydrate formula also has been suggested.[6]

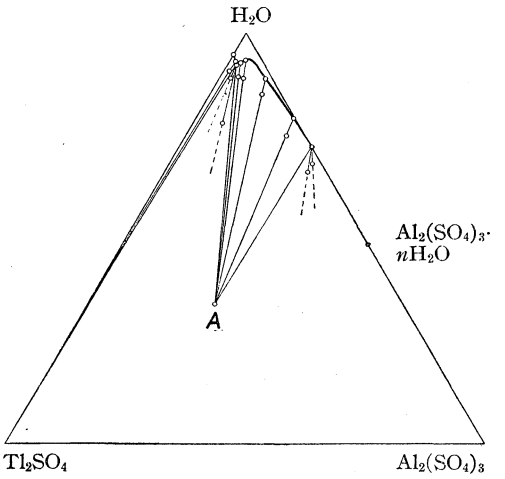


Fig. 1.—The system Tl_2SO_4–$Al_2(SO_4)_3$–H_2O at 25°; A = $TlAl(SO_4)_2 \cdot 12H_2O$.

Solubility equilibrium was found to be reached in this simple system within twenty-four hours, provided that the thallous sulfate was dissolved in the water before the addition of the aluminum sulfate. Only the liquid phases were analyzed. Thallium was determined volumetrically by the method of Zintl and Rienäcker[7] in which thallous ion is oxidized to thallic ion by standard bromate in 5% hydrochloric acid solution at 80° using methyl orange as indicator. In order to determine aluminum it was necessary first to remove thallium by precipitation as the sulfide in hot solution made alkaline with sodium hydroxide to retain the aluminum. After removal of sulfur the fil-

(5) Horan and Skarulis, THIS JOURNAL, **61**, 2689 (1939).

(6) Mellor, "Treatise on Inorganic Chemistry," Vol. **11**, 1922, p. 436; in particular, Weinland and Krebs, *Z. anorg. Chem.*, **49**, 157 (1906).

(7) Zintl and Rienäcker, *Z. anorg. allgem. Chem.*, **153**, 276 (1926).

TABLE II

$TlAl(SO_4)_2$–$NH_4Al(SO_4)_2$–H_2O AT 25°

No.	Original complex, wt. % $TlAl(SO_4)_2$	Original complex, wt. % $NH_4Al(SO_4)_2$	Liquid solution, wt. % $TlAl(SO_4)_2$	Liquid solution, wt. % $NH_4Al(SO_4)_2$	Solid phase, wt. % $TlAl(SO_4)_2$	Solid phase, wt. % $NH_4Al(SO_4)_2$
1 U	....	0.000	6.986	0.000	66.20	0.000
S			6.991			
2 A	12.00	1.000	6.045	.723	62.53	2.992
B	12.00	1.000	6.082	.780	62.62	2.995
3 A	10.00	2.700	4.558	2.039	55.71	8.42
B	10.00	2.700	4.640	1.968	55.03	8.96
4 A	6.455	4.000	3.387	3.107	45.62	16.31
B	6.455	4.000	3.417	3.063	45.72	16.47
5 A	5.300	5.667	2.387	4.004	36.27	23.24
B	5.300	5.667	2.425	3.964	35.86	24.06
6 A	2.500	5.928	1.536	4.780	24.74	32.72
B	2.500	5.928	1.544	4.780	24.80	32.80
7 A	2.000	9.000	0.689	5.563	14.17	41.34
B	2.000	9.000	.764	5.498	13.45	41.86
8 U	0.000	...	.000	6.16	0.00	52.31
S				6.14		

trate was analyzed for aluminum by precipitation with 8-hydroxyquinoline according to the gravimetric method of Kolthoff and Sandell.[8]

Table I shows the results, which are plotted in Fig. 1. The solubilities listed for the pure salts, thallous sulfate and hydrated aluminum sulfate, are averages from closely agreeing measurements from both under- and super-saturation (these approaches to equilibrium are marked U and S, respectively, in this and subsequent similar tables). That for thallous sulfate, 5.213%, is in good agreement with the figures of Berkeley[9] (5.21% by interpolation), and of Noyes and Stewart[10] (5.22%); the figure for the aluminum salt, 27.86%, is in fair agreement with the determinations of Poggiale[11] (27.6%), Wirth[12] (27.82%), Britton[13] (27.70%) and Hill and Kaplan[2] (27.39%). The solid phase over the greater part of the diagram is shown by algebraic extrapolation[14] to be the hydrated double sulfate, thallium alum, and the small average absolute deviation (= 0.24%) between the extrapolated and the theoretical percentage of thallous sulfate in the solid phase is indicative of the experimental accuracy. The solubility curve of the hydrated aluminum sulfate as solid phase is of course too short to be represented on the diagram. Inspection of the figure shows that at 25° the alum is congruently soluble to an extent of about 7% of anhydrous salt (see also Table II).

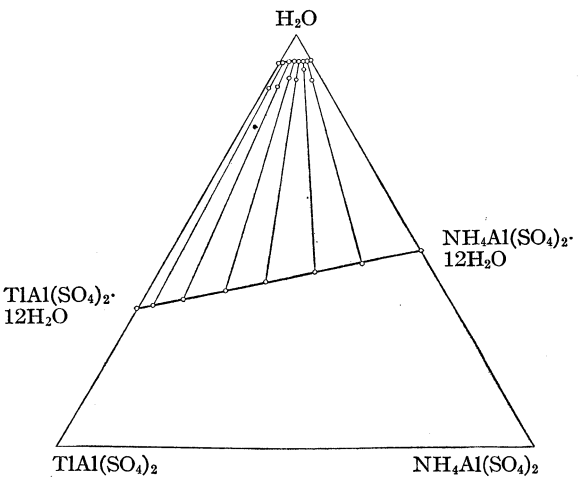


Fig. 2.—The system $TlAl(SO_4)_2$–$NH_4Al(SO_4)_2$–H_2O at 25°.

Thallium Alum, Ammonium Alum, Water at 25°.—Inasmuch as an attempt will be made to relate the distribution of the isomorphous salts between aqueous and crystalline phases, to the molar solubilities, this particular alum pair is of special interest because of the considerable difference in the molecular weights of the pair. Both alums were prepared by mixing solutions of equimolecular quantities of the component salts (analyzed grades) at about 60° and allowing the solution to cool with prolonged stirring. In the case of the ammonium alum this procedure gave a product of composition corresponding to the theoretical value. The thallium alum so prepared, however, as if, apparently, incongruently soluble at higher temperatures, was contaminated with excess thallous sulfate; this difficulty was therefore overcome by returning the crystals to the mother liquor, adding a considerable excess of aluminum sulfate, heating to dissolve the solid, and cooling with stirring for twenty hours. The solubilities of the individual alums were determined from under- and super-saturation

(8) Kolthoff and Sandell, THIS JOURNAL, **50**, 1900 (1928).
(9) Berkeley, *Trans. Roy. Soc. London*, **A203**, 189 (1904).
(10) Noyes and Stewart, THIS JOURNAL, **33**, 1658 (1911).
(11) Poggiale, *Ann. chim. phys.*, (3) **8**, 467 (1843).
(12) Wirth, *Z. anorg. Chem.*, **79**, 360 (1913).
(13) Britton, *J. Chem. Soc.*, **121**, 982 (1922).
(14) Hill and Ricci, THIS JOURNAL, **53**, 4306 (1931).

TABLE III

$TlAl(SO_4)_2$–$KAl(SO_4)_2$–H_2O AT 25°

No.	Original complex, wt. % $TlAl(SO_4)_2$	Original complex, wt. % $KAl(SO_4)_2$	Liquid solution, wt. % $TlAl(SO_4)_2$	Liquid solution, wt. % $KAl(SO_4)_2$	Solid phase, wt. % $TlAl(SO_4)_2$	Solid phase, wt. % $KAl(SO_4)_2$
1	...	0.000	6.989	0.000		0.00
2 A	6.604	3.000	4.202	2.519	51.43	11.97
B	6.604	3.000	4.200	2.506	51.42	11.89
3 A	6.000	5.956	2.606	4.020	37.28	23.56
4 A	2.000	6.352	1.321	5.280	21.42	36.73
B	2.000	6.352	1.323	5.308	21.45	36.63
5 A	1.000	10.000	0.403	6.17	7.035	48.28
B	1.000	10.000	0.402	6.18	7.042	48.20
6 U	0.000	....	0.000	6.59	0.000	
S				6.58		

and the complexes were made from the two alums and water in duplicate as described above. In Table II the complexes marked A were made with thallium alum and those marked B with ammonium alum as the original solid phase. After two or three weeks in the thermostat both liquid and solid phases were analyzed for thallium (volumetrically as described above) and for ammonium by distilling the ammonium liberated by potassium hydroxide into standard acid and titrating the excess acid with standard base. The solid phases were centrifuged and air-dried before being analyzed. The results of analysis are shown in Table II and plotted in Fig. 2.

For comparison with the solubility here reported for thallium alum at 25°, 6.989%, we note that Fock[4] gives 7.07%, Locke[15] 6.97% and Berkeley,[9] by interpolation, 7.19%. The solubility of ammonium alum, 6.15%, which is an average (from both under- and super-saturation) of both ammonium and aluminum analyses, is in satisfactory agreement with the recent determination of Hill and Kaplan,[2] 6.19%. The fact that the ternary results from the duplicate tubes (A and B) are in agreement is proof that they are results at equilibrium. Figure 2 shows that the two alums form a complete series of solid solutions, and the directions of the tie-lines indicate that the concentration of ammonium alum in the liquids (neglecting water content) is always greater than that in the conjugate solids. The over-all accuracy of the analytical procedure was again checked by extrapolating algebraically the tie-lines joining the compositions of the original complexes and the liquid solutions, to the straight line on the diagram joining the points representing the single alums; the average absolute deviation between the observed and the extrapolated compositions of the solid phases was only 0.19%.

Thallium Alum, Potassium Alum, Water at 25°.—This system is one already studied by Fock[4] but as his analyses appear to be of doubtful accuracy it was thought desirable to repeat the work. It may be observed that thallium alum and potassium alum have very similar solubilities by weight but quite different solubilities in molar units, a fact of some interest in connection with interpreting their behavior ultimately.

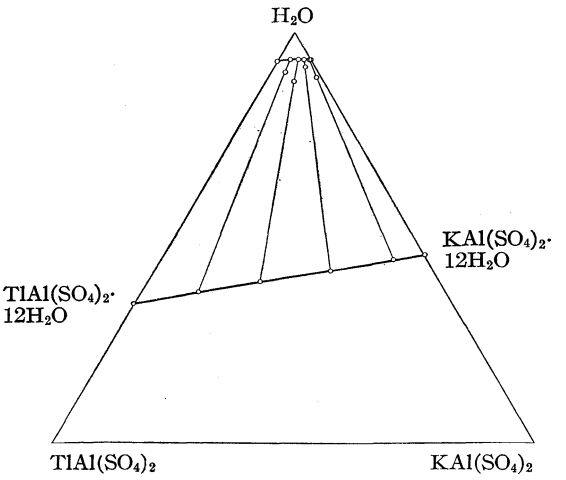


Fig. 3.—The system $TlAl(SO_4)_2$–$KAl(SO_4)_2$–H_2O at 25°.

The complexes were made up in duplicate according to the procedure for the preceding system, the A tubes (Table III) having thallium alum and the B tubes potassium alum present as the initial solid phase. The potassium alum used was recrystallized Baker Analyzed material. After four weeks rotation in the thermostat the equilibrium liquids and solids were analyzed for both thallium and aluminum as described above, the solids being first centrifuged and air-dried. Table III gives the resulting data, which are shown graphically in Fig. 3.

The solubility of potassium alum here reported (6.58%) is again in close agreement with the determination of Hill and Kaplan[2] (6.60%). As shown in Fig. 3, the two alums are completely mutually soluble, the proportion of potassium alum being greater in the liquids than in the conjugate solids, concentrations being on the dry basis. When Fock's figures for this isotherm are plotted on such a triangular diagram, the liquid curve shows considerable irregularity.

(15) Locke, *Am. Chem. J.*, **26**, 166 (1901).

TABLE IV

$NH_4Cr(SO_4)_2$–$KCr(SO_4)_2$–H_2O AT 25°

No.	Original complex, wt. % $NH_4Cr(SO_4)_2$	Original complex, wt. % $KCr(SO_4)_2$	Liquid solution, wt. % $NH_4Cr(SO_4)_2$	Liquid solution, wt. % $KCr(SO_4)_2$	Solid phase, wt. % $NH_4Cr(SO_4)_2$	Solid phase, wt. % $KCr(SO_4)_2$
1 U	....	0.000	13.65	0.000		0.00
S			13.68			
2 A	12.46	5.015	9.99	4.504	43.18	12.05
B	12.46	5.015	10.28	4.612	43.12	12.08
3 A	10.79	12.01	6.86	9.44	30.21	25.45
B	10.79	12.01	6.85	9.40	30.26	25.26
4 A	8.00	16.08	4.882	12.18	21.88	34.09
B	8.00	16.08	4.852	12.14	21.91	34.15
5 A	3.997	17.46	2.958	14.74	13.50	42.69
B	3.997	17.46	2.986	14.75	13.52	42.76
6 A	1.500	20.49	1.162	17.30	5.226	51.32
7 U	0.000	....	0.000	18.79	0.00	56.71
S				18.79		

The internal agreement in the present data can again be judged by the small average absolute deviation (of only 0.09%) between the extrapolated and the observed compositions of the solid phases.

Ammonium Chrome Alum, Potassium Chrome Alum, Water at 25°.—Hydrated chromic salts in general are known to exist in both violet and green forms, but in the case of the (solid) chrome alums only the violet forms appear to have been prepared. A solution of the violet form becomes green on heating, and there is evidence[16,17] that an equilibrium exists in the liquid between the dissolved violet and green forms. In the determinations of the solubility of a chrome alum an abnormally long time is required for complete equilibrium to be reached, the reason for this undoubtedly being related to the additional equilibria involved.

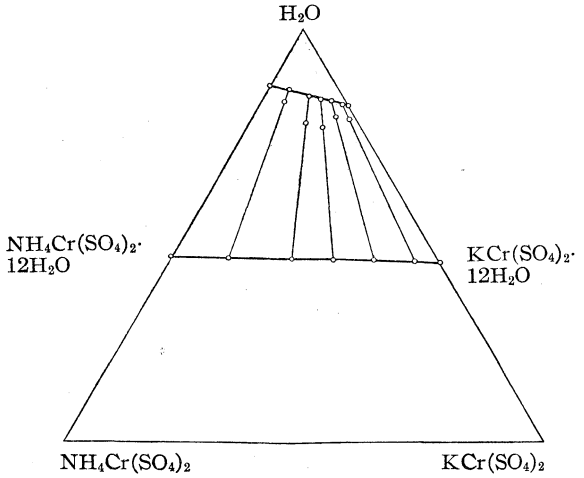


Fig. 4.—The system $NH_4Cr(SO_4)_2$–$KCr(SO_4)_2$–H_2O at 25°.

(16) Montemartini and Vernazza, *L'Ind. Chimica*, **7**, 857 (1932); **8**, 445 (1933); *cf. Brit. Chem. Abstracts*, **A**, 912 (1932); 562 (1933).

(17) Koppel, *Ber.*, **39**, 3738 (1906).

Baker and Adamson chemicals were used in the present work. After recrystallization from water (maximum temperature 60°) the alums were dried in a desiccator over the corresponding partly dehydrated salts. Analysis of the ammonium chrome alum for both ammonium and chromium content showed agreement with theory. The potassium chrome alum, as a result of efflorescence, changed slightly in composition during the preparation of the complexes; this change was taken into consideration in the calculation of the composition of the original complexes listed in Table IV. The complexes were made up in duplicate as already described, the A tubes with potassium chrome alum and the B tubes with ammonium chrome alum as the original solid. Three months of rotation in the thermostat was necessary for equilibrium to be reached as shown by successive analyses of tubes containing the separate alums and water when their single solubilities were being determined from under- and from super-saturation. At the end of such a period of rotating, both the liquid and the solid phases were analyzed for ammonium and chromium content, the former by the ammonia distillation method and the latter by oxidation to chromate with sodium peroxide followed by reduction with iodide and titration with thiosulfate.[18] The solids were centrifuged and air-dried for a short time before analysis. The results are given in Table IV and shown graphically in Fig. 4.

Our figure for the solubility of ammonium chrome alum (13.66%) is in agreement with the value of 13.2% interpolated from Koppel's data[17] but very far from that of Locke[15] (9.63%), whose measurements were made after only a few hours. Locke's figure for potassium chrome alum (11.01%) is subject to the same error, and is consequently very different from the solubility here reported, of 18.78%. As the diagram shows, the alums of this system are completely miscible in the solid state, and again the proportion of the potassium alum in the liquids is seen always to exceed that in the conjugate solids, provided concentrations are taken on the dry basis. The

(18) Scott, "Standard Methods of Chemical Analysis," D. Van Nostrand Co., Inc., New York, N. Y., 1922, pp. 158, 161.

TABLE V

$NH_4Fe(SO_4)_2$–$KAl(SO_4)_2$–H_2O AT 25°

Point	Original complex, wt. % $NH_4Fe(SO_4)_2$	Original complex, wt. % $KAl(SO_4)_2$	Liquid solution, wt. % $NH_4Fe(SO_4)_2$	Liquid solution, wt. % $KAl(SO_4)_2$	Liquid solution, wt. % $KFe(SO_4)_2$	Solid phase, wt. % $NH_4Fe(SO_4)_2$	Solid phase, wt. % $KAl(SO_4)_2$	Solid phase, wt. % $NH_4Al(SO_4)_2$	Moles of water per mole of total double sulfate in solid
1 U	0.00	...	0.00	6.59	0.00	0.000	54.43	0.00	12.00
S				6.58					
2 A[a]	12.21	8.20	...	...	...	7.033	18.47	26.27	12.82
B[a]	12.21	8.20	...	...	...	6.932	19.41	26.61	12.25
3 A	24.34	4.040	21.24	1.100	3.066	26.81	3.22	21.72	13.07
B	24.34	4.040	21.23	1.260	3.054	26.46	5.33	20.99	12.57
4 A	30.18	4.025	24.51	0.637	3.979	37.92	3.82	11.16	12.79
B	30.18	4.025	24.51	.574	4.111	38.61	4.16	11.32	12.19
5 A	32.09	2.016	27.57	.432	2.107	45.94	1.967	7.085	11.88
B	32.09	2.016	27.55	.515	2.124	45.62	1.880	6.910	12.17
6 A	33.05	0.983	29.16	.336	1.223	49.10	0.919	3.514	12.71
B	33.05	.983	29.23	.348	1.252	49.98	.780	3.965	12.10
7 U	...	.000	31.17	.000	0.00	55.17	.000	0.000	12.00
S			31.23						

[a] Liquid solutions 2A, 2.327% $(NH_4)_2SO_4$, 8.251% $Fe_2(SO_4)_3$, 2.191% $Al_2(SO_4)_3$; 2B, 2.324% $(NH_4)_2SO_4$, 8.281% $Fe_2(SO_4)_3$, 2.167% $Al_2(SO_4)_3$.

average absolute deviation between the analytical and the extrapolated compositions of the solid phases in this system was 0.37%.

Ferric Ammonium Alum, Potassium Alum, Water at 25°.—This pair of alums, not containing a common cation, constitutes with water a quaternary system, but only that portion of the system was examined where the total compositions can be expressed in terms of the two alums and water. The complexes were again made up in duplicate from weighed amounts of potassium alum (recrystallized Baker Analyzed), ferric ammonium alum (recrystallized Baker and Adamson) and water, as in the preceding systems. As in the case of potassium chrome alum mentioned above, the composition of the ferric ammonium alum changed during manipulation as a result of efflorescence, and a correction for the change was applied in calculating the compositions of the complexes, by means of a time extrapolation. After one month of rotation in the thermostat, both liquid and solid phases were analyzed, as follows, for ammonium, iron and total iron and aluminum: for ammonium by the ammonia distillation method, for iron by the Zimmermann–Reinhardt reduction followed by titration with standard ceric sulfate, for combined iron and aluminum by the simultaneous precipitation of both cations by 8-hydroxyquinoline.[8,19] The accuracy of the latter procedure was found to be satisfactory by preliminary tests.

These determinations are sufficient for the determination of the complete composition of the phases, provided it can be assumed that in any phase the number of moles of trivalent sulfates equals the number of moles of univalent sulfates, whereupon the remaining constituents can be calculated. This assumption is justified so long as the system remains quaternary, or so long as no hydrolytic products are formed. Actually a very small amount of a finely-divided insoluble solid was formed in all the tubes. This was probably a basic iron complex, but being present in such small quantity it was not analyzed. The liquids were analyzed without interference by waiting long enough for the settling of all solids, before sampling. The main solid phase itself was also easily obtained free of this hydrolytic precipitate because the latter passed through the finest filter paper, so that the main solid was washed free of it by the supernatant liquid. The main solid phases were sucked dry on filters and analyzed while moist.

The results are presented in Table V, in which the A complexes began with ferric ammonium alum and the B complexes with potassium alum as the only solid. The figure for the solubility of ferric ammonium alum (31.20%), which is the average of both iron and ammonium analyses, is slightly higher than the reports of Locke[15] (30.7%) and of Hill and Kaplan[2] (30.85%).

The analytical results are shown calculated in terms of the three alums ammonium–iron, potassium–aluminum, and potassium–iron; the difference, water, is shown, for the solid phases, in the last column, as moles of water per mole of total double sulfate in the solid. The agreement of these figures with the theoretical number 12 required for alums supports the assumption that the solids are all quaternary solid solutions or mixed alums. The internal consistency of the results was further checked by methods of algebraic extrapolation,[14] in which by assuming the theoretical alum hydration for the solids, any one of the three percentages listed under "the solid phase" could be calculated by extrapolation, for comparison with the observed value. The average error found, testing all three columns, was only 0.37%. In these averages, however

(19) Berg, *Z. anal. Chem.*, **76**, 193 (1929).

TABLE VI

$NH_4Fe(SO_4)_2$–$KAl(SO_4)_2$–H_2O AT 25°

Units: moles per 100 grams of mixture or phase (average of duplicates)

Point	Original complex $NH_4Fe(SO_4)_2$	Original complex $KAl(SO_4)_2$	Liquid solution $NH_4Fe(SO_4)_2$	Liquid solution $NH_4Al(SO_4)_2$	Liquid solution $KFe(SO_4)_2$	Liquid solution $KAl(SO_4)_2$	Solid phase $NH_4Fe(SO_4)_2$	Solid phase $NH_4Al(SO_4)_2$	Solid phase $KFe(SO_4)_2$	Solid phase $KAl(SO_4)_2$
1	0	...	0	0	0	0.0255	0	0	0	0.2108
2	0.04590	0.03176	0.03520 .02246	0.01274	0.00614 .01888	.01274	0.02625	0.1378 .1115	0.02625	.04710 .07335
3	.0914	.01566	.07985 .07526	.00457	.01066 .01523	.00457	.10013 .08356	.09006 .10663	.01657	.01657
4	.1136	.01558	.09215 .08980	.00235	.01409 .01644	.00235	.1439 .1284	.04741 .06286	.01545	.01545
5	.1206	.00781	.10361 .10178	.00183	.00737 .00920	.00183	.1721 .1646	.02951 .03696	.00745	.00745
6	.1243	.00381	.10975 .10843	.00133	.00431 .00563	.00133	.1863 .1830	.01577 .01906	.00329	.00329
7	...	0	.1173	0	0	0	.2074	0	0	0

tubes 2A and 2B were not included; these two tubes were found to contain considerably more of the above-mentioned hydrolytic precipitate than any of the other complexes. The very same method of algebraic extrapolation, however, showed that even in this case the main solid phase was evidently quaternary, although the basic solid and consequently also the liquid solution must be of higher order. Extrapolation further indicated that the basic solid contained neither ammonium nor aluminum.

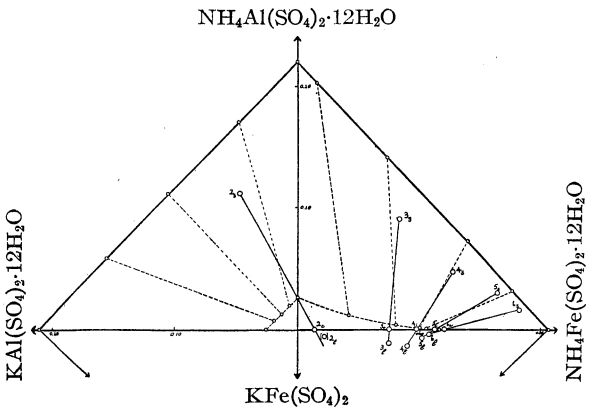


Fig. 5.—Part of the system $KAl(SO_4)_2$–$NH_4Fe(SO_4)_2$–H_2O at 25°. Units: moles of salt per 100 g. of mixture or phase. Subscripts l, c, s denote liquids, complexes and solids, respectively.

The data of Table V were recalculated, using the averages for the duplicate tubes, to moles per 100 g. of mixture, and listed as such in Table VI. Using the graphical method of extrapolation for such reciprocal quaternary systems of Ricci and Loucks[20] the results, in these units, are plotted in Fig. 5, which is a projection on the base of the isothermal tetrahedral pyramid model for the quaternary system. The points are numbered in accordance with the table. It may be pointed out, in elucidation of the figure, that inasmuch as the original complexes were made up from water and the two alums $KAl(SO_4)_2$ and $NH_4Fe(SO_4)_2$, the compositions of the complexes all fall, in this projection, on the horizontal axis connecting these alums. The units of the diagram are moles of the respective salts per 100 g. of mixture (including water), the water being plotted, in the solid model, on a vertical axis perpendicular to the base pictured, at the intersection of the axes joining the reciprocal alums. The ends (not shown) of the four horizontal axes would represent the number of moles of the respective (anhydrous) alums in 100 g. of the pure salt. The dashed curves and tie-lines show the results of Hill and Kaplan on two of the ternary systems making up the main quaternary system. If the complete quaternary system were to be studied, the isothermal model, except for regions of quinary behavior, would probably consist of two surfaces bounded by four edges, the one a curved surface representing liquid and the other also a curved surface representing the saturating solid solutions. The data of Hill and Kaplan, in Fig. 5, therefore give two edges of each surface, and our data some points on these surfaces. Point 2 is in doubt for reasons stated above. Further information concerning the trend in direction of the tie-lines, and general relations between the liquids and the solids in the quaternary system, was obtained by projecting the points and lines of the solid model onto the two diagonal planes of the pyramid passing through

(20) Ricci and Loucks, *J. Chem. Education*, **15**, 329 (1938).

TABLE VII

DISTRIBUTION OF ALUMS BETWEEN LIQUID PHASE AND SOLID PHASE

Point	$NH_4Al(SO_4)_2$ with $TlAl(SO_4)_2$ Mole fraction of $NH_4Al(SO_4)_2$		$KAl(SO_4)_2$ with $TlAl(SO_4)_2$ Mole fraction of $KAl(SO_4)_2$		$NH_4Cr(SO_4)_2$ with $KCr(SO_4)_2$ Mole fraction of $NH_4Cr(SO_4)_2$	
	In dissolved salts Y	In solid solution X	In dissolved salts Y	In solid solution X	In dissolved salts Y	In solid solution X
1	0.000	0.000	0.000	0.000	0.000	0.000
2	.181	.079	.495	.276	.294	.206
3	.438	.219	.717	.509	.560	.437
4	.618	.391	.868	.737	.698	.591
5	.747	.539	.962	.918	.821	.745
6	.847	.703	1.000	1.000	.932	.901
7	.932	.843			1.000	1.000
8	1.000	1.000				

the vertical water axis; these projections however are not shown, for reasons of space-saving. Some of the significant aspects of the distribution of the salts between the liquid and solid phases, however, are shown below, together with similar information on the simpler systems studied.

Distribution between Liquid Solution and Solid Solution.—In order to interpret some of the above data in terms of the Roozeboom[21] classification of solid solutions, the concentrations have been recalculated into mole fractions of the two alums, disregarding water, in the two phases. The results, showing for each system the mole fraction of the more soluble alum, are listed in Table VII, and are plotted in Fig. 6, where the Y values represent the mole fraction of the more soluble alum in the liquid phase and X its mole fraction in the solid phase.

All three ternary systems studied apparently belong to Class I of Roozeboom's classification, in which there is complete miscibility in the solid phase and in which one of the components is present in higher proportion in the liquid than in the conjugate solid phase throughout the series of solid solutions. It is conceivable of course that this relation may not hold true at the extreme edges of the diagram, for which there are no data, but in the light of further theoretical work not yet published such a possibility appears unlikely These curves, it may be noted, all follow the equation previously suggested, $y = x^m$, with m a constant for each system. For the present we observe merely that the component present in greater concentration in the liquid than in the solid is that component with the greater aqueous molar solubility; for example, though ammonium and potassium alums both have smaller weight solubilities than thallium alum, their molar solubilities

(21) Roozeboom, *Z. physik. Chem.*, **8**, 521 (1891); **30**, 385 (1899).

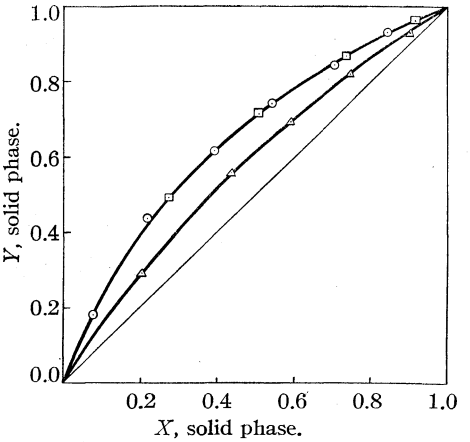


Fig. 6.—Distribution of alums between liquid solution and solid solution at 25°: circles, ○, $TlAl(SO_4)_2$–$NH_4Al(SO_4)_2$; squares, □, $TlAl(SO_4)_2$–$KAl(SO_4)_2$; triangles △, $NH_4Cr(SO_4)_2$–$KCr(SO_4)_2$.

are much greater, a fact to be taken into account in considering the observed distribution.

Similar (partial) calculations are shown in Table VIII, for part of the quaternary system $NH_4Fe(SO_4)_2$–$KAl(SO_4)_2$–H_2O. The table lists the number of moles of $^1/_2K_2SO_4$ and $^1/_2Fe_2(SO_4)_3$ per mole of total double sulfate in both liquid solutions (Y) and solid solutions (X). Although these figures may be interpreted as indicating that the proportion of potassium alum (ferric

TABLE VIII

DISTRIBUTION BETWEEN LIQUID AND SOLID PHASES FOR PART OF THE SYSTEM $NH_4Fe(SO_4)_2$–$KAl(SO_4)_2$–H_2O

Point	Mole fraction of $^1/_2K_2SO_4$ In dissolved salts Y	Mole fraction of $^1/_2K_2SO_4$ In solid solution X	Mole fraction of $^1/_2Fe_2(SO_4)_3$ In dissolved salts Y	Mole fraction of $^1/_2Fe_2(SO_4)_3$ In solid solution X
1	1.000	1.000	0.000	0.000
2	(.349)	(.347)	(.651)	(.653)
3	.160	.080	.952	.484
4	.151	.075	.978	.696
5	.082	.036	.984	.823
6	.049	.016	.989	.907
7	.000	.000	1.000	1.000

or aluminum) is greater in the liquid than in the solid solutions, and the same for (potassium or ammonium) ferric alum, the results do not of course have the significance of those shown above in Table VII and Fig. 6, since Roozeboom's classification applies only to ternary systems.

Summary

1. The system Tl_2SO_4–$Al_2(SO_4)_3$–H_2O has been studied at 25° and the isotherm found to consist of the three solubility curves of Tl_2SO_4, $TlAl(SO_4)_2 \cdot 12H_2O$, and $Al_2(SO_4)_3 \cdot nH_2O$, respectively (n being probably 17).

2. The 25° isotherms for the ternary systems consisting of water and the three alum pairs thallium alum–ammonium alum, thallium alum–potassium alum and ammonium chrome alum–potassium chrome alum have been studied. In all three a complete series of solid solutions has been found, and their assignment to Roozeboom's Class I demonstrated.

3. That part of the quaternary system ferric ammonium alum–potassium alum–water, where the total compositions can be expressed in terms of $NH_4Fe(SO_4)_2$, $KAl(SO_4)_2$ and H_2O, has been studied at 25°. Where the concentration of $KAl(SO_4)_2$ relative to that of $NH_4Fe(SO_4)_2$ in the total composition is large, the behavior becomes that of a system of more than four components, apparently because of slight hydrolysis; all the quaternary solids, however, are solid solutions of alums.

NEW YORK, N. Y. RECEIVED JANUARY 23, 1940

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF STANFORD UNIVERSITY]

Some Properties of Sodium Palmitate Curd as Studied in the Centrifuge

BY JAMES W. McBAIN AND T. FOSTER FORD

Soap curd[1] is a felt of hydrated crystalline fibers enmeshing a mother liquor that is slightly alkaline water with almost no soap. The fibers, although exceedingly fine,[2] yield good X-ray patterns as has been shown by Thiessen and others, and they are strikingly visible in the ultramicroscope. Ordinary solutes diffuse and sediment freely through their interstices.[3] The mechanical structure of the felt is sufficiently firm that sodium palmitate curd more concentrated than 0.2 M does not sediment or crush in a centrifugal field of 250,000 times gravity. Incidentally, this is likewise true of household soap, liquid crystalline sulfonic acid solution of 2 M, and of a potassium coconut oil liquid crystalline neat soap.

The densities of sodium palmitate curds at 20° with and without added salt, referred to water at 20° as 0.99820, are given in Table I. Compositions are given in true weight %.

TABLE I

Wt. % NaP	Wt. % NaCl	Wt. % H_2O	Density of curd
1.39	0	98.61	1.0000
2.105	0	97.895	1.0014
2.78	0	97.22	1.0014
2.065	1.92	96.0	1.0136
2.025	3.77	94.2	1.0269
2.725	1.91	95.3	1.0130
2.67	3.74	93.5	1.0194

The density of the hydrated curd fibers themselves was found by adding sodium palmitate solution to saturated sodium chloride solution until the curd fibers just began to sediment, instead of having a tendency to float. The result, 1.15, agrees fairly well with that calculable from Table I.

Observations in the Air-Driven Spinning Top.—For observation of sedimentation in the one-piece rotor the effective arrangement shown in Fig. 1 was devised. By looking obliquely down into the top, as shown by the arrow, it is possible to see directly the separation of water from curd. Calibration was by observation when known weights of water were added to the empty top, the internal radius of which was 0.80 cm., with opening of radius 0.5 cm., height of annular space 0.26 cm., and volume of annular space 0.32 cc. Forty seconds are required for the 20 mm. rotor to attain its full speed of 2650 r. p. s. at 80 lb. (5 atm.) pressure of air.

Separation of curd from water occurred so rapidly, in about one minute, that sedimentation velocity of curd fibers has not yet been accurately

(1) Jerome Alexander, "Colloid Chemistry, Theoretical and Applied," Vol. I, Chemical Catalog Co., Inc., New York, N. Y., 1926, p. 138.

(2) J. W. McBain, J. M. McDowell and M. E. Worden, THIS JOURNAL, **61**, 2540 (1939).

(3) J. W. McBain and C. Alvarez-Tostado *ibid.*, **59**, 2489 (1937).

measured. However, s is about 5×10^{-11}. The method of using a scraping tool was found inadmissible for soap curds as this may press water out of the structure.

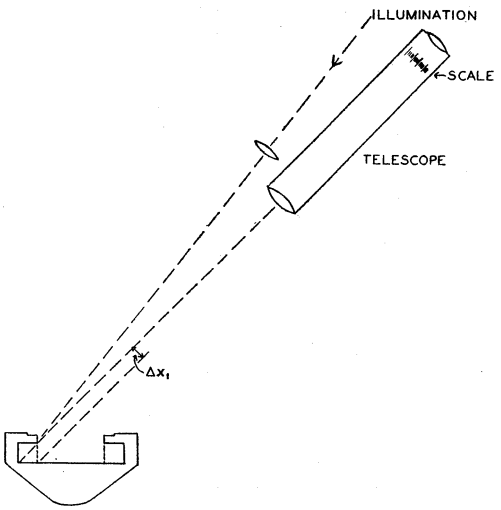


Fig. 1.

Tenth normal sodium palmitate curd shows no sedimentation at 2650 r. p. s.; one-fifteenth normal curd begins to collapse at 1500 r. p. s.; and one-twentieth normal at 1000 r. p. s. A curd collapsed at a high speed does not noticeably rebound when the speed is reduced, although in most cases a slight blurring of the originally sharp boundary between curd and separated water is noticed. This is due perhaps to the Brownian motions and slight diffusion of the curd fibers, but possibly also to a collision effect of molecules that are diffusing back after displacement in the high centrifugal field.

The amount of collapse increases as the centrifugal force increases, but it takes an observable time. The time lag must be due to friction of the water forced through the interstices of the curd structure. With the usual Poiseuille formula for membranes, idealized as consisting of parallel equal capillaries, the radius r of these equivalent capillaries was deduced from the measurements. For example, with a ring of 0.05 N curd of average radius 0.68 cm., 0.32 cc. of curd contained 0.0045 g. of sodium palmitate, of which the effective weight (above that of the aqueous medium) is 0.00067 g., the centrifugal force exerted on the periphery at 2000 r. p. s. is therefore $4\pi^2$ (0.00067) $(0.68)(2000)^2 = 42{,}000$ dynes. The rate of collapse at twenty seconds from the beginning of the experiment calculated from the slope of the collapse curve is 0.0234 g. H_2O/sec. The inner cylindrical surface of the curd being 1.11 sq. cm., by assuming that 1 sq. cm. of this is total pore cross section, it follows that the flow is equivalent to that through twenty-six million capillaries, each 0.3 cm. long and 0.00022 cm. in diameter. The initial calculated pore size is somewhat greater and that at forty seconds somewhat smaller, but the cessation of collapse is not due to the interstices becoming too small to permit capillary flow, but because the structure is stronger. A similar measurement at 800 r. p. s. gave also 0.00022 cm. for the effective pore diameter.

An alternative approach is to evaluate the diameter of the fibers themselves, or much more probably bundles of fibers, from the approximate sedimentation velocity constant, $s = 5 \times 10^{-11}$. Whereas for spheres this would correspond to a radius of about 390 Å., for very long cylinders the diameter would be about 400 Å. Judging by the well-known ultramicroscopic appearance of sodium palmitate curds, this is an effective diameter due to bundling of the parallel individual fibers which, according to the sorption of methylene blue,[2] are much less than 100 Å. in diameter.

Fig. 2a.—N sodium palmitate curd.

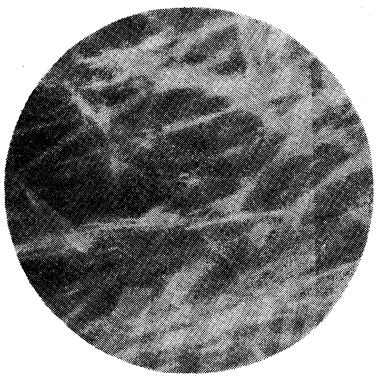


Fig. 2b.—0.25 N sodium palmitate curd.

Photographs of N and 0.25 *N* sodium palmitate curd as seen in the cardioid ultramicroscope are shown in Fig. 2, clearly showing that we are dealing with discrete bundles of fibers.

In Table II is given the final radial thickness, *d*, of the ring of water separated from 0.05 *N* sodium palmitate curds in experiments carried out in triplicate at 10, 20, 40 and 80 lb./sq. in. air pressure, respectively. In all cases the original thickness of the ring of curd was 0.30 cm. In Table III, glycerol was added in two experiments, raising the density to 1.0268, but separations at the higher pressures were greater than without glycerol despite the greater buoyancy of the medium.

TABLE II

FINAL THICKNESS, *d*, OF WATER LAYER SEPARATED FROM 0.30 CC. OF CURD

Lb./sq. in.	(R. p. s.)^2 × 10^{-6}	A	B	C
10	1.117	0.014	0.008	0.005
20	2.66	.052	.034	.030
40	4.92	.078	.052	.052
80	7.02	.090	.070	.070

TABLE III

FINAL THICKNESS, *d*, OF AQUEOUS GLYCEROL LAYER SEPARATED FROM 0.30 CM. OF CURD

Lb./sq. in.	(R. p. s.)^2 × 10^{-6}	D	E
10	1.17	...	...
20	2.66	0.030	0.045
40	4.92	.090	.170
80	7.02	.125	.180
100	8.4	.160	...

Since the properties of sodium palmitate curds depend upon their structure, the exact procedure used in their preparation is important. Thus if the soap solution has been cooled sufficiently that it has already begun to form curd fibers before placing in the top, it forms a soft "mushy" curd yielding considerably more water on collapse than if it were introduced while clear but just above the melting point and allowed to form and set in the slowly rotating top.

The mat separated from mush curd remains in one piece whereas the ordinary curd usually breaks into about seven equal segments in the rotor used owing to radial collapse of the inner circumference. This indicates that the mush curd possesses less oriented structure which agrees with the fact that more free water may be mechanically squeezed from such a mat than from a stiff curd collapsed to an equal extent.

When a curd refuses to collapse further at a given speed, the strength of the structure in the peripheral layer just balances the centrifugal force exerted by the unbalanced mass of the upper (or inner) layers of curd upon this peripheral layer. This pressure exerted inward radially by the outermost or peripheral layer is known as the swelling pressure, although here there is no marked tendency to swell but chiefly a tendency to resist further collapse.

This is a clear case where the origin of the swelling pressure[4] is mechanical rather than osmotic, whereas for many jellies and gels the two factors have not been distinguished in recording swelling pressures and the thermodynamically related vapor pressures. The data are collected in Table IV.

TABLE IV

FINAL THICKNESS, *d*, OF WATER LAYER FROM 0.30 CM. OF VARIOUS CURDS OF SODIUM PALMITATE AND THE SWELLING PRESSURES, *P*, IN DYNES/SQ. CM.

Description of curd	(R. p. s.)^2 × 10^{-6}	*d*	*P* × 10^{-4}
0.05 *N* NaP curd formed in top from soap soln. in which crystals just beginning to form, least collapse obtained	2.66	0.04	4.7
0.05 *N* NaP curd formed from soap soln. just above m. p., least collapse obtained	4.92	0.05	8.7
0.05 *N* NaP curd formed from soap soln. just barely melted clear, least collapse obtained	7.02	0.08	12.8
N/15 NaP curd formed from soap soln. just above melting point, least collapse obtained	7.02	0.038	17.0

Curds were made from 0.05 *N* sodium palmitate solutions with additions of sodium chloride and glycerol, respectively, in such amounts as to make the two curds equal in density. Compared with the original curd in water alone, the glycerol curd collapsed faster and to a greater extent. However, the sodium chloride curd was too rigid to collapse and showed a coarse radial structure yielding water readily upon cutting. The cut curd then collapsed. Since the glycerol medium has a higher viscosity, it is clear that the effect is one of structure and possibly of reduced hydration rather than any retardation of "capillary" flow.

Summary

The behavior of soap curd in the centrifuge is in accord with its brush heap structure with greater or less orientation depending upon previous history; the effective diameter of the interstices between the ultramicroscopic fibers being 10^{-4} cm., that of the fibers, or more probably fiber

(4) J. W. McBain and R. F. Stuewer, *Kolloid-Z.*, **74**, 10 (1936).

bundles, themselves 400 Å.; and the swelling pressure from a chiefly mechanical origin being 10^5 dynes/sq. cm. for 0.05 *N* sodium palmitate curd.

Glycerol softens the curd whereas sodium chloride makes it more rigid.

STANFORD UNIVERSITY, CALIF.
RECEIVED JANUARY 19, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF SOUTH CAROLINA]

Dialkyl Adipates

BY ROBERT A. FEAGAN, JR., AND J. E. COPENHAVER[1]

This work was carried out because of the growing commercial importance of the higher alcohols and adipic acid, as well as to study the type of melting point curve exhibited by the esters of this dibasic acid. This investigation covers the normal alkyl esters from pentyl to eicosyl. Since the first four have been described previously, they were not prepared in this series but for completeness they are included in the curve.

The esters up to and including dinonyl were colorless liquids at room temperature and above that compound they were white waxy solids. The melting points are given in Table I and plotted in Fig. 1. The alternation between the esters of the even and odd carbon alcohols was very slight, the odd esters exhibiting the unusual property of being a little above the mean curve. It will be noted that there is an even number of carbon atoms in all of these compounds.

TABLE I

MELTING POINTS AND ANALYSES OF THE DIALKYL ADIPATES

Diester	M. p. (cor.), °C.	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
Methyl	8[a]	...	...	...	...
Ethyl	−21[b]	...	...	...	...
Propyl	−20.25[c]	...	...	...	...
Butyl	−37.5[c]	...	...	...	...
Pentyl	−14	67.10	66.07	10.56	10.08
Hexyl	−9 to −7	68.75	68.78	10.90	11.08
Heptyl	3.8–4.5	...	...	...	...
Octyl	9.5–9.8	71.31	70.77	11.43	11.56
Nonyl	21.6[d]	72.31	72.50	11.63	11.37
Decyl	27.4	73.19	74.22	11.88	12.02
Undecyl	34.7	73.96	74.57	11.97	11.56
Dodecyl	39.3	74.63	75.17	12.11	12.04
Tridecyl	45.9	75.24	75.33	12.24	12.14
Tetradecyl	49.4	75.78	75.52	12.35	12.55
Pentadecyl	55.0	76.27	76.36	12.45	12.27
Hexadecyl	57.3[e]	76.71	76.63	12.54	12.31
Heptadecyl	61.8	77.11	76.53	12.62	12.27
Octadecyl	63.4	77.48	76.49	12.69	12.08
Nonadecyl	66.7	...	...	...	...
Eicosyl	65.2	...	...	...	...

[a] Bouveault, *Bull. soc. chim.*, **29**, 1042 (1920); M. van Rysselberge, *Bull. soc. acad. roy. Belg.*, [5] **11**, 171–192 (1926).

[b] Timmermans, *Bull. soc. chim. Belg.*, **36**, 502–518 (1927), gave m. p. −21°, while H. Serwy, *Bull. soc. chim.*, **42**, 482–501 (1933), gave −19.9°.

[c] Timmermans, *Bull. soc. chim. Belg.*, **36**, 502 (1927).

[d] Staudinger and Schwalenstöcker, *Ber.*, **68**, 745 (1935), gave m. p. 17–18.5°.

[e] Staudinger and Schwalenstöcker, *ibid.*, gave the m. p. of 53°.

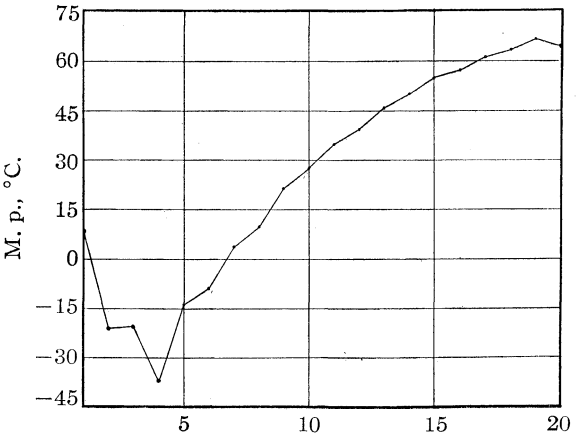


Fig. 1.—Melting points of the dialkyl adipates.

Experimental

Two methods were used for their preparation, *viz.*, the action of the alcohols on the acid or on adipyl chloride. In several cases, both methods were used and the products checked. A slight excess of the acid or the acid chloride was used above the theoretical quantity necessary for the formation of the diester. When adipic acid was used, the reaction mixture was heated at 150–155° for several hours, whereas with adipyl chloride, only slight warming was necessary.

The crude product from either method was dissolved in ether and thoroughly washed with 10% sodium carbonate. The recovered ester was recrystallized from

(1) Presented in part before the Organic Division of the American Chemical Society at its 97th meeting, Baltimore, Maryland, April, 1939.

acetone, in which the higher derivatives were almost insoluble, while the corresponding alcohols were very soluble. Cooling with dry-ice was necessary to remove from solution the esters below tetradecyl.

The melting points were taken, with mechanical stirring, in a 200-cc. bulb, fitted with a side-arm for the thermometer and melting point tube. Standard Anschütz thermometers were used so the melting points may be regarded as corrected.

This problem was suggested by Dr. E. Emmet Reid, Research Adviser, University of South Carolina, and to him the authors wish to express their appreciation for his valuable help. The alcohols from decyl to octadecyl were furnished by Dr. Reid and were from those prepared by Meyer and Reid.[2] Thanks also are due E. I. du Pont de Nemours and Company for furnishing the adipic acid.

Summary

The diesters of adipic acid from *n*-pentyl to *n*-eicosyl alcohols were prepared and the melting points determined. The melting points show slight alternation, the esters of the odd carbon alcohols being slightly higher than the even on the mean curve.

(2) Meyer and Reid, THIS JOURNAL, **55**, 1574–84 (1933).

COLUMBIA, SOUTH CAROLINA RECEIVED FEBRUARY 7, 1940

[CONTRIBUTION FROM THE STERLING CHEMISTRY LABORATORY, YALE UNIVERSITY, AND THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

The Synthesis of 5-Methylchrysene and Related Compounds

BY MELVIN S. NEWMAN[1,2]

In a previous publication,[3] the author pointed out the desirability of synthesizing methyl derivatives of chrysene and described a new synthesis by which chrysene and 6-alkylchrysenes could be prepared readily. In order to explore the generality of this method for the preparation of various chrysene derivatives desired for biological testing in connection with the cancer problem, further work has been done. In this paper, the syntheses of 5-methylchrysene, 5-ethylchrysene and 5,6-dimethylchrysene are described, together with a new and more generally applicable procedure for the preparation of α,γ-diphenylbutyric acid, an important intermediate.

The α,γ-diphenylbutyric acid previously[3] used was prepared in five steps, of which the first was the condensation of benzaldehyde with acetophenone. The second step involved 1,4-addition of hydrogen cyanide to the chalcone thus produced. It was feared that in certain projected syntheses, the corresponding chalcones (bearing alkyl groups on the α-carbon) might prove difficult to prepare or purify and also that conditions for the addition of hydrogen cyanide might be difficult to find.[4] In the present work α,γ-diphenylbutyric acid was prepared by the alkylation of benzyl cyanide with phenethyl bromide using sodium amide.[5] The α,γ-diphenylbutyronitrile thus produced was hydrolyzed to the corresponding acid in excellent yield. Inasmuch as a variety of substituted phenethyl bromides and of substituted benzyl cyanides is easily prepared, the new approach is seen to be quite general.

The cyclization of the acid chloride of α,γ-diphenylbutyric acid by aluminum chloride was further improved (94% yield) by decreasing the time of reaction.[3] It was also determined that if the volatile phosphorus compounds formed when the acid was treated with phosphorus pentachloride were not removed prior to the treatment with aluminum chloride, the yield was decreased to 77%. The remaining steps in the synthesis are indicated in the chart.

The Reformatsky condensations of 1,2,3,4-tetrahydro-1-keto-2-phenylnaphthalene, I, with ethyl α-bromopropionate and ethyl α-bromobutyrate proceeded smoothly and the corresponding unsaturated acids, II (R = CH_3 and C_2H_5), were isolated in fair yields. The double bond is placed in the ring instead of the alternate position of conjugation with the carboxyl group as in the analogous case of 3,4-dihydro-2-phenyl-1-naphthaleneacetic acid.[3] It is interesting to note that from the neutral fraction of the reaction products (after dehydration and hydrolysis) con-

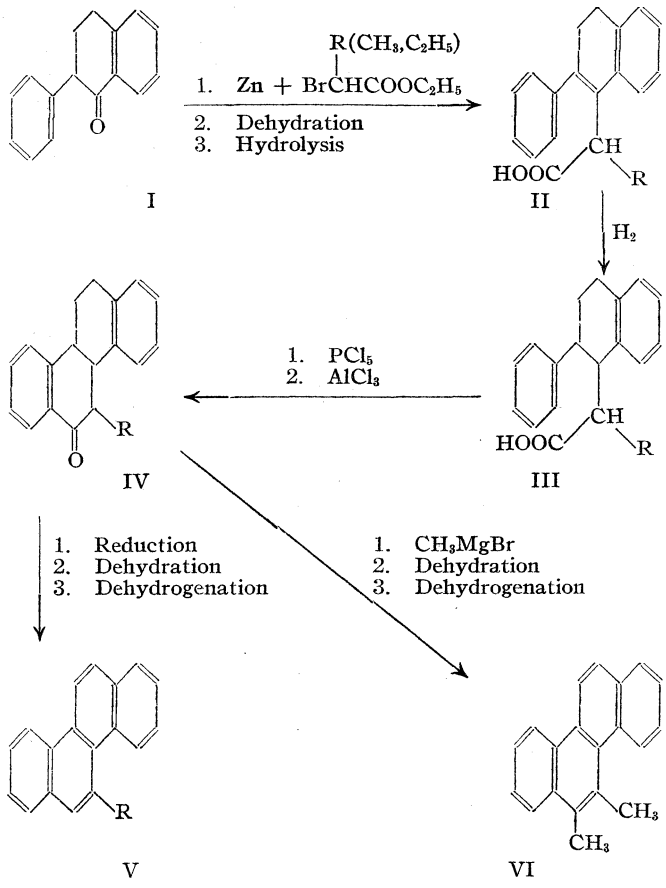
(1) Part of the work herein reported was aided by a grant from the Jane Coffin Childs Memorial Fund for Medical Research, Yale University.

(2) Elizabeth Clay Howald Scholar at The Ohio State University, 1939–1940.

(3) Newman, THIS JOURNAL, **60**, 2947 (1938).

(4) Michael and Weiner, *ibid.*, **59**, 744 (1937), cite no instance of the addition of hydrogen cyanide to unsaturated ketones containing an alkyl group on the α-carbon.

(5) See Bergstrom and Fernelius, *Chem. Rev.*, **12** 138 (1933), and **20**, 455 (1937), for reviews of the use of sodium amide in alkylation studies.



siderable amounts of starting ketone, I, were recovered in spite of varying the amount of excess reagents used in the Reformatsky reactions. In an experiment using ethyl α-bromobutyrate and zinc with I, it has been shown that at least part of the recovered unchanged ketone results from the reaction of its enolic form with the postulated organozinc intermediate according to the equation

$$\underset{\text{I}}{\text{R—COCHR}} + \text{BrZnCH(C}_2\text{H}_5\text{)COOC}_2\text{H}_5 \longrightarrow \underset{\text{Ia}}{\text{R—C(OZnBr)=CR}} + \text{C}_2\text{H}_5\text{CH}_2\text{COOC}_2\text{H}_5$$

Upon hydrolysis, the bromozinc enolate, Ia, regenerates I. This explanation is supported by the isolation (in 15% yield) of ethyl butyrate from the reaction products. Such behavior of a ketone in the Reformatsky reaction has its analogy in similar reactions of ketones with Grignard reagents.[6]

Another interesting observation had to do with the use of iodine for initiation of the reaction. If strictly anhydrous conditions were carefully observed and sandpapered zinc foil[7] used, the reactions always started easily without the use of iodine. However, the yield of desired product was better if a small amount of iodine was used to initiate the reaction. Thus, in comparable runs using I and ethyl α-bromopropionate, the yield of unsaturated acid, II (R = CH_3), was 23.0% when no iodine was used and 37.6% when it was.

Difficulty was again encountered in the reduction of the unsaturated acids, II. Reduction was finally accomplished by high pressure hydrogenation over a copper-barium chromite catalyst[8] at 200°. A small amount of decarboxylation also took place but at lower temperatures reduction was incomplete. The reduction of the esters over a nickel catalyst supported on kieselguhr was also tried but at 200° saturation of the double bond was incomplete and it was feared that at higher temperatures the aromatic rings might have been hydrogenated.

No attempts were made to separate in a pure condition the stereoisomeric reduced acids, III, although in one case a separation into crystalline and non-crystalline fractions was made. Both fractions yielded the same end-products when put through the remaining steps of the synthesis. No crystalline ketone corresponding to IV was isolated. To form the 5-alkylchrysenes, the crude ketones were reduced to the alcohols using the aluminum isopropylate procedure.[9] The alcohols were dehydrated by heating with a trace of iodine and the tetrahydrochrysenes dehydrogenated by heating with sulfur. The hydrocarbons, 5-methylchrysene, m. p. 117.2–117.8°, and 5-ethylchrysene, m. p. 91.4–92.4°, were obtained in fair yields. In connection with the latter, it should be pointed out that the ethylchrysene, m. p. 236°, prepared from the acetylchrysene, m. p. 254°, is not the 5-derivative as tentatively advanced.[10]

After treating IV (R = CH_3) with methylmagnesium bromide, followed by dehydration and

(6) For example, the enolization of acetomesitylene, Kohler and Baltzly, THIS JOURNAL, **54**, 4015 (1932).

(7) Natelson and Gottfried, *ibid.*, **61**, 970 (1939). The zinc foil was obtained from the J. T. Baker Chemical Company, Phillipsburg, N. J.

(8) Catalyst 37KAF, Connor, Folkers, and Adkins, *ibid.*, **54**, 1138 (1932).

(9) Lund, *Ber.*, **70**, 1520 (1937).

(10) Funke and Müller, *J. prakt. Chem.*, **144** 242 (1936).

dehydrogenation, a mixture of hydrocarbons was obtained. By fractional crystallization of the picrates formed from this mixture followed by adsorption of the picric acid on alumina, 5,6-dimethylchrysene, VI, was obtained. The nature of the impurity has not been determined positively but it is probably 5-methylchrysene, since the melting point of the mixture of hydrocarbons obtained was not depressed by the addition of 5-methylchrysene.

The new hydrocarbons are being tested for biological activity. Unpublished results would indicate a very slight carcinogenic activity for 6-methylchrysene[3] as it has produced one sarcoma in twenty mice during eighteen months.[11]

Experimental[12,13]

α,γ-Diphenylbutyric acid.—To 39 g. of powdered sodium amide[14] under 500 cc. of dry sulfur-free benzene in a three-necked flask fitted with mercury-sealed stirrer, reflux condenser, gas inlet tube, and dropping funnel was added 106 g. of benzyl cyanide[15] with stirring and cooling, the air in the system having been displaced with dry nitrogen. Ammonia was evolved copiously and the benzene took on a deep red color. The mixture was refluxed for one hour and on cooling a light colored complex separated from a deep red solution. Owing to the vigorous exothermic reaction two hours were required for the addition (with cooling) of 156 g. of phenethyl bromide. After three hours of stirring at room temperature, during which time the color became light brown and much white solid appeared, the mixture was refluxed for thirty minutes, cooled, and treated with an excess of dilute hydrochloric acid. The benzene layer was washed and the product distilled to give 114 g. (61%) of a clear yellow viscous oil, b. p. 147–151 at 0.5–1 mm. A fairly large higher boiling residue accounted for the low yield. In spite of several modifications of procedure, the yield varied from 56 to 63%. In a typical hydrolysis, 165 g. of nitrile was refluxed with 600 cc. of acetic acid and 100 cc. of 70% sulfuric acid for two days to yield 170 g. (95%) of acid, m. p. 70–72°. Alkaline hydrolysis of the nitrile was not as satisfactory.

1,2,3,4-Tetrahydro-1-keto-2-phenylnaphthalene. I.—The yield of this ketone was increased to 94% when the directions previously given[3] were modified to include in the following order: one-half hour for addition of aluminum chloride at room temperature; one-half hour each at 40 and at 60°; and a final cooling to room temperature during one-half hour before decomposition. In a comparable experiment in which the acid chloride was treated directly with aluminum chloride without removing any of the volatile phosphorus compounds formed in the reaction of the acid with phosphorus pentachloride, the yield fell to 77%.

The Reformatsky Reactions.—Considerable experimentation upon the Reformatsky reaction was carried out, the best conditions found being illustrated by the following description: to a hot solution of 44.4 g. (0.2 mole) of I and 54 g. (0.3 mole) of ethyl α-bromopropionate in 250 cc. of dry sulfur-free benzene contained in a 1-liter flask fitted with a ground-in condenser was added 20 g. (0.3 mole) of zinc foil which had been freshly sandpapered[7] and about 0.2 g. of iodine. After the initial reaction moderated the benzene was kept gently refluxing for three hours. The solid complex which separated was decomposed with dilute hydrochloric acid. The organic reaction products were heated at 230° with a small crystal of iodine to effect dehydration and then distilled at 2 mm. The fraction boiling from 180 to 210° was refluxed for sixteen hours with alcoholic potassium hydroxide. From the neutral portion of the hydrolyzed products was isolated 12.3 g. of I (27.3%) and from the acid fraction, by crystallization from benzene–ligroin, 20.92 g. (37.6%, or 52.5% if allowance for recovered ketone is made) of **3,4-dihydro-α-methyl-2-phenyl-1-naphthaleneacetic acid, II** (R = CH_3), m. p. 204–210°. A sample recrystallized for analysis separated as small colorless dense prisms, m. p. 210.2–210.6°.

Anal. Calcd. for $C_{19}H_{18}O_2$: C, 81.99; H, 6.52. Found: C, 82.15; H, 6.52.

In decomposing the insoluble complex formed in the Reformatsky reaction, there was always a certain amount which was not easily decomposed by shaking with dilute acid at room temperature. In a run using 0.1 mole of ketone, this insoluble complex was collected by filtration and decomposed by boiling with dilute hydrochloric acid and a little alcohol. On cooling 3.2 g. of organic matter crystallized. This crystalline material proved to be ethyl 1,2,3,4 - tetrahydro - 1 - hydroxy - α - methyl - 2 - phenyl-1-naphthaleneacetate, m. p. 90.4–91.4°, as shown by analysis and by dehydration and hydrolysis to II (R = CH_3).

Anal. Calcd. for $C_{21}H_{24}O_3$: C, 77.75; H, 7.46. Found: C, 77.49; H, 7.51.

In a comparable reaction using 44.4 g. of I, 58.5 g. of ethyl α-bromobutyrate, 20 g. of zinc, and 0.2 g. of iodine, there was isolated 21.4 g. (48%) of unchanged ketone and 16.0 g. (27.6% or 53.4% if allowance for recovered ketone is made) of a mixture of isomeric unsaturated acids, m. p. 151–168°, designated as **3,4-dihydro-α-ethyl-2-phenyl-1-naphthaleneacetic acid.** No attempt was made to separate pure isomers and the portion for analysis, crystallized from benzene–ligroin, melted at 156–169°.

Anal. Calcd. for $C_{20}H_{20}O_2$: C, 82.16; H, 6.90. Found: C, 82.39; H, 6.88.

Isolation of Ethyl Butyrate.—In an exactly similar reaction using 0.1 mole of ketone, the organic reaction products were extracted with benzene and after washing, the benzene removed in an insulated column packed with glass helices. The remaining material was distilled with steam and after salting out the distillate with ammonium chloride, the non-aqueous layer was dried over sodium sulfate

(11) Private communication from Dr. M. J. Shear.

(12) All melting points corrected.

(13) The author acknowledges the valuable assistance of Mr. O. Woolfolk in the preparation of several intermediates and of Mr. J. H. Walker who performed the semi-micro analyses. Their assistance was made possible by The Ohio State W. P. A. Project No. 65-1-42-89.

(14) The sodium amide used was prepared by Dr. M. Orchin essentially according to the method of Dennis and Browne, THIS JOURNAL, **26**, 587 (1904), using ammonia from a tank.

(15) The benzyl cyanide was purified according to Johnson, "Organic Syntheses," Vol. 16, John Wiley and Sons, Inc., New York, p. 89.

and distilled. A forerun, b. p. 80–121°, was discarded and 1.7 g. of ethyl butyrate, b. p. 121.2–121.5°, was obtained. On hydrolysis, butyric acid was identified by odor and by its *p*-bromphenacyl ester,[16] m. p. and mixed m. p. 62.6–63.0°.

The Reduced Acids. III.—After several methods of reduction had been attempted unsuccessfully, the acids were reduced smoothly in dioxane over catalyst 37KAF[8] under an initial hydrogen pressure of 1900 lb. (127 atm.). A temperature of 200° was necessary, as at lower temperatures reduction was incomplete. The reduced acids, III, contain three asymmetric carbon atoms and no attempt was made to separate pure isomers. By the reduction of 10.0 g. of II (R = CH_3) there was obtained 5.91 g. of colorless needles, m. p. 143–148°, of **1,2,3,4-tetrahydro-α-methyl-2-phenyl-1-naphthaleneacetic acid, III** (R = CH_3), by a single crystallization from benzene–ligroin. On evaporation of the mother liquors to dryness, 4.06 g. of a pale yellow viscous oil was obtained which consisted of a mixture of isomeric acids. A small amount of the crystals was recrystallized from benzene–ligroin to yield colorless rosets of needles, m. p. 147.6–148.8°.

Anal. Calcd. for $C_{19}H_{20}O_2$: C, 81.40; H, 7.19. Found: C, 81.42, 81.44; H, 6.94, 6.92.

In the case of the corresponding acid, III (R = C_2H_5), no crystalline fraction was obtained and the pale colored oil obtained in over 90% yield was used directly for the succeeding steps.

5-Methylchrysene, V(R = CH_3).—Either the crystalline or non-crystalline acid III (R = CH_3) could be used for the preparation of 5-methylchrysene. In a typical experiment, 2.00 g. of acid III (R = CH_3) in 10 cc. of benzene was treated with 1.5 g. of phosphorus pentachloride. After refluxing for several minutes, all volatile compounds were removed under reduced pressure at 80°. The pale yellow residue was dissolved in 15 cc. of dry sulfur-free benzene and 1.0 g. of aluminum chloride added in three portions with cooling. After swirling at room temperature until the evolution of hydrogen chloride slackened, the reaction mixture was warmed slowly to 50°. The bromine colored solution was cooled after thirty minutes and was decomposed by adding dilute hydrochloric acid. The benzene solution was washed with acid and alkali and the organic matter remaining after the evaporation of the solvent was pale brown in color. This crude ketone IV (R = CH_3) was suitable for the further steps described below. A solution of the above ketone in isopropanol containing aluminum isopropylate (from 0.5 g. of aluminum) was distilled slowly until no further test for acetone was given by the distillate.[9] The reaction mixture was treated with dilute hydrochloric acid and the organic product dehydrated by heating at 230° for ten minutes under reduced pressure after the addition of a crystal of iodine. The residue was dehydrogenated by heating at 240 to 250° for forty minutes with 0.23 g. of sulfur. After vacuum distillation from a small amount of zinc dust, the hydrocarbon was isolated by crystallization from benzene–alcohol as almost colorless needles, m. p. 115–117°, in 36% yield (0.621 g.). A sample purified for biological testing and analysis by recrystallization of the picrate followed by chromatographic adsorption on alumina formed colorless needles, m. p. 117.2–117.8°, with brilliant blue-violet fluorescence in ultraviolet light.

Anal. Calcd. for $C_{19}H_{14}$: C, 94.18; H, 5.82. Found: C, 94.04, 93.96; H, 5.96, 5.59.

The **picrate** crystallized from alcohol in orange-red needles, m. p. 142.6–143.0°.

Anal. Calcd. for $C_{25}H_{17}O_7N_3$: C, 63.69; H, 3.64; N, 8.91. Found: C, 63.93; H, 3.49; N, 8.70.

The ***s*-trinitrobenzene derivative** crystallized from benzene–alcohol in shining orange needles, m. p. 172.6–173.6°.

Anal. Calcd. for $C_{25}H_{17}O_6N_3$: C, 65.93; H, 3.76; N, 9.23. Found: C, 66.20; H, 3.74; N, 9.24.

5,6-Dimethylchrysene. VI.—A solution of the ketone, IV (R = CH_3), prepared as above from 4.26 g. of acid, III (R = CH_3), in 25 cc. of benzene was refluxed with an excess of ethereal methylmagnesium bromide for thirty minutes. The alcohol thus formed was dehydrated by heating at 220° under reduced pressure and then distilled at 10 mm. The pale yellow distillate (3.60 g.) was heated with 0.89 g. of sulfur at 230–240° for one hour, when the evolution of hydrogen sulfide had ceased. The product was distilled from a small amount of zinc dust and, since the solids obtained by crystallization had an unsharp melting point (118–125°), the entire product was treated with picric acid. After fractional crystallization of the picrates from benzene–alcohol followed by chromatographic adsorption on alumina, there was obtained 1.06 g. of colorless **5,6-dimethylchrysene, VI**, m. p. 128.6–129.8°, having intense blue-violet fluorescence in ultraviolet light. If a benzene–alcohol solution of the hydrocarbon were cooled rapidly, thin plates, m. p. 128.0–129.0°, were obtained. On slow cooling needles of m. p. 128.6–129.8° separated. From other fractions of the picrates, 0.71 g. of a hydrocarbon mixture, m. p. 118–128°, was obtained and no depression of melting point was noticed on mixing in some 5-methylchrysene, m. p. 117°.

Anal. Calcd. for $C_{20}H_{16}$: C, 93.71; H, 6.29. Found: C, 93.47, 93.61; H, 6.15, 6.20.

The **picrate** crystallized from benzene–alcohol in red needles, m. p. 134.4–135.4° with decomposition.

Anal. Calcd. for $C_{26}H_{19}O_7N_3$: C, 64.33; H, 3.95; N 8.66. Found: C, 64.52; H, 3.82; N, 8.34.

The ***s*-trinitrobenzene derivative** crystallized from benzene–alcohol in bright orange needles, m. p. 158.6–159.4°.

Anal. Calcd. for $C_{26}H_{19}O_6N_3$: C, 66.52; H, 4.08; N, 8.95. Found: C, 66.66; H, 3.88; N, 9.11.

5-Ethylchrysene, V(R = C_2H_5).—No crystalline acid corresponding to III (R = C_2H_5) was isolated. A solution of 4.16 g. of acid III (R = C_2H_5) in 20 cc. of benzene was treated with 3.0 g. of phosphorus pentachloride. The acid chloride was cyclized in benzene solution using 2.0 g. of aluminum chloride, the ketone reduced, the alcohol dehydrated, and the residue dehydrogenated as above to yield a total of 1.15 g. (32%) of **5-ethylchrysene**, m. p. 88–90°. A sample purified for analysis by crystallization of the picrate and chromatographic adsorption on alumina formed colorless needles, m. p. 91.4–92.4°, having an intense blue-violet fluorescence in ultraviolet light.

Anal. Calcd. for $C_{20}H_{16}$: C, 93.71; H, 6.29. Found: C, 93.49, 93.39; H, 6.16, 6.10.

(16) Judefind and Reid, THIS JOURNAL, **42**, 1043 (1920).

The **picrate** crystallized from benzene–alcohol in red needles, m. p. 99.2–100.6°.

Anal. Calcd. for $C_{26}H_{19}O_7N_3$: C, 64.33; H, 3.95; N, 8.66. Found: C, 64.33; H, 3.61; N, 8.46.

The ***s*-trinitrobenzene derivative** crystallized from benzene–alcohol in orange rectangular prisms, m. p. 125.2–125.8°.

Anal. Calcd. for $C_{26}H_{19}O_6N_3$: C, 66.52; H, 4.08; N, 8.95. Found: C, 66.45; H, 3.82; N, 8.76.

Summary

The synthesis of 5-methylchrysene, 5-ethylchrysene, and 5,6-dimethylchrysene is described, together with a new and more generally applicable synthesis for α,γ-diphenylbutyric acid.

The recovery of a considerable amount of 1,2,3,4-tetrahydro-1-keto-2-phenylnaphthalene from the Reformatsky reaction between this ketone and ethyl α-bromobutyrate despite a large excess of reagents is noted. An explanation is offered involving reaction of the enol form of the ketone with an organozinc intermediate to produce a bromozinc enolate and ethyl butyrate. This explanation is supported by the isolation of ethyl butyrate from the reaction mixture.

COLUMBUS, OHIO RECEIVED FEBRUARY 5, 1940

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, No. 212]

The Condensation of Esters with Aromatic Hydrocarbons by Means of Aluminum Chloride

BY JAMES F. NORRIS AND PAUL ARTHUR, JR.[1]

Preliminary results of the study of the condensation of ethyl acetate and of phenyl acetate with benzene were given in a recent paper[2] from this Laboratory. The work was continued because the reaction appeared to give a new and valuable method for the preparation of aromatic ketones. When the investigation was about completed, an abstract of a German patent,[3] bearing on the subject, was published. Our results are not in accord with certain statements in the patent; these will be considered in the experimental part of this paper.

In a communication by Bowden[4] on the alkylation of benzene by esters by the Friedel–Crafts reaction one phase of the condensation is described. In our work special attention was paid to acylation and the study of the conditions to be used to produce alkylation alone or simultaneous alkylation and acylation.

A study of possible mechanisms of the reactions involved was made in order to gain information to be used as a guide in directing the syntheses. The results led to the following steps in the case of methyl acetate

(1) $CH_3COOCH_3 + AlCl_3 \xrightarrow{\text{cold}} CH_3COOCH_3.AlCl_3 \xrightarrow{\text{hot}} CH_3COOAlCl_2 + CH_3Cl$

(2) $CH_3Cl + C_6H_6 + AlCl_3 \longrightarrow C_6H_5CH_3 + C_6H_4(CH_3)_2$ etc. $+ HCl$

(3) $CH_3COOAlCl_2 + C_6H_6(C_6H_5CH_3$, etc.) $+ AlCl_3 \longrightarrow C_6H_5COCH_3 + C_6H_4CH_3COCH_3$ (etc.) $+ AlOCl$

From work to be discussed later it is probable that a third step is involved in the alkylation, namely, the formation of an intermediate which contains three components, the hydrocarbon, the alkyl chloride and aluminum chloride.

One mole of aluminum chloride dissolves in one mole of methyl acetate and forms a compound which melts at about 60°. When this was heated it was stable at 132°, decomposed moderately rapidly at 143°, and rapidly at 170°. The yield of methyl chloride isolated was 0.7 mole. The solid residue ($CH_3COOAlCl_2$) obtained after the pyrolysis of the complex made from ethyl acetate and aluminum chloride, was condensed with benzene by aluminum chloride; the yield of acetophenone was 42% of the theoretical.

When methyl acetate, toluene, and aluminum chloride were heated, the products were dimethyl- and trimethylbenzene and a 60% yield of a mixture of methyl acetophenones. Since all of the dimethyl acetophenones have not been described, it was necessary to synthesize certain isomers by methods which gave evidence in regard to structure. The product obtained contained mostly 2,4-dimethylacetophenone; a smaller amount of 4-methylacetophenone was shown to be present.

(1) From the thesis presented by Paul Arthur, Jr., in partial fulfillment of the requirements for the degree of Doctor of Philosophy, 1938.

(2) Norris and Sturgis, THIS JOURNAL, **61**, 1413 (1939).

(3) *Chem. Abs.*, **51**, 703 (1937).

(4) Everett Bowden, THIS JOURNAL, **60**, 645 (1938).

In the case of ethyl acetate, alkylation alone took place at room temperature; at 90° both alkylation and acylation occurred. By control of the temperature it was possible to obtain as the chief product of the reaction either *m*-diethylbenzene or ethyl derivatives of acetophenone.

Alkylation of benzene was effected by the use of methyl and ethyl formates. Attempts to acylate with these reagents and thus form aldehydes were not successful.

Details of Experiments

Pyrolysis of Molecular Compounds of Esters and Aluminum Chloride.—The pyrolysis was effected in a tube with a side-arm connected to a U-tube containing enough water to cover the bend and to absorb the hydrogen chloride formed. The other gases, after passing through a drying tube, entered a spiral condenser cooled by dry-ice. The condensate was collected in a graduated tube placed in a toluene-bath kept cold by two test-tubes filled with dry-ice. Any permanent gases formed were collected. The tube in which pyrolysis took place was heated by the vapor of a boiling liquid which was selected according to the temperature required.

It has been shown that the compound formed from aluminum chloride and ethyl benzoate contains its components in the molecular ratio of 1:1. One mole of aluminum chloride dissolves in one mole of methyl acetate, with the evolution of heat. The compound solidifies and begins to melt at 60°. When more chloride was added it did not dissolve in the melted complex and no appreciable amount of heat was evolved. A compound was prepared from 4.5 cc. of methyl acetate and 7.8 g. of aluminum chloride (mole ratio 1:1). No methyl chloride was formed when it was heated for fifty minutes at 110°. At 143° in fifty minutes 0.05 mole was collected. When the temperature was held at 170° for two and one-half hours the total yield of methyl chloride was 0.7 mole. Heating was continued at 184° and 220° until the evolution of hydrogen chloride ceased (0.38 mole). No acetyl chloride was found. The titration of the acid and the determination of chloride ion by precipitation gave the same results.

Since ketones are formed from esters, it appeared possible that a compound of acetyl chloride and aluminum chloride was formed along with methyl chloride as the result of pyrolysis. A search for acetyl chloride was made. Combes[5] has shown that under certain conditions acetyl chloride is converted in part by aluminum chloride into acetylacetone as the result of the loss of hydrogen chloride. The test for the ketone with ferric chloride was applied. The color produced was the same, but not so strong as that produced by a sample of acetylacetone. The behavior was tested of a mixture of acetyl chloride and aluminum chloride when heated to the temperature used in the pyrolysis. No acetyl chloride was recovered, but the product gave a test with ferric chloride. No acetylacetone was separated by using copper sulfate or dinitrophenylhydrazine. It is probable that a compound of the composition $CH_3COOAlCl_2$ is involved in the ketone synthesis, which is similar to a compound derived from benzoic acid and is the intermediate in the formation of benzophenone from the acid.

Pyrolysis of the Compound $CH_3COOC_2H_5 \cdot AlCl_3$.—The compound began to decompose slowly at 139°; in 9.7 hours 0.67 mole of ethyl chloride was obtained. At 170° there were obtained 0.5 mole in two hours and 0.85 mole in 6.3 hours.

The residue from the pyrolysis (14.1 g.) which appears to have the formula $CH_3COOAlCl_2$ was heated on a steam-bath for three hours with benzene and aluminum chloride (mol ratio 1:2:1.2, respectively). The yield of acetophenone melting at 17.5–18° was 42% of the theoretical.

Pyrolysis of the Compound $CH_3COOC_4H_9(n) \cdot AlCl_3$.—The compound has been studied.[6] It is liquid at 0°. When it was heated at 132° hydrogen chloride and a permanent gas were formed fairly rapidly. The liquid formed at 170° was shown to be *n*-butyl chloride (5%); the hydrogen chloride was 1.26 moles. The chief products were evidently butylenes and hydrogen chloride.

Pyrolysis of the Compounds Containing Methyl and Ethyl Formate and Aluminum Chloride.—The compound containing methyl formate decomposed slowly at 110°. When heated at 143°, as long as methyl chloride was formed, the yield of the latter was 88% of the theoretical. The residue when heated at 185° gave practically equivalent amounts of hydrogen chloride and carbon monoxide. The residue obtained at 143° appeared to have the same composition as the compound made from formic acid and aluminum chloride as the result of the loss of hydrogen chloride. The compound prepared in this way, when heated at 185°, yielded carbon monoxide and hydrogen chloride. This residue, obtained at 143°, should condense with benzene to give benzaldehyde, provided it behaved as the analogous residue obtained from an acetate. For this reason it was studied. Zinc chloride lowered the temperature of its pyrolysis to 140°; cuprous chloride had no effect. It did not yield an aldehyde when an attempt was made to condense it with benzene. When anhydrous formic acid was dropped into phosphorus trichloride at room temperature, a steady stream of carbon monoxide was produced.

The compound of ethyl formate and aluminum chloride gave 82% of the theoretical yield of ethyl chloride when heated at 110° for one and one-quarter hours. Subsequent heating at 184° yielded 0.93 mole of hydrogen chloride and 0.43 mole of carbon monoxide.

Alkylation of Aromatic Hydrocarbons with Esters.—The pyrolysis of compounds of esters and aluminum chloride showed that the alkyl–oxygen bond broke at a lower temperature than the acyl–oxygen bond; that the compounds which contained ethyl esters decomposed at a lower temperature than those containing methyl esters. It was shown also that one molecular quantity of aluminum chloride is used in the formation of the alkyl halide and as a result an additional mole of aluminum chloride is required for the condensation in which ketones are formed. These facts made it possible to select experimental conditions for the syntheses. The molecular ratios of the reactants used were kept constant in order to determine the influence of factors other than concentration on the products of the reactions.

(5) Combes, *Ann. chim. phys.*, (6) **12**, 207 (1887).

(6) Gault and Beloff, *Bull. soc. chim.*, (v) **5**, 295 (1938).

Ethylation of Benzene with Ethyl Acetate.—Aluminum chloride (117.3 g.) was added slowly to a mixture of 39.2 cc. of ethyl acetate and 71 cc. of benzene in a flask placed in ice water. The mixture stood at room temperature for about twenty-five hours and was shaken occasionally. After decomposition with ice, the dried product was fractionated through a V-packed column equivalent to 17 theoretical plates. There were obtained 33 cc. of benzene, 6 cc. of ethylbenzene, 16 cc. of *m*-diethylbenzene; 12.3% of the ester was converted into ethylbenzene and 51.3% into diethylbenzene. The latter was shown to be the meta isomer by comparing it and its derivatives with those of an authentic sample, obtained from the Eastman Kodak Company, which furnished details of the method used in its purification. These included fractional sulfonation of the diethylbenzene made from ethylene and benzene, recrystallization of the barium sulfonate, hydrolysis of the sulfonic acid, and distillation of the hydrocarbon. The physical constants obtained are given below: the constants of the *m*-diethylbenzene from the Eastman Kodak Company are given in parentheses and those reported in the literature in brackets: b. p. 181.6° at 751 mm. (181–182°) [180.5°]; m. p. $<-55°$ ($<-55°$) [$<-20°$]; $n^{25}D$ 1.4922 (1.4922) [1.4926]; tetrabromo derivative, m. p. 77.8–78.2° (77.8–78.2°) [74°]. Mixed melting point showed no depression. The tetrabromo derivative of *o*-diethylbenzene melts at 64.5° and that of the para compound at 112°. Benzoylbenzoic acid by condensation with phthalic anhydride, m. p. 121.5–123° (120–121°) [114–116° (uncor.)]; neutralization equivalent of acid 281.2 (theoretical 282).

These results are not in accord with the patent, previously mentioned, which states that the para isomer is formed on alkylation of an aromatic nucleus with which an alkyl group is combined. The method appears to be the best for the preparation of *m*-diethylbenzene because it does not involve a tedious treatment to remove isomers.

Agitation of the reactants during the course of the experiment affects the relative proportions of the products formed. With very little agitation 12.2% of the ester was converted into ethylbenzene, 29% into *m*-diethylbenzene, and 17.8% into triethylbenzene. In an experiment in which the reactants were stirred for eleven hours, the corresponding figures were 18.5% ethylbenzene, 48.5% *m*-diethylbenzene and 8% triethylbenzene.

Ethylation with Ethyl Formate.—The formate was condensed with benzene under the conditions used with ethyl acetate; 11.9% of the ester was converted into ethylbenzene, 24% into diethylbenzene and 23.7% into triethylbenzene. The index of refraction of the diethylbenzene was $n^{20}D$ 1.4958; that of the meta isomer is $n^{20}D$ 1.4947. Benzene was ethylated with ethyl formate under the conditions favorable for the formation of *s*-triethylbenzene. The mole ratios used were benzene 1, aluminum chloride 5, ethyl formate 3. The reagents were mixed at the temperature of an ice-bath and then slowly heated during one hour to 70°, and finally at 94° for forty minutes. The hydrocarbon obtained was distilled with steam and fractionated; only 0.5 cc. boiled between 60 and 201°. The yield of *s*-triethylbenzene, boiling at 208–209° (uncor.), was 50.5%. The index of refraction of the part boiling at 209° was $n^{25}D$ 1.4925. The value is in accord with the index of a sample of *s*-triethylbenzene purified by sulfonation, etc.

Methylation with Methyl Acetate.—An experiment was made under the condition used with ethyl acetate. No alkylation took place; the result was the same when hydrogen chloride was passed into the reactants or when they were heated at 60° for two and one-half hours. At 90–96° both alkylation and acylation occurred (see later).

Methylation with Methyl Formate.—Benzene and methyl formate yielded only 5% of toluene when condensed at room temperature. The ester was condensed with toluene. To 139.4 g. of aluminum chloride suspended in 88.4 cc. of toluene was added a mixture of 44.2 cc. of toluene and 25 g. of methyl formate (mole ratio methyl formate 1, aluminum chloride 2.5, toluene 3). To the mixture was added 5 g. of cuprous chloride. The mixture stood for 107 hours and then was heated for two periods of one-half hour each at 60° and at 80°. The products recovered were benzene 0.1 mole, toluene 1.7 moles, *m*-xylene 0.45 mole. The xylene was shown to be the meta isomer by condensing it with phthalic anhydride; the aroylbenzoic acid melted at 222–224°, which is the melting point for the compound made from *m*-xylene. This condensation appears to be a good method for preparing *m*-xylene free from its isomers.

Methyl formate was condensed with benzene under favorable conditions for the preparation of mesitylene (mol ratio: C_6H_6 1, aluminum chloride 5, methyl formate 3; time of heating was one hour at 70–85° and four hours on the steam-bath). The yield of mesitylene (b. p. 165.5–166°) was 46% of the theoretical. No benzene, toluene, or xylene was obtained.

Acylation of Aromatic Hydrocarbons by Means of Esters.—Acylation with esters requires a higher temperature than alkylation. The effect of the molecular ratio of aluminum chloride to the ester was studied in the case of methyl acetate. With the ratio 1 CH_3COOCH_3 to 0.62 aluminum chloride, the yield of ketones was 19% and with 1 CH_3COOCH_3 to 2.2 aluminum chloride, 51% of the theoretical.

Methyl Acetate and Toluene.—To a cooled mixture of 96 cc. of methyl acetate and 266 cc. of toluene, contained in a 1-liter flask provided with a return condenser and a wide tube, was added slowly 366 g. of aluminum chloride (mol ratio: 1:2:2.2, respectively). The mixture was heated on a steam-bath for two hours; it was left at room temperature for ten hours and finally heated for five and one-half hours. The product, after decomposition with ice and drying, was distilled through a column equivalent to 16 theoretical plates. The fractions up to 180° were collected at atmospheric pressure, the next at 50 mm. up to 180°, and finally at 2 mm. The moles of the products from 1 mole of methyl acetate were as follows: benzene 0.25, toluene 0.36, xylene 0.05, $C_6H_3(CH_3)_3$ 0.13, ketones 0.60; 9 cc. of high boiling liquids and 2 g. of solid materials were also obtained.

The fraction boiling at 80° was shown to be benzene by its melting point, 4.5–5°. The fraction boiling at 137–139° was condensed with tetrachlorophthalic anhydride; the melting point of the product was 206–215°, showing that it consisted principally of *m*-xylene. The fraction at 164° was nearly pure mesitylene (b. p. 165°). The crude compound prepared from it and phthalic anhydride melted at 200–211°, and after recrystallization at 210–212°, the recorded melting point is 211–212°.

That part of the ketone fraction (b. p. 135–138°) which boiled at 136° was studied. A part was treated with sodium hypochlorite. The neutralization equivalent of the acids obtained was 147.2. Since the equivalent of toluic acid is 136 and dimethylbenzoic acid 150, it appeared that the fraction examined contained about 80% of dimethylacetophenone. A sample of the mixed ketones was treated with 2,4-dinitrophenylhydrazine. Two hydrazones crystallized from the reaction mixture separately, the *p*-methyl derivative first. One compound had the same melting point (174.2–175.2° (cor.)) as the 2,4-dinitrophenylhydrazone prepared from a pure sample of 2,4-dimethylacetophenone. The quantity of hydrazone obtained showed that the original mixture of ketones contained about 80% of 2,4-dimethylacetophenone. When *p*-nitrophenylhydrazine was used, a small amount of the hydrazone of *p*-methylacetophenone was isolated. It melted at 192–193° (cor.). These results are not in accord with the patent mentioned before, which states that the ketone formed from an alkylbenzene and a simple ester is the 2,5-dialkylated ketone.

Methyl Acetate and Benzene.—The moles of reactants used were benzene 2, methyl acetate 1, aluminum chloride 2.2. The mixture was heated at 60–70° for one hour; at 70–80° for one hour, and at the reflux temperature for six and one-half hours. There was obtained a 45% yield of a mixture of ketones of which about 83% was *p*-methylacetophenone; the latter was identified by the melting point of its 2,4-dinitrophenylhydrazone and the mixed melting point of the compound and an authentic sample; the rest of the mixture was principally 2,4-dimethylacetophenone.

Ethyl Acetate and Benzene.—The mole ratio used was benzene 2; ethyl acetate 1; aluminum chloride 2.2. The mixture was heated gradually to 90° and refluxed for 2.6 hours. The yield of mixed ketones was 48%. The fraction boiling at 242–243° contained 70% *p*-ethylacetophenone; the fraction boiling at 252–262° contained 25% *p*-ethylacetophenone; the higher boiling ketone was not identified.

Phenylhydrazones Used in Identification.—Several of these derivatives, some of which have not been described, were prepared from ketones synthesized by methods that furnished evidence of structure.

4-Nitrophenylhydrazone of 2,4-Dimethylacetophenone.—The compound was prepared from a sample of the ketone, made in this Laboratory by Dr. J. N. Ingraham by condensing pure *m*-xylene with acetyl chloride. The hydrazone prepared in the usual way consisted of bright yellow crystals. The product was recrystallized from a mixture of dichloromethane and petroleum ether and melted at 154.6–154.8° (cor.). % N found, 14.9 and 14.8; theory, 14.83.

2,4-Dinitrophenylhydrazone of 2,4-Dimethylacetophenone.—After crystallization from alcohol and water, the compound was obtained as long needles that matted together; m. p. 174.2–175.2°; % N found, 16.8 and 16.8; theory, 17.07.

4-Nitrophenylhydrazone of 2,5-Dimethylacetophenone.—The ketone was prepared from *p*-xylene, acetyl chloride, and aluminum chloride. The reaction took place at 15°, with stirring for two and one-half hours, and standing at 25° for twenty minutes. That no rearrangement of the alkyl groups took place was shown by the fact that the hydrocarbon recovered was *p*-xylene which melted at 11–12°. The 4-nitrophenylhydrazone prepared from the ketone melted at 159.8–160.1° (cor.); % N found, 14.95 and 14.83; theory, 14.83. The mixed melting point of this compound with the corresponding derivative of 2,4-dimethylacetophenone (m. p. 154.4–154.8°) was 135–142°.

2,4-Dinitrophenylhydrazone of 2,5-Dimethylacetophenone.—The compound was recrystallized from alcohol; m. p. 174.2–175.2° (cor.); % N found, 17.0 and 16.9; theory, 17.07. The melting point of a mixture of this compound and the 2,4-dinitrophenylhydrazone of 2,5-dimethylacetophenone (m. p. 174.2–175.2°) was 155–162°.

2,4-Dinitrophenylhydrazone of 3,4-Dimethylacetophenone.—The ketone was prepared from *o*-xylene, acetyl chloride and aluminum chloride in the presence of carbon disulfide; the time of reaction was forty minutes at room temperature. The index of refraction of the ketone was $n^{20}D$ 1.5390 (literature 1.5388). The 2,4-dinitrophenylhydrazone of the ketone melted at 255.2–255.8° (cor.). A mixed melting point with the 2,4-dinitrophenylhydrazone of 4-methylacetophenone (258.6–259.4°) gave 245–250° with decomposition.

Summary

1. The condensations of methyl and ethyl formates and acetates with benzene and toluene by means of aluminum chloride have been investigated. At lower temperatures alkylation alone takes place; at higher temperatures the acetates yield derivatives of acetophenone, the structures of which have been determined.

2. The pyrolysis of the compounds of the esters and aluminum chloride has been studied. The first decomposition yielded alkyl chlorides with excellent yields. The residue obtained in this way from ethyl acetate gave acetophenone when it was condensed with benzene.

3. A number of new 4-nitro- and 2,4-dinitrophenylhydrazones of 2,4-, 2,5- and 3,4-dimethylacetophenones have been prepared and used in the identification of the ketones formed from methyl acetate.

CAMBRIDGE, MASS. RECEIVED DECEMBER 6, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

Monothioacetals of Galactose

BY M. L. WOLFROM AND D. I. WEISBLAT

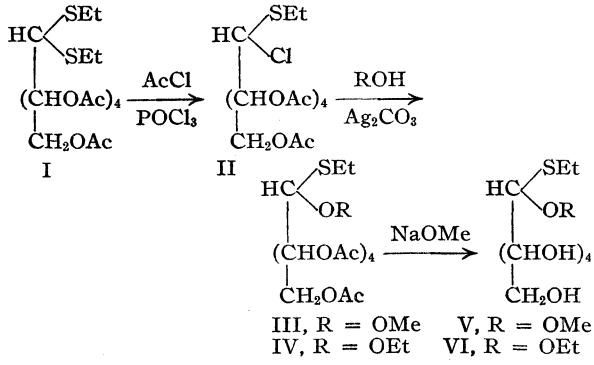
Geuther and Bachmann[1] treated the diethyl acetal of acetaldehyde with phosphorus pentachloride and obtained the 1-chloro-1-ethoxyethane (α-monochlorodiethyl ether), previously synthesized by Wurtz and Frapolli[2] from acetaldehyde, ethanol and hydrogen chloride. Blaise[3] and recently Post[4] postulated the probable formation of this same halogen compound in the reaction of acetaldehyde diethyl acetal with benzoyl chloride.

As thioacetals and acetals of the simple alcohols are available in the sugar series, we were interested in the possible extension of the above reactions to these carbohydrate derivatives. We have found that galactose dimethyl acetal reacts readily with acetyl chloride with the replacement of one methoxyl group by chlorine to form 1-chloro-1-methoxy-galactose pentaacetate. This general type of derivative is the open chain analog of the well-known acetohalogen sugars. Such a derivative had been prepared in the arabinose series by Montgomery, Hann and Hudson[5] through halogen replacement of the 1-acetate in the two isomeric *aldehydo*-1-methoxy-arabinose pentaacetates obtained by the acetolysis of the methyl arabinopyranosides. A corresponding galactose derivative had been obtained in this Laboratory[6] by halogen replacement of the 1-acetate in 1-ethoxy-galactose hexaacetate obtained by the acetylation of *aldehydo*-galactose pentaacetate ethyl hemiacetal.

We have found that galactose diethyl mercaptal pentaacetate (I) reacts with a mixture of acetyl chloride and phosphorus oxychloride to replace one ethylmercapto group with chlorine. The resulting *aldehydo*-1-chloro-1-ethylmercapto-galactose pentaacetate (II) reacts with methanol or ethanol to produce the monothioacetal pentaacetate (III and IV) from which the monothioacetals (V and VI) can be obtained by saponification. No evidence was obtained for the presence of more than one form of these derivatives in any of our reactions, although such a result is a possibility on stereochemical grounds. The halogen in the above halogen compounds is extremely reactive and the halogen derivatives are difficult to obtain in pure form. Montgomery, Hann and Hudson[5] likewise report the same experience with the arabinose derivative which they also used for acetal synthesis.

These monothioacetals of galactose and their pentaacetates are beautifully crystalline substances and are formed in high yield from the chloro compound. Such mixed oxygen, sulfur acetals have been postulated by Green and Pacsu[7] as a probable intermediate in the reaction of sugar mercaptals with mercuric chloride in alcoholic solution in the presence of mercuric oxide.

Work is in progress in this Laboratory on the extension of these reactions to other sugar structures and on the study of the behavior of the monothioacetals under ring-closure conditions.



Experimental

***aldehydo*-1-Chloro-1-ethylmercapto-*d*-galactose Pentaacetate (II).**—*d*-Galactose diethyl mercaptal pentaacetate[8] (30 g.) was dissolved in 20 cc. of freshly distilled acetyl chloride and the solution heated to boiling. Phosphorus oxychloride (10 cc.) was added to the boiling solution under reflux until a reddish-brown coloration began to develop (two to five minutes). The flask was then stoppered, quickly immersed in an ice-bath and the whole placed in an icebox. Crystallization in rosets of small needles began in a few hours and after standing overnight at icebox temperature the crystals were removed by filtration and washed thoroughly with a mixture of petroleum ether (5 parts) and ether (1 part). This crude material was re-

(1) A. Geuther and A. Bachmann, *Ann.*, **218**, 38 (1883).
(2) A. Wurtz and A. Frapolli, *Ann. chim. phys.*, [3] **56**, 139 (1859).
(3) E. E. Blaise, *Compt. rend.*, **140**, 66 (1905).
(4) H. W. Post, *J. Org. Chem.*, **1**, 231 (1936).
(5) Edna M. Montgomery, R. M. Hann and C. S. Hudson, THIS JOURNAL, **59**, 1124 (1937).
(6) M. L. Wolfrom and M. Konigsberg, *ibid.*, **60**, 288 (1938).
(7) J. W. Green and E. Pacsu, *ibid.*, **60**, 2288 (1938).
(8) M. L. Wolfrom, *ibid.*, **52**, 2464 (1930).

crystallized rapidly from benzene by the addition of anhydrous ether; yield 13–18 g., m. p. 108–111°. The material at this stage of purity still decomposed rapidly and evolved ethyl mercaptan. After two more recrystallizations from four parts of benzene by the addition of approximately seven parts of dry ether, pure material was obtained; yield 7–7.5 g., m. p. 111–113°, spec. rot. −27° (22°, *c* 3.7, abs. $CHCl_3$).[9] Due to the instability of the compound, the constants recorded are probably not quite the maximum.

In absolute chloroform the rotation changed slowly in the *dextro* direction. In one experiment the specific rotation was −13° after fifteen hours. At this point the solution had darkened somewhat and an odor of ethyl mercaptan was distinctly noticeable. It is believed that this mutarotation represents decomposition, probably by reaction with traces of moisture.

The substance was readily soluble in the common organic solvents but was practically insoluble in cold ether, petroleum ether and water. It reduced Fehling's solution and evolved ethyl mercaptan on boiling with dilute alkali or acid. The substance was found to be stable only when kept in a vacuum desiccator over soda lime. An investigation of mother liquors yielded no other definite substance or any methanol reaction product different from that described below (III).

Anal. Calcd. for $C_8H_{12}O_5(CH_3CO)_5SCl$: Cl, 7.5; saponification value (six equivalents), 12.8 cc. 0.1 *N* NaOH per 100 mg. Found: Cl, 6.9; saponification value, 12.9 cc.

d-Galactose S-Ethyl O-Methyl Monothioacetal Pentaacetate (III).—*aldehydo*-1-Chloro-1-ethylmercapto-*d*-galactose pentaacetate (II, 10 g.) was added to a previously cooled suspension of 20 g. of Drierite (anhydrous calcium sulfate) and 10 g. of silver carbonate in 50 cc. of anhydrous methanol in a three-necked flask equipped with a mercury-sealed mechanical stirrer and a drying tube. The reaction was then allowed to run at room temperature for approximately sixteen hours. The inorganic salts were removed by filtration through a bed of Super-cel (Johns-Manville) and the clear, colorless filtrate was made just opalescent with water. The product crystallized on standing at icebox temperature; yield 5.6 g., m. p. 114–117°, spec. rot. +42.5° (abs. $CHCl_3$). Pure material was obtained on recrystallization (92–95% return) from five parts of hot methanol containing a few drops of pyridine; m. p. 119–120°, spec. rot. +42.5° (19°; *c*, 3.3; abs. $CHCl_3$).

The substance crystallized in beautiful diamond-shaped plates and was readily soluble in chloroform, ether, acetone and warm alcohol but was practically insoluble in water and petroleum ether. It showed no reduction toward hot Fehling's solution and evolved ethyl mercaptan on heating with dilute hydrochloric acid.

Anal. Calcd. for $C_9H_{15}O_6(CH_3CO)_5S$: S, 6.87; CH_3CO, 10.7 cc. 0.1 *N* NaOH per 100 mg. Found: S, 7.08; CH_3CO, 10.8 cc.

d-Galactose Diethyl Monothioacetal Pentaacetate (IV).—This substance was synthesized from *aldehydo*-1-chloro-1-ethylmercapto-*d*-galactose pentaacetate (II, 10 g.) exactly as described for the synthesis of the corresponding methoxy compound (III) except that 60 cc. of absolute ethanol was substituted for the methanol. The product was isolated from the reaction mixture in the same manner; yield 5.3 g., m. p. 102–102.5°, spec. rot. +50° (abs. $CHCl_3$). Pure material was obtained on recrystallization (93–95% return) from six parts of hot absolute ethanol containing a few drops of pyridine; m. p. 104–105°, spec. rot. +50° (20°; *c*, 3.5; abs. $CHCl_3$).

The substance crystallized in beautiful prisms and exhibited properties and solubilities similar to those of the corresponding methoxy compound (III).

Anal. Calcd. for $C_{10}H_{17}O_6(CH_3CO)_5S$: S, 6.67; CH_3CO, 10.4 cc. 0.1 *N* NaOH per 100 mg. Found: S, 6.62; CH_3CO, 10.4 cc.

d-Galactose S-Ethyl O-Methyl Monothioacetal (V).—*d*-Galactose S-ethyl O-methyl monothioacetal pentaacetate (III, 8.5 g.) was dissolved at room temperature in 20 cc. of anhydrous methanol, 4 cc. of 0.2 *N* sodium methylate added and the solution cooled rapidly in an ice-bath. Crystallization occurred immediately upon shaking. After a few hours of standing the crystalline material was removed by filtration and washed thoroughly with ether; yield 4.6 g. (98%), m. p. 144–146°, spec. rot. +48° (H_2O). Pure material was obtained on recrystallization (90–95% return) from six parts of hot anhydrous methanol; m. p. 146–147°, spec. rot. +50° (20°; *c*, 3; H_2O).

The substance crystallized in the form of elongated prisms. It showed no reduction toward hot Fehling's solution but on acid hydrolysis ethyl mercaptan was liberated and the hydrolyzate was reducing. The material was soluble in water and warm methanol and was practically insoluble in ether, acetone and chloroform.

Anal. Calcd. for $C_9H_{20}O_6S$: C, 42.13; H, 7.87; S, 12.51. Found: C, 41.86; H, 7.70; S, 12.28.

d-Galactose Diethyl Monothioacetal (VI).—*d*-Galactose diethyl monothioacetal pentaacetate (IV, 9.6 g.) was dissolved in 30 cc. of warm ethanol and to the warm solution 5 cc. of 0.2 *N* sodium methylate was added. The solution was immediately immersed in an ice-bath and crystallization began immediately. After a few hours of standing the material was removed by filtration and washed with ether; yield 5.2 g. (93%), m. p. 155–156°, spec. rot. +53° (20°; *c*, 3; H_2O). The product was pure and identical constants were obtained on material after four recrystallizations from 14 parts of hot absolute ethanol from which it could be obtained in 94% return.

The substance crystallized in elongated prisms exhibiting a beautiful pearly luster and showed properties and solubilities similar to those of the corresponding methoxy compound (V).

Anal. Calcd. for $C_{10}H_{22}O_6S$: S, 11.86. Found: S, 11.82.

***aldehydo*-1-Chloro-1-methoxy-*d*-galactose Pentaacetate.**—*d*-Galactose dimethyl acetal pentaacetate[10] (1 g.) was dissolved in 3.5 cc. of boiling, freshly distilled acetyl chloride and the stoppered container placed in the icebox, whereupon the product crystallized. After several hours the product was removed by filtration and washed with ether; yield 0.9 g., m. p. 140–145°. Pure material was obtained on recrystallization from dry benzene by the addi-

(9) All specific rotations are recorded to the D-line of sodium light; 22° is the temperature; *c* is the concentration in g. per 100 cc.

(10) M. L. Wolfrom, L. J. Tanghe, R. W. George and S. W. Waisbrot, THIS JOURNAL, **60**, 132 (1938); H. A. Campbell and K. P. Link, *J. Biol. Chem.*, **122**, 635 (1938).

tion of ligroin; m. p. 155–156°; spec. rot. −38° ⟶ +15° (25°; *c*, 5; abs. $CHCl_3$, 24 hrs.); spec. rot. −53° ⟶ −42.5° (26°; *c*, 5; dry benzene; 10 hrs.).

Anal. Calcd. for $C_7H_{10}O_6(CH_3CO)_5Cl$: Cl, 8.04; saponification value (six equivalents), 13.6 cc. 0.1 *N* NaOH per 100 mg. Found: Cl, 7.96; saponification value, 13.7 cc.

We are indebted to Mr. John Walker (W. P. A. Project 18062) for assistance rendered in the analytical determinations. We also acknowledge the assistance of Mr. Irving Auerbach (N. Y. A. Project O. S. U. 167).

Summary

1. *aldehydo*-1-Chloro-1-methoxy-*d*-galactose pentaacetate was synthesized by the action of acetyl chloride upon *d*-galactose dimethyl acetal pentaacetate.

2. *aldehydo*-1-Chloro-1-ethylmercapto-*d*-galactose pentaacetate (II) was synthesized by the action of a mixture of acetyl chloride and phosphorus oxychloride upon *d*-galactose diethyl mercaptal pentaacetate.

3. *d*-Galactose diethyl monothioacetal and *d*-galactose S-ethyl O-methyl monothioacetal and their pentaacetates have been synthesized from II.

COLUMBUS, OHIO RECEIVED JANUARY 26, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

The Thermal Decomposition of Diacetyl

BY W. D. WALTERS

In a previous investigation[1] the rate of decomposition of diacetyl in the range 424–470° was obtained by pressure measurements and the products of the reaction analyzed. Since diacetyl can be determined quantitatively by conversion to dimethylglyoxime, which, on addition of a nickel salt, precipitates as nickel dimethylglyoxime, it is possible to analyze for the amount of diacetyl remaining after the decomposition has been allowed to proceed for a definite time. The present work was undertaken to investigate the kinetics of the decomposition by this method, thereby avoiding any assumptions regarding the relation between the pressure increase and the amount of decomposition. The effect of propylene on the rate of decomposition and the variation of the ketene concentration during the decomposition also were studied.

Experimental

The diacetyl, obtained from the Eastman Kodak Company, was dried over calcium sulfate and purified by four fractional distillations under vacuum, the middle two-thirds being used for each subsequent operation. The diacetyl used in this investigation was analyzed quantitatively, as indicated later, and found to be pure within the limits of error of the method, ±0.1%. The diacetyl was protected from light and between runs kept at −80°. The propylene, obtained from the Ohio Chemical Company, was of 99.5% purity.

The cylindrical Pyrex vessel, 75 × 120 mm., was contained in a furnace similar in design to the one previously used.[1] By means of a chromel–alumel thermocouple located at the center of the reaction vessel, the temperature was determined to within 0.1°. A temperature control of ±0.25° was obtained by causing light reflected from the mirror of a galvanometer in the thermocouple-potentiometer circuit to fall on a photoelectric cell, which controlled additional heating current. All thermocouples were standardized at the boiling point of sulfur and the absolute accuracy of the temperatures measured should be at least ±0.5°. In runs 29–50 inclusive, from which the activation energy was determined, a new thermocouple, standardized before use at the sulfur boiling point and after use against a standard thermocouple, was used every day.[2]

In order to obtain a pressure of diacetyl in the reaction vessel higher than its vapor pressure at room temperature, a small side arm was connected to the line leading from the storage bulb to the reaction vessel. This T-section was separated by a stopcock I from the reaction vessel and separated by another stopcock II from the line leading to the storage bulb. To introduce a sample into the reaction bulb, stopcock I was closed and stopcock II opened. Using dry-ice–acetone mixture the desired amount of diacetyl was condensed in the lower part of the side arm. After stopcock II was closed and I opened, the dry-ice-bath was replaced by a heated liquid-bath, vaporizing the diacetyl within fifteen seconds. The external tubing adjacent to the reaction bulb was heated with resistance wire to approximately 85° to prevent condensation of diacetyl. Stopcocks I and II which were also heated were "no-lube" stopcocks ground for high vacuum, and to these it was necessary to apply only a small amount of high vacuum grease. The diacetyl storage bulb was fitted with a small stopcock and ground glass joint so that it could be removed, the grease wiped off the

(1) Rice and Walters, *J. Chem. Phys.*, **7**, 1015 (1939).

(2) Roeser and Wensel, *Bur. Standards J. Research*, **14**, 277 (1935).

joint with ether, and the bulb weighed without admitting air. These weighings were reproducible to within at least 0.4 mg. To ensure that no trace of air entered the reaction bulb, the diacetyl was outgassed at −80° in the storage bulb and again in the side arm before every run. Moreover, blank determinations showed that under the conditions used no diacetyl was lost. In the runs with propylene the same procedure was followed except that the desired amount of propylene was placed in the furnace prior to the introduction of the diacetyl.

Before using a new reaction vessel, or after contact with air, it was flushed out at an elevated temperature with several charges of diacetyl, one of which was allowed to remain in the vessel overnight. A similar treatment was given the packed bulb, which was filled with thin-walled Pyrex tubes. The reaction bulb was evacuated to a pressure less than 10^{-3}–10^{-4} mm. before every run.

After a definite time in the reaction vessel, the products of the reaction, as well as diacetyl, were removed by expansion into a condensing apparatus consisting of two long spirals of 8-mm. tubing, a trap fitted with a ground glass joint, and a U-tube in series, all of which could be immersed in a dry-ice–acetone mixture. Since undecomposed diacetyl, which is readily condensable, represented the major portion of the gas in most of the runs, about 85% of the charge could be removed within a few seconds. Then after forty seconds the remainder of the gas in the reaction bulb was led through the condensing apparatus by connecting the U-tube to the pumping system. At −80° all the diacetyl condensed out and the permanent gases and ketene were removed. No diacetyl could be detected in the effluent gases. By noting the pressure in the reaction vessel during removal, a correction could be applied for the decomposition occurring as the charge was being removed. This usually corresponded to about twenty seconds' additional heating. All the diacetyl was distilled into the removable trap, which was then taken off and kept at −80° while a solution of hydroxylamine hydrochloride and nickel chloride was added. Then this bulb was fitted with a ground glass cap and allowed to warm up to 0°. The rest of the analysis for diacetyl was a modification of the method described by Schmalfuss and Rethorn.[3] To precipitate quantitatively any nickel dimethylglyoxime remaining in solution after the first filtration, a second period of heating of the filtrate with simultaneous evaporation and subsequent addition of ammonium hydroxide was necessary.

To follow the reaction and determine the time of removal, pressure measurements were made using a heated click gage calibrated before and after every run. The volume of the click gage together with external tubing amounted to about 1% of the total volume. The extrapolated and calculated initial pressures ordinarily agreed to within 1%.

The determination of ketene was accomplished by its reaction with water to form acetic acid, which could be titrated with dilute alkali. The gases from the reaction vessel were removed by expansion into an evacuated 2-liter bulb, which was connected to the apparatus by a ground glass joint so that it could be rotated. At the time the gases entered, ice at −80° was contained in a finger attached to the bulb. By quickly melting the ice and rotating the bulb, the water, which ran into the bulb, would cover a large part of the inner surface of the bulb, thus facilitating the reaction between the ketene and the water. In the presence of diacetyl an excess of alkali must be avoided, since in alkaline solutions reactions involving diacetyl apparently destroy a portion of the alkali. However, with continuous stirring the titration of acetic acid in the presence of diacetyl to the brom thymol blue end-point with dilute alkali could be used satisfactorily. Blank determinations using standard acetic acid and diacetyl showed that a small correction of about 1% was necessary.

(3) Schmalfuss and Rethorn, *Z. Untersuch. Lebensm.*, **70**, 233 (1935).

Results

To determine whether diacetyl undergoes some reaction at low temperatures, a few preliminary experiments with initial pressures in the neighborhood of 150 mm. were made at 114, 242, 304, and 346° with reaction times of sixty-six minutes or more. Within the limits of experimental error no reaction could be detected either from the pressure measurements or from the analyses for diacetyl. The results of experiments at higher temperatures where decomposition does occur are given in Table I. The majority of runs were carried to only small amounts of decomposition, 20% or less, so as to avoid as much as possible any interference by the products. The data from the runs at 408° with initial pressures from 147 to 287 mm. indicate that the fraction decomposed within a certain time is practically independent of the initial pressure. Since similar results over a wider range of initial pressures were obtained in the previous investigation using pressure measurements, first order constants were calculated for all the runs and they are given in the last column of Table I.

In the runs near 418 and 436° which were carried to larger amounts of decomposition, the first order constants decrease as the percentage decomposition increases, indicating that probably the reaction is complex and inhibited to some extent by the products. From the measured pressure increases and the amounts of diacetyl disappearing, it was possible to correlate the pressure increase with the fraction of diacetyl decomposed at 418 and 436°, as shown in Fig. 1. These curves could then be used to transform the pressure measurements during a run into percentages of decomposition. During a single run at either of these temperatures, although the first order

TABLE I

DECOMPOSITION OF DIACETYL

Run	Temp., °C.	Time, sec.	P_0, mm.	$\Delta P/P_0$, %	Diacetyl in bulb, g.	Diacetyl decompn. (anal.), %	$k_{1st\ order} \times 10^5$, sec.$^{-1}$
			Unpacked Bulb				
42	383.1	24205	198.3	20.1	0.2086	17.4	0.788
49	383.1	23850	201.7	19.1	.2121	17.4	.802
39	383.1	23905	210.5	19.6	.2225	16.6	.758
46	391.5	13410	172.9	20.0	.1786	16.6	1.36
31	391.8	13355	202.7	20.5	.2104	17.6	1.45
35	398.2	8070	204.8	20.6	.2102	16.2	2.19
19	399.1	7280	218.0	19.6	.2236	16.7	2.51
20	399.1	3880	230.1	11.0	.2372	9.4	2.53
36	407.1	4310	213.7	21.2	.2156	15.4	3.87
12	408.0	7750	147.2	34.7	.1499	29.8	4.56
21	408.0	4330	169.8	23.0	.1715	17.7	4.50
18	408.0	4670	197.8	24.5	.2014	19.3	4.59
15	408.0	7630	210.5	34.4	.2141	29.2	4.53
22	408.0	4360	287.0	22.9	.2890	18.3	4.63
47	417.7	10320	218.5	69.0	.2161	53.6	7.44
48	417.7	21650	195.7	100.1	.1935	74.3	6.27
50	417.7	36505	160.1	119.4	.1572	85.9	5.36
32	418.0	1895	188.1	21.5	.1866	15.5	8.92
33	418.0	4170	209.6	38.3	.2063	29.0	8.21
38	425.6	1160	196.8	22.3	.1921	15.7	14.7
37	425.6	1100	226.4	21.1	.2208	14.9	14.6
40	435.8	577	213.6	22.6	.2042	16.0	30.1
41	435.8	628	198.3	23.4	.1892	16.9	29.5
23	435.9	760	213.4	28.1	.2004	21.1	31.2
24	435.9	1965	209.1	55.3	.1965	41.8	27.5
25	435.9	3885	237.6	80.2	.2256	60.4	23.9
29	436.2	10855	216.4	124.0	.2043	84.6	17.3
30	436.2	23460	212.2	148.8	.2028	94.9	12.7
			Packed Bulb[a]				
45	383.1	22635	192.1	20.1	.1545	19.2	0.943
44	398.2	8055	192.4	20.2	.1508	18.3	2.51
43	425.5	1180	208.5	21.5	.1571	15.3	14.1

[a] Surface to volume ratio increased eighteen-fold.

constants fall off as the reaction proceeds, the decrease from the initial value does not exceed 5% until more than 25% of the diacetyl has decomposed. However, to fit the experimental results fairly satisfactorily over the whole decomposition, a 1.6 order would be required at 436° and a 1.5 order at 418°.

The results from experiments on the packed bulb with the surface to volume ratio increased by a factor of 18 are also shown in Table I. The rate at 425.5°, although somewhat slower, is essentially in agreement with the rate in the unpacked bulb. At the lower temperatures the rate is slightly faster than the rate in the unpacked bulb, but even at the lowest temperature, 383.1°, where the heterogeneous reaction would be expected to become more important, the rate in the packed bulb is only 20% greater than the rate in the unpacked bulb, indicating about 1% of heterogeneous reaction.

The activation energy was obtained, as shown in Fig. 2, from runs with initial pressures near 200 mm. in which the amount of decomposition was low and approximately constant, averaging about 16%. This procedure will tend to eliminate any errors arising from the falling off of the rate constants as the reaction proceeds, since, as already mentioned, this effect is not appreciable until more than 25% decomposition has occurred. Using the value of 63,200 cal. for the activation energy, the reaction rate constant can be expressed as

$$k = 8.7 \times 10^{15} e^{-63200/RT}\ \text{sec.}^{-1}$$

It is known that ketene is produced during

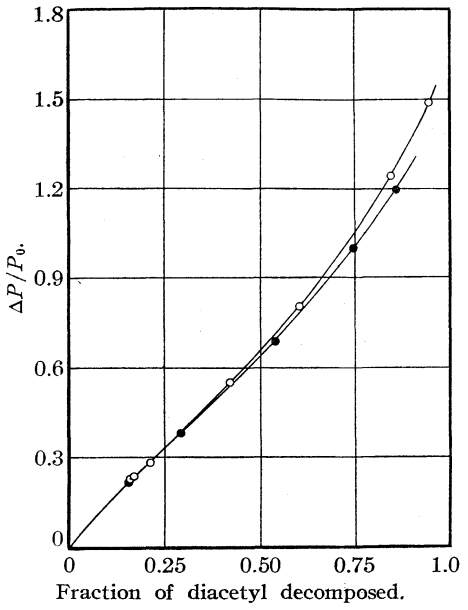


Fig. 1.—Plot of pressure increase against fraction of diacetyl decomposed: ●, 418°; ○, 436°.

the decomposition of diacetyl,[1,4] and the reaction which has been proposed for its formation is

$$CH_3COCOCH_3 \longrightarrow CH_4 + CO + CH_2{=}CO$$

Assuming the correctness of this equation, a comparison of the pressure increases in Table I with the amounts of diacetyl decomposed indicates that polymerization of the ketene is occurring. Moreover, the rise of the curves in Fig. 1 near the end of the decomposition points to the presence of an intermediate which decomposes with an increase in volume. Apparently ketene undergoes decomposition as well as polymerization.[5] However, it is uncertain whether the polymerization and the decomposition are competing reactions, or, as Hurd and Williams[6] suggest, the polymerization to acetylketene occurs first, followed by the decomposition of the acetylketene. In any case, it is to be expected that if diacetyl does decompose according to the equation given above, the yield of ketene will increase as the percentage of diacetyl decomposed decreases. The results of the analyses for ketene are shown in Table II and Fig. 3. The percentages of decomposition were obtained from pressure increases using the data shown in Fig. 1 and Table I.

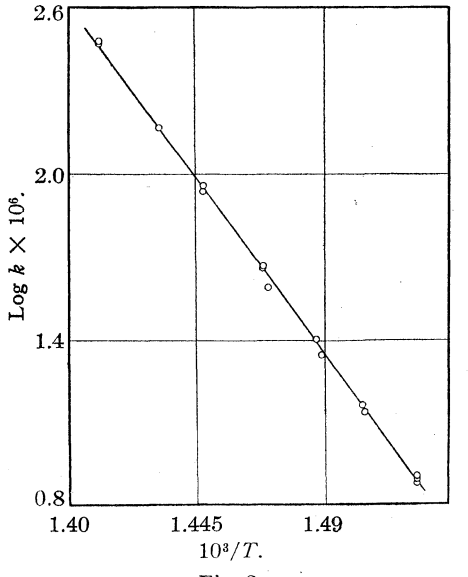


Fig. 2.

(4) Hurd and Tallyn, THIS JOURNAL, **47**, 1779 (1925).

TABLE II

KETENE PRESENT DURING DIACETYL DECOMPOSITION

P_0, mm.	Time, sec.	$\Delta P/P_0$, %	Diacetyl decompn. (calcd.), %	$P_{ket.}/P_0$, %	Ketene yield, %
		Temp. 436°			
214.1	327	12.2	8.6	5.8	67
202.3	609	23.4	16.8	8.7	52
192.4	1965	57.3	43.2	12.0	28
215.5	3850	82.6	62.0	10.0	16
212.5	10840	122.5	83.5	6.5	7.8
211.5	23400	144.3	93.3	4.5	4.8
		Temp. 408°			
204.7	1140	6.1	4.2	2.8	67
195.6	2340	12.2	9.0	4.0	44

Although the highest yield of ketene at 436° was found to be 67% at 8.6% decomposition, the yield of ketene is increasing rapidly and will presumably extrapolate to some value close to 100% at zero decomposition. At the lower tem-

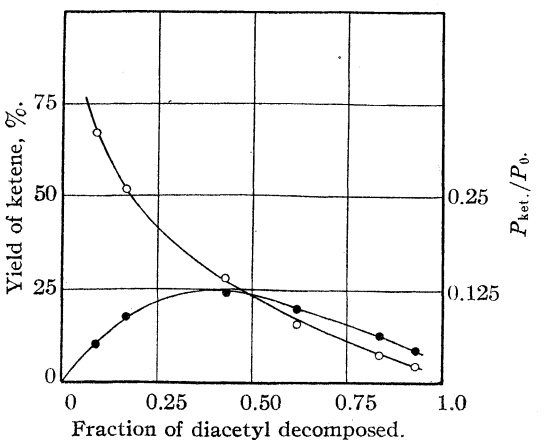


Fig. 3.—Ketene present during the decomposition of diacetyl at 436°: ●, $P_{ket.}/P_0$; ○, % yield of ketene.

(5) Williamson, *ibid.*, **56**, 2216 (1934).

(6) Hurd and Williams, *ibid.*, **58**, 962 (1936).

perature for the same percentage decomposition a somewhat smaller yield of ketene was obtained. In this connection, it can be seen from the data in Table I and Fig. 1 that as the temperature decreases the pressure increase corresponding to a given amount of decomposition of diacetyl decreases. This fact together with the smaller yield of ketene at the lower temperature may be explained by the increasing importance of the polymerization of ketene as the temperature decreases.

Inhibition by Propylene.—For a number of chain reactions it has been demonstrated that unsaturated compounds, particularly propylene[7] and also ethylene,[8] inhibit the decomposition. In cases where nitric oxide is not satisfactory as an inhibitor, such as the decompositions of aldehydes and ketones, inhibition by propylene has been regarded as an indication of a chain reaction. Therefore, the effect of propylene on the decomposition of diacetyl was investigated and the results of successive runs with and without propylene are shown in Table III.

TABLE III

INHIBITION BY PROPYLENE AT 418°

Initial pressures, mm. P_{Ac_2}	$P_{C_3H_6}$	Time, sec.	$\Delta P/P_{Ac_2}$	Diacetyl decompn. (anal.), %	$k_{1st\ order} \times 10^5$, sec.$^{-1}$
167.7	100.6	1915	15.0	..	5.97[a]
164.1	0	1915	22.0	..	9.23[a]
195.9	99.0	1915	15.5	10.7	5.92
191.0	0	1910	21.0	15.0	8.51
193.6	150.1	1920	14.4	10.3	5.66
188.1	0	1895	21.5	15.5	8.92

[a] Calculated from pressure increases instead of analyses.

The first two runs, on which only pressure measurements were made, indicated that propylene was definitely an inhibitor. However, to avoid the possibility that the slower pressure increase might be due to some cause other than the slower decomposition of diacetyl, analyses for the amount of diacetyl present, as well as pressure measurements, were carried out in the succeeding runs. For comparison the results of run 32 which had been made earlier are given in the last line of the table. The analytical results, which show that the rate of decomposition is approximately 35% slower in the presence of 150 mm. of propylene, are in agreement with the pressure measurements.

(7) Rice and Polly, *J. Chem. Phys.*, **6**, 273 (1938); Echols and Pease, THIS JOURNAL, **61**, 1024 (1939).

(8) Fletcher and Rollefson, *ibid.*, **58**, 2129. 2135 (1936); Staveley, *Proc. Roy. Soc.* (London), **162A**, 557 (1937).

Discussion

On the basis of the inhibition with propylene and also the kinetics of the ordinary decomposition, it would appear that the decomposition of diacetyl is probably a chain reaction. Moreover, the fact that small amounts of diacetyl can promote the chain decomposition of other compounds,[9] such as diethyl ether, acetaldehyde, and acetone, gives evidence that free radicals are produced when diacetyl decomposes. Although the experimental results do not exclude the possibility that some decomposition occurs through intramolecular rearrangement, it is probable that the major portion of the decomposition is a chain reaction. Therefore, as in the previous investigation, the following simplified chain mechanism for the decomposition of diacetyl, designated by M_1, will be assumed.

$$M_1 \longrightarrow 2R_1 \quad (1)$$

$$R_1 + M_1 \longrightarrow R_1H + R_2 \quad (2)$$

$$R_2 \longrightarrow R_1 + M_2 \quad (3)$$

$$R_1 + R_2 \longrightarrow R_1R_2 \quad (4)$$

Under conditions where the amount of decomposition according to reaction (1) can be neglected in comparison with the chain decomposition, the rate of decomposition has been shown to be[10]

$$\frac{d(M_1)}{dt} = -\sqrt{\frac{k_1k_2k_3}{k_4}}(M_1) \quad (I)$$

In the presence of an inhibitor, such as propylene, which acts by removal of radicals R_1[11]

$$R_1 + M_3 \longrightarrow X \quad (5)$$

the rate equation[12] becomes

$$\frac{d(M_1)}{dt} = -\left[\left(\frac{k_1k_2k_3}{k_4}(M_1)^2 + \frac{k_5^2k_3^2}{16k_4^2}(M_3)^2\right)^{1/2} - \frac{k_5k_3}{4k_4}(M_3)\right] \quad (II)$$

That unsaturated compounds are present in the products was shown in the previous investigation, in which the unsaturates were determined as a group including ethylene. From the retarding effect of propylene, these unsaturated products would be expected to exert an inhibiting influence. If the inhibitor, M_3, in reaction (5) can be identified with one of the products which increases as the amount of decomposition increases, the rate of reaction during a single run would reduce to

$$dx/dt = (k_A^2(1-x)^2 + k_B^2x^2)^{1/2} - k_Bx \quad (III)$$

(9) Rice and Walters, unpublished results.

(10) Rice and Herzfeld, THIS JOURNAL, **56**, 284 (1934).

(11) For discussion of possible mechanisms for the removal of radicals by propylene, see Ref. 7.

(12) This equation is similar to equation (36) derived by Rice and Polly.

where x is the fraction decomposed and k_A and k_B are constants. At low percentages of decomposition equation III will approach the value given in equation I. Actually the experimental results during a single run at 418 or 436° can be expressed to within 5% by an empirical equation of the above type. This, of course, is a necessary, but not a sufficient, condition to prove the validity of the above equations. The deviation is greatest near the beginning where the rate does not fall off as rapidly as would be predicted from the equation.

Comparison of the fractional times from the pressure measurements for runs at 436° (with initial pressures near 200 mm.) shows that the rates of decomposition in the earlier work[1] are on the average about 9% slower than those obtained in the present study. Most of this difference may be due to a slight difference in temperature scales since a variation of 1° causes a change of approximately 7% in the rate. The present value of 63.2 kcal. for the activation energy is almost within the limits of experimental error of the value 66.5 ± 3 kcal. obtained previously at higher temperatures by pressure measurements, corrected for the change in the pressure increase with temperature. At present it is not possible to state whether the difference is due in part to an increase of activation energy with temperature or is entirely the result of the fact that different methods were used to measure the rate. Although the frequency factor of 8.7×10^{15} is somewhat lower than the earlier value, it is still higher than that found in most decompositions, one outstanding exception being azomethane[13] with a frequency factor of 3.5×10^{16}.

Assuming that expression (1) is correct, a high frequency factor might be due to a high frequency factor for one or more of the rate constants in the numerator, or to a small frequency factor for a rate constant in the denominator. On the basis of the Eyring theory[14] of absolute reaction rates, a high frequency factor for a rate constant in the numerator would result if the reaction involved a large entropy of activation.

That there is restricted rotation around the bond joining the two carbonyl groups in diacetyl has been shown by Zahn[15] using dipole measurements, and a similar effect might be expected in a radical with adjacent carbonyl groups. In the detailed scheme[1] for the decomposition of diacetyl

$$CH_3COCOCH_3 \longrightarrow 2CH_3CO \quad (1')$$

or

$$\longrightarrow CH_3 + CH_3COCO \quad (1'')$$

$$CH_3CO \longrightarrow CH_3 + CO \quad (1'a)$$

$$CH_3COCO \longrightarrow CH_3 + 2CO \quad (1''a)$$

$$CH_3 + CH_3COCOCH_3 \longrightarrow CH_4 + CH_2COCOCH_3 \quad (2')$$

$$CH_2COCOCH_3 \longrightarrow CH_2{=}CO + CH_3CO \quad (3')$$

$$CH_3 + CH_2COCOCH_3 \longrightarrow CH_3CH_2COCOCH \quad (4')$$

reactions (3′) and (1′), assuming for the moment that (1′) is the primary reaction, will involve the breaking of the bond joining the carbonyl groups. In both of these reactions a contribution to the entropy of activation would result from the free rotation around this bond in the activated complex. However, with a reasonable estimate of the potential barrier from the dipole data, the entropy of activation, using Pitzer's values,[16] although appreciable, does not appear to be sufficient to account entirely for the high experimental frequency factor. By analogy with acetone,[17] any entropy of activation corresponding to free rotation of the methyl groups in the activated complex probably would be small. Moreover, other reasons for a high frequency factor in a chain reaction[18] do not seem applicable to the decomposition of diacetyl.

In trying to decide whether reaction (1′) or reaction (1″) is more probable, an attempt was made to estimate the strength of the carbon–carbon bond joining the two acetyl groups using the heats of combustion of diacetyl,[19] acetone[20] and ethane.[21] The energy necessary to dissociate diacetyl into two acetyl groups was found to be $A + (A - E) - 7$ with a possible error of ±6 kcal., where A is the energy of dissociation of acetone into a methyl and acetyl radical, and E, the energy of dissociation of ethane into two methyl radicals. On account of the variations in the values assigned by different investigators to these carbon–carbon bonds, an attempt to evaluate numerically the above expression at the present time does not seem justified. However, unless there is a large difference in the carbon–carbon bond in acetone and ethane, the middle carbon–bond in diacetyl will have a value near that of acetone, in other words, approximately the strength of an ordinary single bond. On the

(13) Taylor and Jahn, *J. Chem. Phys.*, **7**, 470 (1939).
(14) Eyring, *ibid.*, **3**, 107 (1935).
(15) Zahn, *Phys. Rev.*, **40**, 291 (1932).
(16) Pitzer, *J. Chem. Phys.*, **5**, 469 (1937).
(17) Schumann and Aston, *ibid.*, **6**, 485 (1938).
(18) Rice and Herzfeld, *ibid.*, **7**, 673 (1939).
(19) Landrieu, *Compt. rend.*, **142**, 580 (1906).
(20) Emery and Benedict, *Am. J. Physiol.*, **28**, 307 (1911).
(21) Rossini, *Bur. Standards J. Research*, **12**, 735 (1934).

other hand, LuValle and Schomaker's observations[22] of a shortening of 0.07 Å. in the bond between the adjacent carbonyl groups would indicate that this middle bond is somewhat stronger than a single carbon–carbon bond. Although it is difficult to make any decision as to which primary step actually occurs, on the basis of this latter evidence, reaction (1″) would seem to be more probable than reaction (1′).

Summary

1. The kinetics of the decomposition of diacetyl between 383 and 436° have been investigated by analyzing for the diacetyl present after different time intervals. The pressure increases corresponding to the different amounts of decomposition have been determined.

2. With variation of the initial pressure the reaction is first order, but during a run the first order constants fall off.

3. The first order rate constant can be expressed as $k = 8.7 \times 10^{15} e^{-63,200/RT}$ sec.$^{-1}$.

4. Determinations of the amount of ketene present during the decomposition show that the yield of ketene increases as the percentage of decomposition decreases.

5. Addition of propylene retards the decomposition of diacetyl.

(22) LuValle and Schomaker, THIS JOURNAL, **61**, 3520 (1939).

ROCHESTER, NEW YORK RECEIVED DECEMBER 29, 1939

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

The Heat Capacity and Entropy, Heats of Fusion and Vaporization and the Vapor Pressure of Methyl Chloride[1]

BY G. H. MESSERLY AND J. G. ASTON

This paper presents the results of a low temperature calorimetric investigation of methyl chloride. The work was begun several years ago to permit a comparison between the third law entropy and the value calculated from molecular constants for an organic compound containing methyl groups uncomplicated by the question of restricted rotation. The measurements had to be discontinued, however, because of the destruction by fire of a considerable portion of the Cryogenic Laboratory and have only recently been completed. Egan and Kemp have since published low temperature calorimetric data on methyl bromide and found good agreement between the calorimetric and "spectroscopic" entropy.[2] Our data on methyl chloride confirm the results of Egan and Kemp with methyl bromide.

Purification of Methyl Chloride.—A commercial sample was used as the starting material. About 150 cc. of liquid was distilled in the absence of air through an efficient vacuum-jacketed low temperature fractionating column (section 1 × 70 cm. packed with glass helices). An 80-cc. middle portion was redistilled and the middle cut of about 50 cc. after drying over P_2O_5 and removal of the last traces of air, was condensed in a weighed glass sample bulb. Vapor pressure measurements taken on the first and last portions of the final sample as the distillation proceeded had shown that no further purification of the material could be effected by fractionation. Two samples from different batches of starting material were prepared in this way. The second of these was used for all measurements. Only the melting point of the first sample was determined.

The Apparatus.—When the first sample prepared was being cooled to liquid hydrogen temperatures in the apparatus previously described[3] most of the apparatus was destroyed by a fire in the laboratory. The rebuilt apparatus was similar to the one destroyed except that the calorimeter itself was made entirely of gold and somewhat larger (present capacity 47 cc.) than the original gold-plated copper calorimeter. Heat conduction was provided for by eight radial vanes instead of the horizontal copper disks previously used. The single standard thermocouple at the bottom of the old calorimeter was replaced by two standard thermocouples which were fastened into horizontal platinum wells gold-welded on the top and bottom of the new calorimeter. The hydrogen liquefier that was an integral part of the old apparatus has been eliminated; liquid hydrogen produced in the laboratory liquefier and other refrigerants are added to the dewar surrounding the cryostat can through a vacuum jacketed german silver transfer tube. The present calorimeter is thus practically identical with the one described by Giauque and Egan.[4] It will hereafter be designated calorimeter C. The earlier calorimeter, only the winding of which was destroyed, is designated calorimeter

(1) Presented before the Low Temperature Symposium of the Division of Physical and Inorganic Chemistry at the Boston meeting of the American Chemical Society, September, 1939.

(2) Egan and Kemp, THIS JOURNAL, **60**, 2097 (1938).

(3) Aston and Messerly, *ibid.*, **58**, 2354 (1936).

(4) Giauque and Egan, *J. Chem. Phys.*, **5**, 45 (1937).

A. Calorimeter C was used in all the thermal measurements reported.

At the time that this apparatus was being rebuilt, data upon the performance of the adiabatic calorimeter[5] had not yet been obtained. It was for this reason that the destroyed isothermal calorimeter was replaced with one of the same type rather than the adiabatic apparatus, which has shown itself capable of greater accuracy than the isothermal calorimeter above 190 °K.

The Heat Capacity Measurements.—The method, temperature scale, and accuracy were as already described.[3] Standard thermocouples S-4 and S-7 were used for all temperature measurements. Their calibration was checked at the freezing and boiling points of hydrogen and oxygen, and at the upper transition point of oxygen. There was satisfactory agreement with the original scale.[6] The results of this and other similar comparisons made in this Laboratory from time to time will be discussed in a forthcoming paper. Standard thermocouple S-2 was used for the melting point determination in sample one.

TABLE I

THE MOLAL HEAT CAPACITY OF METHYL CHLORIDE

Mol. wt., 50.495; 0.86666 mole (sample two) in calorimeter; 0 °C. = 273.16 °K.

Temp., °K.	C_p, cal./deg.	Approx. ΔT, °K.	Temp., °K.	C_p, cal./deg.	Approx. ΔT, °K.
Series I			169.60	15.96	5.5
96.13	11.251	4.8	182.24	17.83	6.4
101.52	11.800	5.6	189.80	17.77	6.1
109.12	12.401	5.0	197.54	17.75	6.0
114.73	12.839	5.9	204.89	17.68	5.7
120.57	13.215	5.6	211.95	17.78	6.0
163.00	15.600	5.6	214.73	17.79	5.4
168.04	15.879	4.2	228.97	17.83	5.1
171.38	16.040	2.3	239.22	17.94	4.8
173.19	16.011	1.1	245.24	18.06	4.2
174.26	16.543	0.8	249.67	18.07	3.7
Series II			Series III		
56.64	7.716	4.6	11.95	0.393	1.4
61.69	8.299	5.1	14.11	0.640	2.4
67.48	8.989	1.2	17.61	1.187	4.2
74.28	9.645	6.7	21.27	1.865	3.2
81.03	10.215	5.8	26.07	2.751	4.0
86.32	10.760	5.3	30.00	3.503	3.4
92.01	11.101	4.9	33.77	4.127	3.9
97.51	11.454	5.7	38.74	5.509	5.6
118.87	13.093	6.5	44.45	6.037	5.4
125.75	13.427	6.7	50.68	7.014	6.5
132.86	13.917	7.0	Series IV		
140.23	14.375	7.2	162.89	15.58	5.7
147.86	14.729	6.7	168.20	15.89	4.3
156.81	15.21	7.3	171.62	15.99	2.3
164.11	15.63	5.0	174.01	16.92	2.3

(5) Aston and Eidinoff, THIS JOURNAL, **61**, 1533 (1939).

(6) Aston, Willihnganz and Messerly, *ibid.*, **57**, 2354 (1935).

One defined calorie was taken as equal to 4.1835 international joules. The density of liquid methyl chloride was obtained from the data of Timmermans.[7a] The heat capacity results are given in Table I and plotted in Fig. 1, where are also plotted some earlier heat capacity data on methyl chloride by Eucken and Hauck.[7b] These latter data may be seen to be unsuitable for third law calculations. The series number in Table I designates to which set of continuous measurements the particular measurement belongs.

The Vapor Pressure Measurements.—The measurements were made as already described,[3] and the results are given in Table II. Except for the lowest pressures the accuracy depends only upon the temperature. Column 1 gives the temperature as read by standard thermocouple S-7; column 2 the observed pressure and column 3 the difference between the observed pressure and that calculated from equation (1). Column 4 gives the temperature difference corresponding to the pressure difference in column 3.

TABLE II

THE VAPOR PRESSURE OF METHYL CHLORIDE (SAMPLE TWO)

°C. = 273.16 °K.; b. p., 248.943 °K.; (g for State College = 980.124 I. C. T.)

P obsd. int. mm. Hg	T obsd., °K.	P obsd. − P calcd., mm.	T calcd. − T obsd., °K.
26.32	191.424	−0.02	−0.011
26.24	191.378	− .01	− .006
33.56	194.556	− .01	− .004
47.54	199.272	− .01	− .004
77.41	206.324	+ .01	+ .002
122.58	213.539	− .06	− .008
122.47	213.526	− .08	− .010
212.90	222.999	− .15	− .013
313.07	230.184	.00	.000
442.57	237.125	− .19	− .009
579.23	242.845	+ .11	+ .004
681.09	246.441	+ .33	+ .011
761.47	248.998	+ .33	+ .010
735.42[a]	248.943	+ .39	+ .012
Triple point pressure			
6.569			
6.566			
6.563			
6.566 (mean)	175.44	+0.09	+0.16

[a] After distilling off half of sample.

$$\text{Log}_{10} P_{\text{mm.}} = -1822.60/T - 9.287119 \log_{10} T + 0.00555556\, T + 31.07167 \quad (1)$$

The first thirteen measurements were made with the calorimeter full of material. The measure-

(7) (a) Timmermans, *Bull. soc. chim. Belg.*, **30**, 65 (1921); (b) Eucken and Hauck, *Z. physik. Chem.*, **134**, 161 (1928).

ment marked (*a*) was made after half of the sample had been removed from the calorimeter. The boiling range of the sample is thus negligible.

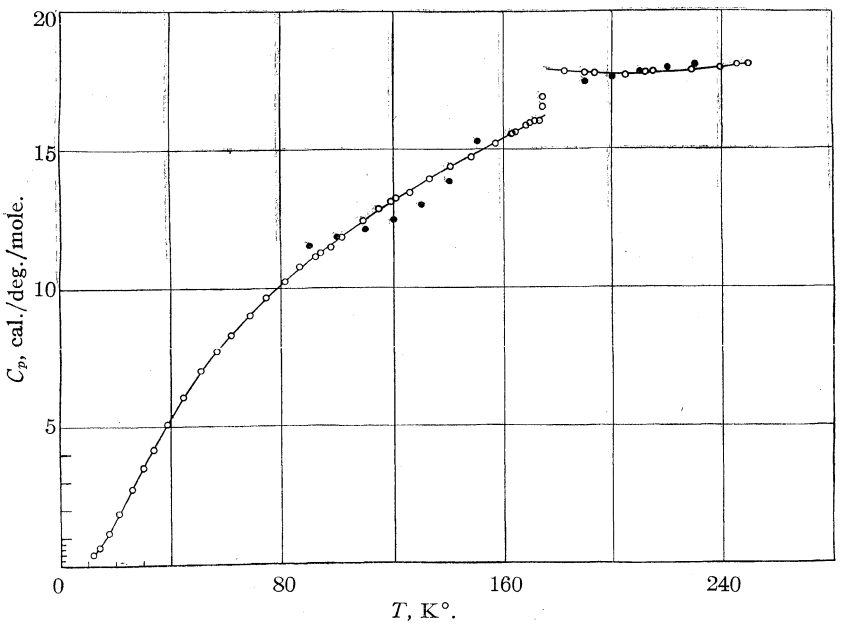


Fig. 1.—The molal heat capacity of methyl chloride: this research, ○; Eucken and Hauck,[7b] ●.

TABLE IIIA

MELTING POINT OF METHYL CHLORIDE (SAMPLE ONE)
0°C. = 273.16°K.

% melted	T, °K. resistance thermometer	T, °K. thermocouple S-2
6	175.423	175.421
6[a]	175.423	175.423
13	175.426	175.426
19	175.426	175.427
25	175.428	175.428
45	175.428	175.430
80	175.429	175.430
Melting point	175.43	175.43

[a] This observation taken one-half hour after the previous one.

TABLE IIIB

MELTING POINT OF METHYL CHLORIDE (SAMPLE TWO)
0°C. = 273.16°K.

% melted	T, °K. resistance thermometer	T, °K. thermocouple S-4	T, °K. thermocouple S-7
1	175.283	175.329	175.342
10	175.438	175.434	175.447
10[a]	175.436	175.436	175.448
19	175.437	175.438	175.450
41	175.437	175.433	175.447
80	175.438	174.440	175.452
Melting point	175.44	175.44	175.45

[a] This observation taken one hour after the previous one.

Triple Point.—At the bottom of Table II are given the determinations of the triple point pressure.

The Melting Point.—The equilibrium temperature of both samples was observed over periods of fifteen and eighteen hours with increasing fractions of the sample melted as determined by the heat input. From these results and the heat of fusion, the solid insoluble impurity for both samples was found to be 0.002 ± 0.001 mole per cent. Tables IIIA and IIIB summarize the data.

Values of the melting point were obtained with two different samples and three different standard thermocouples. The value on sample I with thermocouple S-2 was obtained with calorimeter A. The values on sample II were obtained with the rebuilt apparatus.

The final value taken for the melting point was 175.44 ± 0.05°K. (−97.72°C.). Other values given in the literature for the melting point of methyl chloride are: −102.9,[8] −97.6,[9] −91.5,[10] −93[11] (all in °C.).

By solving equation (1) for one atmosphere 248.94 ± 0.02°K. (−24.22°C.) is obtained for the normal boiling point of methyl chloride. Other values given by earlier investigators for the normal boiling point are: −23.73,[12] −24.09,[13] −23.7,[14] −23.7,[7a] −23.8[15] (all in °C.). The values of the physical constants indicate that methyl chloride would be a suitable material for thermometric fixed points. It is curious that the values obtained in this research seem to be the only reliable ones for such a common substance.

The Heats of Fusion and Vaporization.—The heats of fusion were measured as already described, and the results are given in Table IV. The heat of vaporization at the boiling point has

(8) Lndenburg and Krügel, *Ber.*, **33**, 638 (1900).
(9) McIntosh, *J. Chem. Soc.*, **85**, 915 (1904).
(10) Baume, *Compt. rend.*, **148**, 1322 (1909).
(11) Baume and Borowski, *J. chim. phys.*, **12**, 281 (1915).
(12) Regnault, *Jahresber. uber. Fort. Chem.*, 70 (1863).
(13) Gibbs, THIS JOURNAL, **27**, 851 (1905).
(14) Holst, *Commun. Phys. Lab. Univ. Leiden*, No. 144c (1914).
(15) D. N. Shorthose, Food Investigation Board, Dept. of Scientific and Industrial Research (Great Britain), Special Report 19 (1924).

TABLE IV

HEAT OF FUSION OF METHYL CHLORIDE

0°C. = 273.16°K.; mol. wt., 50.495; 0.86666 mole (sample II); m. p., 175.44 ± 0.05°K.

Temperature interval, °K.	Corrected heat input, cal./mole	$\int C_p\,dt$, cal./mole	ΔH fusion, cal./mole
172.458–179.835	1715.2	178.1	1537.1
171.691–180.681	1754.2	217.7	1536.5
172.679–179.213	1693.1	156.4	1536.7
		Mean	1537 ± 1

been calculated from our vapor pressure equation and the equation of state data of Holst,[14] with the liquid density mentioned already. A direct experimental result has been published by Shorthose.[15] These values are compared in Table V. To obtain a final value, the experimental value of Shorthose was averaged with the one derived from the data of Holst. Double weight was given to the latter value. The heat of vaporization also has been calculated assuming a modified Berthelot equation of state for the gas with critical constants cited by Centnerszwer.[16] The agreement obtained justifies the later use of the Berthelot equation in calculating the entropy to the ideal gas state. This comparison could equally well have been made between the gas volumes, but in this case the experimental data of Shorthose would have received no weight.

TABLE V

THE HEAT OF VAPORIZATION OF METHYL CHLORIDE AT THE BOILING POINT

B. p., 248.94°K.; mol. wt., 50.495

		ΔH, cal./mole
(1)	Calculated from eqn. (1) and state data Holst[14] (1914)	5138 ± 10
(2)	Measured (Shorthose,[15] 1924)	5166 ± 20
	Average (2 × (1) + (2))/3	5147 ± 15
(3)	Calculated from eqn. (1) and modified Berthelot eqn. T_c = 143.2°C.;[16] P_c = 65.7 atm.[16]	5157

The Entropy from Thermal Data.—The calculation is summarized in Table VI. The entropy of the gas at 298.16°K. has been obtained by extrapolation using the spectroscopic data discussed by Stevenson and Beach.[17] The corrections for gas imperfection are based upon a modified Berthelot equation of state for the gas. For completeness the entropy of the superheated liquid has been estimated at 298.16°K.

The Entropy from Molecular Data.—Stevenson and Beach[11] have calculated the entropy of methyl chloride to be 55.99 e. u. for the ideal gas

(16) Centnerszwer, *Z. physik. Chem.*, **49**, 199 (1904).
(17) Stevenson and Beach, *J. Chem. Phys.*, **6**, 25 (1938).

TABLE VI

THE ENTROPY OF METHYL CHLORIDE FROM THERMAL DATA

Mol. wt., 50.491; 0°C., 273.16°K.

	E. u./mole
0 – 10.00°K., Debye extrapolation	0.075
10.00 – 175.44°K., Graphical	18.402
Fusion 1537/175.44	8.760
175.44 – 248.94°K., Graphical	6.239
Vaporization, 5147/248.94	20.677
Entropy of actual gas	54.153
Correction for gas imperfection[a]	0.119
Entropy of ideal gas, 248.94°K., 1 atm.	54.27 ± 0.15
Entropy of ideal gas, 298.16°K., 1 atm.	55.94
Entropy of liquid, 298.16°K.	36.74

[a] $S_{ideal} - S_{real} = 27\,RT_c\,{}^3P/32T^3\,Pc$ T_c = 143.2°C.;[16] P_c = 65.7 atm.[16]

at 298.1°K. The same vibrational frequency assignment was used in the present calculation for the ideal gas at the boiling point. This calculation is summarized in Table VII. The nuclear spin entropy is not included and the effect of isotopic composition has been neglected.

TABLE VII

THE ENTROPY OF METHYL CHLORIDE FROM MOLECULAR DATA AT ONE ATMOSPHERE PRESSURE

Mol. wt., 50.491; 0°C. = 273.16°K.

C–H = 1.10Å. R = 1.9871 cal.(15°)/deg./mole
C–Cl = 1.76Å.
∠H–C–H = 111° hc/k = 1.4325 cm. deg.
I_1 = 5.46 × 10^{-40} g. cm.²
I_2 = I_3 = 61.36 × 10^{-40} g. cm.²

	E. u./mole 248.94°K.	298.16°K.
$S_{trans.}$ = 3/2 R ln M + 5/2 R ln T − R ln P − 2.300	36.785	37.683
$S_{rot.}$ = R/2 ln $I_1I_2I_3$ × 10^{120} + 3/2 R ln T − R ln 3 − 6.851	17.271	17.809
$S_{vib.}$ = Σ_n $S_{Einstein}$	0.252	0.490
Total	54.31	55.98
Experimental	54.27 ± 0.15	55.94

The agreement between the entropy calculated from calorimetric and from molecular data further confirms the validity of applying the third law to organic compounds.

We gratefully acknowledge the help of the Research Corporation in providing a grant-in-aid which made the work possible. We wish to thank Mr. S. C. Schuman and Mr. R. M. Kennedy for help with the experimental work. We are indebted to Mr. C. W. Brouse for the execution of the fine mechanical work in the apparatus and the supervision of its construction.

Summary

The heat capacity of methyl chloride has been measured from 12°K. to the boiling point.

The melting and boiling points of methyl chloride are 175.44 and 248.94°K. respectively (0°C. = 273.16°K.).

The heat of fusion is 1537 cal./mole and the heat of vaporization is 5147 cal./mole at the boiling point.

The vapor pressure of methyl chloride is represented from the triple point to the boiling point by the equation, $\log_{10} P_{mm.} = -(1822.60/T - 9.287119 \log_{10} T + 0.00555556 T + 31.07167$.

The triple point pressure is 6.57 int. mm.

The entropy of methyl chloride in the ideal gas state has been found from calorimetric data to be 54.27 e. u. and 55.94 e. u. at 284.94 and 298.16°K., respectively. The corresponding values calculated from spectroscopic and molecular data are 54.31 e. u. and 55.98 e. u.

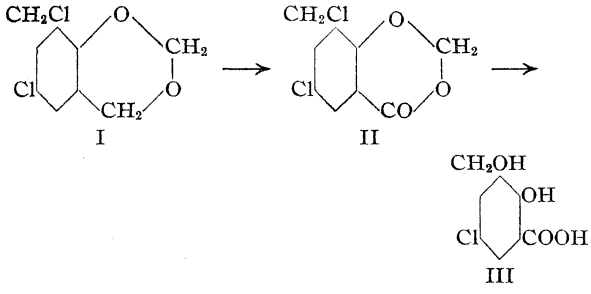
STATE COLLEGE, PA. RECEIVED JANUARY 12, 1940

[CONTRIBUTION FROM THE DABNEY CHEMICAL LABORATORY, UNIVERSITY OF TENNESSEE]

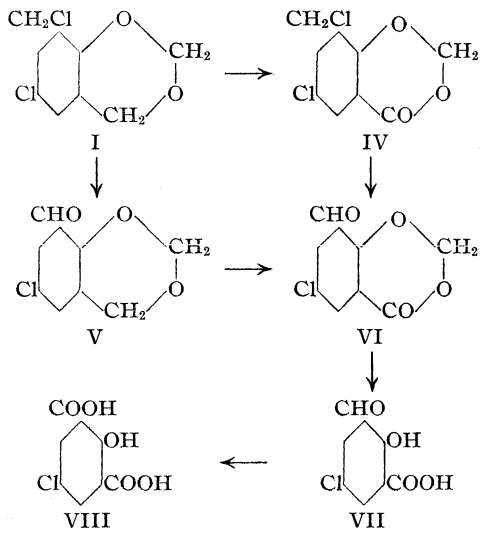
Proof of Structure of 6-Chloro-8-chloromethyl-1,3-benzodioxane by Oxidation[1]

BY C. A. BUEHLER, B. CALVIN BASS, ROBERT B. DARLING AND MILTON E. LUBS

In studying the action of formaldehyde on *p*-chlorophenol[2] in the presence of hydrochloric acid, a compound (I) thought to be 6-chloro-8-chloromethyl-1,3-benzodioxane was obtained. That the condensation product was a dioxane was shown by oxidation with chromium trioxide in acetic acid by the method of Borsche and Berkhout.[3] The 6-chloro-8-chloromethyl-1,3-benzodioxane-4-one, II, thus obtained gave, on alkaline hydrolysis, 2-hydroxy-3-methylol-5-chlorobenzoic acid, III.



To prove the structure of the original dioxane, I, a new oxidizing mixture, potassium permanganate in acetic acid, was tried and it was found that complete disruption of the dioxane ring was possible in one step. In this oxidation five products, IV, V, VI, VII and VIII, were isolated. Considering the effect of time and concentration of oxidizing agent on the amounts of the products obtained, we are inclined to support the oxidation sequence as indicated below. Of the first-formed products, IV appears in greater amounts than V although the former apparently is consumed more rapidly as the oxidation proceeds.



The 6-chloro-8-chloromethyl-1,3-benzodioxane-4-one, IV, and 6-chloro-8-aldo-1,3-benzodioxane, V, were isolated only in small quantities. The former, identical with II, gave the corresponding alcohol on alkaline hydrolysis while the latter was identified by conversion into its phenylhydrazone.

Of all the oxidation products, perhaps 6-chloro-8-aldo-1,3-benzodioxane-4-one, VI, is the most interesting because of the ease with which the dioxanone ring is broken. Not only does this opening occurs on standing and on titration with standard alkali, since the neutral equivalent is fairly satisfactory and 2-hydroxy-3-aldo-5-chlorobenzoic acid, VII, may be recovered from the titration mixture, but catalytic reduction, in which

(1) Presented at the 99th meeting of the American Chemical Society, Cincinnati, Ohio, April, 1940.

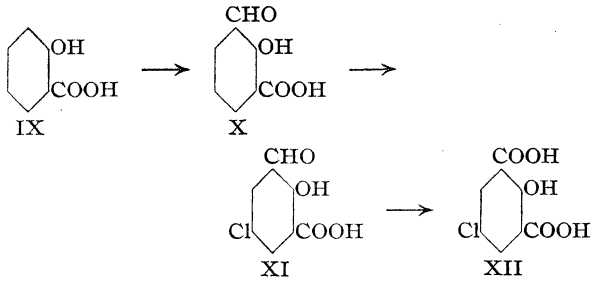
(2) For a similar reaction of phenol, see *Chem. Zentr.*, **103**, I, 2997(1932).

(3) Borsche and Berkhout, *Ann.*, **330**, 92 (1904).

the product is purified from slightly acidified water, gives 2-hydroxy-3-methylol-5-chlorobenzoic acid, III, rather than the expected 6-chloro-8-methylol-1,3-benzodioxane-4-one. Of indefinite melting point, this unstable dioxanone reacts positively with Tollens' reagent, a test which serves to distinguish it clearly from its decomposition product, 2-hydroxy-3-aldo-5-chlorobenzoic acid, VII, which does not affect this reagent.

2-Hydroxy-3-aldo-5-chlorobenzoic acid, VII, formed an oxime and could be oxidized readily to 2-hydroxy-5-chloroisophthalic acid, VIII, a compound which is fluorescent in ultraviolet light. The latter formed a diethyl ester.

None[4] of the oxidation products is recorded in the literature. To establish their constitution the synthesis below was carried out



Salicylic acid, IX, was converted into the known 2-hydroxy-3-aldobenzoic acid, X, by the Reimer–Tiemann reaction. On chlorination X gave a chloro derivative, XI, identical with VII. From an examination of the oxidation and synthetic series of reactions it is apparent that this identity could occur only if the formula for VII and XI was that of 2-hydroxy-3-aldo-5-chlorobenzoic acid. As further proof of structure, XI was oxidized with potassium permanganate in acetic acid to give the dicarboxylic acid, XII, which proved to be identical with VIII.

Experimental

Preparation of 6-Chloro-8-chloromethyl-1,3-benzodioxane.—To a mixture of 500 cc. of concentrated hydrochloric and 15 cc. of concentrated sulfuric acid warmed to 40°, 20 g. of Eastman Kodak Co. practical *p*-chlorophenol and 80 cc. of U. S. P. 40% formaldehyde were added. Hydrogen chloride was bubbled rapidly through the stirred mixture, kept at 40°, for one and one-half hours, at which point the solution had clarified with the separation of some solid. This crude solid, 30 g., was crystallized three times from methanol and gave 18.5 g. melting at 103°.

Anal. Calcd. for $C_9H_8O_2Cl_2$: Cl, 32.37; mol. wt., 219.1. Found: Cl, 32.31, 32.42; mol. wt. (cryoscopic, benzene), 217, 218.

Oxidation of 6-Chloro-8-chloromethyl-1,3-benzodioxane to 6-Chloro-8-chloromethyl-1,3-benzodioxan-4-one.—The dioxane, 3 g., was oxidized by the method of Borsche and Berkhout.[2] The crude benzodioxanone, washed with water until free from color, was crystallized from 95% ethanol, on the addition of water, in white, glistening plates, 1 g., melting at 181–182°. The compound gave a positive test for chlorine with aqueous silver nitrate, but no coloration was produced with ferric chloride nor was there any fluorescence in ultraviolet light.

Anal. Calcd. for $C_9H_6O_3Cl_2$: Cl, 30.43; mol. wt., 233.1. Found: Cl, 30.48, 30.22; mol. wt. (cryoscopic, acetic acid), 238, 242.

Hydrolysis of the Benzodioxanone to 2-Hydroxy-3-methylol-5-chlorobenzoic Acid.—6-Chloro-8-chloromethyl-1,3-benzodioxane-4-one, 1 g., was warmed with sodium hydroxide solution and then acidified as recommended by Borsche and Berkhout. The crude product when crystallized from 95% ethanol, upon the addition of water, gave a white powder, 0.5 g., melting at 165.5–166°. The pure acid produced a mulberry-purple color with ferric chloride and a bluish-green fluorescence in ultraviolet light.

Anal. Calcd. for $C_8H_7O_4Cl$: Cl, 17.50, neut. equiv., 202.6. Found: Cl, 17.61, 17.64; neut. equiv., 206.

Oxidation of 6-Chloro-8-chloromethyl-1,3-benzodioxane with Potassium Permanganate.—To a solution of 3 g. of 6-chloro-8-chloromethyl-1,3-benzodioxane in 100 cc. of glacial acetic acid there was added 160 cc. of distilled water, which causes considerable precipitation, and 9 g. of potassium permanganate. This mixture was refluxed vigorously for two hours while a stream of air was introduced to prevent bumping. After partial cooling, sulfur dioxide was bubbled through the solution to remove the color and dissolve the suspended material. To prevent resinification the resulting amber colored solution, having a greenish-blue fluorescence, was evaporated in a stream of air to one-half its volume or until organic material began to separate. Twice the volume of distilled water was then added, and the mixture was allowed to stand for three to four hours when about 0.2 g. of 6-chloro-8-aldo-1,3-benzodioxane, usually mixed with a smaller amount of 6-chloro-8-chloromethyl-1,3-benzodioxane-4-one, separated out. The total solid was dissolved in about 10 cc. of methanol and then thrown out by the addition of 50 to 75 cc. of cold water as 6-chloro-8-aldo-1,3-benzodioxane, a white solid melting at 138–138.5°.

After the removal of the crude 6-chloro-8-aldo-1,3-benzodioxane, concentrated hydrochloric acid was added to the filtrate until the amber color just disappeared. At the same time the solution became cloudy, and the fluorescence changed to blue-violet. This mixture was allowed to stand, usually twelve hours or more, until about 0.3 g. of 2-hydroxy-3-aldo-5-chlorobenzoic acid separated out. This product, when crystallized from water three or four times, gave 0.1 g. of long needles melting at 213.5–215.5°. More of the compound may be recovered by the addition of hydrochloric acid to the filtrate.

The filtrate obtained on removing the aldo acid was extracted with about 75-cc. portions of ether four times, the aqueous layer being discarded. On evaporating the com-

(4) German Patent 216,924 refers to a product, melting at 201°, which was thought to be 2-hydroxy-3-aldo-5-chlorobenzoic acid.

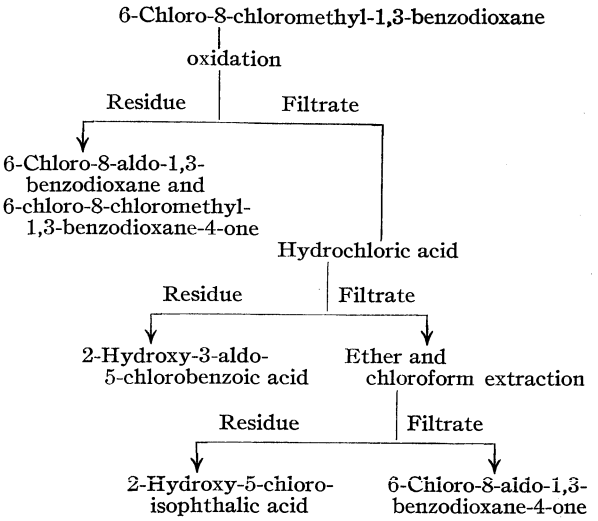
bined ether extractions to dryness, a mixture of about 1 g. of 6-chloro-8-aldo-1,3-benzodioxan-4-one and 2-hydroxy-5-chloroisophthalic acid, containing small amounts of 2-hydroxy-3-aldo-5-chlorobenzoic acid, was recovered. This residue was extracted with two 75-cc. portions of chloroform, and the combined chloroform solutions were then evaporated to about 90 cc., during which process some solid separated. This solid was removed and added to that remaining from the two chloroform extractions.

The chloroform filtrate was evaporated to about 25 cc., and the solid separating, about 0.4 g., which was removed by filtration, was crude 6-chloro-8-aldo-1,3-benzodioxan-4-one. This compound proved to be difficult to purify by the usual methods. Our best product was obtained by recrystallization twice from chloroform, in which process the first crystals, consisting largely of 2-hydroxy-5-chloroisophthalic acid, were discarded. The fact that 2-hydroxy-5-chloroisophthalic acid was fluorescent in ultraviolet light was of great assistance in this purification. Because of its instability the melting point of the 6-chloro-8-aldo-1,3-benzodioxan-4-one obtained, about 0.3 g., was indefinite. If heated rapidly, it melted in the neighborhood of 165–170°, then solidified, and finally sublimed around 190–200°. If heated slowly, the compound did not melt, but began to sublime around 175°, the process being complete near 200°.

The residue, about 0.3 g., remaining from the chloroform extractions was crude 2-hydroxy-5-chloroisophthalic acid. It was purified by solution in hot water followed by cooling in an ice-bath. After removing some 2-hydroxy-3-aldo-5-chlorobenzoic acid, which separated out first as an impurity, by filtration, concentrated hydrochloric acid was added to the filtrate and 2-hydroxy-5-chloroisophthalic acid precipitated. This compound, after five crystallizations, gave about 0.1 g. of a white, hair-like product melting at 238–240°.

Either varying the time or concentration of oxidizing agent exerted an influence on the amounts of the oxidation products. For instance, in a forty-five minute oxidation, fairly pure 6-chloro-8-chloromethyl-1,3-benzodioxan-4-one separated at the point at which impure 6-chloro-8-aldo-1,3-benzodioxane normally appeared. This dioxanone, after crystallization from methanol, weighed 0.25 g. and melted at 178–181°. A three-hour oxidation, in which the 6-chloro-8-aldo-1,3-benzodioxane-4-one produced was converted into 2-hydroxy-3-aldo-5-chlorobenzoic acid during the purification of 2-hydroxy-5-chloroisophthalic acid, gave 0.4 g. of the aldo acid. Likewise, a five and one-half hour oxidation gave 0.3 g. of 2-hydroxy-5-chloroisophthalic acid.

The scheme of separation employed for the oxidation products of 6-chloro-8-chloromethyl-1,3-benzodioxane may be represented diagrammatically as shown



Oxidation Products and Derivatives

(1) 6-Chloro-8-chloromethyl-1,3-benzodioxan-4-one.—This dioxanone, m. p. 178–181°, was identical with that previously described as melting at 181–182°. On hydrolysis it gave 2-hydroxy-3-methylol-5-chlorobenzoic acid also previously described.

(2) 6-Chloro-8-aldo-1,3-benzodioxane.—This compound, a white powder, m. p. 138–138.5°, gave negative tests with aqueous silver nitrate, ferric chloride, litmus and ultraviolet light.

Anal. Calcd. for $C_9H_7O_3Cl$: Cl, 17.85. Found: Cl, 17.82, 17.96.

(a) The phenylhydrazone separated from an alcoholic solution on the addition of water as pale yellow needles, m. p. 152.5–155°.

Anal. Calcd. for $C_{15}H_{13}O_2ClN_2$: Cl, 12.28. Found: Cl, 12.31, 12.21.

(3) 6-Chloro-8-aldo-1,3-benzodioxan-4-one.—The melting point of this dioxanone is of little significance as has been indicated above. The compound did not affect aqueous silver nitrate nor fluoresce in ultraviolet light, but it gave a mulberry-purple color with ferric chloride and a deposit of silver with Tollens reagent. In hot alkali it was sufficiently soluble for a neutral equivalent determination. Conversion to 2-hydroxy-3-aldo-5-chlorobenzoic acid was accomplished on standing or by heating in neutral or alkaline solution.

Anal. Calcd. for $C_9H_5O_4Cl$: Cl, 16.68; neut. equiv., 212.6. Found: Cl, 16.71, 16.88; neut. equiv., 202, 198.

(a) The oxime of 2-hydroxy-3-aldo-5-chlorobenzoic acid was obtained from the dioxanone and hydroxylamine hydrochloride in 10% sodium hydroxide solution. By the addition of water to an ethanol solution, it crystallized as a white, needle-like solid, m. p. 199.5–200.5°.

Anal. Calcd. for $C_8H_6ClNO_4$: Cl, 16.45; neut. equiv., 215.6. Found: Cl, 16.48; neut. equiv., 207.

(b) By reduction of the dioxanone in ethyl acetate with hydrogen (Raney catalyst) at 39 lb. (2.5 atm.) pressure followed by evaporation of the solvent and taking up the residue in warm water, 2-hydroxy-3-methylol-5-chlorobenzoic acid separated as the solution, slightly acidified with hydrochloric acid, cooled for several hours. Purification by the same process gave a product of m. p. 166.5–167°. The identity of this acid with that previously described was established by analysis and mixed melting point.

(4) 2-Hydroxy-3-aldo-5-chlorobenzoic Acid.—This aldo acid, one of the most abundant oxidation products, crystallized easily though not with a sharp melting point from

aqueous solution. The crude product, m. p. 208–214°, rose in melting point to 217–221° after ten crystallizations. The crystals separated in clusters from a dilute and in a hair-like mat from a concentrated solution. Aqueous silver nitrate reacted negatively, but ferric chloride gave a cherry-red coloration. In solution the substance gave a green fluorescence in reflected light, but there was no effect in the ultraviolet except on standing when fluorescence developed slowly due to the formation of 2-hydroxy-5-chloroisophthalic acid. Potassium permanganate in acetic acid converted the aldo acid to the corresponding dicarboxylic acid in good yield. The compound first formed was a monohydrate.

Anal. Calcd. for $C_8H_5ClO_4 \cdot H_2O$: Cl, 16.27; neut. equiv., 218.6. Found: Cl, 16.57, 16.49; neut. equiv., 208, 212.

Heating at 115–120° for three hours gave the anhydrous form.

Anal. Calcd. for $C_8H_5ClO_4$: Cl, 17.68; neut. equiv., 200.6. Found: Cl, 17.66, 17.80; neut. equiv., 201.

(a) The oxime, m. p. 199.5–200.5°, prepared in the usual manner, was shown by analysis and mixed melting point to be identical with that previously described. It gave a dark purple color with ferric chloride; its aqueous solution in reflected light produced a blue, while the solid in ultraviolet gave a yellowish-green, fluorescence.

(5) **2-Hydroxy-5-chloroisophthalic Acid.**—This dicarboxylic acid separated from water as a white mat resembling filter paper. When heated it shrank at about 225°, darkened at about 235°, and then melted with slight decomposition at 238–240°. Its aqueous solution in reflected light possessed a blue-violet, while the solid in ultraviolet gave a bright greenish-blue, fluorescence. Silver nitrate did not affect a solution of the acid, but ferric chloride produced a dark red color. The compound separating from water was a monohydrate.

Anal. Calcd. for $C_8H_5ClO_5 \cdot H_2O$: Cl, 15.11; neut. equiv., 117.3. Found: Cl, 15.23, 15.38; neut. equiv., 116, 115.

By heating for five hours at 115–120°, the anhydrous acid resulted.

Anal. Calcd. for $C_8H_5ClO_5$: Cl, 16.37; neut. equiv., 108.3. Found: Cl, 16.40, 16.42; neut. equiv., 115, 116.

(a) The diethyl ester was produced from ethanol and hydrogen chloride. By the addition of cold water to an ethanol solution, it crystallized as white needles, m. p. 50–51°. In ultraviolet light the solid produced a bluish-green fluorescence.

Anal. Calcd. for $C_{12}H_{13}ClO_5$: Cl, 13.00. Found: Cl, 13.04, 13.11.

Synthetic Products and Derivatives

(1) **2-Hydroxy-3-aldobenzoic Acid.**—This acid was prepared by the Reimer–Tiemann reaction[5] modified as follows. A solution of 200 g. of sodium hydroxide in 450 cc. of water was prepared and to 300 cc. of it at room temperature, containing 50 cc. of chloroform, there was added slowly, with constant stirring, 90 g. of salicylic acid. The resulting solution was placed in a three-necked, round-bottomed flask in which it was stirred while being refluxed on a water-bath at 80°. After the initial foaming and refluxing had subsided somewhat, another 50 cc. of chloroform and the remainder of the sodium hydroxide solution were added gradually through the condenser over a period of three hours. After another hour of stirring at 80°, the mixture was allowed to cool. Any chloroform layer was siphoned off, and 1:1 hydrochloric acid was added cautiously to the remainder of the reaction mixture until it became neutral, a fact indicated by its light, almost transparent appearance. After filtering off any resinous material present, 150 cc. more of 1:1 hydrochloric acid was added and a voluminous tan precipitate formed. This solid was permitted to settle while being cooled to about 20°, and then it was filtered off in a Büchner and washed five times with about 50-cc. portions of cold water.

The residue was now dissolved in an amount of 1:10 ammonium hydroxide sufficient to produce an orange to red solution. To this solution about 100 cc. of a 20% copper sulfate solution was added, with constant stirring, until the suspension which formed assumed a pea-green color. More 1:10 ammonium hydroxide, about 100 cc., was then added until the color became a much darker green.[6] After warming at 60° with constant stirring, the mixture was filtered, the green residue being washed three or four times with cold water.

In a solution of 15 cc. of concentrated sulfuric acid in 1200 cc. of water, the above residue was dissolved and, on stirring, the free 2-hydroxy-3-aldobenzoic acid separated as a flocculent white to yellow precipitate. So much resinous material was present, however, that the precipitate was redissolved in the mother liquor by heating barely to boiling, to avoid additional resinification, and the mixture was filtered rapidly. On cooling, tan crystals, melting at 167–173°, separated from the filtrate. For purification, the crude product was dissolved at room temperature in the least possible quantity of methanol, and this solution was poured several times through boneblack. Crystallization occurred after adding 3 volumes of water and cooling to 20°. Two more crystallizations from methanol gave 3 g. of tan needles melting at 178–179° (Reimer and Tiemann give 179°).

(2) **2-Hydroxy-3-aldo-5-chlorobenzoic Acid.**—Into a solution of 3.0 g. of 2-hydroxy-3-aldobenzoic acid in 75 cc. of glacial acetic acid surrounded with ice, dry chlorine was bubbled at the rate of 60 to 70 bubbles per minute until 1.3 g. of the gas had dissolved. After standing at room temperature for twenty-four hours, the reaction mixture was diluted with approximately three times its volume of distilled water. Upon cooling in a refrigerator for two hours, 2-hydroxy-3-aldo-5-chlorobenzoic acid had precipitated as a white, fluffy solid. By crystallization three times from water the acid, 2.7 g., melted at 226°. An analysis, as shown below, indicated that the compound was isomeric with the hydrated oxidation acid melting at 217–221°.

Anal. Calcd. for $C_8H_5ClO_4 \cdot H_2O$: Cl, 16.27; neut.

(5) Reimer and Tiemann, *Ber.*, **10**, 1563 (1877).

(6) The success of the experiment depends largely on the skill in arriving at the proper shade of color. Since the copper salts of 2-hydroxy-3-aldobenzoic and 2-hydroxy-5-aldobenzoic acids have different solubilities in ammonium hydroxide, a satisfactory separation is possible at the proper concentration. However, if the alkali is excessive, both isomeric salts dissolve.

equiv., 218.6. Found: Cl, 16.41, 16.61; neut. equiv., 212, 219.

That the two acids were identical was shown by a mixed melting of the oximes (synthetic aldoxime, m. p. 202°; oxidation aldoxime, m. p., 199.5–200.5°).

(3) **2-Hydroxy-5-chloroisophthalic Acid.**—To a solution of 1.2 g. of synthetic 2-hydroxy-3-aldo-5-chlorobenzoic acid in 40 cc. of glacial acetic acid, 64 cc. of distilled water and 4 g. of potassium permanganate were added. The mixture was stirred about a minute, until a noticeable reaction began, and then it was allowed to stand for two hours. After clarification with sulfur dioxide, evaporation to about half its volume, and then cooling, the crude 2-hydroxy-5-chloroisophthalic acid, which had separated, was removed. Upon purifying and heating as before, the anhydrous synthetic dicarboxylic acid melted at 245–246°. The analysis, as given below, indicated that the compound was isomeric with the anhydrous oxidation dicarboxylic acid whose hydrate melted at 238–240°.[7]

Anal. Calcd. for $C_8H_5ClO_5$: Cl, 16.37; neut. equiv., 108.3. Found: Cl, 16.48, 16.17; neut. equiv., 113, 113.

That the two dicarboxylic acids were identical was shown by a mixed melting point of the two diethyl esters (synthetic ester, m. p. 50°; oxidation ester, m. p. 50–51°).

(7) For both 2-hydroxy-3-aldo-5-chlorobenzoic and 2-hydroxy-5-chloroisophthalic acids the melting points of the hydrates do not differ appreciably from those of the anhydrous forms.

Summary

1. 6-Chloro-8-chloromethyl-1,3-benzodioxane has been obtained by the action of formaldehyde on *p*-chlorophenol in the presence of hydrochloric acid.

2. Oxidizing the above dioxane with potassium permanganate in acetic acid gave five products: 6-chloro-8-chloromethyl-1,3-benzodioxane-4-one, 6-chloro-8-aldo-1,3-benzodioxane, 6-chloro-8-aldo-1,3-benzodioxane-4-one, 2-hydroxy-3-aldo-5-chlorobenzoic acid and 2-hydroxy-5-chloroisophthalic acid.

3. The structure of 6-chloro-8-chloromethyl-1,3-benzodioxane was established through the identity of 2-hydroxy-3-aldo-5-chlorobenzoic and 2-hydroxy-5-chloroisophthalic acids with two isomeric acids synthesized from salicylic acid.

KNOXVILLE, TENN. RECEIVED FEBRUARY 1, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY, HOWARD UNIVERSITY]

The Acetylation of alpha-Bromo Ketones and their Derivatives

BY R. P. BARNES AND VICTOR J. TULANE

In an attempt to obviate certain difficulties experienced with glacial acetic acid solutions of freshly fused potassium acetate as an acetylating agent for alpha haloketones, we turned to acetic anhydride solutions of the acetate instead. The results were so surprising that we decided to test further the power of this acetylating combination. Thus the following compounds were investigated: phenyl bromobenzyl diketone (I), bromodibenzoylmethane (II), desyl bromide (III), acetylbenzoin (IV) and benzoin (V).

$C_6H_5CHBrCOCOC_6H_5$ (I)

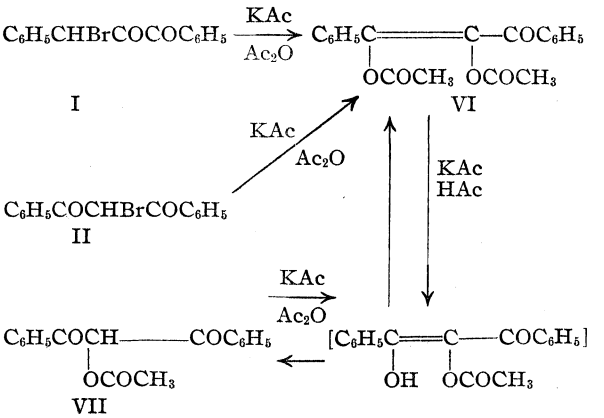
$C_6H_5COCHBrCOC_6H_5$ (II)

$C_6H_5CHBrCOC_6H_5$ (III)

$C_6H_5CH(OCOCH_3)COC_6H_5$ (IV)

$C_6H_5CHOHCOC_6H_5$ (V)

We have found that both bromo ketones (I) and (II) upon refluxing with a solution of freshly fused potassium acetate in acetic anhydride lead to the diacetate of phenylbenzoyl acetyleneglycol (VI). This diacetate, upon treatment with a solution of freshly fused potassium acetate in glacial acetic acid with subsequent distribution of the acetic acid by pouring into a large volume of water, is changed quantitatively into dibenzoylcarbinol acetate (VII). While other methods of acetylation fail,[1] dibenzoylcarbinol acetate is acetylated quantitatively by means of acetic anhydride–fused potassium acetate, giving the diacetate (VI).



(1) A. H. Blatt and W. Lincoln Hawkins, THIS JOURNAL, **58**, 81 (1936).

Neither phenyl bromobenzyl diketone (I) nor bromodibenzoylmethane (II) is enolic as indicated by alcoholic ferric chloride, and both are unaffected by acetic anhydride and by acetyl chloride. It is our experience that unless an alpha-bromo diketone is enolic, it is not acetylated by either of these reagents. It seems reasonable therefore that in these acetylations, bromine is first split out by metathesis with subsequent enolization and acetylation to the diacetate, since we have found[2] that compounds of the type R—C(OCOCH$_3$)=C(Br)—COR, which result from the acetylation of enolic bromo diketones, do not acetylate further under any known conditions.

We believe that these reactions give a feasible explanation of the behavior of the bromo diketones (I) and (II) on treatment with a solution of freshly fused potassium acetate in glacial acetic acid.[3]

The diacetate (VI) when dissolved in cold concd. sulfuric acid and poured onto finely crushed ice, gives the separation of a pale yellow solid. This solid oils out so rapidly that its melting point cannot be determined. However, its alcoholic solution gives with ferric chloride solution a deep greenish-blue color which fades rapidly, decolorizes iodine solution, and bleaches indophenol. These properties are characteristic of ene–diols. Thus the mesityl group in phenylmesitoylacetyleneglycol[4] and other ene–diols[4] does exert a stabilizing influence upon the ene–diol. On exposure to atmospheric oxygen the ene–diol (VIII) is changed to diphenyl triketone (IX).

$$C_6H_5C(OCOCH_3)\equiv C(OCOCH_3)—COC_6H_5 \xrightarrow{H_2SO_4}$$

VI

$$C_6H_5C(OH)\equiv C(OH)—COC_6H_5 \xrightarrow{O_2} C_6H_5COCOCOC_6H_5 + H_2O_2$$

VIII IX

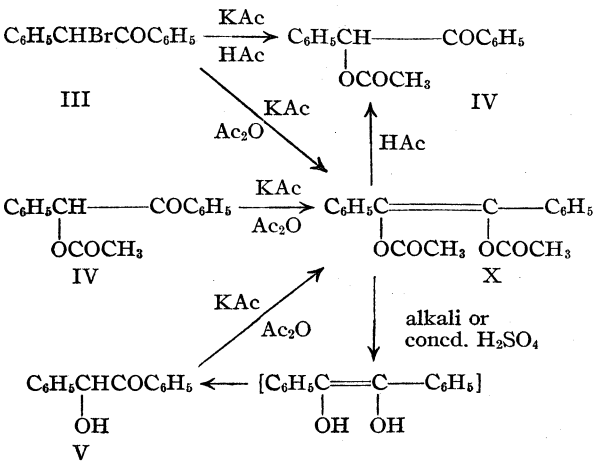
In a similar manner, desyl bromide (III), acetyl benzoin (IV), and benzoin (V), are acetylated by acetic anhydride–fused potassium acetate to the alpha-diacetate of diphenyl acetyleneglycol[5] (X), whereas potassium acetate and acetic acid convert desyl bromide into acetyl benzoin.

(2) Unpublished graduate thesis.

(3) A. H. Blatt, *J. Wash. Acad. Sci.*, **28**, 1 (1938).

(4) R. P. Barnes and Leila S. Green, THIS JOURNAL, **60**, 1549 (1938); R. B. Thompson, *ibid.*, **61**, 1283 (1939); Reynold C. Fuson and Joseph Corse, *ibid.*, **61**, 975 (1939).

(5) Johannes Thiele, *Ann.*, **306**, 142 (1899).



The driving power in these reactions seems to be the concentration of potassium acetate. The diacetate (X) is hydrolyzed to acetylbenzoin by boiling acetic acid, and either aqueous alkali or concd. sulfuric acid converts the diacetate (X) to benzoin. Thus again the stabilizing effect of the mesityl group is manifested, since Thompson[4] and Fuson[4] have found that the two geometrically isomeric ene–diols resulting from the reduction of dimesitoyl are quite stable.

Experimental

Phenylbenzoylacetyleneglycol Diacetate (VI).—A solution of 10 g. of either phenyl bromobenzyl diketone or bromodibenzoylmethane in 50 cc. of acetic anhydride is refluxed gently for thirty minutes with 5 g. of freshly fused potassium acetate, after which it is poured into 500 cc. of cold water and stirred vigorously until the acetic anhydride is decomposed. The resulting yellow oil solidifies. It is filtered immediately, washed with water and dried, yielding a practically quantitative amount of crude material. It is recrystallized from hot methyl alcohol, and melts at 133°.

Anal. Calcd. for $C_{19}H_{16}O_5$: C, 70.3; H, 4.9. Found: C, 70.0; H, 4.8.

A solution of 10 g. of dibenzoylcarbinol acetate in 50 cc. of acetic anhydride with 5 g. of freshly fused potassium acetate is treated as described above, yielding a practically quantitative yield of phenylbenzoylacetyleneglycol diacetate, melting and mix-melting at 133°.

The Action of Glacial Acetic Acid on Phenylbenzoylacetyleneglycol Diacetate.—A solution of 5 g. of the diacetate in 25 cc. of glacial acetic acid is refluxed gently for thirty minutes with 2.5 g. of freshly fused potassium acetate and worked up as above. The product is recrystallized from methyl alcohol, melting and mix-melting with pure dibenzoylcarbinol acetate at 94°.

Phenyl bromobenzyl diketone and bromodibenzoylmethane are both recovered unchanged after refluxing for four hours with either acetyl chloride or acetic anhydride Neither gives any color with alcoholic ferric chloride.

Hydrolysis of Phenylbenzoylacetyleneglycol Diacetate.—Solution of 2.0 g. of the diacetate in 10 cc. of cold concd.

sulfuric acid produces a deep orange color. This solution is poured with stirring onto crushed ice. A light yellow solid separates out which soon becomes sticky. It cannot be crystallized from alcohol. Its alcoholic solution gives a deep greenish-blue color with ferric chloride, which color fades rapidly; it bleaches iodine and indophenol solutions instantly. On exposure to atmospheric oxygen, it changes to a yellow solid which is identified as diphenyltriketone, melting and mix-melting with an authentic sample at 70°.

Diphenylacetyleneglycol Diacetate (X).—Separate solutions of 10.0 g. each of desyl bromide, acetylbenzoin and benzoin in 50 cc. of acetic anhydride are refluxed gently with equal weights of freshly fused potassium acetate for thirty minutes. Each solution turns yellow to light brown. After cooling, they are poured into large volumes of cold water and stirred vigorously until the acetic anhydride is decomposed. A cream-colored granular solid separates out. The solid is filtered, washed with water, and dried over solid potassium hydroxide. It is then crystallized from methyl alcohol, yielding 3.0 g. of a crystalline solid, melting at 153° and 6.0 g. of material melting at 70°. The material melting at 70° mix-melts with acetylbenzoin at 70°, and is hydrolyzed quantitatively by alkali to benzoin. Repeated recrystallizations do not change the melting point of 70°. When refluxed with acetic anhydride and potassium acetate, it yields the 153° substance. It is a mixture of acetylbenzoin and diphenylacetyleneglycol diacetate. The diacetate, melting at 153°, is hydrolyzed quantitatively by both alkali and cold concd. sulfuric acid to benzoin, identified by its melting point and mixed-melting point. Hot glacial acetic acid converts the diacetate to acetylbenzoin.

Acetylbenzoin (IV).—A solution of 10.0 g. of desyl bromide in 50 cc. of glacial acetic acid is refluxed with 10.0 g. of freshly fused potassium acetate for thirty minutes, cooled and poured into a large volume of water. An oily solid separates, which is crystallized from methyl alcohol, melting and mix-melting with acetylbenzoin at 84°.

Summary

Herein is reported the use of an acetylating combination which seems to be more powerful than acetic anhydride in the presence of concd. sulfuric acid, converting certain compounds which have the group —CH(Br)— or —CH(OCOCH$_3$)— or —CH(OH)— adjacent to a >C=O group, into diacetates of acetyleneglycol.

The properties of the ene–diol, phenylbenzoylacetyleneglycol, resulting from the hydrolysis of its diacetate are given.

Further possibilities of this acetylating combination are now under investigation.

WASHINGTON, D. C. RECEIVED JANUARY 22, 1940

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. XCV. Acid Isomerization of Pseudosapogenins to Sapogenins

BY RUSSELL E. MARKER AND EWALD ROHRMANN

The reaction of the sapogenins with acetic anhydride to yield the isomeric pseudosapogenins is now a well-established reaction which has been applied to sarsasapogenin,[1] *epi*-sarsasapogenin,[2] sarsasapogenone,[2] isosarsasapogenin,[2] tigogenin[3] and chlorogenin.[2] Although there may be some question concerning the structure of the pseudosapogenins all of the available evidence indicates the presence of an ethylenic linkage at C-16, C-17 and a reactive grouping at C-22 possibly as in I.[4]

In studying the reduction of pseudosarsasapogenone[2] by the Clemmensen method, it was observed that the essential reaction product was desoxysarsasapogenin and not desoxypseudosarsasapogenin. That this isomerization of the pseudosapogenin side chain to the sapogenin side chain is due to the presence of hydrochloric acid is clearly shown in succeeding experiments.

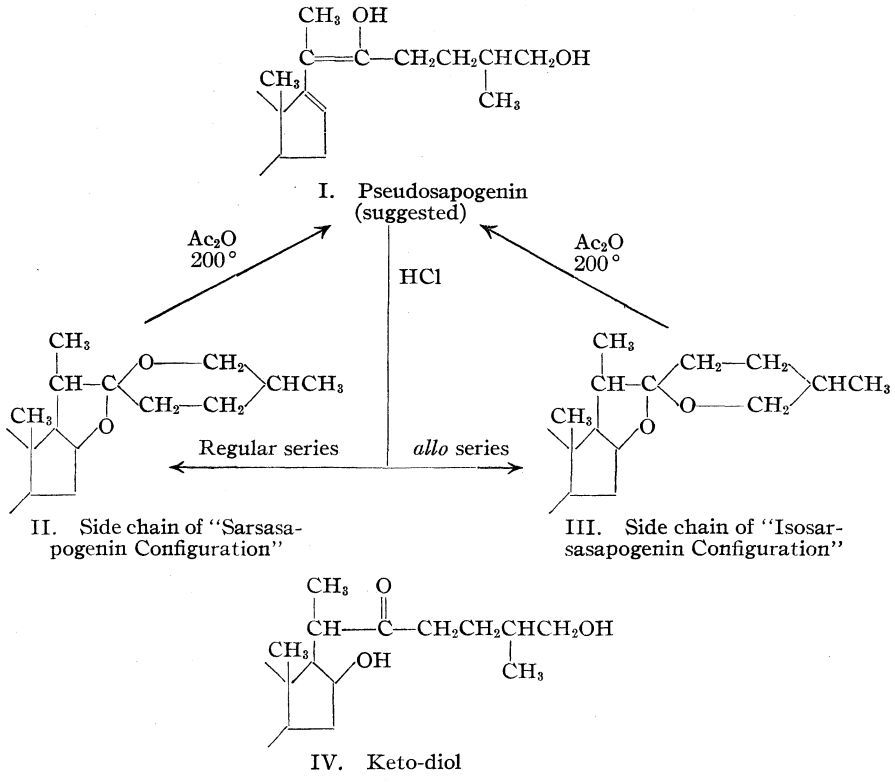
Pseudosarsasapogenin upon standing with aqueous ethanolic hydrochloric acid at 25° for one day is almost quantitatively converted into sarsasapogenin. Pseudotigogenin and pseudochlorogenin readily were converted into the corresponding sapogenins by short refluxing with aqueous ethanolic hydrochloric acid. It seems probable that this reaction involves the addition of hydrogen chloride to ethylenic linkages followed by elimination of hydrogen chloride and subsequent ring closure to yield the spiro ketal system. It is significant that dihydropseudosarsasapogenin[4] is unaffected by similar treatment.

In previous work we have shown that the side chains of tigogenin, chlorogenin and diosgenin and probably of gitogenin and digitogen differ in

(1) Marker and Rohrmann, THIS JOURNAL, **62**, 518 (1940).
(2) Marker, Rohrmann and Jones, *ibid.*, **62**, 648 (1940).
(3) Marker and Rohrmann, *ibid.*, **62**, 898 (1940).
(4) Marker and Rohrmann, *ibid.*, **62**, 521 (1940).

configuration from the side chain of sarsasapogenin. This was shown by the conversion of sarsasapogenin to neotigogenin,[5,6] a substance differing from tigogenin only in the configuration of the side chain. That the configuration of the side chain of the sapogenins derived from the acid isomerization of the pseudosapogenins is determined largely by the configuration at C-5 is indicated by the fact that pseudosarsasapogenin (pseudoisosarsasapogenin[2]) yields largely sarsasapogenin rather than isosarsasapogenin, while pseudotigogenin yields largely tigogenin rather than neotigogenin. Thus it may be generalized that pseudosapogenins having the regular configuration at C-5 give rise to a spiro ketal side chain of the "sarsasapogenin configuration" (II), while those having the *allo*-configuration give rise to one having the "isosarsasapogenin configuration" (III). It seems most probable that these reactions are of an equilibrium nature and that the isomerization of pseudosarsasapogenin probably gives rise to small amounts of isosarsapogenin besides the sarsasapogenin. Likewise the isomerization of pseudotigogenin probably gives small amounts of neotigogenin in addition to the tigogenin.

The behavior of the pseudosapogenins on acid isomerization raises the interesting question concerning the structure of the side chains of unhydrolyzed saponins. It would appear that some of these substances such as tigonin[7] and amolonin,[8] the parent saponins of tigogenin, give rise to more sugar groups on acid hydrolysis than one would reasonably expect to be attached to a single hydroxyl group such as exists in tigogenin. This suggests that the nucleus of the saponins may be that of the pseudosapogenins (I) or more probably that of the keto-diol IV, which is the equivalent of a spiro ketal (II and III). Such substances, during the course of the acid hydrolysis necessary for the cleavage of the glycoside linkages, would be converted to spiro ketals (II and III). The existence of a nucleus such as I or IV, on the basis of the previously mentioned equilibrium, satisfactorily explains the existence of smilagenin[9,10,11] (isosarsasapogenin) and neotigogenin[6] among the hydrolysis products of the saponins.



I. Pseudosapogenin (suggested)

II. Side chain of "Sarsasapogenin Configuration"

III. Side chain of "Isosarsasapogenin Configuration"

IV. Keto-diol

We wish to thank Parke, Davis and Company for their generous help and assistance in the various phases of this work.

Experimental Part[12]

Clemmensen Reduction of Pseudosarsasapogenone.—To a boiling solution of 200 mg. of pseudosarsasapogenone in 50 cc. of ethanol in the presence of 5 g. of 20-mesh zinc was added 8 cc. of concentrated hydrochloric acid over a period of two hours. Water was added and the precipitated solid taken up in ether and crystallized from acetone to give white plates, m. p. 214–216°. This gave no depression with a sample of desoxysarsasapogenin of m. p. 214–216°.

Anal. Calcd. for $C_{27}H_{44}O_2$: C, 80.9; H, 11.1. Found: C, 81.2; H, 11.1.

(5) Marker and Rohrmann, THIS JOURNAL, **62**, 647 (1940).
(6) Goodson and Noller, *ibid.*, **61**, 2420 (1939).
(7) Tschesche, *Ber.*, **69**, 1665 (1936).
(8) Jurs and Noller, THIS JOURNAL, **58**, 1251 (1936).
(9) Farmer and Kon. *J. Chem. Soc.*, 414 (1937).
(10) Askew, Farmer and Kon, *ibid.*, 1399 (1936).
(11) Kon, Soper and Woolman, *ibid.*, 1201 (1939).
(12) Microanalyses by Dr. John R. Adams, Jr., of this Laboratory.

Isomerization of Pseudosapogenins. (a) **Pseudosarsasapogenin.**—To a solution of 500 mg. of pseudosarsasapogenin, m. p. 170–173°, in 100 cc. of 95% ethanol was added a mixture of 85 cc. of ethanol and 15 cc. of concentrated hydrochloric acid. After standing at 25° for twenty hours, water was added and the precipitated solid taken up in ether and crystallized from acetone to give 400 mg. of white needles, m. p. 199–201°. This gave no depression with a sample of sarsasapogenin, m. p. 199–201°.

With chromic anhydride at room temperature, this gave a neutral product which crystallized from acetone as white plates, m. p. 223–226°. This gave no depression with a sample of sarsasapogenone, m. p. 223–226°.

With hot acetic anhydride an acetate was formed which was crystallized repeatedly from acetone–methanol to give white plates, m. p. 125–127°. When mixed with a sample of sarsasapogenin acetate, m. p. 143–145°, the mixture melted from 126–144°. When seeded with a crystal of sarsasapogenin acetate, m. p. 143–145°, a product of m. p. 142–144° was obtained. This gave no depression with sarsasapogenin acetate.

Anal. Calcd. for $C_{29}H_{46}O_4$: C, 75.9; H, 10.1. Found: C, 75.8; H, 10.2.

Similar results were obtained when pseudosarsasapogenin was refluxed in ethanol solution with aqueous hydrochloric acid for ninety minutes.

Dihydropseudosarsasapogenin, m. p. 169°, was recovered unchanged after refluxing for two hours in aqueous ethanolic hydrochloric acid solution.

(b) **Pseudotigogenin.**—Pseudotigogenin when refluxed for one hour with aqueous ethanolic hydrochloric acid gave a good yield of a product which crystallized from acetone as white needles, m. p. 203–205°. This gave no depression with a sample of tigogenin, m. p. 204–206°.

With boiling acetic anhydride this yielded an acetate, m. p. 202–204°, which gave no depression with an authentic sample of tigogenin acetate, m. p. 202–204°.

Anal. Calcd. for $C_{29}H_{46}O_4$: C, 75.9; H, 10.1. Found: C, 75.7; H, 10.0.

(c) **Pseudochlorogenin.**—Pseudochlorogenin when treated as described for pseudotigogenin gave a good yield of a product which crystallized from acetone as white needles, m. p. 269–272°. This gave no depression with a sample of chlorogenin, m. p. 270–273°.

With boiling acetic anhydride this yielded a diacetate, m. p. 149–151°, which gave no depression with a sample of chlorogenin diacetate, m. p. 149–151°.

Anal. Calcd. for $C_{31}H_{48}O_6$: C, 72.05; H, 9.4. Found: C, 72.1; H, 9.3.

Summary

Pseudosarsasapogenin, pseudotigogenin and pseudochlorogenin are isomerized by hydrochloric acid to the original sapogenins.

STATE COLLEGE, PENNA. RECEIVED JANUARY 29, 1940

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. XCVI. *allo*-Pregnanediols from Tigogenin

BY RUSSELL E. MARKER AND EWALD ROHRMANN

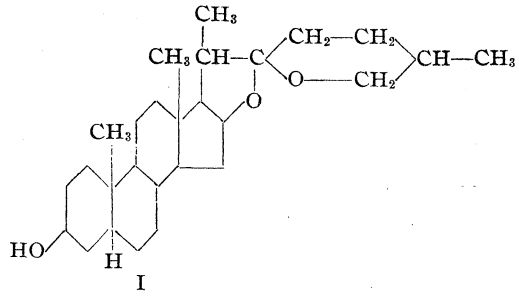
In a recent publication[1] the conversion of sarsasapogenin to $\Delta^{16,17}$-pregnenedione-3,20 and the subsequent reduction of this to various pregnane derivatives was described. In the present work we have extended some of these reactions to tigogenin (I), a substance having the *allo*-configuration at C-5.

Tigogenin upon treatment with acetic anhydride at 200° is converted to pseudotigogenin which upon mild oxidation with chromic anhydride is converted to an unsaturated diketone of the composition $C_{21}H_{30}O_2$. This substance is undoubtedly $\Delta^{16,17}$-*allo*-pregnenedione-3,20 (II) a substance first reported by Butenandt, Mamoli and Heusner.[2] Their product was prepared from androsterone by conversion to the nitrile, reaction with methyl Grignard reagent and subsequent oxidation. The product was reported to melt at 205–208°, while our product from tigogenin melts at 210–212°.

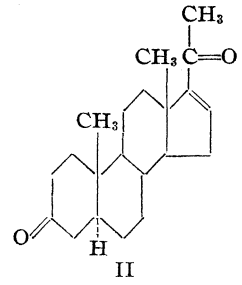
Reduction of the unsaturated diketone with sodium and ethanol yields *allo*-pregnanediol-3(β),20(α) while reduction with Adams catalyst yields *allo*-pregnanediol-3(β),20(β). The ease of reduction with sodium and ethanol indicates the presence of an α,β-unsaturated ketone grouping.

Although data have been presented indicating that the configuration of the C-3 hydroxyl group in tigogenin is *beta*, none of this evidence can be considered conclusive inasmuch as it has been derived from digitonin precipitation data[3] and from reduction experiments on $\Delta^{4,5}$ unsaturated ketones,[4] reactions which might conceivably be influenced by the presence of the complex side chain.

(1) Marker and Rohrmann, THIS JOURNAL, **62**, 518 (1940).
(2) Butenandt, Mamoli and Heusner, *Ber.*, **72**, 1614 (1939).
(3) Tschesche and Hagedorn, *ibid.*, **68**, 2247 (1935).
(4) Marker and Rohrmann, THIS JOURNAL, **61**, 1291 (1939).



I



II

The conversion of tigogenin to *allo*-pregnanediol-3(β),20(β) and *allo*-pregnanol-3(β)-one-20 by reactions in which the original C-3 hydroxyl group remains intact definitely proves that the configuration of the C-3 hydroxyl group is *beta*. Pseudotigogenin was acetylated and oxidized with chromic anhydride under relatively mild conditions, giving a non-crystalline product. Reduction of this with Adams catalyst followed by mild oxidation with chromic anhydride and subsequent hydrolysis yielded *allo*-pregnanol-3-(β)-one-20, while direct hydrolysis of the reduction product yielded *allo*-pregnanediol-3(β),20(β).

We wish to thank Parke, Davis and Company for their generous help and assistance in the various phases of this work.

Experimental Part

Pseudotigogenin.—A mixture of 3.6 g. of tigogenin and 25 cc. of acetic anhydride was heated at 195–200° for eight hours. The solvent was removed *in vacuo* and the residue hydrolyzed with ethanolic potassium hydroxide. The neutral material was crystallized from aqueous acetone to give white crystals, m. p. 193–196°. When mixed with tigogenin, m. p. 204°, it gave a depression in melting point to 180–186°, yield 3.1 g.

Anal. Calcd. for $C_{27}H_{44}O_3$: C, 77.8; H, 10.6. Found: C, 77.5; H, 10.5.

$\Delta^{16,17}$-*allo*-Pregnenedione-3,20 from Pseudotigogenin.—To a solution of 1.5 g. of pseudotigogenin in 100 cc. of acetic acid was added a solution of 1.5 g. of chromic anhydride in 25 cc. of 90% acetic acid. It was allowed to stand at 25–28° for two hours, poured into water and extracted with ether. The ethereal solution was washed with 2% sodium hydroxide solution and the product remaining after evaporation of the ether was sublimed in a high vacuum at 120–125°. This was crystallized from ether–pentane and finally from ether to give small white crystals, m. p. 210–212°. It gave a 25° depression with *allo*-pregnanedione-3,20, m. p. 210°; yield 425 mg.

Anal. Calcd. for $C_{21}H_{30}O_2$: C, 80.2; H, 9.6. Found: C, 80.0; H, 9.5.

The substance was unchanged by refluxing with acetic anhydride.

***allo*-Pregnanediol-3(β),20(α) from $\Delta^{16,17}$-*allo*-Pregnenedione-3,20.**—To a solution of 200 mg. of $\Delta^{16,17}$-*allo*-pregnenedione-3,20 in 50 cc. of boiling absolute ethyl alcohol was added 4 g. of sodium in small pieces. After the sodium had dissolved, water was added and the product was extracted with ether. It was recrystallized from methanol and acetone, giving white crystals, m. p. 213–214°. It gave no depression in melting point when mixed with *allo*-pregnanediol-3(β),20(α), m. p. 214–217°; yield 160 mg.

Anal. Calcd. for $C_{21}H_{36}O_2$: C, 78.8; H, 11.3. Found: C, 78.7; H, 11.3.

This product gave an acetate with hot acetic anhydride which was crystallized from methanol as white crystals, m. p. 166–168°. It gave no depression in melting point when mixed with the diacetate of *allo*-pregnanediol-3(β),20(α), m. p. 166–168°.

Anal. Calcd. for $C_{25}H_{40}O_4$: C, 74.2; H, 10.0. Found: C, 74.0; H, 9.9.

***allo*-Pregnanediol-3(β),20(β) from $\Delta^{16,17}$-*allo*-Pregnenedione-3,20.**—A solution of 200 mg. of $\Delta^{16,17}$-*allo*-pregnenedione in 100 cc. of acetic acid was shaken with 100 mg. of Adams catalyst under a pressure of 45 pounds (3 atm.) of hydrogen for three hours. The product was crystallized from ethanol to give white crystals, m. p. 192–193°. It gave no depression in melting point when mixed with *allo*-pregnanediol-3(β),20(β), m. p. 192–194°.

Anal. Calcd. for $C_{21}H_{36}O_2$: C, 78.8; H, 11.3. Found: C, 78.6; H, 11.2.

Oxidation of Pseudotigogenin Acetate with Chromic Oxide.—A solution of 1.6 g. of pseudotigogenin in 10 cc. of acetic anhydride was refluxed for thirty minutes. The excess acetic anhydride was removed *in vacuo* and the residue was dissolved in 100 cc. of glacial acetic acid. To this was added 2 g. of chromic oxide in 10 cc. of 80% acetic acid. After standing at 28° for two hours, water was added and the precipitated solid taken up in ether. The acids were removed by washing with water and sodium carbonate solution. Upon evaporation of the ether the residue failed to crystallize from acetone or ethanol, probably due to some by-products of the oxidation. The total product was dissolved in acetic acid and shaken with hydrogen under 45 pounds (3 atm.) pressure in the presence of Adams catalyst for one hour. A portion of the reduction product was hydrolyzed by refluxing for thirty minutes with alcoholic potassium hydroxide solution. This product was crystallized from ethyl alcohol to give white crystals, m. p. 192–194°. Mixed with *allo*-pregnanediol-3-(β),20(β), m. p. 192–194°, it gave no depression in melting point.

Anal. Calcd. for $C_{21}H_{36}O_2$: C, 78.7; H, 11.3. Found: C, 78.4; H, 11.3.

The remainder of the reduction product was dissolved

in 20 cc. of acetic acid and oxidized by adding 1 g. of chromic anhydride in dilute acetic acid. The neutral fraction was refluxed for fifteen minutes with alcoholic potassium hydroxide, then crystallized from dilute ethanol to give a product melting at 192–193°. Mixed with *allo*-pregnanol-3(β)-one-20, m. p. 192–193°, it gave no depression in melting point.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.2; H, 10.7. Found: C, 79.3; H, 10.6.

Summary

Tigogenin reacts with acetic anhydride to yield pseudotigogenin which on mild oxidation with chromic anhydride yields $\Delta^{16,17}$-*allo*-pregnenedione-3,20.

Reduction of $\Delta^{16,17}$-*allo*-pregnenedione-3,20 with sodium gives *allo*-pregnanediol-3(β),20(α) while reduction with Adams catalyst gives *allo*-pregnanediol-3(β),20(β). The configuration of the hydroxyl group in tigogenin is shown to be *beta*.

STATE COLLEGE, PENNA. RECEIVED JANUARY 2, 1940

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. XCVII. Sarsasapogenin

BY RUSSELL E. MARKER AND EWALD ROHRMANN

We find that sarsasapogenin reacts with both ethylmagnesium bromide and methylmagnesium iodide to yield products which contain two esterifiable hydroxyl groups. Oxidation of the diacetate of the ethyl Grignard product with chromic anhydride at 90° gave 3-hydroxy-*etio*-bilianic acid.[1]

The dimethyl ester[1] of the 3-hydroxy-*etio*-bilianic acid readily was converted to a monomethyl ester by hydrolysis with one equivalent of alkali. This indicates that one of the carboxyl groups in the acid is hindered, as might be anticipated from the structure. This is also in accord with the results of Litvan and Robinson[2] concerning the analogous acid derived from *o*-methylestrone. The mono-methyl ester yielded a crystalline acetate which, upon treatment with thionyl chloride and diazomethane by the procedure of Arndt and Eistert,[3] yielded a nicely crystalline diazo ketone.

Attempts to convert the diazo ketone to a crystalline acid by treatment with silver oxide were unsuccessful. The non-crystallline acid obtained from this reaction was treated with acetic anhydride to give, after alkaline hydrolysis, a ketone of the composition $C_{19}H_{30}O_2$, m. p. 117–119°. For purposes of comparison we prepared *etio*-cholanol-3(β)-one-17 by the method used by Ruzicka and co-workers.[4] This product after purification melted at 117° when crystallized from pentane. Ruzicka reports his product to melt at 151–152°. Evidently this ketone, as in the case of many other sterol ketones, exists in several polymorphic forms with different melting points. This product did not depress in melting point when mixed with the product prepared from 3-hydroxy-*etio*-bilianic acid. Both products formed semicarbazones melting at 240–242° with decomposition.

As further proof of the identity of the above product, it was reduced by sodium in amyl alcohol and the 3-OH group epimerized to the α-form. This product was identical with *etio*-cholanediol-3(α),17(α) prepared by the reduction of *epi-etio*-cholanolone with sodium in ethanol. The *etio*-cholanediol-3(α),17(α) was converted into its diacetate and this subjected to partial hydrolysis with methanolic potassium hydroxide, followed by oxidation with chromic anhydride. The resulting product was then hydrolyzed to yield *etio*-cholanone-3-ol-20. This substance was converted readily to testosterone by bromination and subsequent removal of hydrogen bromide with pyridine.

We wish to thank Parke, Davis and Company for their generous assistance.

Experimental Part

Reaction of Sarsasapogenin Acetate with Ethylmagnesium Bromide.—To a Grignard reagent prepared from 6.1 g. of magnesium, 27.5 g. of ethyl bromide and 100 cc. of ether was added a solution of 5 g. of sarsasapogenin acetate in 200 cc. of ether. Most of the ether was distilled off and the residual liquid was refluxed for fifteen hours with 25 cc. of benzene. The mixture was decomposed with dilute hydrochloric acid and the solid taken up in ether. The product was crystallized from ethyl acetate–pentane as flaky white needles, m. p. 159–161.5°.

(1) Marker and Rohrmann, THIS JOURNAL, **61**, 2722 (1939).
(2) Litvan and Robinson, *J. Chem. Soc.*, 1997 (1938).
(3) Arndt and Eistert, *Ber.*, **68**, 200 (1935).
(4) Ruzicka, Goldberg, Meyer, Brungger and Eichenberger, *Helv. Chim. Acta.*, **17**, 1395 (1934).

Anal. Calcd. for $C_{29}H_{50}O_3$: C, 77.9; H, 11.3. Found: C, 77.9; H, 11.2.

When refluxed with an excess of acetic anhydride the product yielded a diacetate which crystallized from aqueous methanol as white needles, m. p. 87.5–89°.

Anal. Calcd. for $C_{33}H_{54}O_5$: C, 74.7; H, 10.3. Found: C, 74.8; H, 10.1.

Reaction of Sarsasapogenin Acetate with Methylmagnesium Iodide.—This reaction was carried out as described above. The product was crystallized from ethyl acetate–pentane as white plates, m. p. 179–181.5°.

Anal. Calcd. for $C_{28}H_{48}O_3$: C, 77.7; H, 11.2. Found: C, 77.7; H, 11.2.

When treated with *p*-nitrobenzoyl chloride in pyridine at 60° the substance formed a **di-*p*-nitrobenzoate**, which crystallized from ether as white crystals, m. p. 192–194°.

Anal. Calcd. for $C_{43}H_{56}O_9N_2$: C, 69.3; H, 7.6. Found: C, 69.2; H, 7.6.

Oxidation of Diacetate of Ethyl Grignard Product.—To a stirred solution of 3 g. of the diacetate of the ethyl Grignard product in 60 cc. of acetic acid heated at 90° was added a solution of 7 g. of chromic anhydride in 40 cc. of 80% acetic acid over a period of one hour. The mixture was stirred for an additional hour at 90° when ethanol was added and the mixture concentrated *in vacuo* to about one-third volume. Water was added and the solid taken up in ether and washed with water and 3% sodium hydroxide. The alkaline water layer was heated on the steam-bath for twenty minutes, cooled, acidified with hydrochloric acid and the precipitated acid taken up in ether and crystallized from chloroform as small white crystals, m. p. 220–222°. This gave no depression with a sample of 3-hydroxy-*etio*-bilianic acid, m. p. 220–222°; yield 1.1 g.

Anal. Calcd. for $C_{19}H_{30}O_5$: C, 67.4; H, 8.9. Found: C, 67.2; H, 8.9.

Mono-methyl Ester of 3-Hydroxy-*etio*-bilianic Acid.—A solution of 2.68 g. of the dimethyl ester of 3-hydroxy-*etio*-bilianic acid in 25 cc. of methanol was refluxed for ninety minutes with a solution of 0.292 g. (1 mol) of sodium hydroxide in 8 cc. of water. The mixture was diluted with water, acidified with hydrochloric acid and the precipitated acid taken up in ether. The ethereal extract was washed with 0.5% potassium hydroxide solution. Evaporation of the ethereal solution gave approximately 1 g. of unchanged dimethyl ester.

The alkaline extract was acidified with hydrochloric acid and the precipitate taken up in ether and crystallized from ether–pentane as small compact white crystals, m. p. 211–213°.

Anal. Calcd. for $C_{20}H_{32}O_5$: C, 68.1; H, 9.2. Found: C, 68.3; H, 9.1.

When refluxed with an excess of acetic anhydride the monomethyl ester yielded an **acetate** which, after treatment in acetone with Norite, crystallized from aqueous acetone and aqueous methanol as compact white crystals, m. p. 181.5–183.5°.

Anal. Calcd. for $C_{22}H_{34}O_6$: C, 66.95; H, 8.7. Found: C, 67.0; H, 8.8.

Diazoketone from Monomethyl Ester.—A solution of 2 g. of the acetate of the monomethyl ester of 3-hydroxy-*etio*-bilianic acid in 10 cc. of dry benzene and 2 cc. of thionyl chloride (colorless) was refluxed on the steam-bath for two hours. The solvents were evaporated and the residual sirup was evaporated repeatedly *in vacuo* with dry benzene.

The acid chloride was not obtained crystalline. The product was dissolved in 60 cc. of ether and to this solution at 0° was added a cold ethereal solution of diazomethane (from 4 g. of methylnitrosourea). The solution was allowed to stand at room temperature for sixteen hours, when the solvent was evaporated. The residue was crystallized from ether–acetone–pentane as pale yellow needles, m. p. 159–160° dec. (gas); yield 1.2 g.

Anal. Calcd. for $C_{23}H_{33}O_5N_2$: C, 66.1; H, 8.0; N, 6.7. Found: C, 66.1; H, 8.1; N, 6.4.

Conversion of Diazoketone to *etio*-Cholanol-3(β)-one-17.—To a solution of 1 g. of the diazoketone in 25 cc. of absolute ethanol heated at 70–80° was added 2 g. of dry, freshly prepared silver oxide. The mixture was warmed at 70–80° for one hour, after which time the evolution of gas had ceased. The mixture was filtered and the filtrate diluted with water and the precipitated solid taken up in ether. Evaporation of the ether gave a non-crystalline sirup which was hydrolyzed with hot ethanolic potassium hydroxide. The resulting acid could not be crystallized. The sirup was refluxed with acetic anhydride for twenty-five minutes and the excess acetic anhydride was distilled off up to 250°. The residue was heated at 250° for one hour and then sublimed in high vacuum at 4 mm. pressure at 200–250°.

The sublimate was hydrolyzed with ethanolic potassium hydroxide and the neutral fraction treated with Girard reagent. The resulting ketonic material was sublimed in high vacuum and crystallized from ether–pentane as white needles, m. p. 117–119°.

Anal. Calcd. for $C_{19}H_{30}O_2$: C, 78.5; H, 10.4. Found: C, 78.2; H, 10.7.

When treated with semicarbazide acetate the product yielded a **semicarbazone** which crystallized from aqueous ethanol as white crystals, m. p. 241–242.5° dec.

Anal. Calcd. for $C_{20}H_{33}O_2N_3$: C, 69.1; H, 9.6. Found: C, 69.0; H, 9.3.

etio-Cholanolone was prepared by the oxidation of coprostanol by the method described by Ruzicka and coworkers.[5] It was isolated as the semicarbazone, m. p. 240–242°.

Anal. Calcd. for $C_{20}H_{33}O_2N_3$: C, 69.1; H, 9.6. Found: C, 69.0; H, 9.3.

A solution of 1 g. of the above semicarbazone was refluxed with 30 cc. of ethanol and 5 cc. of concentrated sulfuric acid in 10 cc. of water for three hours. The product was extracted with ether, the solvent removed and the residue was sublimed at 120–130° in a high vacuum. It was then crystallized from pentane giving white needles, m. p. 117–118°. It gave no depression in melting point when mixed with the same product obtained from 3-hydroxy-*etio*-bilianic acid.

Anal. Calcd. for $C_{19}H_{30}O_2$: C, 78.5; H, 10.4. Found: C, 78.4; H, 10.7.

***etio*-Cholanediol-3(α),17(α).**—To a solution of 200 mg. of *etio*-cholanolone in 80 cc. of amyl alcohol was added 5 g.

of sodium. The solution was refluxed for ten hours to ensure epimerization of the 3 hydroxyl group. The product was sublimed in high vacuum and crystallized from ethyl acetate, m. p. 233–235°. It gave no depression in melting point with an authentic sample of *etio*-cholanediol-3(α),17(α) prepared by the reduction of *epi-etio*-cholanolone.

Anal. Calcd. for $C_{19}H_{32}O_2$: C, 78.0; H, 11.0. Found: C, 78.1; H, 11.1.

With boiling acetic anhydride the product gave a diacetate which was crystallized from methanol as white crystals, m. p. 124–125°.

Anal. Calcd. for $C_{23}H_{36}O_4$: C, 73.4; H, 9.7. Found: C, 73.3; H, 9.8.

Ruzicka and co-workers[5] report a m. p. of 236–236.5° for the diol and of 124.5–125.5° for the diacetate.

Partial Hydrolysis of the Diacetate of *etio*-Cholanediol-3(α),17(α).—To a solution of 1.5 g. of the diacetate of *etio*-cholanediol-3,17 in 1 liter of absolute methanol was added 0.8 mol (titration) of potassium hydroxide in 100 cc. of methanol. After standing at room temperature for fifty hours, it was carefully neutralized with sulfuric acid and the methanol removed *in vacuo*. The residue was extracted with ether, washed well with water and the ether evaporated. The residue was dissolved in 25 cc of acetic acid, vacuum evaporated twice, and then dissolved in 25 cc. of acetic acid at room temperature. To this solution was added 700 mg. of chromic anhydride in 10 cc. of 80% acetic acid. After standing for forty-five minutes the mixture was diluted with water and extracted with ether. After washing with dilute sodium carbonate solution and water the ether was evaporated and the residue was dissolved in 50 cc. of ethyl alcohol. To this was added 2 g. of Girard reagent and the product was refluxed for twenty minutes. Water was added and the precipitated product extracted with ether. The aqueous layer was decomposed with hydrochloric acid and the solid product extracted with ether. The ether was evaporated and the residue dried with benzene. To the residue was added 1.5 g. of succinic anhydride and 5 cc. of pyridine and the mixture heated for ninety minutes. Ether was added and the pyridine removed by shaking with dilute hydrochloric acid. The ethereal extract was washed with potassium carbonate solution and the aqueous layer acidified and extracted with ether. Evaporation of the ether gave a residue which was hydrolyzed with ethanolic potassium hydroxide. The resulting product was treated with Norite in acetone and crystallized from ether–pentane (1:1). After standing overnight in a refrigerator the crystalline material was filtered. This product was not very soluble in ether, and was crystallized directly from this solvent, to give a small amount of a product melting at 145–148°, which gave no depression in melting point with *etio*-cholanone-17-ol-3(α), m. p. 149–150°.

The filtrate was evaporated and the residue crystallized from pentane to give white crystals, m. p. 139–141°. When mixed with *etio*-cholanone-17-ol-3(α) of a melting point of 148° it gave a depression of 24°. This product was *etio*-cholanone-3-ol-17.

Anal. Calcd. for $C_{19}H_{30}O_2$: C, 78.5; H, 10.4. Found: C, 78.2; H, 10.4.

Testosterone.—To a solution of 225 mg. of *etio*-cholanone-3-ol-17 in 20 cc. of glacial acetic acid acidified with hydrobromic acid was added 7.5 cc. of a 0.1 *M* solution of bromine in acetic acid. The solution was diluted with water and extracted with ether. The ethereal solution was shaken with dilute sodium bicarbonate solution, filtered, and the ether evaporated. The residue was crystallized from pentane–acetone. It melted over a range of 150–156°, but was not further purified.

To 100 mg. of this product was added 10 cc. of pyridine and the solution was refluxed for nine hours. Ether and water were added and the pyridine removed by shaking with dilute hydrochloric acid. The product was sublimed in a high vacuum and the sublimate crystallized from pentane to give white crystals, m. p. 149–151°, which gave no depression in melting point when mixed with an authentic sample of testosterone, m. p. 150–152°.

Anal. Calcd. for $C_{19}H_{28}O_2$: C, 79.1; H, 9.8. Found: C, 79.0; H, 9.7.

Summary

Sarsasapogenin has been converted into testosterone.

STATE COLLEGE, PENNA. RECEIVED DECEMBER 9, 1939

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY OF PRINCETON UNIVERSITY]

Glycofuranosides and Thioglycofuranosides. VII. Crystalline Alkyl Furanosides and Dimethylacetal of *d*-Mannose

BY ALLEN SCATTERGOOD[1] AND EUGENE PACSU

The general method of Pacsu and Green[2] for the preparation of glycofuranosides from the sugar mercaptals was applied to mannosediethylmercaptal which was previously obtained[3] from sirupy mannose by Fischer and from crystalline mannose by Levene and Meyer.[4] It was found that this starting material could be prepared conveniently and in good yield directly from the readily available α-methyl-*d*-mannopyranoside[5] by the action of hydrochloric acid and ethyl mercaptan. As was reported in a preliminary communication,[2f] the reaction between mannosediethylmercaptal and mercuric chloride in methyl alcoholic solution under neutral conditions resulted in a 60% yield of pure α-methyl-*d*-mannofuranoside (m. p. 118°; $[\alpha]^{20}D$ 108.4° in water solution) previously prepared by Haworth and co-workers through the dicarbonate[6] and direct from mannose[7] and methyl alcoholic hydrogen chloride. Green and Pacsu used pyridine to remove the excess mercuric chloride necessary to carry this type of reaction to completion. During the course of this work it was found that metallic mercury was also suitable for this purpose, the reaction being $Hg^{++} + Hg \rightarrow Hg_2^{++}$. On acetylation by acetic anhydride and sodium acetate, α-methyl-*d*-mannofuranoside readily gave a crystalline tetraacetate (m. p. 61–62°; $[\alpha]^{20}D$ 108.8° in chloroform solution) which was identical with the compound obtained[7a] by Haworth and co-workers by the pyridine method of acetylation. The substance had a specific rotation[8] of 105.3° in *trans*-dichloroethylene and 120.3° in *cis*-dichloroethylene.

When the sirupy residue of the mother liquor of α-methyl-*d*-mannofuranoside was treated with a saturated aqueous solution of calcium chloride, crystallization of a non-reducing, negatively rotating substance started immediately. After recrystallization by the addition of isobutyl alcohol to its concentrated methyl alcoholic solution, the substance had a specific rotation of −58.5° in water solution. It represented a calcium chloride addition compound of β-methyl-*d*-mannofuranoside with the composition of $C_7H_{14}O_6 \cdot CaCl_2 \cdot 3H_2O$. Subsequent investigation revealed that the sirupy residue of the mother liquor of α-methyl-*d*-mannofuranoside prepared according to Haworth and co-workers[7] would also combine with calcium chloride to yield the same addition compound. Furthermore, it was also obtained directly from mannose and methyl alcoholic hydrogen chloride at room temperature in the presence of calcium chloride. Considering the difficulties involved in the preparation of crystalline mannose, it is probably best to prepare this calcium chloride compound from the mercaptal. Removal of the calcium chloride from the addition compound by silver oxalate resulted in the pure β-methyl-*d*-mannofuranoside, which was obtained from ethyl acetate solution in long needles. Irvine and Burt[9] first suggested the existence of this substance as they believed that the "γ-methylmannoside" which they obtained in the sirupy condition was a mixture of two forms. Recently Haworth and co-workers obtained[10] β-methyl-*d*-mannofuranoside by the carbonate method but were unable to secure it in the crystalline condition. Our purest preparation which had been recrystallized three times from ethyl acetate melted at 47° and had a specific rotation of −112.6° in water solution as against −107° observed first[2f] on a slightly reducing sample. From the rotation of the calcium chloride compound (−58.5°) a rotation of −108.2° is calculated for the optically active portion of

(1) This paper is based upon a thesis submitted by Allen Scattergood, Albert Plaut Fellow in Chemistry, former Research Assistant on Special Funds from the Rockefeller Foundation, to the Faculty of Princeton University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) (a) Pacsu and Green, THIS JOURNAL, **58**, 1823 (1936); (b) Green and Pacsu, *ibid.*, **59**, 1205 (1937); (c) Green and Pacsu, *ibid.*, **59**, 2569 (1937); (d) Green and Pacsu, *ibid.*, **60**, 2056 (1938); (e) Green and Pacsu, *ibid.*, **60**, 2288 (1938); (f) Pacsu and Scattergood, *ibid.*, **61**, 534 (1939); (g) Pacsu, *ibid.*, **61**, 1671 (1939).

(3) Fischer, *Ber.*, **27**, 678 (1894).

(4) Levene and Meyer, *J. Biol. Chem.*, **74**, 695 (1927).

(5) Hudson, "Organic Syntheses," Vol. VII, John Wiley and Sons, Inc., New York, N. Y., 1927, p. 64.

(6) (a) Haworth and Porter, *J. Chem. Soc.*, 151 (1930); (b) *ibid.*, 649 (1930).

(7) (a) Haworth, Hirst and Webb, *ibid.*, 654 (1930); (b) Haworth, Hirst and Wood, *ibid.*, 2108 (1932).

(8) Unless otherwise stated, the rotations given in this paper are all for sodium light at 20°.

(9) Irvine and Burt, *J. Chem. Soc.*, **125**, 1343 (1924).

(10) Haworth, Porter and Waine, *Rec. trav. chim.*, **57**, 541 (1938).

this substance by multiplying by the formula weight ratio of 359/194. In a special experiment we found that addition of the calculated amount of calcium chloride to the aqueous solution of the pure furanoside changed the observed rotation from −6.65 to −6.40°. Further amounts of calcium chloride added to the solution did not appreciably change the rotation of the solution. This experiment clearly indicated that calcium chloride has a perturbing effect upon the rotation of the glycoside with which it is combined and that it is unsafe to calculate the rotation of a sugar or sugar derivative from the rotation of its calcium chloride compound by multiplying by the formula weight ratio.

By application of the furanoside synthesis to mannosediethylmercaptal in ethyl, normal propyl, and isopropyl alcohols, respectively, the corresponding α-alkyl mannofuranosides were obtained in the crystalline state. Table I contains the more important constants of the furanosides prepared in the course of the present work.

TABLE I

ALKYL MANNOFURANOSIDES WITH THEIR MELTING POINTS, OBSERVED AND CALCULATED ROTATIONS AND A_x'' VALUES

d-Manno-furanosides	Mol. wt.	M. p., °C.	$[\alpha]^{20}D$ in water	[M]	A_x'' [M] − $B_{\alpha\beta}$[a]	$[\alpha]_D$ calcd. from (A_x[b] + $B_{\alpha\beta}$[a] + F[c])
α-Methyl	194	118	108.4	21,030	21,455	...
β-Methyl	194	47	−112.8	−21,880	−21,455	...
α-Ethyl	208	90	105.0	21,840	22,265	105.4
α-n-Propyl	222	89	96.0	21,310	21,735	100.2
α-i-Propyl	222	82–84	96.7	21,470	21,895	100.8

[a] $B_{\alpha\beta}$ = −425, one-half the sum of the molecular rotation of α- and β-methyl-d-mannofuranoside. [b] A_x designates the following "normal" values for the aldoses: A_{OMe} = 18,700; A_{OEt} = 19,600; A_{OPr} = 19,925; $A_{Oi\text{-}Pr}$ = 20,060. [c] F = 2755 obtained from $A''_{OMe} - A_{OMe}$.

When the pentaacetate of mannosediethylmercaptal was submitted to the action of mercuric chloride in absolute methyl alcohol under neutral conditions, mannosedimethylacetal pentaacetate was formed. On deacetylation, this substance gave rise to crystalline mannosedimethylacetal with m. p. 101° and $[\alpha]^{20}D$ 0.6° in water solution. The dimethylacetal was stable in neutral and alkaline media but it suffered gradual hydrolysis at room temperature in a 0.05% hydrochloric acid solution. The specific rotation in the latter medium changed in forty-eight hours from the initial value of 0.6° to −34°. This change was probably due to the formation of a mixture of the α- and β-methylmannofuranoside from the dimethylacetal and the reaction followed a first order course with the velocity constant of 10^4k = 240. After the point of maximum levorotation had been reached, the rotation changed slowly to the final value of +12.8°, the approximate final rotation of d-mannose. This second change apparently represented the hydrolysis of the furanosides to methyl alcohol and mannose and it proceeded about one-twentieth as rapidly ($10^4 k$ = 11.8) as the first stage of the hydrolysis reaction.

Mannopyranose and its derivatives have been known for a long time to present a notable exception to the validity of van't Hoff's hypothesis of optical superposition as applied by Hudson to the sugars and certain of their derivatives. By the preparation of the crystalline β-methylmannofuranoside, it has now become possible to test Hudson's isorotation rules in the mannofuranose series also. It is seen in Table I that half of the rotational difference of the two mannofuranosides, A''_{OMe} = 21,455, is considerably larger than the "normal" value, A_{OMe} = 18,700, for the methylglycosides of the aldoses. It appears, therefore, that the isorotation rules do not hold for the furanoid derivatives of mannose just as they are not applicable directly to mannose and its pyranoid derivatives where the value of the same coefficient is A'_{OMe} = 14,225. In a recent communication[11] it has been shown that by introduction of a new term (F) in the simple equations used for the calculation of the rotations, correct values are obtained for d-mannose and l-sorbose and its pyranoid derivatives from the "normal" A_x and a_x coefficients for the aldoses and ketoses, respectively. The numerical value of F is calculated by subtraction of the value of any "normal" A_x coefficient from that of the corresponding "abnormal" coefficient. It represents a constant characteristic of a particular sugar and its derivatives in a certain solvent. Thus, F = −4475 was calculated from $A'_{OMe} - A_{OMe}$ (14,225 − 18,700) for d-mannopyranose and all its glycosidic derivatives in water solution. It is to be expected that by introduction of a similar constant for the mannofuranose series the calculated and observed rotations of the glycosidic derivatives will show satisfactory agreement. The pertinent data in Table I reveal that this, indeed, is the case. The value of the new term, F = 2755, represents the difference between the "abnormal" and the "normal" coefficients of

(11) Pacsu, THIS JOURNAL, 61, 2669 (1939).

$A''_{OMe} = 21{,}455$ and $A_{OMe} = 18{,}700$, respectively, and it remains practically constant for the different alkyl mannofuranosides.

As to the physical significance of F, it has been suggested[11] that this constant probably represents the numerical value of the contribution of a hitherto unrecognized optical factor, the ring conformation, to the total rotation of the molecule. In the furanose series, where the ring is almost certainly planar, large deviations from the isorotation rules should not be found if ring conformation were the only disturbing factor. However, it is quite certain that the B coefficient of the sugars and their derivatives consists of at least four optical factors without considering a possible solvent effect. These factors are the number (N) of the different atoms, the conformation (C) of the ring, the configuration (C_f) of the hydrogen atoms and hydroxyl groups around the asymmetric centers, and the orientation (O) about the C–O bonds of all the hydroxyl groups. The last factor is probably due to the formation of hydrogen bonds. Obviously these factors must have nearly constant values for both the α- and β-isomers of those pyranoid or furanoid sugars and sugar derivatives which obey the rules of isorotation in first approximation, since in such instances only will the difference between the B parts of the isomers be zero, and, consequently, the value of A_x be a constant quantity. On the other hand, in instances where the isorotation rules are not valid, the value of at least one of the factors must be different for the α- and β-forms, since the difference, in such cases, between the B parts of the α,β-isomers will not be zero and, consequently, the value of A_x will be modified by this difference. Of the four factors under consideration, factor N represents a constant characteristic of certain groups of sugars, such as pentoses, aldohexoses, ketohexoses, etc., and it must have the same value for both the ring and the α,β-isomers of any member within these groups. Similarly, the factor C_f should have a constant value characteristic of the individual members of the different groups of sugars and should not change either for the ring isomers or for the α,β-isomers of a particular sugar. With regard to factor C, any simple sugar molecule containing a strainless six-membered ring should, according to Haworth,[12] be theoretically capable of existing in two *trans* and six *cis* forms constituted on the Sachse principle. However, Pacsu[11] recently reported that attempts to build up these forms from the Fisher–Hirschfelder atom models resulted in the discovery that only one *cis* and one *trans* form could be constructed. The diameters of these atom models are the so-called collision diameters obtained from the kinetic theory or from a rule of Pauling that the collision diameter is equal to 3.2 times the covalent radius. Figures 1 to 8 represent the skeleton models of a pyranose molecule constructed from these atom models in the eight conformations advocated by Haworth.

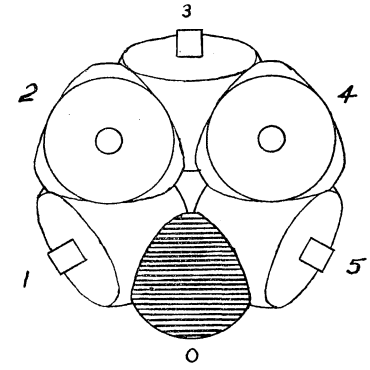


Fig. 1.—*trans*-Form, O above plane of paper, C_3 below plane of paper. A —CH_2OH group projecting outward on C_5 (*d*-form) would not interfere with groups attached to neighboring carbon atoms. This conformation is possible for the *d*-aldohexoses but not for the *l*-forms, which would have the —CH_2OH group on the lower valence of C_5 where it would block groups on the lower valences of C_1 and C_3. This does not mean that the *d*- and *l*-forms of an aldohexopyranose will not be mirror images. It simply indicates that the mirror image of the *d*-form will be derived from a different figure (Fig. 2).

It becomes evident by handling these models that *d*-hexopyranose molecules with conformations represented by Figs. 2, 4, 5, 6, 7, and 8 cannot be constructed because more or less obstruction occurs between certain atoms or atomic groups such as the hydrogen atom and the hydroxyl group of one or more ring carbon atoms and the —CH_2OH group which would be on carbon atom 5 of an aldohexose molecule. On the other hand, molecules with either of the two conformations represented by Figs. 1 and 3 can be constructed readily without obstructions occurring between any of the addenda of the ring. Since theoretical considerations[13] indicate that a *cis* form would be unstable and would pass over to the *trans* form because of large repulsion both in the ring and among the

(12) Haworth, "The Constitution of Sugars," Edward Arnold and Co., London, 1929, p. 91.

(13) Gorin, Kauzmann and Walter, *J. Chem. Phys.*, **7**, 327 (1939).

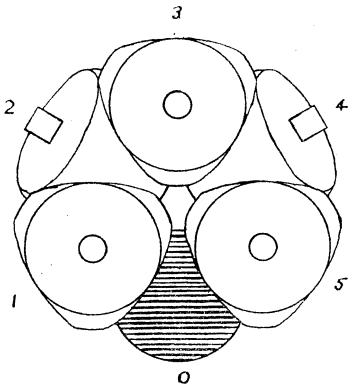


Fig. 2.—*trans*-Form, O below plane of paper, C_3 above plane of paper. Bottom view of Fig. 1. A $-CH_2OH$ group projecting upward on C_5 (*d*-form) partially covers the upper valences of C_1 and C_3. Even with hydrogen atoms on the two latter positions, there would be some interference. This conformation is possible for the *l*-aldohexoses but not for the *d*-forms. The *d*-form of a given aldohexose would be derived from Fig. 1 while the *l*-form, its mirror image, would be derived from Fig. 2.

subsidiary groups, there remains only one *trans* form (Fig. 1) from which all the *d*-hexopyranose molecules and their derivatives must be derived. In such a case factor C will have the same value for the α- and β-form of any pyranoid sugar or sugar derivative. Finally, factor O for the α-form (O_α) of any sugar may differ considerably from the same factor for the β-isomer (O_β) and, therefore, will not cancel out in the calculation of the numerical value of A_x. This appears to be the case in mannose, rhamnose, sorbose, etc., and their pyranoid derivatives where large deviations from the isorotation rules have been observed.

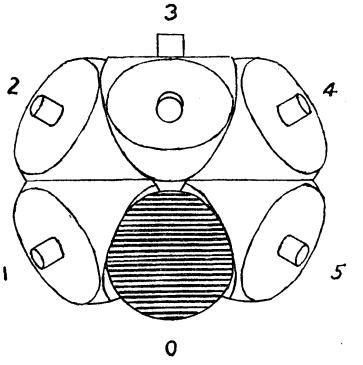


Fig. 3.—Symmetrical *cis*-form, O and C_3 above plane of paper. A $-CH_2OH$ group projecting outward on C_5 (*d*-form) would not interfere with groups of neighboring carbon atoms. This conformation is possible for the *d*-aldohexoses but not for the *l*-forms, which would have the $-CH_2OH$ group on the lower valence of C_5 where it would partially cover the lower valences of C_1 and C_4.

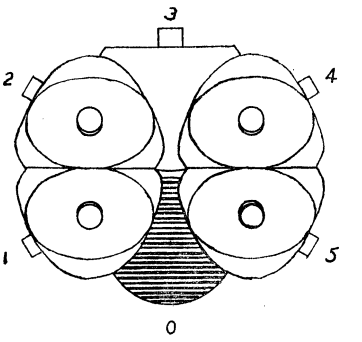


Fig. 4.—Symmetrical *cis*-form, O and C_3 below plane of paper. Bottom view of Fig. 3. A $-CH_2OH$ group projecting upward on C_5 (*d*-form) partially covers the upper valences of C_1 and C_4. This conformation is possible for the *l*-aldohexoses but not for the *d*-forms.

In the mannopyranose series $F = -4475$ represents, therefore, the numerical value of half of such difference $[(O'_\alpha - O'_\beta)/2]$. Since factor C is necessarily constant for all the furanosides (planar ring) any large deviation from the rules in this series must also be ascribed to the difference in the rotation values of the O factors for the α- and β-isomers. Obviously this is the case in the alkyl mannofuranosides where $F = 2725$ represents the numerical value of half of such difference $[(O''_\alpha - O''_\beta)/2]$. In both the pyranose and furanose series, therefore, the physical significance of F appears to be confined to the disturbing optical effect of the different orientation of the hydroxyl groups in the α- and β-isomers of certain sugars. As pointed out previously,[11] the occurrence of such disturbances at present cannot be predicted, neither can the effect be measured by physical or chemical methods. In many

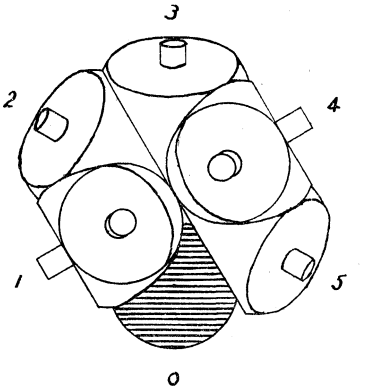


Fig. 5.—Asymmetrical *cis*-form, C_1 and C_4 above plane of paper. In both the *d*- and *l*-forms there would be interference between OH groups and H atoms on the upper valences of C_1 and C_4. Neither form can exist in this conformation.

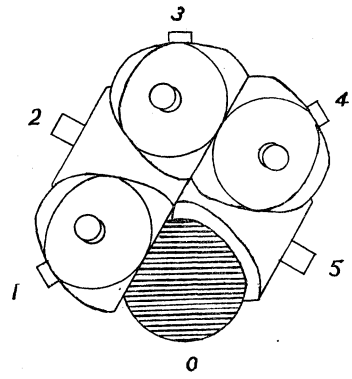


Fig. 6.—Asymmetrical *cis*-form, C_2 and C_5 below plane of paper. Bottom view of Fig. 5. In both the *d*- and *l*-forms there would be no interference on the top face of the molecule. However, on the bottom face of C_2 and C_5 there would always be interference. Neither form can exist in this conformation.

instances the optical effect of the orientation appears to be negligible (glucose-arabinose series) but for certain sugars (mannose, sorbose, etc.) it must be eliminated from the calculations by the introduction of term *F*, a characteristic constant for each of these sugars.

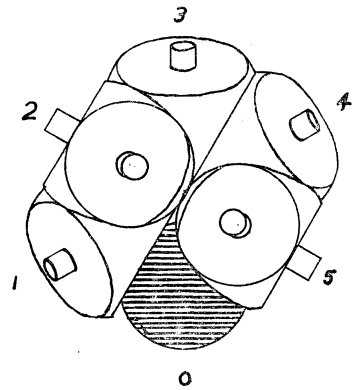


Fig. 7.—Asymmetrical *cis*-form, C_2 and C_5 above plane of paper. Mirror image of Fig. 5. A $-CH_2OH$ group projecting upward on C_5 (*d*-form) partially covers the upper valence of C_2. Even for the *l*-form, with H atoms on the upper valences of C_2 and C_5, there is interference. Neither form can exist in this conformation.

Experimental Part

Preparation of Mannosediethylmercaptal from α-Methyl-*d*-mannopyranoside.—One hundred cc. of ethyl mercaptan was added to 100 g. of crude α-methylmannopyranoside[5] in 100 cc. of concd. hydrochloric acid and the mixture was shaken for twenty hours at room temperature. At the end of this time the reaction product was treated with ice-cold water (150 cc.) and the crystals which soon formed were filtered and washed with small quantities of ice water. The crude product was purified by crystallization from water containing enough ammonia

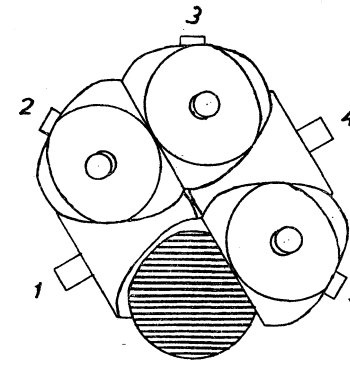


Fig. 8.—Asymmetrical *cis*-form, C_1 and C_4 below plane of paper. Bottom view of Fig. 7, mirror image of Fig. 6. A $-CH_2OH$ group projecting upward on C_5 (*d*-form) partially covers the upper valence of C_3. There would also be interference for both the *d*- and *l*-forms on the bottom valences of C_1 and C_4. Neither form can exist in this conformation.

to make the solution alkaline and decolorized by the use of activated carbon; yield, 54%; m. p. 131–133°.

Preparation of α-Methylmannofuranoside and its Tetraacetate.—A warm solution of 109 g. of mercuric chloride (0.4 mole) in 500 cc. of absolute methyl alcohol was added slowly to a suspension of 87 g. of yellow mercuric oxide in a solution of 57.6 g. of mannosediethylmercaptal (0.2 mole) in 500 cc. of absolute methyl alcohol. During the addition the mixture was either shaken mechanically or stirred. After the addition had been completed, the mixture was stirred or shaken for three hours. A test for the completion of the reaction was usually made after this time by heating the clear filtrate of a sample of the mixture with water. The reaction was complete if no precipitate of mercaptoethyl mercuric chloride would form. The insoluble mercury compounds were then filtered off and washed with methyl alcohol. The filtrate and washings contain mercuric chloride, which must be removed. This can be accomplished either by the use of pyridine according to Pacsu and Green[2] or by means of metallic mercury. In the latter procedure the united liquids were shaken with 7 cc. of mercury until the solution was free of chloride ion. This usually required four days of continuous shaking. After this time the mixture was filtered and the solution was evaporated *in vacuo* to a sirup which often crystallized spontaneously. If this was not the case then the sirup was dissolved in two or three times its volume of normal propyl alcohol and the solution was inoculated with seed crystals secured by evaporation of a methyl alcoholic solution of a small sample of the sirup in a stream of air. In either case the crystals were washed with cold normal propyl alcohol until the rotation of the washings became positive. Evaporation of the filtrate and washings *in vacuo* or in a stream of air gave a sirup which deposited more crystals on addition of an equal volume of normal propyl alcohol. After a thorough chilling the crystals were filtered and washed with ice-cold normal propyl alcohol in 10-cc. portions until the washings became positively rotating. The total yield of

the crude product was 25 g. or 64%. The strongly negative rotating filtrate and washings were saved for the preparation of the β-isomer. Haworth and co-workers[7a] used a mixture of methyl alcohol and ether to crystallize α-methylmannofuranoside. Six crystallizations were reported necessary with this combination of solvents. In the present work, normal propyl alcohol was found to be a better solvent, as pure material was obtained after two recrystallizations. The substance was dissolved in ten times its weight of normal propyl alcohol at 75°. The hot solution was filtered through a steam-jacketed funnel and the filtrate was kept in the icebox overnight. After the second recrystallization the substance had m. p. 118° and $[\alpha]^{20}D$ 108.4° in water solution, in agreement with the data of Haworth, Hirst and Wood.[7b]

Anal. Calcd. for $C_7H_{14}O_6$: OCH_3, 15.97. Found: OCH_3, 15.92.

For acetylation, 1 g. of α-methylmannofuranoside was boiled for two minutes with 5 cc. of acetic anhydride containing 0.25 g. of anhydrous sodium acetate. After the solution had been worked up in the usual manner, the product crystallized spontaneously from its chloroform solution upon evaporation in a stream of air. After recrystallization from aqueous alcohol it had m. p. 61–62° and $[\alpha]^{20}D$ 108.8° in chloroform (*c*, 1.23), 105.3° in *trans*-dichloroethylene (*c*, 1.56) and 120.3° in *cis*-dichloroethylene (*c*, 1.18). Haworth, Hirst and Webb[7a] prepared this substance by acetylation of the furanoside in pyridine at 0°. By the above procedure the acetate was secured in the crystalline condition without the difficulty which Haworth and co-workers encountered.

Preparation of the Calcium Chloride Compound of β-Methylmannofuranoside.—From the combined filtrate and washings of the α-methylmannofuranoside a strongly negatively rotating sirup was obtained by evaporation of the solution *in vacuo*. A saturated aqueous solution of 8 g. of calcium chloride was added to the sirup. Crystallization of the calcium chloride mannoside compound started within a few minutes, and was initiated by stirring. During the crystallization an equal volume of normal propyl alcohol was stirred in so that the mixture would not set to a solid. The crystalline slush was chilled in ice for several hours and then filtered with suction. The crystals were washed with cold absolute ethyl alcohol, in which they were insoluble. The substance was dried *in vacuo* over calcium chloride; yield, 8 g. or 13%. From the mother liquor, after the removal of the excess calcium chloride by means of silver oxalate, several small quantities of α-methylmannofuranoside were obtained. A careful search failed to reveal the presence of any mannosedimethylacetal.

The crude calcium chloride compound was dissolved in a minimum quantity (about 20 cc.) of cold methyl alcohol. The formation of the solution is a slow process and an excess of methyl alcohol is to be avoided. Isobutyl alcohol was then added to the solution, a few cc. at a time, until a total of 60 cc. had been added at room temperature. Crystallization started at this point and 20 cc. of isobutyl alcohol was added during the crystallization, making a total of 80 cc. The crystals were kept in the icebox overnight and then filtered and washed with isobutyl alcohol; yield, practically quantitative; $[\alpha]^{20}D$ −58.5° in water solution (*c*, 1.711). A similar process of recrystallization by the use of water instead of methyl alcohol and normal propyl alcohol instead of isobutyl alcohol was employed to prepare a sample of the substance for analysis, since the methyl alcohol method gave high values to the methoxyl content.

Anal. Calcd. for $C_7H_{14}O_6 \cdot CaCl_2 \cdot 3H_2O$: Ca, 11.16; Cl, 19.74; H_2O, 15.04; OCH_3, 8.64. Found: Ca, 11.08; Cl, 19.70; H_2O, 15.13; OCH_3, 8.70.

The compound was very soluble in water and methyl alcohol and almost insoluble in ethyl alcohol and higher alcohols. It was devoid of action toward Fehling solution. In testing the compound with Fehling solution it was found that an excess of the alkaline tartrate portion of the reagent would keep the calcium in solution as a complex ion during the test. The substance was hydrolyzed in 0.575 *N* hydrochloric acid at 19° in two days to give mannose with $[\alpha]D$ 14.0°.

The same substance was obtained from the mother liquor of the α-methylmannofuranoside prepared according to Haworth and co-workers.[7a] After several crops of the α-compound were removed, a sirup was obtained which was strongly negatively rotating. This was treated with an equal volume of a saturated aqueous solution of calcium chloride and the crystalline compound formed was filtered with some ethyl alcohol; yield, 0.5 g. from 10 g. of mannose.

The calcium chloride compound of β-methylmannofuranoside was also prepared direct from mannose in the following way. To 360 cc. of methyl alcohol containing 1% of dry hydrogen chloride, there was added 11 g. of calcium chloride (0.1 mole) and 18 g. of *d*-mannose (0.1 mole). The mixture was shaken on the machine until the mannose had all dissolved. After twenty hours of standing at room temperature the solution showed its lowest negative rotation. The acid was then neutralized by shaking the solution with silver carbonate. After filtration the solution was evaporated *in vacuo* to a sirup which was dissolved in 125 cc. of warm normal propyl alcohol. On inoculation with a crystal of the calcium chloride compound the product crystallized at 0°; yield 6 g. or 17%; $[\alpha]^{20}D$ −58.0° in water solution.

Preparation of β-Methylmannofuranoside from its Calcium Chloride Compound.—A solution of 3.6 g. of the calcium chloride compound in 50 cc. of water was shaken for thirty minutes with an equivalent quantity of silver oxalate, which was prepared by mixing 21 cc. each of normal solutions of potassium oxalate and silver nitrate and washing the resulting precipitate thoroughly by decantation. The reaction mixture was filtered, the filtrate was rendered alkaline by a few drops of ammonia, then evaporated *in vacuo* to a sirup which was repeatedly treated with alcohol, each time the solvent being evaporated *in vacuo* to ensure the removal of water. Seed crystals were secured by extraction of a small portion of the sirup with 25 cc. of hot ethyl acetate and slow evaporation of the solution in a vacuum desiccator. The main portion of the sirup was then extracted with warm ethyl acetate in several portions, which were kept in separate flasks. Each ethyl acetate extract deposited a small quantity of sirup at room temperature. The solutions were decanted into clean flasks and inoculated with crystals. The crystallization of the substance was slow and the flasks were al-

lowed to remain at 0° for several days. The furanoside was deposited in the form of buttons made up of fine needles. The crystals (1 g.) were filtered and shaken at room temperature with 25-cc. portions of ethyl acetate until all but a trace had dissolved. The combined solutions were kept in the icebox for three days. Well developed crystals of the β-furanoside were obtained; yield, 70%; m. p. 46–47°; $[\alpha]^{20}D$ −112.6° in water solution (*c*, 2.952). Further recrystallization did not change the rotation or the melting point.

Re-formation of the Calcium Chloride Compound from β-Methylmannofuranoside.—A solution of 0.1476 g. of β-methylmannofuranoside in 5 cc. of water gave an observed rotation of −6.65° in a 2-dm. tube. This corresponds to a specific rotation of −112.6°. To 3 cc. of this solution there was added 84 mg. of calcium chloride, a small excess over the calculated quantity to form the addition compound. The rotation of this solution was −6.40° which corresponds to a specific rotation of −108.4°. Thus the specific rotation of the furanoside is lowered 4.2° by the addition of calcium chloride. From the specific rotation of the crystalline calcium chloride addition compound (−58.5°) a rotation of −108.2° is calculated for the optically active portion of this substance by multiplying by the formula weight ratio 359/194. Further quantities of calcium chloride added to this solution did not appreciably change the rotation. Evaporation of this solution resulted in the formation of a crystalline substance which on recrystallization from methyl alcohol and isobutyl alcohol had $[\alpha]^{20}D$ −58.5° in water solution. This experiment indicates that the same calcium chloride compound may be re-formed from crystalline β-methylmannofuranoside.

Preparation of α-Alkylmannofuranosides.—A hot solution of 22.8 g. of mannosediethylmercaptal in the desired alcohol was made (200 cc. of ethyl alcohol, 400 cc. of either *n*- or *i*-propyl alcohol). To the cooled solution, 34 g. of yellow mercuric oxide[2b] was added. A warm solution of 43.6 g. of mercuric chloride in 200 cc. of ethyl alcohol, in 325 cc. of normal propyl alcohol or in 280 cc. of isopropyl alcohol was added under vigorous stirring to the mercaptal solution at room temperature. The mixture was shaken or stirred for the required period (three hours for isopropyl alcohol, six hours for ethyl alcohol and overnight for normal propyl alcohol) until a test showed that the reaction was complete. The reaction mixture was filtered and the filtrate and washings were treated by either of the procedures given for the preparation of α-methylmannofuranoside. The sirups obtained crystallized spontaneously. The products were recrystallized from ethyl acetate and showed the constants given in Table I.

Anal. Calcd. for $C_6H_{11}O_5(OR)$: OR, 21.6 (R, C_2H_5), 26.6 (R, C_3H_7). Found: OR, 21.2 (R, C_2H_5), 26.1 (R, *n*-C_3H_7), 25.4 (R, *i*-C_3H_7).

Preparation of Mannosedimethylacetal.—The starting material, mannosediethylmercaptal pentaacetate, was prepared by acetylation of the mercaptal with hot acetic anhydride containing anhydrous sodium acetate. It was identical with the substance previously prepared by Pirie,[14] who acetylated the mercaptal in pyridine. The demercaptalation of the acetate was carried out in an apparatus fitted with a separatory funnel, a reflux condenser and a mercury-sealed mechanical stirrer. A solution of 12 g. of the acetate in 120 cc. of methyl alcohol was gently refluxed and stirred for five hours with 6 g. of yellow mercuric oxide and a solution of 22.5 g. of mercuric chloride in 45 cc. of warm methyl alcohol. After this time, the mixture was stirred at room temperature overnight, then filtered and the filtrate and washings evaporated *in vacuo* to dryness. The chloroform extract of the residue contained, beside the mannosedimethylacetal pentaacetate, a small quantity of mercuric chloride. It was found in this investigation that metallic copper was an ideal reagent for removal of mercury in non-aqueous solvent. Moist bright copper turnings were added to the chloroform solution and the mixture was shaken until a sample no longer amalgamated a fresh copper turning. The reaction mixture was filtered and the combined filtrate and chloroform washings were evaporated *in vacuo* to a sirup. For deacetylation by the procedure of Zemplén and Pacsu[15] this sirup was dissolved in 50 cc. of absolute methyl alcohol and 2 cc. of 0.1 *N* sodium methylate in methyl alcohol was added to the solution. The mixture was kept at room temperature overnight, then the filtered solution was evaporated *in vacuo* to a sirup which crystallized spontaneously. The crude mannosedimethylacetal was then dissolved in a small volume of absolute ethyl alcohol and crystallized by the addition of isopropyl ether at 0°. The substance was then recrystallized twice from hot ethyl acetate; m. p. 101°; $[\alpha]^{20}D$ 0.6° in water solution (*c*, 6.86).

Anal. Calcd. for $C_6H_{12}O_5(OCH_3)_2$: OCH_3, 27.4. Found: OCH_3, 27.6.

The acetal is non-reducing but is easily hydrolyzed by dilute aqueous acids. A study of the rate of hydrolysis was made and the data are reported in Table II.

TABLE II

HYDROLYSIS OF A SOLUTION OF 0.074 G. OF MANNOSEDIMETHYLACETAL IN 2 ML. OF 0.05% HYDROCHLORIC ACID AT 23° IN A 2-DM. TUBE.

Time, hours	Specific rotation	*k* (first order)
0	0.6	
0.1	.6	
.4	.2	
.8	− .4	
1	− .85	0.018
2	− 2.4	.019
3	− 5.0	.025
4	− 6.8	.026
5	− 9.1	.028
6	−10.4	.028
48	−34.0	Mean 0.024
48	−34.0	..
60	−33.0	0.00078
72	−31.4	.00103
240	− 7.3	.00153
317	− 4.0	.00140
560	+12.8	Mean 0.00118

It will be noticed that the solution of the acetal became negatively rotating as the reaction proceeded. This is

(14) Pirie, *Biochem. J.*, **30**, 374 (1936).

(15) Zemplén and Pacsu, *Ber.*, **62**, 1613 (1929).

interpreted as evidence of the formation of a β-glycoside. Since the acetal eventually became hydrolyzed to mannose as shown by the final rotation, it was concluded that the intermediate must have been β-methylmannofuranoside or a mixture of this substance and its α-form. The formation of these intermediates from the acetal proceeded about twenty times faster than the hydrolysis of these intermediates into mannose and methyl alcohol.

Acknowledgment is made to Mr. Richard C. Johnson, a student at the Union Junior College, Roselle, New Jersey, for making the drawings of the models.

Summary

1. By application of the general method of Pacsu and Green to mannosediethylmercaptal prepared directly from α-methylmannopyranoside, crystalline β-methyl, α-ethyl, α-*n*-propyl and α-isopropyl mannofuranosides have been obtained. The β-methylmannofuranoside has been isolated from its crystalline calcium chloride addition compound, $C_6H_{11}O_5OCH_3 \cdot CaCl_2 \cdot 3H_2O$, which was obtained from the mother liquor of the α-methylmannofuranoside. The same calcium chloride compound also has been obtained directly from the reaction products of mannose and methyl alcoholic hydrogen chloride and from the mother liquor of α-methylmannofuranoside prepared according to Haworth and co-workers.

2. It has been found that calcium chloride has a perturbing effect upon the rotation of the β-methylmannofuranoside with which it is combined and therefore it is unsafe to calculate the rotation of a sugar or a sugar derivative from the rotation of its calcium chloride compound by multiplying by a formula weight ratio.

3. Crystalline mannosedimethylacetal has been prepared and its hydrolysis has been studied.

4. It has been shown that Hudson's rules of isorotation hold closely in the mannofuranose series provided that a factor F is introduced in the equations. The numerical value of F has been determined to be 2725 for the furanoid derivatives of mannose in water solution.

5. It has been suggested that the factor F probably represents the disturbing optical effect of the different orientation of the hydroxyl groups in the α- and β-isomers of certain sugars and their pyranoid or furanoid derivatives.

PRINCETON, NEW JERSEY RECEIVED JANUARY 16, 1940

[CONTRIBUTION NO. 185 FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, THE UNIVERSITY OF TEXAS]

Disubstituted Aminoacetones Containing Two Unlike Substituents[1]

BY J. WM. MAGEE[2] WITH HENRY R. HENZE

Continuing our attempts to prepare compounds possessing satisfactory activity as soporifics, we reported[3] recently our synthesis of ten disubstituted aminoacetones which subsequently were converted into disubstituted aminohydantoins. The ketones thus employed were all of the simple type $CH_3COCH_2NR_2$ in which the two substituents are identical and are either alkyl or allyl. We have now been interested in obtaining examples of the less well-known type CH_3COCH_2NRR', in which the two substituents are different, since these compounds present greater opportunity for variation in the combination of the groups most usually present in useful sedatives.

We have completed the synthesis of ten disubstituted aminoacetones, six of which had not been reported previously, by interaction of bromoacetone and the appropriate mixed secondary amine.[3] Most of the amines employed were produced in almost quantitative yield by catalytic reduction of the appropriate Schiff base by high pressure hydrogenation in the presence of Raney nickel catalyst.

(1) From the Ph.D. dissertation of J. Wm. Magee, June, 1938.

(2) Present address, Federal Bureau of Investigation, United States Department of Justice, Washington, D. C.

(3) Magee with Henze, THIS JOURNAL, **60**, 2148 (1938).

Experimental

Preparation of the Mixed Secondary Amines.—The monomethylaniline and monoethylaniline were redistilled immediately before use. Cyclohexylmethylamine was obtained by heating one mole of methylaniline for eight hours at 200° in the presence of Raney nickel catalyst and an initial hydrogen pressure of 3500 lb. (233 atm.). The product was of such purity as to permit use immediately upon filtration from the catalyst. In the other instances, one mole of benzaldehyde, or a derivative, was warmed on a steam cone with one mole of a primary amine for fifteen minutes. After cooling to room temperature and separating the water formed from the unsaturated base, the latter was reduced in thirty minutes at 75° under initial hydrogen pressure of 2000 lb. (133 atm.). Here, too, the mixed amines were obtained in excellent yield and in a state of practical purity.

TABLE I

DISUBSTITUTED AMINOACETONES, $RR'NCH_2COCH_3$

	−R	−R′	Yield, %	B. p. (cor.), °C.	Mm.	Density, d^{20}_4	Ref. index $n^{20}D$	Surface tension γ^{20}, dynes/cm.	Free surface energy $\gamma(m/d)^{2/3}$
1	$-C_6H_5$	$-CH_3$	46	110.7[a]	3.0	1.0490	1.5578	40.21	1163.2
2	$-C_6H_5$	$-CH_2CH_3$	50	123.5[b]	3.0	1.0275	1.5488	38.27	1186.0
3	$-CH_2C_6H_5$	$-C_6H_5$	28	187.9[c]	4.5	1.0971	1.5961	42.37	1534.6
4	$-CH_2C_6H_5$	$-CH_3$	45	129.5	16.0	0.9899	1.5108	36.17	1149.2
5	$-CH_2C_6H_5$	$-CH_2CH_3$	47	113.8	3.0	.9759	1.5060	34.90	1177.5
6	$-CH_2C_6H_5$	$-CH_2CH_2CH_3$	53	130.0	6.0	.9670	1.5030	32.81	1167.6
7	$-CH_2C_6H_5$	$-CH_2CH_2CH_2CH_3$	51	147.5	8.0	.9551	1.4994	31.77	1191.3
8	$-CH_2C_6H_4(CH_3)$-*o*	$-CH_3$	54	137.3	10.0	.9769	1.5092	33.62	1133.6
9	$-CH_2C_6H_4(CH_3)$-*p*	$-CH_3$	51	132.3	9.0	.9769	1.5090	33.48	1128.9
10	$-C_6H_{11}$	$-CH_3$	46	93.2[d]	4.0	.9387	1.4673	32.54	1038.6

Compound	Carbon, % Calcd.	Found	Hydrogen, % Calcd.	Found	Molecular refraction Calcd.	Found	ΔMR	Parachor Calcd.	found	ΔP
1	73.58	73.86	8.03	7.92	50.25	50.15	−0.10	401.7	382.9	−18.8
2	74.52	74.67	8.53	8.72	54.87	54.90	+ .04	440.7	428.3	−12.4
3	80.32	80.47	7.16	7.14	74.37	74.31	− .06	574.7	556.1	−18.6
4	74.52	74.69	8.53	8.47	53.35	53.57	+ .22	440.7	439.3	− 1.4
5	75.35	75.53	8.96	8.90	57.97	58.23	+ .26	479.7	476.4	− 3.3
6	76.05	76.22	9.33	9.17	62.58	62.76	+ .16	518.7	508.1	−10.6
7	76.66	76.89	10.36	10.33	67.20	67.46	+ .26	557.7	545.2	−12.5
8	75.35	75.51	8.96	8.86	57.97	58.46	+ .49	479.7	471.5	− 8.2
9	75.35	75.78	8.96	8.92	57.97	58.46	+ .49	479.7	471.0	− 8.7
10	70.96	71.12	11.32	11.41	50.13	50.06	− .07	434.7	430.7	− 4.0

[a] Meisenheimer, Angerman, Finn and Vieweg [*Ber.*, **57B**, 1744 (1924)] reported b. p. 119–120° (7 mm.).

[b] Stevens, Cowan and MacKinnon [*J. Chem. Soc.*, 2570 (1931)] reported b. p. 143° (11 mm.).

[c] Bauer and Bühler [*Arch. Pharm.*, **262**, 128 (1924)] reported b. p. 320–334° (atm. pres.) with slight decomposition.

[d] Reference *a*, reported b. p. 106° (11 mm.).

Preparation of Disubstituted Aminoacetones.—The two general procedures previously described[3] for preparing dialkylaminoacetones were employed in this investigation. Thus 0.4 mole of methylaniline, ethylaniline, benzylmethylamine or benzylphenylamine, diluted with 400 cc. of ether was added to 0.2 mole of bromoacetone in 50 cc. of ether and cooled to aid in the separation of the hydrobromide of the secondary amine. After evaporation of the ether, it was found desirable to dissolve 90–95% of the keto amine by addition of 6 *N* hydrochloric acid, to extract the acid solution with ether before neutralizing with alkali and again extracting with ether. Upon distillation the aminoacetones were obtained in yields of 45–50% of the theoretical.

For the aminoacetones derived from the more expensive mixed secondary amines, slightly higher yields of product were obtained by suspending 0.2 mole of the amine in 150 cc. of water containing 0.2 mole of sodium carbonate and adding 0.2 mole of bromoacetone dropwise with efficient stirring. The sodium bicarbonate separating from solution was removed by suction filtration. A small amount of unreacted bromoacetone could be removed efficiently from the keto amine by extraction with 1 *N* hydrochloric acid. Fractionation under diminished pressure yielded these aminoacetones in about 50% yield.

The substituted aminoacetones prepared in this study are colorless oils when first prepared but develop a dark color quite quickly. But sparingly soluble in water, the keto amines are readily soluble in 6 *N* acid solutions and in the usual organic solvents. Data obtained by analysis or measurement of the physical properties of these ten compounds are listed in Table I. The surface tensions were measured by means of Cassel's[4] precision capillarimeter at 20°. In calculating the parachors, the atomic parachor values of Sugden[5] were used.

Preparation of Semicarbazones from the Substituted Aminoacetones.—Solid, crystalline semicarbazones were obtained readily and in good yield from each of the ten substituted aminoacetones, best by dissolving the ketone in dilute alcohol, adding slightly more than the equivalent quantity of semicarbazide hydrochloride and making the solution barely alkaline with sodium hydroxide solution. The derivatives were recrystallized from dilute alcohol.

TABLE II

SEMICARBAZONES OF DISUBSTITUTED AMINOACETONES

$$R{-}NCH_2{-}C{=}NNHCONH_2$$
$$\quad\;\; |\qquad\;\; |$$
$$\quad\;\; R'\qquad CH_3$$

	−R	−R′	M. p., °C. (cor.)	Nitrogen, % Calcd.	Found
1	$-C_6H_5$	$-CH_3$	158	25.46	25.77
2	$-C_6H_5$	$-CH_2CH_3$	140	23.92	23.96
3	$-CH_2C_6H_5$	$-C_6H_5$	141	18.91	19.05
4	$-CH_2C_6H_5$	$-CH_3$	132	23.92	24.02
5	$-CH_2C_6H_5$	$-CH_2CH_3$	135	22.56	22.68
6	$-CH_2C_6H_5$	$-CH_2CH_2CH_3$	125	21.36	21.47
7	$-CH_2C_6H_5$	$-CH_2CH_2CH_2CH_3$	113	20.27	20.34
8	$-CH_2C_6H_4(CH_3)$-*o*	$-CH_3$	134	22.56	22.68
9	$-CH_2C_6H_4(CH_3)$-*p*	$-CH_3$	133	22.56	22.61
10	$-C_6H_{11}$	$-CH_3$	171	24.76	24.85

(4) Cassel, *Chem. Ztg.*, **53**, 479 (1929).

(5) Sugden, *J. Chem. Soc.*, **125**, 1180 (1924).

The corrected melting points and the analytical data of the ten semicarbazones are to be found in Table II.

Summary

1. Ten disubstituted aminoacetones, CH_3COCH_2NRR', have been prepared from mixed secondary amines, this being the initial report of the synthesis of six of the amino ketones.

2. Catalytic hydrogenation of seven Schiff bases, derived from benzaldehyde, by the use of Raney nickel and hydrogen under pressure afforded an easy and convenient method of preparing the corresponding mixed secondary amines in good yield.

AUSTIN, TEXAS RECEIVED JANUARY 29, 1940

[CONTRIBUTION NO. 187 FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, THE UNIVERSITY OF TEXAS]

5,5-Dimethylhydantoins Containing a —NRR′ Substituent[1]

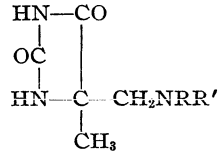
BY HENRY R. HENZE AND J. WM. MAGEE[2]

Recently we reported[3] the synthesis of ten 5,5-dimethylhydantoins containing a dialkylamino constituent. This synthesis was accomplished by adaptation of Bucherer's[4] procedure to the utilization of aminoacetone derivatives of the type $CH_3COCH_2NR_2$. In this manner, for example, we were able to convert dimethylaminoacetone into 5-dimethylamino-5-methylhydantoin despite the fact that this conversion had not been obtained by other investigators[5] using the closely related method of Bergs.[6]

It has been possible now to extend our investigation to the preparation of hydantoins from substituted aminoacetones of the type CH_3COCH_2NRR' in which R— and R′— represent different groupings. Further, since phenyl and benzyl groups are present in the structure of many anticonvulsants[7] and antispasmodics, one or both of these are present in all but one of the mixed secondary amines from which the substituted aminoacetones were prepared.

TABLE I

DISUBSTITUTED AMINODIMETHYLHYDANTOINS,



—R	—R′	Yield, %	M. p., °C. (cor.)	Nitrogen, % Calcd.	Nitrogen, % Found	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found
—C_6H_5	—CH_3	90	190	18.02	17.96	61.78	61.94	6.49	6.55
—C_6H_5	—C_2H_5	80	171	16.99	17.02	63.14	63.35	6.93	6.99
—$CH_2C_6H_5$	—C_6H_5	91	213	13.85	13.90	69.88	70.07	6.19	6.65
—$CH_2C_6H_5$	—CH_3	77	204	16.99	17.08	63.14	63.37	6.93	7.17
—$CH_2C_6H_5$	—C_2H_5	92	165	16.08	16.22	64.34	64.51	7.33	7.61
—$CH_2C_6H_5$	—C_3H_7-*n*	91	157	15.26	15.40	65.43	65.59	7.69	7.86
—$CH_2C_6H_5$	—C_4H_9-*n*	96	169	14.46	14.61	66.40	66.61	8.01	8.14
—$CH_2C_6H_4CH_3$(*o*)	—CH_3	90	177	16.08	16.19	64.34	64.51	7.33	7.59
—$CH_2C_6H_4CH_3$(*p*)	—CH_3	91	178	16.08	16.19	64.34	64.48	7.33	7.62
—C_6H_{11}	—CH_3	68	199	16.96	17.09	58.18	58.30	10.92	10.98

Experimental

For the preparation of the ten hydantoins included in this investigation, 0.1 mole of the appropriate substituted aminoacetone, whose synthesis has been reported previously,[8] 0.15 mole of potassium cyanide, 0.3 mole of ammonium carbonate and 7–8 volumes of 50% alcohol were warmed under a reflux condenser for about ten hours at 55–65°. After concentration of the solution to about one-half volume, cooling in an ice-bath caused separation of most of the hydantoin and only an additional small quantity was obtained upon neutralization of the filtrate with con-

(1) From the Ph.D. dissertation of J. Wm. Magee, June, 1938.

(2) Present address, Federal Bureau of Investigation, United States Department of Justice, Washington, D. C.

(3) Magee with Henze, THIS JOURNAL, **60**, 2148 (1938).

(4) Bucherer and Lieb, *J. prakt. Chem.*, [2] **141**, 5 (1934).

(5) Slotta, Behnisch and Szyszka, *Ber.*, **67B**, 1529 (1934).

(6) Bergs, German Patent 566,094 (1932).

(7) Through the courtesy of Eli Lilly and Company the 5-(di-*n*-butylaminomethyl)-5-methylhydantoin and the 5-(diethylaminomethyl)-5-methylhydantoin have been shown to possess approximately 50% and 40%, respectively, of the anticonvulsant value of 5,5-diphenylhydantoin.

(8) Magee with Henze, THIS JOURNAL, **62**, 910 (1940).

centrated hydrochloric acid. Because of their amino substituent, these hydantoins possess solubility in acid as well as the usual solubility in alkali.

The hydantoins were recrystallized readily from dilute alcohol, and are soluble in the ordinary organic solvents, and are insoluble in water. The compounds are stable, white, crystalline solids which melt without decomposition to clear straw-colored liquids. Analytical data and corrected melting points for the hydantoins are reported in Table I.

Summary

1. Ten examples have been prepared of a new type of disubstituted aminohydantoin in which the two substituents are not alike.

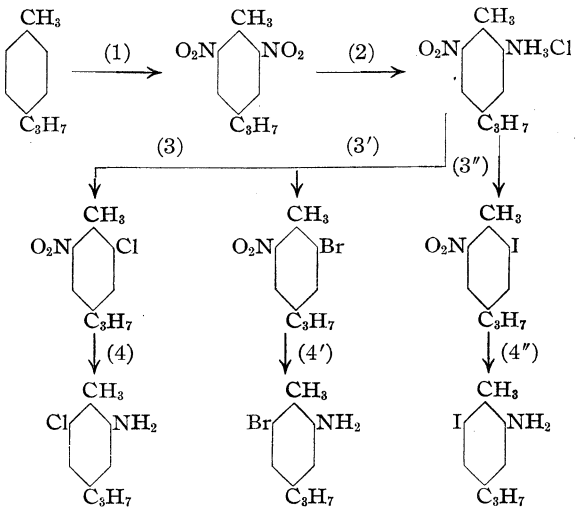
AUSTIN, TEXAS RECEIVED JANUARY 29, 1940

[CONTRIBUTION FROM THE VENABLE CHEMICAL LABORATORY OF THE UNIVERSITY OF NORTH CAROLINA]

The Preparation and Properties of 6-Halogenated Carvacrylamines from *p*-Cymene

BY R. W. BOST AND GRANVIL C. KYKER[1]

The preparation of 6-halogenated carvacrylamines by a method which locates the position of the halogen has not been reported. Wheeler and Early[2] and Inoue and Horiguchi[3] independently obtained a product by the direct chlorination of 2-nitro-*p*-cymene from which a chloronitro-*p*-cymene was separated. In each case the substance was taken to be 2-chloro-6-nitro-*p*-cymene and the subsequent reduction product to be 6-chlorocarvacrylamine. The chlorination is accompanied by low yields and a mixture of difficultly separable products since positions 3, 5 and 6 are open to substitution and other chlorination products were recognized.[2] The method of these investigators[2,3] is not applicable to the preparation of analogous bromine and iodine compounds. A method for preparing 6-halogenated carvacrylamines from *p*-cymene which is equally applicable to chloro, bromo, and iodocarvacrylamines has been investigated. The steps in the process are shown in the diagram.



Steps (1) and (2) have been reported in a previous paper.[4]

Since the position of the substituents in 2,6-dinitro-*p*-cymene and 6-nitrocarvacrylamine have been established[5] an orientation of the substituent groups in 6-halogenated carvacrylamines is obtained.

Diazotized 6-nitrocarvacrylamine gave 2-chloro-6-nitro-*p*-cymene when treated with cuprous chloride according to the procedure of Marvel and McElvain.[6] An azo dye, 2-nitro-5(?)-(6-nitrocarvacrylazo)-6-hydroxy-*p*-cymene was isolated from the reaction product; its occurrence is explained by the formation of 6-nitrocarvacrol, through a side reaction, which served as a coupler with the diazo compound. The reduction of 2-chloro-6-nitro-*p*-cymene with either tin or a mixture of tin and zinc in hydrochloric acid yielded 6-chlorocarvacrylamine.

Various derivatives of 6-chlorocarvacrylamine were studied. The amine produced crystalline salts with hydrochloric, hydrobromic, nitric, sulfuric, phenylsulfonic, *p*-tolylsulfonic, dichloroacetic, trichloroacetic, oxalic, 3,5-dinitrobenzoic, 2,4,6-trinitrobenzoic and picric acids. These salts are soluble in alcohol, insoluble in water, easily hydrolyzed, and stable in the dry state. The amine has been characterized by its acetyl, benzoyl, 3,5-dinitrobenzoyl, benzenesulfonyl, *p*-tolyl-

(1) This paper is an abstract of part of the dissertation submitted by Granvil C. Kyker to the Graduate Faculty of the University of North Carolina in partial fulfillment of the requirements for the degree of Doctor of Philosophy, in June, 1938.

(2) Wheeler and Early, unpublished thesis by Early, "The Chlorination of 2-Nitro-*p*-cymene," Department of Chemistry, University of North Carolina, 1933.

(3) Inoue and Horiguchi, *J. Soc. Chem. Ind., Japan*, **36**, Suppl. binding 189–190 (1933).

(4) Kyker and Bost, THIS JOURNAL, **61**, 2469 (1939).

(5) Wheeler and Harris, *ibid.*, **49**, 494 (1927).

(6) Marvel and McElvain, "Org. Syntheses," John Wiley and Sons, Inc., New York, N. Y., 1932, Coll. Vol. I, p. 163.

TABLE I

	Wheeler and Early[2]	Inoue and Horiguchi[3]	This study
	2-Chloro-6-nitro-*p*-cymene		
B. p., °C.	123–125 at 6–7 mm.	146–148 at 15 mm.	132–133 at 2 mm.
Density	1.1965^{20}	1.1592^{20}_4	1.1834^{25}_4
Refractive index	1.4934^{26}	1.53917^{20}	1.5397^{25}
	6-Chlorocarvacrylamine		
B. p., °C.	130–132 at 7–8 mm.	156–157 at 15 mm.	134–136 at 1 mm.
Density	1.0968^{20}	1.0866^{20}_4	1.0977^{20}_4
Refractive index	1.5583	1.50930	1.5604^{20}
M. p., °C. HCl	200–205		225–226
n-Benzoyl-		134	139
Azo-2-naphthol-		162	202

sulfonyl, *p*-bromosulfonyl, *m*-nitrobenzenesulfonyl and picryl derivatives all of which are easily prepared and purified and possess very sharp melting points. The picryl derivative has a melting point almost identical to that of the picrate but the two are easily distinguished by crystal form, solubility, color, stability to water, and mixed melting point. A substituted urea was made by condensing the amine hydrochloride with potassium cyanate. 2,2′-Diazoamino-6,6′-dichloro-*p*-cymene resulted from coupling the amine with itself in half-saturated sodium acetate.

The diazotized 6-chlorocarvacrylamine gave an azo dye with 2-naphthol and disazo dyes with phenol, resorcinol, phloroglucinol, and 1,8-dihydroxy-3,6-naphthalene disulfonic acid. *m*-Phenylenediamine, 1-naphthylamine, 2-naphthylamine, naphthionic acid and 1-amino-8-hydroxy-4-naphthalenesulfonic acid coupled easily to give dyes but these dyes resisted every attempt toward purification and no analyses were obtained on these dyes. Each of the dyestuffs was applied to wool, silk, cotton, and rayon giving varying shades of red, yellow, and brown to the fibers. The vegetable fibers were previously mordanted with tannic acid. The colors are very brilliant on animal fibers and are fast to light, washing, alkali, and perspiration.

The data of previous studies[2,3] are compared to those of this investigation in Table I.

6-Bromocarvacrylamine hydrochloride and 6-iodocarvacrylamine hydrochloride were prepared in two steps from 6-nitrocarvacrylamine, the former by a process similar to that used for the chloro analog and the latter by the method of Griess.[7] The intermediate compounds, 2-bromo-6-nitro-*p*-cymene and 2-iodo-6-nitro-*p*-cymene and the free bases of these amines have not been isolated and characterized.

(7) Griess, *Ann.*, **137**, 76 (1866).

Experimental Part

2-Chloro-6-nitro-*p*-cymene.—Precipitated cuprous chloride, prepared from 312 g. (1.25 moles) of hydrated copper sulfate, 87.5 g. (1.5 moles) of sodium chloride, 66.6 g. (0.64 mole) of sodium bisulfite, and 44 g. (1.1 moles) of sodium hydroxide, was washed several times by decantation and dissolved in 400 cc. of concd. hydrochloric acid in a stoppered flask. At 0°, 230.5 g. (1 mole) of 6-nitrocarvacrylamine hydrochloride was stirred for thirty minutes with 1200 cc. of water, 575 g. (6 moles) of concd. hydrochloric acid, and 74.5 g. (1.08 moles) of sodium nitrite. The excess nitrous acid was destroyed with urea. With vigorous stirring the cold diazo solution was added rapidly to the cuprous chloride solution which had been cooled previously to 0°. Stirring was continued for two hours at room temperature and for thirty minutes at 60°.

The oily layer was separated and distilled with superheated steam at 155–160°. About 10 liters of distillate was collected. The yellowish-red oil in the distillate was separated, stirred with an equal volume of concd. sulfuric acid at 0° for an hour, diluted and stirred with 1 kg. of cracked ice, separated, washed successively with water, dilute sodium hydroxide and water, taken up with ether and dried over anhydrous calcium chloride. After removal of the drier and ether the oil was distilled at reduced pressure. The fraction boiling at 132–133° at 2 mm. was collected. The distillate was a highly refractive, light yellow oil, n^{25} 1.5397, d^{25}_4 1.1834, soluble in ethanol, methanol, ether, acetone, carbon tetrachloride, benzene, petroleum ether and other organic solvents; yield 165.7 g.; 77.5%.

A more rapid isolation of the product was obtained by ether extraction in place of superheated steam distillation, followed by the same treatment as above but purification was easier when the steam distillation was used.

Anal. Calcd. for $C_{10}H_{12}O_2NCl$: Cl, 16.60. Found: Cl, 16.60, 16.49.

2-Nitro-5(?)-(6-nitrocarvacrylazo)-6-hydroxy-*p*-cymene.—A solid, insoluble in water and ether, was found in the isolation of 2-chloro-6-nitro-*p*-cymene as a residue in the steam distillation and as a flocculent precipitate at the interface in the ether extraction. It was purified by crystallization from acetone. The brilliant red, irregular platelets melted at 186–187°.

Anal. Calcd. for $C_{20}H_{24}O_5N_4$: N, 13.99. Found: 13.82, 13.84.

TABLE II

Procedure	Salt	Color	Crystal form	M. p., °C.	Analysis for acid, % Calcd.	Found
A	Hydrobromide	White	Needles	231–232	30.60	30.61
A	Nitrate	White	Needles	153	25.56	25.49
A	Oxalate	White	Plates	155	19.69	19.75
A	Trichloroacetate	White	Blades	157	47.09	47.01
A	2,4,6-Trinitrobenzoate	Light yellow	Needles	161	58.33	58.54
B	3,5-Dinitrobenzoate	White	Needles	133–134	53.60	53.55
B	Picrate	Deep yellow	Needles	151	55.53	55.76
C	Acid sulfate	White	Needles	166	34.82	34.72
C	Phenylsulfonate	White	Needles	184	46.27	46.69
C	*p*-Tolylsulfonate	White	Needles	193–194	48.39	48.60
D	Dichloroacetate	White	Irreg. plates	92–93	41.24	41.25

6-Chlorocarvacrylamine. (A) Hydrochloride.—To a 3-liter flask, under reflux condenser and heated on a steam-bath containing 107 g. (0.5 mole) of 2-chloro-6-nitro-*p*-cymene, 50 cc. of ethanol and 178 g. of mossy tin, was added with frequent shaking 280 cc. of concd. hydrochloric acid during a period of two hours. Refluxing and shaking was continued for two hours after the addition of the acid. The cooled reaction product was treated with an excess of sodium hydroxide, a cold saturated solution containing about 450 g. The oil was extracted with five 300-cc. portions of ether. A troublesome emulsion accompanied the extraction. The combined extracts were dried over solid sodium hydroxide, decanted from the drier, and saturated with dry hydrogen chloride. The precipitated salt weighed 100 g., was decomposed by water, stable and only slightly soluble in hydrochloric acid, and gave glistening white needles when crystallized from alcohol and hydrochloric acid; yield 91%; softens at 210–220°; m. p. 225–226° with decomposition.

Less troublesome emulsions were encountered in the ether extraction when the reduction was obtained by using a mixture of tin (10%) and zinc (90%). After completion of the reduction, the hot solution was decanted from any undissolved material and cooled. The crystals which formed were filtered and the filtrate was concentrated and cooled as long as it yielded more crystals. The above procedure of making alkaline and isolating the amine was repeated.

Anal. Calcd. for $C_{10}H_{15}NCl_2$: HCl, 16.57. Found: HCl, 16.66, 16.68.

(B) Free Base.—The hydrochloride suspended in 500 cc. of water was made alkaline with dilute sodium hydroxide. The oil was extracted with ether (five 100-cc. portions), dried over solid sodium hydroxide, decanted, ether removed and distilled at 1 mm.; b. p. 134–136°. The colorless amine became red when exposed to light and air, was soluble in common organic solvents, n^{20} 1.5604, and d^{20}_4 1.0977.

Anal. Calcd. for $C_{10}H_{14}NCl$: Cl, 19.32. Found: Cl, 19.38, 19.48.

Salts of 6-Chlorocarvacrylamine.—The following procedures gave good yields of pure salts: (A) To a dry ether solution containing the required amount of acid was added 0.005 mole of the amine in ether solution. The precipitated salt was filtered and washed with ether. (B) The amine and acid, 0.005 mole of each, were dissolved in a small amount of alcohol and heated on a steam-bath. Water was added until a slight turbidity was produced and the salt separated on cooling; it was recrystallized from alcohol and water. (C) The amine, 0.005 mole, was boiled with sufficient quantity of 5% solution of the acid to dissolve it. The hot charcoaled, filtered solution gave the salt in crystalline form when cooled. (D) The amine and acid, 0.005 mole of each, were dissolved in 10 cc. of benzene and heated to boiling on a steam-bath. The hot solution was diluted with 20 cc. of hot heptane and cooled in ice. The salt was washed in cold benzene and heptane mixture.

The data on the salts are found in Table II.

N-Acyl Derivatives of 6-Chlorocarvacrylamine.—To the amine, 0.005 mole, dissolved in pyridine, 0.006 mole, was added the acyl chloride, 0.006 mole. The mixture was stirred and placed on a steam-bath for ten to fifteen minutes. The reaction product was worked with cracked ice until it solidified. The solid was washed successively with water, dilute alkali, water, dilute acid and water and recrystallized from a suitable solvent. In each case a needle crystal resulted, white in color except in the presence of nitro groups where a straw color was observed. The data on the acyl derivatives are found in Table III.

TABLE III

Acyl derivative	Solvent	M. p., °C.	Cl Analyses, % Calcd.	Found
N-Acetyl	Heptane–pet. ether	117–118	15.72	15.68
N-Benzoyl	Alc.–water (3:1)	139	12.33	12.40
N-3,5-Dinitroben-zoyl	Alc.–water (4:1)	197–198	9.39	9.40

Sulfonyl Derivatives of 6-Chlorocarvacrylamine.—The amine, 0.005 mole, dissolved in pyridine, 0.006 mole, was treated with the sulfonyl chloride, 0.006 mole, stirred and warmed on a steam-bath for ten to fifteen minutes. The solid was stirred with water and ice until it solidified, then filtered, washed, dissolved in 2% sodium hydroxide, stirred with charcoal, filtered, and acidified with hydrochloric acid. The filtered and washed precipitate was recrystallized in each case from alcohol and water mixture (2:1). The crystals were white in each case except in the presence of a nitro group where a yellow color was noted. The data on the sulfonyl derivatives are given in Table IV.

6-Chlorocarvacrylpicrylamine.—Picryl chloride, 0.75 g. (0.003 mole), and 1.10 g. (0.006 mole) of 6-chlorocarvacrylamine were mixed in a test-tube, heated at 100° for an hour and then for an hour at 145°. During the latter

TABLE IV

Sulfonyl derivative	Crystal form	M. p., °C.	Halogen analyses, % Calcd	Found
N-Benzenesulfonyl	Platelets	117.5	10.96	11.07
N-*p*-Tolylsulfonyl	Needles	115.5	10.50	10.75
N - *p* - Bromobenzenesulfonyl	Needles	131.5	28.66[a]	28.86[a]
N - *m* - Nitrobenzenesulfonyl	Needles	129.5	9.62	9.63

[a] Chlorine and bromine.

period the reaction mixture solidified. The solid recrystallized from alcohol as reddish-orange spear-shaped crystals which melted at 150.5–151.5°.

Anal. Calcd. for $C_{16}H_{15}O_6N_4Cl$: Cl, 8.99. Found: Cl, 8.84.

2-Ureido-6-chloro-*p*-cymene.—In 5 cc. of water, 0.74 g. (0.004 mole) of 6-chlorocarvacrylamine was suspended and treated with 2.5 g. of potassium cyanate and 1.25 cc. of concd. hydrochloric acid. A pink flocculent precipitate soon appeared. The solution was left on a steam-bath for three hours after evaporation to dryness. The solid was washed several times with water. The product recrystallized from alcohol and water (3:2) and melted at 180–182° with decomposition; at 185–187° with decomposition if placed in a bath at 160° and heated.

Anal. Calcd. for $C_{11}H_{15}ON_2Cl$: Cl, 15.59. Found: Cl, 15.44.

2,2′-Diazoamino-6,6′-dichloro-*p*-cymene.—Two grams of 6-chlorocarvacrylamine hydrochloride (0.009 mole) in 20 cc. of water at 0° was treated with 0.318 g. (0.0046 mole) of sodium nitrite. After twenty minutes of stirring, an equal volume of cold saturated solution of sodium acetate was added. The reaction product stood for an hour at 0°, then was filtered, dried, and recrystallized from petroleum ether; m. p. 110°.

Anal. Calcd. for $C_{20}H_{25}N_3Cl_2$: Cl, 18.75; N. 11.11. Found: Cl, 18.47; N, 11.16.

Azo Dyes from 6-Chlorocarvacrylamine.—Diazotization of 1.1 g. (0.005 mole) 6-chlorocarvacrylamine hydrochloride was carried out in the usual manner and the excess nitrous acid was destroyed with urea. The diazo solution was added to the solution of the coupler dissolved in a slight excess of sodium hydroxide and stirred for ten to fifteen minutes. The dye was precipitated by making acid and was recrystallized from a suitable solvent. An azo dye was obtained with 2-naphthol whereas the other couplers gave diazo dyes. Data on the dyes are given in Table V.

6-Bromocarvacrylamine Hydrochloride.—Cuprous bromide was prepared by dissolving 62.4 g. (0.25 mole) copper sulfate and 35.6 g. (0.30 mole) potassium bromide in 300 cc. of boiling water. To this solution was added slowly with stirring 150 cc. of alkaline sodium sulfite prepared from 13.3 g. (0.128 mole) of sodium bisulfite and 8.8 g. (0.22 mole) of sodium hydroxide. The precipitated cuprous bromide was washed several times by decantation, dissolved in 100 cc. of 48% hydrobromic acid and 50 cc. of water, stoppered, and cooled to 0°.

According to the general method of diazotization, 38.8 g. (0.2 mole) of 6-nitrocarvacrylamine suspended in 600 cc. of water was treated with 68 cc. of 48% hydrobromic acid and 14.9 g. (0.216 mole) of sodium nitrite dissolved in 200 cc. of water. The diazo solution was rapidly poured into the cold cuprous bromide solution. A purplish-brown addition product separated. The mixture was stirred for two hours at room temperature and for thirty minutes at 50 to 60°.

The oil which separated was stirred with an equal volume of concd. sulfuric acid at 0° for an hour, diluted with an equal volume of cracked ice, separated, washed with water, dilute sodium hydroxide, and water, and dried over calcium chloride; 39 g. oil.

A portion of the crude 2-bromo-6-nitro-*p*-cymene, 12.8 g., was reduced with 18.4 g. of tin and 28 cc. of concd. hydrochloric acid. The reduction product was rendered strongly alkaline with sodium hydroxide and extracted with ether. The dried ether solution was saturated with dry hydrogen chloride. The precipitated salt gave 10 g. of white needles when recrystallized from alcohol and hydrochloric acid; m. p. 213–214° with decomposition; yield 57.5%.

Anal. Calcd. for $C_{10}H_{15}NClBr$: HCl, 13.79. Found: HCl, 13.77.

6-Iodocarvacrylamine Hydrochloride.—6-Nitrocarvacrylamine, 48.5 g. (0.25 mole) in 500 cc. of water at 0° was treated with 57 g. of concd. sulfuric acid and 18.6 g. (0.27 mole) of sodium nitrite in 100 cc. of water. The excess nitrous acid was destroyed with urea. To the diazo solution was added gradually with stirring 72.6 g. (0.44 mole) of potassium iodide in 150 cc. of solution at 0°. The mixture was stirred for an hour after reaching room temperature and then for an hour on a steam-bath. The oily layer was separated, stirred for an hour at 0° with an equal volume of cracked ice, washed with water, dilute alkali, and water, and dried over calcium chloride; 46.5 g. of oil.

Part of the crude 2-iodo-6-nitro-*p*-cymene, 14.8 g., was reduced with 18.4 g. of tin and 28 cc. of hydrochloric acid. The reaction product was made strongly alkaline with sodium hydroxide and extracted with ether. The dried ether solution was saturated with dry hydrogen chloride. The hydrochloride gave 11.5 g. of white needles when crystallized from alcohol and hydrochloric acid; m. p. 244–245° with decomposition; yield 46.5%.

TABLE V

Coupler	Solvent	Color	Crystal form	M. p., °C.	Cl Analyses, % Calcd.	Found
2-Naphthol	Gl. AcOH	Red	Needles	202	10.47	10.37
Phenol	Gl. AcOH	Brown	Needles	192–193	14.68	14.54
Resorcinol	Dil. AcOH–acetone	Dark red	Powder	233	14.21	14.10
Phloroglucinol	Benzene	Red	Plates	278	13.77	13.89
$C_{10}H_4$-1,8-$(OH)_2$-3,6-$(SO_3H)_2$	Gl. AcOH–ether	Purplish-black	Powder	Above 300	N, 7.90	7.83

Anal. Calcd. for $C_{10}H_{15}NClI$: HCl, 11.71. Found: HCl, 11.59, 11.49.

Summary

1. A direct method for the synthesis of 6-halogenated carvacrylamines from *p*-cymene in good yields has been accomplished.

2. 6-Chlorocarvacrylamine as previously described has been shown to be impure.

3. The position of substituents in 2-chloro-6-nitro-*p*-cymene, 6-chloro, 6-bromo, and 6-iodocarvacrylamines has been located by synthesis.

4. 6-Chlorocarvacrylamine has been characterized by twelve salts, three acyl and four sulfonyl derivatives, a secondary picrylamine, a substituted urea, 2,2′-diazoamino-6,6′-dichloro-*p*-cymene, one azo and four diazo dyes.

5. The dyes gave varying shades of yellow, red and brown when applied to wool, silk, cotton, and rayon; they were fast to washing, light, alkali, and perspiration.

CHAPEL HILL, NORTH CAROLINA
RECEIVED JANUARY 27, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, COLLEGE OF AGRICULTURE, UNIVERSITY OF WISCONSIN]

Synthesis of Glycol Glucosides[1]

BY SULO KARJALA AND KARL PAUL LINK

During the last ten years the production and extensive use of the glycol solvents has created a need for comprehensive toxicological studies on these compounds. This Laboratory recently undertook the preparation of large quantities of diethylene glycol β-*d*-monoglucoside for pharmacological investigations.[2] The synthesis of glucosides of other members of the glycol solvent series was studied during the course of this work.

Prior to the time that the work reported in this communication was started, ethylene glycol β-*d*-monoglucoside prepared by Fischer and Fischer[3] was the only substance of this class that had been obtained in the crystalline state. Subsequently Vintilescu, Ionescu and Kizyk[4] reported the enzymatic synthesis of this glucoside by emulsin. Bourquelot, Bridel and Aubry[5] had previously reported the biochemical synthesis of sirupy propylene glycol glucoside by the same enzyme.

A short time after our work was started, Helferich and Hiltmann[6] reported the preparation of the monoglucosides of ethylene glycol monomethyl ether, trimethylene glycol, tetramethylene glycol and the *cis* and *trans* forms of cyclopentanediol, as well as the diglucosides of ethylene, trimethylene, pentamethylene and hexamethylene glycols. Some of the work reported by them already had been completed in this Laboratory, and reference is made in the experimental part to agreement in data obtained.

(1) Published with the permission of the Director of the Wisconsin Agricultural Experiment Station.

(2) The pharmacological studies are being made by Dr. E. M. K. Geiling, Department of Pharmacology, University of Chicago.

(3) Fischer and Fischer, *Ber.*, **43**, 2529 (1910).

(4) Vintilescu, Ionescu and Kizyk, *Bull. soc. chim., Romania*, **16**, 151 (1934); *Chem. Abst.*, **29**, 4390 (1935).

(5) Bourquelot, Bridel and Aubry, *Compt. rend.*, **160**, 214 (1915).

(6) Helferich and Hiltmann, *Ann.*, **531**, 160 (1937).

Experimental

β-*d*-Acetobromoglucose.—The following procedure gave a stable product in yields above those reported previously.[7,8]

To 60 g. of acetic anhydride in a 500-cc. round-bottomed flask, fitted with a rubber stopper bearing an inlet tube reaching to the bottom of the flask and with a calcium chloride tube outlet, was added 60 g. of glucose pentaacetate. The suspension was cooled in ice and dry hydrogen bromide was introduced through the inlet tube. After all the glucose acetate had gone into solution, the passage of hydrogen bromide was interrupted, and an additional 60-g. portion of the acetate was added. Passage of the gas was resumed until the second portion of acetate had gone into solution and the mixture was saturated. With the use of a conventional naphthalene generator,[9] about 350 g. of bromine is required. The reaction takes about five hours. After the solution had stood overnight at room temperature, it was evaporated to a sirup under reduced pressure. Crystallization occurred during the concentration or upon the addition of a small amount of anhydrous ether. The crystalline product was dried and recrystallized from anhydrous ether. The mother liquors were concentrated and worked up in the same way. The yield is 109 g. (86%); m. p. 88–89°. The product could be kept indefinitely in a desiccator over phosphorus pentoxide.

Ethylene Glycol β-*d*-Monoglucoside Tetraacetate.—To 40 g. of ethylene glycol were added 12 g. of acetobromoglucose and 14.4 g. of dry silver carbonate. The mixture

(7) Freudenberg, Noë and Knopf, *Ber.*, **60**, 238 (1927).

(8) Levene and Raymond, *J. Biol. Chem.*, **90**, 247 (1931).

(9) Houben–Weyl, "Die Methoden der organischen Chemie," 3rd ed., Vol. III, Leipzig, 1930, p. 1156.

was shaken until no more carbon dioxide was evolved. Anhydrous benzene (75 cc.) was added and the mixture shaken overnight. The silver salts were removed, the two layers in the filtrate separated, and the glycol layer repeatedly extracted with anhydrous benzene. The benzene fractions were combined and concentrated[10] to a sirup which crystallized readily. Ten grams (87%) of the crude product, after recrystallization from water, gave 8 g. of the pure product; m. p. 105–106°, $[\alpha]^{23}D$ −26.3° (*c*, 3.5; H_2O).

Anal. Calcd. for $C_{16}H_{24}O_{11}$: C, 48.95; H, 6.17. Found: C, 49.15; H, 6.15.

Fischer and Fischer[3] reported a m. p. 101–103° cor., $[\alpha]D$ −26.23° in water (yield of 45%) and an uncrystallizable sirup which appeared to be an isomeric glucoside acetate. When we prepared the β-*d*-monoglucoside acetate following the original directions of Fischer and Fischer we again obtained a product melting at 105–106°. Helferich and Hiltmann[6] gave no constants on this compound.

Ethylene Glycol β-*d*-Monoglucoside.—Six grams of the above glucoside acetate was deacetylated by the method of Fischer and Fischer.[3] After standing for one month at 0°, the oily sirup was inoculated with a minute crystal of diethylene glycol β-*d*-monoglucoside (m. p. 116.5–118°). Crystallization occurred immediately. Upon recrystallization from absolute alcohol 2 g. of product was obtained; m. p. 117.5–118°, $[\alpha]^{22}D$ −28.5° (*c*, 3.4; H_2O). The melting point of a mixture with diethylene glycol *d*-monoglucoside was 102–106°.

Anal. Calcd. for $C_8H_{16}O_7$: C, 42.85; H, 7.19. Found: C, 42.73; H, 7.0.

Instead of 117.5–118°, Fischer and Fischer as well as Vintilescu, Ionescu and Kizyk[4] report a melting point of 137°. We were able to obtain this higher melting product by deacetylating a second portion of the glucoside acetate by the method of Zemplén and Pacsu.[11] The sirup crystallized readily, giving a product which after recrystallization from absolute alcohol melted at 136–137°. When a portion of the lower melting product was recrystallized using the higher melting form for inoculation, the crystals obtained melted at 136–137°. A mixture of the two products melted at 136–137°, with preliminary sintering at 123°.

The rotation of the higher melting form was $[\alpha]^{28}D$ −29.4° (*c*, 2.1; H_2O). Fischer and Fischer reported $[\alpha]^{16}D$ −30.20°, while Vintilescu, *et al.*, found $[\alpha]^{20}D$ −25.62°.

Ethylene Glycol bis-β-*d*-Glucoside Octaacetate.[12]—To 7 g. of ethylene glycol monoglucoside tetraacetate (m. p. 105–106°) in 100 cc. of anhydrous benzene was added acetobromoglucose (4 g.) and dry silver carbonate (5 g.). The mixture was shaken for twenty-four hours, filtered and the filtrate concentrated to a thick sirup. This sirup was heated to 60–70° with 350 cc. of water and filtered. The crystalline residue and the crystals obtained from the filtrate on cooling were recrystallized from absolute alcohol: yield, 3.8 g. (54%); m. p. 169–170° (cor.); $[\alpha]^{23}D$ −31.76° (*c*, 4.6; $CHCl_3$). Helferich and Hiltmann[6] report m. p. 170–171° (cor.), $[\alpha]D$ −31.80° ($CHCl_3$).

Diethylene Glycol β-*d*-Monoglucoside Tetraacetate.—This compound was prepared by the procedure used for ethylene glycol β-*d*-monoglucoside tetraacetate. The crude product (10 g., m. p. 81–84°) on recrystallization from a benzene–petroleum ether mixture gave 8 g. (63%) of the pure compound, m. p. 92–93° (cor.); $[\alpha]^{24}D$ −27.62° (*c*, 3.4; H_2O).

Anal. Calcd. for $C_{18}H_{28}O_{12}$: C, 49.52; H, 6.47. Found: C, 49.54; H, 6.58.

In order to prepare this compound in large quantities the following procedure was adopted. A solution of 100 g. of acetobromoglucose and 400 g. of diethylene glycol in 400 cc. of anhydrous dioxane was shaken for twenty-four hours at room temperature with 70 g. of dry silver carbonate. The silver salts were removed and the filtrate concentrated to remove the dioxane. The concentrate, after filtration through asbestos, was diluted with 400 cc. of water. This solution was extracted 6–8 times with thiophene-free benzene (1 liter). The combined benzene fractions were dried over sodium sulfate and concentrated until the crystallization of the glucoside acetate made distillation difficult. Enough petroleum ether (about 600 cc.) was added to throw out the glucoside acetate, and the mixture was allowed to stand overnight at 0° to ensure complete crystallization. The total yield from five such runs was 386 g., or an average of 77 g. to a run, representing a yield of 73%. The melting point of the crude product was 85–88°. This product was satisfactory for deacetylation.

Diethylene Glycol β-*d*-Monoglucoside.—Three grams of the above pure tetraacetate was dissolved in 50 cc. of absolute methanol and 2 cc. of 0.1 *N* sodium methoxide was added. The solution was refluxed for three minutes, cooled and concentrated to a sirup. A small amount of absolute alcohol was added, and the sirup warmed. Crystallization began immediately. After standing for twelve hours at 0°, 1.55 g. (84%) of the deacetylated product was obtained. Upon recrystallization from absolute alcohol, the product melted at 116.5–118°; $[\alpha]^{23}D$ −22.4° (water; *c*, 3.1).

Anal. Calcd. for $C_{10}H_{20}O_8$: C, 44.74; H, 7.52. Found: C, 44.81; H, 7.52.

For the deacetylation of large quantities of the glucoside tetraacetate the same procedure was used with 50 g. of the crude tetraacetate (m. p. 85–88°) in 200 cc. of absolute methanol and 5 cc. of 0.2 *N* sodium methoxide. By this procedure 386 g. of the tetraacetate gave 210 g. (89%) of the crude, slightly colored glucoside (m. p. 113–115°), which was recrystallized twice (carbon clarification) from two liters of absolute alcohol, yielding 202 g. of glucoside (m. p. 115–116.5°).

Diethylene Glycol bis-β-*d*-Glucoside Octaacetate.—Nineteen grams of diethylene glycol β-*d*-monoglucoside tetraacetate, 10 g. of silver carbonate and 12 g. of acetobromoglucose were shaken in 100 cc. of anhydrous dioxane for twenty-four hours, filtered, the precipitate washed with hot dioxane, and the filtrate concentrated to a thick sirup, which was heated in 400 cc. of water. The hot aqueous solution was decanted from the insoluble oil, which was washed with small portions of hot water and allowed to crystallize. On recrystallization from ab-

(10) All solvents were removed under a reduced pressure of 12 mm. unless otherwise stated.

(11) Zemplén and Pacsu, *Ber.*, **62**, 1613 (1929).

(12) Helferich and Hiltmann system of nomenclature[6] where "bis" connotes a *diglucoside*.

solute alcohol 7 g. (31%) of the product was obtained, m. p. 125.5–126.5°; $[\alpha]^{22}D$ −23.5° (*c*, 3.0; $CHCl_3$).

Anal. Calcd. for $C_{32}H_{46}O_{21}$: C, 50.12; H, 6.06. Found: C, 50.20; H, 6.07.

Deacetylation of Diethylene Glycol bis-β-*d*-Glucoside Octaacetate.—Three grams of the octaacetate, on deacetylation with sodium methoxide as described above, yielded an oil which could not be induced to crystallize. The oil was quite insoluble in cold absolute alcohol. An attempt was made to distil the product in a molecular still at 190° and 0.004 mm. pressure. The pressure changed from 0.004 mm. to 0.1 mm. during the distillation. Apparently cleavage of the glucoside occurred.

Propylene Glycol β-*d*-Monoglucoside Tetraacetate.—To 50 g. of freshly distilled racemic propylene glycol were added 12 g. of acetobromoglucose, 14.4 g. of silver carbonate and 50 cc. of anhydrous benzene. The mixture was shaken for twenty-four hours. After filtration and repeated extraction of the propylene glycol with benzene, the combined benzene extracts were concentrated to a sirup. A portion of the sirup, on scratching on a watch glass, crystallized, and the crystals were used to inoculate the main portion, which then slowly crystallized to give a mass of colorless crystals and a small amount of a red oil. The mass was treated with 100–150 cc. of water in which the red oil, which probably consisted of some diglucoside, was insoluble. The aqueous solution on evaporation to dryness gave a mass of colorless crystals which were taken up in cellosolve and treated with petroleum ether. When the solution was kept at 0°, an oil separated, but when it was allowed to stand for some time at 10–15°, a small amount of crystalline material, m. p. 67–72°, was obtained. Repeated recrystallization from cellosolve–petroleum ether or alcohol–petroleum ether mixture slowly raised the melting point until it finally remained constant at 99–101°. The yield was about 1 g. of pure material; $[\alpha]^{26}D$ −6.8° (*c*, 2.9; $CHCl_3$).

Anal. Calcd. for $C_{17}H_{26}O_{11}$: C, 50.24; H, 6.45. Found: C, 50.20; H, 6.49.

The intermediate fractions could be obtained crystalline upon evaporation to dryness. However, when the crystals were taken up in solvents, in an effort to separate the isomers by fractional crystallization, oily products were obtained.

Propylene Glycol β-*d*-Monoglycoside.—The deacetylation was carried out as above with sodium methoxide, 0.8 g. of the tetraacetate yielding 0.2 g. (43%) of product melting at 136–138°. The product was crystallized from absolute alcohol–ether; $[\alpha]^{22}D$ −25.5° (*c*, 2.0; H_2O).

Anal. Calcd. for $C_9H_{18}O_7$: C, 45.37; H, 7.62. Found: C, 45.47; H, 7.62.

A small portion of the glucoside gave a faint, but definitely positive, iodoform test which indicates that the glucosidic linkage is on the primary alcohol group of propylene glycol. Ethylene glycol β-*d*-monoglucoside, as would be expected, gave a negative test under the same conditions.

Triethylene Glycol β-*d*-Monoglucoside Tetraacetate.—To a solution of 100 g. of freshly distilled triethylene glycol and 12 g. of acetobromoglucose in 100 cc. of anhydrous benzene was added 14.4 g. of dry silver carbonate. After shaking for twenty-four hours the mixture was filtered, and the homogeneous filtrate was treated with 100 cc. of water. The aqueous solution was extracted repeatedly with benzene, the benzene solution dried over anhydrous sodium sulfate and concentrated. The resulting oil could not be induced to crystallize and was not investigated further.

Ethylene Glycol Monoethyl Ether β-*d*-Monoglucoside Tetraacetate.—A mixture of 25 g. of freshly distilled cellosolve, 6 g. of acetobromoglucose and 7.2 g. of silver carbonate was shaken until no more carbon dioxide was evolved. The reaction was very rapid, and a slight evolution of heat was observed. The mixture was filtered, the precipitate washed with hot cellosolve, and the filtrate concentrated at 45–50° to a colorless sirup, which soon crystallized. Upon recrystallization from cellosolve–water the product was isolated as long rods, yield 5 g. (82%); m. p. 65–67°; $[\alpha]^{23}D$ −19.5° ($CHCl_3$; *c*, 3.4).

Anal. Calcd. for $C_{18}H_{28}O_{11}$: C, 51.43; H, 6.72. Found: C, 51.25; H, 6.72.

Ethylene Glycol Monoethyl Ether β-*d*-Monoglucoside.—Five grams of the glucoside acetate was deacetylated with sodium methoxide. The free glucoside crystallized on evaporation of the methanol under reduced pressure and was recrystallized from absolute alcohol. The yield of the substance was 2.5 g. (83%); m. p. 139–140°; $[\alpha]^{23}D$ −26.0° (*c*, 3.1; H_2O).

Anal. Calcd. for $C_{10}H_{20}O_7$: C, 47.61; H, 7.99. Found: C, 47.5; H, 7.9.

Trimethylene Glycol β-*d*-Monoglucoside Tetraacetate.—This substance was prepared in 78% yield by the same method used for the preparation of ethylene glycol β-*d*-monoglucoside tetraacetate. Recrystallized from water, it melted at 97–98°; $[\alpha]^{26}D$ −17.3° (*c*, 4.1; $CHCl_3$). Helferich and Hiltmann[6] report a melting point of 97.5–98.5° (cor.) and $[\alpha]D$ −17.0° for this compound.

A small amount of water-insoluble material was isolated. Upon recrystallization from absolute alcohol, 0.5 g. of substance melting at 171–172° (uncor.) was obtained; $[\alpha]^{26}D$ −15.8° (*c*, 2.8; $CHCl_3$).

This substance is without doubt trimethylene glycol *bis*-β-*d*-glucoside octaacetate, for which Helferich and Hiltmann[6] report a melting point of 175–176.5° (cor.) and an $[\alpha]D$ of −16.9°.

Diethylene Glycol Monoethyl Ether β-*d*-Monoglucoside Tetraacetate.—The procedure was the same as that given for the triethylene glycol β-*d*-monoglucoside tetraacetate. A colorless sirup was obtained which could not be crystallized. The sirup was taken up in benzene which was then extracted two times with water. From the benzene solution an oil was obtained again. The aqueous extract, on evaporation to dryness, yielded crystals. On recrystallization from absolute alcohol–petroleum ether the product had m. p. 104–105.5°. This substance was identical with the monoglucoside acetate of ethylene glycol, m. p. 105–106°, a mixture of the two having m. p. 105–106°. Thus the original carbitol solution contained significant quantities of ethylene glycol as an impurity.

Distillation of the carbitol glucoside acetate in a molecular still at 160–180° and 0.004 mm. pressure gave a glassy film on the condenser. The film reverted to an uncrystallizable oil when brought to room temperature.

Deacetylation of the above Carbitol Glucoside Acetate.—A portion of the oil obtained above was deacetylated with a trace of sodium methoxide, yielding an uncrystallizable oil. Upon distillation in a molecular still at 180° and 0.004 mm. pressure a slight decrease in vacuum (to 0.01 mm.) was observed. The substance distilled, however, to give a glassy film similar to the one obtained above which reverted to an oil on warming to room temperature.

We are indebted to Dr. H. A. Campbell, Research Assistant in Biochemistry, for the micro carbon and hydrogen determinations. Our thanks are also due to Dr. P. N. Leech, Director of the Chemical Laboratory of the American Medical Association, Chicago, Illinois, and Dr. E. W. Schoeffel, chemist for the A. M. A. Chemical Laboratory, for the chemicals used in this study. Dr. Schoeffel also has checked some of the C–H determinations.

Summary

1. The properties of the monoglucosides, the monoglucoside tetraacetates, the diglucosides and the diglucoside octaacetates of ethylene and trimethylene glycol were checked with those appearing in the literature. Improvements in the methods of preparation of these glucosides are described.

2. The β-*d*-monoglucosides and the β-*d*-monoglucoside tetraacetates of diethylene glycol, propylene glycol and ethylene glycol monoethyl ether, and the β-diglucoside octaacetate of diethylene glycol have been prepared and the constants reported.

3. Triethylene glycol β-*d*-monoglucoside tetraacetate, the β-monoglucoside tetraacetate of diethylene glycol monoethyl ether and the free glucoside from the latter have been obtained as sirups.

4. A procedure is described for the large-scale preparation of diethylene glycol β-*d*-monoglucoside tetraacetate and diethylene glycol β-*d*-monoglucoside.

MADISON, WIS. RECEIVED JANUARY 22, 1940

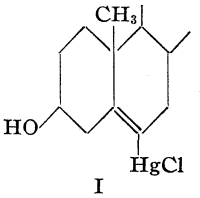
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

The Mercuration of Cholesterol

BY R. H. LEVIN AND M. A. SPIELMAN

Merz[1] mercurated cholesterol with mercuric acetate in hot glacial acetic acid, and after treating the product with sodium chloride he was able to isolate in poor yield a chloromercuricholesterol of unknown constitution. The chloromercuri derivative reacted smoothly with iodine to give an iodocholesterol which, because of the inertness of the halogen atom, resisted all efforts at structure proof. This paper presents a reinvestigation of the problem.

We have prepared chloromercuricholesterol and iodocholesterol with minor modifications of the Merz method. In agreement with him we have found iodocholesterol to be an exceedingly inert compound. Hydrolysis was, however, achieved with the aid of copper catalysis in a steel bomb at 225°. The product was a saturated hydroxy ketone identified as 6-ketocholestanol (III) by comparison with a synthetic specimen made by the usual methods.[2] It follows, therefore, that the compounds in question are 6-chloromercuricholesterol (I) and 6-iodocholesterol (II). The dibasic acid $C_{27}H_{43}O_4I$ from the sodium hypobromite oxidation of 6-iodocholesterol is without doubt 6-iodo-Diels' acid (IV).



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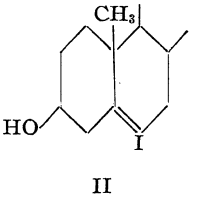

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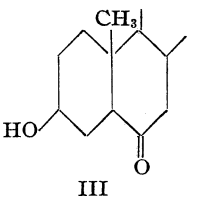

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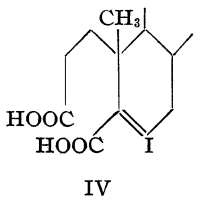


IV

No other products of mercuration could be isolated from the sirupy mercury-containing residues after isolation of the 6-chloromercuricholesterol. The large amounts of mercurous acetate formed indicate dehydrogenation, but no

(1) Merz, *Z. physiol. Chem.*, **154**, 225 (1926). Compare also Montignie, *Bull. soc. chim.*, [4] **43**, 1403 (1928); [5] **2**, 1367 (1935).

(2) Mauthner and Suida, *Monatsh.*, **24**, 652 (1903); Heilbron Jackson, Jones and Spring, *J. Chem. Soc.*, 102 (1938).

ketones were present and spectroscopic examination revealed no absorption in the region characteristic of 7-dehydrocholesterol.[3]

Experimental Part[4]

6-Chloromercurichlesterol.—The method of Merz was used with essentially the same results. A product melting at 185–205° and giving no antimony trichloride color reaction was found satisfactory for the subsequent experiment. The yield was 27% of theoretical, or corrected for recovered cholesterol, 35%. The numerous crystallizations from acetone necessary to produce a white preparation melting at 200–205° reduced the yield to 17–20% of theoretical. The mother liquors were freed of mercury by hydrolysis with hydrochloric acid. The thick brown residue gave a purple color with antimony trichloride in chloroform. No pure product could be isolated from it other than cholesterol.

6-Iodocholesterol.—The Merz method was modified as follows. Twenty-five grams of crude chloromercurichlesterol was dissolved in 300 cc. of chloroform; the solution was filtered and 10 g. of iodine was added in portions with shaking. The mixture was allowed to stand six hours and was then filtered to remove the vermilion precipitate of mercuric iodochloride. Excess iodine was eliminated by adding 30 cc. of water and bubbling in sulfur dioxide for fifteen minutes. The solution was again filtered, 50 cc. of water was added and the chloroform was removed by distillation. The water was decanted and the residue was taken up in 500 cc. of hot absolute alcohol. The mixture was treated twice with norite and allowed to cool; 9.5 g. of 6-iodocholesterol separated, and concentration of the mother liquor yielded 4.5 g. more. Crystallization from glacial acetic acid gave colorless needles melting at 156–158°; yield 50%. When pure chloromercurichlesterol was used the yield was 75% of the theoretical.

Anal. Calcd. for $C_{27}H_{45}OI$: C, 63.2; H, 8.85. Found: C, 63.4; H, 9.06.

6-Iodocholesterol benzoate is a new compound prepared by benzoylation in pyridine at room temperature for thirty minutes. Crystallization from chloroform–ether, and from dioxane, gave colorless prisms; m. p. 214–215°.

Anal. Calcd. for $C_{34}H_{49}O_2I$: C, 66.2; H, 8.02. Found: C, 66.2; H, 8.30.

6-Ketocholestanol Benzoate.—Ten grams of 6-iodocholesterol was placed in a small steel bomb (80 cc. void) together with 6 g. of sodium bicarbonate, 20 cc. of water and 50 mg. of cupric chloride. The mixture was heated to 225° for nine hours with continuous shaking. The water was decanted after cooling and the residue was taken up in chloroform. The residue after evaporation of the chloroform was benzoylated in pyridine at room temperature with 4 cc. of benzoyl chloride. The product was crystallized from methanol–chloroform and from ethanol–ether. It melted at 171–172° in agreement with the figure given by Windaus[5]; yield 89%; $[\alpha]^{20}D$ +4.0 in chloroform.

Anal. Calcd. for $C_{34}H_{50}O_3$: C, 80.6; H, 10.0. Found: C, 80.9; H, 10.1.

6-Ketocholestanol was obtained by saponification of the benzoate. It formed needles, m. p. and mixed m. p. 143–144°.[5]

Anal. Calcd. for $C_{27}H_{46}O_2$: C, 80.5; H, 11.5. Found: C, 80.6; H, 11.8.

The 6-ketocholestanol was also characterized as the acetate, m. p. and mixed m. p. 129–130°; the formate, m. p. 104–105°; and the *p*-nitrophenylhydrazone, m. p. 194°. Melting points all agreed with literature values.[5]

6-Ketocholestanol 3,5-dinitrobenzoate is a new derivative made by benzoylation in cold pyridine during twenty-four hours. Repeated crystallizations from chloroform–methanol yielded colorless crystals melting at 226–228°.

Anal. Calcd. for $C_{37}H_{48}O_7N_2$: C, 68.4; H, 8.1. Found: C, 68.2; H, 8.2.

Summary

1. Mercuric acetate in acetic acid mercurates cholesterol at position 6.

2. The mercurated product has been converted by a series of reactions to 6-ketocholestanol.

MADISON, WISCONSIN RECEIVED FEBRUARY 12, 1940

(3) Milas and Heggie, THIS JOURNAL, **60**, 984 (1938).

(4) Preliminary experiments by John Legler, M.S. Thesis, University of Wisconsin, 1937.

(5) Windaus, *Ber.*, **36**, 3754 (1903).

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE UPJOHN COMPANY]

Physiologically Active Amines. III. Secondary and Tertiary β-Phenylpropylamines and β-Phenylisopropylamines

BY E. H. WOODRUFF, JOHN P. LAMBOOY[1] AND WILLIAM E. BURT[2]

It is known[3,4] that the N-alkylation of analogs of phenethylamine has an effect on their physiological activity. The quantitative effect of this change in structure, as well as whether an increase or decrease of activity results, is variable, so that a prediction of expected properties is subject to doubt. In continuing the studies of amines it was desirable to determine the effect on the pressor and bronchodilator activity of the introduction of N-alkyl and N-aralkyl groups into the primary amines previously prepared in this Laboratory.[5,6] The synthesis of the secondary and tertiary amines described here was accomplished by one or the other of two methods.

Method I.—

$$C_6H_5CH(CH_3)CH_2NH_2 \longrightarrow C_6H_5CH(CH_3)CH_2N{=}CHC_6H_5$$

$$C_6H_5CH(CH_3)CH_2N{=}CHC_6H_5 + RI \longrightarrow C_6H_5CH(CH_3)CH_2\underset{\displaystyle I}{\overset{\displaystyle R}{\overset{|}{\underset{|}{N}}}}{=}CHC_6H_5$$

$$C_6H_5CH(CH_3)CH_2\underset{\displaystyle I}{\overset{\displaystyle R}{\overset{|}{\underset{|}{N}}}}{=}CHC_6H_5 + H_2O \longrightarrow C_6H_5(CH)CH_3NHR\cdot HI$$

The hydrolysis of the quaternary salt formed by the reaction of a benzalamine and an alkyl halide is that of Decker and Becker.[7,8,9] This method gave good results when R = CH_3 but variable and generally unsatisfactory results when used for the introduction of larger alkyl groups. The time required for the formation of the quaternary ammonium compound becomes progressively longer as the size of the alkyl group is increased. Decker and Becker[10] state that when a certain temperature or duration of heating is exceeded, by-products are obtained. This was evidently true where the hydrolysis of the ammonium compound failed to give products that could be isolated and identified and thereby limits the usefulness of the procedure.

Method II.—

$$C_6H_5CH(CH_3)CH_2NH_2 + RCHO \xrightarrow[\text{Raney Ni}]{H_2} C_6H_5CH(CH_3)CH_2NH(CH_2R)$$

$$C_6H_5CH(CH_3)CH_2NH(CH_2R) + RCHO \xrightarrow[\text{Raney Ni}]{H_2} C_6H_5CH(CH_3)CHN(CH_2R)_2$$

This is the reduction of a mixture of an amine and an aliphatic aldehyde without isolation of the intermediate reaction product.[11-18] This direct reduction procedure has been termed "reductive alkylation."

The reduction of the isolated Schiff base[19] is satisfactory when an aromatic aldehyde is used and the Schiff base readily isolated. When aliphatic aldehydes are used, Skita and Keil[11] and Emerson and Walters[17] prefer reductive alkylation. While platinum oxide catalyst is quite satisfactory for the reduction of the isolated Schiff base,[19] experiments by the authors as well as Emerson and Walters show it to be less satisfactory than Raney nickel when the reductive alkylation method is used. Skita, *et al.*,[12] on the other hand, found colloidal platinum superior to their nickel catalyst.

The procedure of Emerson and Walters, using Raney nickel and hydrogen, has been used for the reductive alkylation (II, R = H, CH_3, C_2H_5) of amines as indicated in the table of compounds. This catalyst was also successfully used to reduce the isolated benzal amine.

The only previous catalytic reductive alkylation experiments reported using formaldehyde (II, R = H) were with secondary amines.[15] Contrary

(1) Kalamazoo College Fellow 1937–1938. A part of the data is from the thesis of John P. Lambooy for the degree of Master of Science from Kalamazoo College, June, 1938.

(2) Kalamazoo College Fellow 1938–1939. A part of the data is from the thesis of William E. Burt for the degree of Master of Science from Kalamazoo College, June, 1939.

(3) Chen and Schmidt, *Medicine*, **9**, 1 (1930).

(4) Hartung, *Chem. Rev.*, **9**, 390 (1931).

(5) Woodruff and Conger, THIS JOURNAL, **60**, 465 (1938).

(6) Woodruff and Pierson, *ibid.*, **60**, 1075 (1938).

(7) Decker and Becker, *Ann.*, **395**, 362 (1913).

(8) Buck, THIS JOURNAL, **54**, 3661 (1932).

(9) Späth and Bruck, *Ber.*, **70B**, 2450 (1937).

(10) Decker and Becker, *Ann.*, **395**, 328 (1913).

(11) Skita and Keil, *Ber.*, **61B**, 1452 (1928).

(12) Skita, Keil, Baesler and Boente, *ibid.*, **61B**, 1682 (1928).

(13) Skita, Keil and Boente, *ibid.*, **62B**, 1142 (1929).

(14) Skita and Keil, *Monatsh.*, **53–54**, 753 (1929).

(15) Skita, Keil, Havemann and Lawrosky, *Ber.*, **63B**, 34 (1930).

(16) Winans and Adkins, THIS JOURNAL, **54**, 306 (1932).

(17) Emerson and Walters, *ibid.*, **60**, 2023 (1938).

(18) Emerson and Robb, *ibid.*, **61**, 3145 (1939).

(19) Buck, *ibid.*, **53**, 2192 (1931).

TABLE I

Amine	B. p. of benzal deriv. of primary amine, °C.	Mm.	B. p. of free amine Mm.	°C.	Yield, %	M. p. of hydrochloride, °C.[a]	Empirical formula	Analyses, % Carbon Calcd.	Found	Hydrogen Calcd.	Found	Nitrogen Calcd.	Found	Chlorine Calcd.	Found
β-Phenylisopropylmethylamine[b]	170–171	12	78–80		93	135–136	$C_{10}H_{16}NCl$	64.62	64.68	8.68	8.55	7.54	7.46		
β-*o*-Methoxyphenylisopropylmethylamine[b]	183	6	100–102		93	137–138	$C_{11}H_{18}ONCl$	61.24	61.29	8.41	8.19	6.49	6.62		
β-*m*-Methoxyphenylisopropylmethylamine[b]	192–194	12	135–137		90	142–143	$C_{11}H_{18}ONCl$	61.24	61.38	8.41	8.42	6.49	6.68	16.44	16.50
β-*p*-Methoxyphenylisopropylmethylamine[b]	191–193	14	117–119		29	178.5–179.5	$C_{11}H_{18}ONCl$	61.24	61.01	8.41	8.19	6.49	6.30		
β-Phenylpropylmethylamine[b]	174–176	12	96–98		80	148–159	$C_{10}H_{16}NCl$	64.62	64.52	8.68	8.84	7.54	7.49		
β-*o*-Methoxyphenylpropylmethylamine[b]	185–187	10	115–117		79	199–200	$C_{11}H_{18}ONCl$	61.24	61.25	8.41	8.17	6.49	6.33		
β-*p*-Methoxyphenylpropylmethylamine[b]	213	12	127–128		75.5	166.5–167.5	$C_{11}H_{18}ONCl$	61.24	61.42	8.41	8.45	6.49	6.45		
β-*o*-Methoxyphenylisopropylethylamine[b]			104		93	158–159	$C_{12}H_{20}ONCl$	62.73	62.94	8.77	8.76	6.14	5.96		
β-*m*-Methoxyphenylisopropylethylamine[c]			140		70	123–124	$C_{12}H_{20}ONCl$	62.73	62.62	8.77	8.72	6.14	6.31	15.42	15.28
β-*p*-Methoxyphenylisopropylethylamine[c]			137		48	156–157	$C_{12}H_{20}ONCl$	62.73	62.52	8.77	8.73	6.14	6.25	15.42	15.30
β-Phenylpropylethylamine[c]			127		94	159–160	$C_{11}H_{18}NCl$	66.10	66.43	9.08	9.27	7.01	7.15		
β-*p*-Methoxyphenylpropylethylamine[c]			137		48	156–157	$C_{12}H_{20}ONCl$	62.73	62.52	8.77	8.73	6.10	6.25	15.44	15.30
β-Phenylisopropyldimethylamine[c]			100		67	159–161	$C_{11}H_{18}NCl$	66.10	65.44	9.08	9.09	7.01	7.00	17.75	17.60
β-*o*-Methoxyphenylisopropyldimethylamine[c]			125		80.0	157–158	$C_{12}H_{20}ONCl$	62.73	62.77	8.77	8.56	6.14	6.14	15.42	15.30
β-*m*-Methoxyphenylisopropyldimethylamine[c]			132		85.5	134–135	$C_{12}H_{20}ONCl$	62.73	62.63	8.77	8.77	6.14	6.27		
β-*p*-Methoxyphenylisopropyldimethylamine[c]			137		51.3	161–162	$C_{12}H_{20}ONCl$	62.73	62.91	8.77	8.60	6.14	6.29	15.42	15.36
β-*m*-Methoxyphenylpropyldimethylamine[c]			130		63.5	175–176	$C_{12}H_{20}ONCl$	62.73	62.82	8.77	8.57	6.14	6.30	15.42	15.54
β-*p*-Methoxyphenylpropyldimethylamine[c]			129		64.1	198–199	$C_{12}H_{20}ONCl$	62.73	62.56	8.77	8.97	6.14	6.31	15.42	15.28
α-(α-Dimethylamino)-benzyl alcohol[c] (methylephedrine)			86.5–87.5[d,e]		84	190–191[e]									
β-Phenylisopropylbenzylamine			178	13	72	198–199	$C_{16}H_{20}NCl$	73.40	73.45	7.70	7.54	5.35	5.55		
β-*o*-Methoxyphenylisopropylbenzylamine			194	9	64	130–131	$C_{17}H_{22}ONCl$	69.98	70.15	7.60	7.48	4.80	4.92	12.15	12.30
β-*m*-Methoxyphenylisopropylbenzylamine			196	10	55	143–144	$C_{17}H_{22}ONCl$	69.98	69.83	7.60	7.55	4.80	4.99	12.15	12.21
β-*o*-Methoxyphenylpropylbenzylamine			197	10	85	146–147[f]	$C_{17}H_{22}ONCl$	69.98	70.10	7.60	7.80	4.80	4.61	12.15	12.26
						161–162									12.15
β-*m*-Methoxyphenylpropylbenzylamine			181	10	50	148–149	$C_{17}H_{22}ONCl$	69.98	69.83	7.60	7.58	4.80	5.03	12.15	11.97
β-*p*-Methoxyphenylpropylbenzylamine			209–212	13	78	154	$C_{17}H_{22}ONCl$	69.98	69.83	7.60	7.39	4.80	4.96		

[a] All melting points taken on a thermometer standardized against a set of Bureau of Standards Anschütz thermometers. [b] Decker and Becker method. [c] Reductive alkylation. [d] Melting point. [e] Smith, *J. Chem. Soc.*, 2056 (1927), gives m. p. 87–88° for free amine and m. p. 189–190° for the hydrochloride. [f] Two forms of this hydrochloride were obtained. Simple crystallization was sufficient to make the change, though when the melting point would change could not be predicted. In fifteen consecutive crystallizations six crops were of the high melting form and nine were of the lower melting form. No further investigation is being made of this phenomenon.

to what might be expected from the work of Emerson and Walters it was not possible to isolate any secondary amine from the reaction product when formaldehyde was used as the alkylating agent. The products were identified as the N-dimethyl derivatives and were obtained in yields ranging from 51 to 85% of the theoretical. This result resembles that obtained when other than catalytic means of reduction are employed in the reductive alkylation of an amine with formaldehyde, such as the Eschweiler reaction,[20,21,22,23] and gives a convenient method for the preparation of N-dimethylamines from the corresponding primary amine. The use of this method to convert l-ephedrine to l-methylephedrine shows that the alcoholic hydroxyl is not disturbed in the reaction. Reductive alkylation with formaldehyde therefore offers a general one step method for the preparation of N-dimethylamines without affecting the aliphatic portion of the molecule.

With higher aldehydes (II, R = CH_3, C_2H_5) the monosubstitution products were isolated, the yield increasing as the alkyl groups became larger.[17,18,24]

This change in type of product, *e. g.*, from N-dimethyl to a mixture of the higher N-alkyl and N-dialkyl amines, also resembles results obtained by the

(20) Decker and Becker, *Ber.*, **45**, 2404 (1912); *Ann.*, **395**, 342 (1913).

(21) Clarke, Gillespie and Weisshaus, THIS JOURNAL, **55**, 4571 (1933).

(22) Forsee and Pollard, *ibid.*, **57**, 1788 (1935).

(23) Baltzly and Buck, *ibid.*, **62**, 161 (1940).

(24) Unpublished data show the yield of β-3,4-dimethoxyphenylpropylethylamine was 36.3% and of β 3,4-dimethoxyphenylpropylpropylamine 64.1%.

reduction of aldehydes in the presence of ammonia.[11]

Experimental difficulties with crystallization have retarded the reporting of more N-ethyl and N-propyl amines as well as the identification of the higher boiling N-diethyl and N-dipropyl amines.

Experimental

The preparation of the methoxy primary amines used in these syntheses has been described previously.[5,6]

Alkylation by the Method of Decker and Becker.[7,8,9]—The Schiff bases used were prepared by refluxing for thirty minutes equimolecular quantities of the amine and benzaldehyde dissolved in 95% ethyl alcohol. The solvent was removed and the product distilled *in vacuo*. The Schiff bases were obtained in yields of 95% and were mostly yellow oils with a few low melting solids. They were used without further purification or analysis.

Equimolecular proportions of a benzal amine (Schiff base) and the appropriate alkyl iodide were introduced into a thoroughly dried Carius tube. After sealing, the tube was heated at 100° by steam for five to twenty-four hours, the longer time being used for the higher halides. The reaction was considered complete when the whole contents of the tube upon cooling was a red to orange viscous oil or a partially crystalline mass. A layer of mobile liquid above the viscous mass showed the reaction to be incomplete. After opening, the contents of the tube were washed out with an alcohol, methyl alcohol for the methylated product and ethyl alcohol for the higher alkylated product, to which had been added one-eighth of its volume of water. The mixture was refluxed for thirty minutes, after which it was poured into an equal volume of water and boiled until the odor of benzaldehyde had disappeared. The solution was made weakly acid with acetic acid and extracted three times with ether. After basification with 30% sodium hydroxide the amine was extracted with ether, the ethereal solution dried with anhydrous magnesium sulfate, and after removal of the solvent the residue was distilled *in vacuo*. The hydrochlorides were prepared from an anhydrous ether solution by the addition of gaseous hydrogen chloride and were recrystallized from ether–alcohol mixtures.

Reductive Alkylation.—One-tenth mole of amine, 0.3 mole of the desired aldehyde, and 1.0 g. of anhydrous sodium acetate in 100 cc. of ethyl alcohol were reduced by 58 g. of Raney nickel and hydrogen (initial pressure 50 pounds (3 atm.)) in an Adams[25] reduction machine as described by Emerson and Walters.[17] When hydrogenation was complete the catalyst was removed by filtration[26] and the alcoholic solution of the amine evaporated to dryness. The amine is extracted from the sodium acetate by ether, the ethereal solution dried with anhydrous magnesium sulfate and the residual oil fractionated. The amine hydrochlorides were prepared and purified as in Method I. Amines of the type prepared here are not sufficiently volatile with steam for this to be a practicable method to effect any separation.

Solution formaldehyde U. S. P. XI was used as the source of formaldehyde. Acetaldehyde and propionaldehyde were materials of usual purity.

Reduction of Schiff Bases with Raney Nickel.—0.05 mole of benzal amine, 30 g. of Raney nickel and 100 cc. of ethyl alcohol were shaken in the Adams[25] reduction machine under an initial hydrogen pressure of 50 pounds (3 atm.). The theoretical amount of hydrogen was absorbed in about two hours. The catalyst was removed by filtration, the solvent distilled off and the residue distilled *in vacuo;* yield, 55–85%. When less catalyst is used the reduction proceeds more slowly. These results parallel those obtained with platinum oxide[19] as a catalyst. The hydrochlorides of the benzyl amines are less soluble in absolute alcohol than those of the N-alkyl amines.

The authors wish to thank Mr. C. H. Emerson for the microanalyses reported in this work.

Summary

For the purpose of pharmacological testing a group of N-alkyl, N-dimethyl, and N-benzylphenylpropyl and isopropylamines have been prepared.

The reductive dimethylation of primary amines by means of formaldehyde and Raney nickel has been described.

KALAMAZOO, MICH. RECEIVED JANUARY 29, 1940

(25) Adams and Voorhees, "Organic Syntheses," Coll. Vol. I, 1932, p. 53.

(26) If suction is used the catalyst should always be kept covered with alcohol as it ignites quickly if sucked dry.

[CONTRIBUTION FROM THE GEORGE HERBERT JONES CHEMICAL LABORATORY OF THE UNIVERSITY OF CHICAGO]

Chlorinations with Sulfuryl Chloride. III. (a) The Peroxide-Catalyzed Chlorination of Aliphatic Acids and Acid Chlorides. (b) The Photochemical Sulfonation of Aliphatic Acids

BY M. S. KHARASCH AND HERBERT C. BROWN[1]

In an earlier paper[2] it was shown that various types of hydrocarbons can be chlorinated rapidly and conveniently by sulfuryl chloride in the presence of a small quantity of an organic peroxide. It was suggested that the reaction depends upon the initiation by the peroxide of a chain reaction involving chlorine atoms.

We have extended the study of the action of sulfuryl chloride to other types of organic compounds. The present paper is devoted to the chlorination of aliphatic acids and acid chlorides and to a preliminary report of the photochemical sulfonation of aliphatic acids.

Chlorination of Acids and Acid Chlorides

In the dark and in the absence of catalysts sulfuryl chloride does not react with aliphatic acids or acid chlorides to any appreciable extent at temperatures as high as the boiling point of the reaction mixtures (70–90°). In the presence of a small quantity of peroxide, however, chlorination of acids and acid chlorides takes place readily. Acetic acid and acetyl chloride, however, are exceptions to this generalization.

The chlorination of acids and acid chlorides by this method has been carried out, for the most part, in accordance with the general procedure described in the first paper of this series.[2] A slight modification of this procedure, however, was found to be advisable. Except in the case of acetic acid, the chlorination of the carboxylic acids is a vigorous reaction, and it was found desirable to add a small quantity of a diluent. The acid chlorides react much less violently, and the addition of a diluent is unnecessary.

In the absence of added peroxides, acetic acid is not chlorinated to any extent by sulfuryl chloride. Upon heating of a mixture of the two compounds in the dark, the sulfuryl chloride under the catalytic influence of the acid is slowly dissociated into sulfur dioxide and chlorine, and the acetic acid can be recovered unchanged. In the presence of an added peroxide, chlorination occurs. The yield of chloroacetic acid, however, is poor compared to the almost quantitative yields which can be obtained in the chlorination of the higher homologs of acetic acid. Even under optimum conditions, the yield of chloroacetic acid is not greater than 50%[3] because of loss of sulfuryl chloride by dissociation.

Acetyl chloride differs even more from its higher homologs than does acetic acid: the compound cannot be chlorinated to any appreciable extent by the use of sulfuryl chloride and either lauroyl or benzoyl peroxide. This inactivity cannot be due to the low boiling point of acetyl chloride since addition of chlorobenzene to the reaction mixture (to raise the boiling point) has no effect, while addition of cyclohexane or toluene leads immediately to a vigorous reaction in which chlorination of the hydrocarbon occurs.

In marked contrast to the inactivity of acetic acid and acetyl chloride to the reagent, is the action of trimethylacetic acid and its acid chloride. These compounds, which are usually considered to be very unreactive toward substituting reagents, are chlorinated with remarkable ease by sulfuryl chloride in the presence of benzoyl peroxide. The beta chloro derivatives are formed.

Propionic acid and propionyl chloride are chlorinated readily by the reagent to yield both the alpha and the beta chloro isomers with the beta in excess.

The preferential chlorination of an aliphatic acid or acid chloride in the beta position is rather unusual in view of the emphasis usually placed upon the activity of the alpha position in these compounds. However, the study of the chlorination of *n*-butyric acid and isobutyric acid and the corresponding acid chlorides has established the fact that the above instance is no exception. In all the cases that we have investigated, *substitution takes place preferentially on a carbon atom which is some distance removed from the carboxyl group, with the result that the yields of beta or beta and gamma chlorinated derivatives which are obtained far exceed the amount of the alpha isomer.*

(1) Eli Lilly Fellow, 1938–1939.

(2) Kharasch and Brown, THIS JOURNAL, **61**, 2142 (1939).

(3) The yields are based on the sulfuryl chloride.

The relative yields of isomers obtained in these reactions are listed in Table I.

TABLE I

PRODUCTS OF THE CHLORINATION OF ALIPHATIC ACIDS AND ACID CHLORIDES BY SULFURYL CHLORIDE AND PEROXIDES

Compound chlorinated	Products
Propionic acid	45% α-chloropropionic acid
	55% β-chloropropionic acid
Propionyl chloride	40% α-chloropropionyl chloride
	60% β-chloropropionyl chloride
Isobutyric acid	15% α-chloroisobutyric acid
	85% β-chloroisobutyric acid
Isobutyryl chloride	20% α-chloroisobutyryl chloride
	80% β-chloroisobutyryl chloride
n-Butyric acid	10% α-chloro-*n*-butyric acid
	45% β-chloro-*n*-butyric acid
	45% γ-chloro-*n*-butyric acid
n-Butyryl chloride	15% α-chloro-*n*-butyryl chloride
	55% β-chloro-*n*-butyryl chloride
	30% γ-chloro-*n*-butyryl chloride

An examination of the effect of the ordinary chlorination catalysts upon mixtures of sulfuryl chloride and organic acids or acid chlorides yielded more conventional results. For example, the addition of iodine to a reaction mixture of propionyl chloride and sulfuryl chloride kept at 70° initiates a slow reaction. The alpha chloro derivative was the only product which was isolated.

Results similar to those obtained in the peroxide-catalyzed reaction have been reported in the *photochemical* chlorination of carefully purified acids and acid chlorides in the absence of halogen carriers.[4] On the other hand, the chlorination of aliphatic acids and acid chlorides with the aid of halogen carriers as catalysts yields only the alpha-substituted derivatives.[5]

Obviously different mechanisms must operate in reactions giving such divergent products. Our entire experience suggests that both the photochemical chlorination and the peroxide-catalyzed reaction with sulfuryl chloride (which, alike, favor substitution in positions of the carbon chain other than the alpha) proceed through chain mechanisms involving chlorine atoms; on the other hand, chlorination of acids and acid chlorides with the aid of halogen carriers (in which substitution takes place only in the alpha position) must involve the action of some other form of active chlorine[6] upon the organic compound.

If, as seems probable, the active agent in the peroxide-catalyzed reactions of sulfuryl chloride is the chlorine atom, the explanation for the fact that the alpha position is not substituted to a degree commensurate with that calculated on a statistical basis is to be sought in the deactivating effect of the carboxyl and the acid chloride groups on the carbon–hydrogen bonds at the alpha position.

This is substantiated by the facts that neither the carboxyl nor the acid chloride groups can inhibit the peroxide-catalyzed reaction of sulfuryl chloride with other substances,[7] and observations that the sensitivity of the carbon–hydrogen bond to attack by chlorine atoms can be markedly decreased by substituents on an adjacent carbon atom. Thus, (1) secondary hydrogen atoms are substituted more readily than primary, (2) substitution of a second chlorine atom upon a carbon atom already holding a halogen substituent is difficult, and (3) a second chlorine atom tends to substitute a point on the carbon chain as far removed from the first chlorine substituent as possible.

The inertness of acetyl chloride toward chlorine atoms (produced from sulfuryl chloride and a peroxide) is therefore interpreted on the basis of a combined effect of the relatively high energy of activation and dissociation of primary hydrogen–carbon bonds and the further deactivation of these bonds induced by the acid chloride group. This suggestion is further supported by the fact that methyl chloroform also does not undergo the peroxide-catalyzed reaction with sulfuryl chloride.

Sulfonation of Aliphatic Acids

As has been mentioned, aliphatic acids do not react with sulfuryl chloride in the absence of catalysts and light. If light is not excluded, however, reaction occurs, leading not to chlorination but to sulfonation of the acid. In this way we have been able to prepare β-sulfopropionic acid and a sulfobutyric acid from the action of sulfuryl chloride on the corresponding acids.

The direct sulfonation of aliphatic acids and acid chlorides in the past has been accomplished by the action of sulfur trioxide or chlorosulfonic

(4) Michael and Garner, *Ber.*, **34**, 4046 (1901).

(5) Markownikow, *Ann.*, **153**, 241–242 (1870); Wolffenstein and Rolle, *Ber.*, **41**, 735–736 (1908); Bass, U. S. Patent 2,010,685. In the case of the aliphatic acids of high molecular weight, such as stearic acid, it is reported that treatment with chlorine yields a mixed product; the rule that substitution takes place predominantly in the alpha position no longer holds.

(6) This problem will be taken up in detail in a forthcoming publication.

(7) Kharasch and Brown, THIS JOURNAL, **61**, 2148 (1939). Furthermore, the presence of an equimolar portion of acetyl chloride does not prevent the chlorination of either cyclohexane or toluene; the acetyl chloride acts only as an inert diluent.

acid upon the organic compound. In all cases, the product formed is reported to be the alpha sulfo derivative.

On the other hand, the photochemical sulfonation of aliphatic acids mentioned above does not lead to the alpha sulfo derivative. Indeed, a careful study of the product obtained from the action of sulfuryl chloride on propionic acid[8] indicates that the only sulfopropionic acid formed is the beta derivative. Thus, here again is an example of different mechanisms favoring different positions for substitution: attack of acids by reagents through what appears to be an ionic mechanism leads predominantly to alpha substitution, while attack through an atomic or free-radical mechanism favors beta substitution.

The generality of this sulfonation reaction of aliphatic acids was investigated, and it was found that while acetic acid does not react, *n*-butyric and isovaleric acids can be sulfonated by this means. The yields are somewhat poorer than that obtained with propionic acid. The position of the sulfonic acid group in these products was not established.

This reaction, photochemical sulfonation with sulfuryl chloride, appears to be catalyzed by the carboxyl group. This view is based upon the observation that aliphatic hydrocarbons can be sulfonated by sulfuryl chloride in the presence of acetic acid. The yields, however, are poor, indicating that the carboxylic acids are comparatively inefficient catalysts for this reaction. Since more efficient catalysts are now available,[9] the study of this catalytic activity of organic acids was not extended.

Experimental Part

Apparatus and Materials.—The types of reaction vessels and fractionating columns which were used in this work are described in an earlier article.[2] The acids used were either Eastman Kodak Co. or commercial chemicals with one exception, trimethylacetic acid.[10] The acid chlorides available commercially were not used: impurities present in these substances (volatile sulfur and phosphorus compounds) could be removed only with difficulty. Pure acid chlorides were prepared more conveniently by the action of benzoyl chloride upon the corresponding acids.[11]

Chlorination of Acetic Acid.—The following experiments are typical of the attempts made to chlorinate acetic acid with sulfuryl chloride.

The reaction mixture, consisting of 36.0 g. of anhydrous acetic acid[12] (0.6 mole) and 40.5 g. of sulfuryl chloride (0.3 mole), was refluxed in the dark for two hours, until evolution of gas ceased. Fractionation of the reaction mixture yielded better than 90% recovery of acetic acid (b. p. 117–119°). The formation of chloroacetic acid could not be demonstrated.

A similar reaction mixture of acetic acid and sulfuryl chloride was made up, and benzoyl peroxide (0.75 g., 0.003 mole) was added. Upon heating of this mixture a vigorous reaction occurred and was complete in fifty minutes. Fractionation of the product indicated a 30% yield of chloroacetic acid (b. p. 106–109° at 40 mm.).

An attempt was made to improve the yield by adding a diluent. The reaction mixture consisted of 36.0 g. of acetic acid, 40.5 g. of sulfuryl chloride, 0.75 g. of benzoyl peroxide, and 92.4 g. of carbon tetrachloride (0.6 mole). Refluxing of the reaction mixture initiated a slow reaction. At the end of three hours, and again at the end of six hours, 0.75-g. portions of benzoyl peroxide were added. At the end of nine hours, the reaction was but 70% complete (on basis of loss of weight). The chloroacetic acid isolated amounted to 50% of the calculated yield.

Acetyl Chloride.—Acetyl chloride could not be induced to undergo the peroxide-catalyzed reaction. Since the results are negative, the experiments need not be described in any detail. One reaction mixture, consisting of equimolar parts of sulfuryl chloride and acetyl chloride, was heated for twenty-four hours in the presence of 2 mole per cent. of benzoyl peroxide without effect. Addition of solvents (carbon tetrachloride, chlorobenzene) was unavailing. The inactivity cannot be due to any inhibiting properties of the molecule since acetyl chloride can be used as an inert solvent in the chlorination of toluene or cyclohexane.

Propionic Acid and Propionyl Chloride.—Propionic acid and propionyl chloride are chlorinated readily by the reagent. The isomeric chloropropionyl chlorides can be separated easily by fractionation. Since this method of analysis cannot be utilized for the separation of the isomeric chloropropionic acids without considerable difficulty, these isomers were separated by fractionation only after they had been transformed into the corresponding acid chlorides.

The reaction mixture consisted of 59.2 g. of propionic acid (0.8 mole), 54.0 g. of sulfuryl chloride (0.4 mole), and 61.6 g. of carbon tetrachloride (0.4 mole). Benzoyl peroxide (0.5 g., 0.002 mole) was added, and the mixture was heated gently under reflux in the dark. After one and one-half hours, no more gas was evolved, and the reaction was considered complete. An excess of thionyl chloride was added (190.4 g., 1.6 moles) and the heating continued for four hours more. The carbon tetrachloride, excess thionyl chloride and propionyl chloride were distilled at atmospheric pressure; the remainder was fractionated at 100 mm. The relative yields[13] of α-chloro-

(8) The sulfonation of this acid was studied most thoroughly because of the relatively high yields which can be obtained, and the ease of separation and identification of the two possible isomers.

(9) Kharasch and Read, THIS JOURNAL, **61**, 3089 (1939).

(10) "Organic Syntheses," Coll. Vol. I, 1932, p. 510.

(11) Brown, THIS JOURNAL, **60**, 1325 (1938).

(12) The acetic acid was heated under reflux with 10% of its weight of acetic anhydride for twenty-four hours, and then carefully distilled through an efficient fractionating column.

(13) The total yield of monochloropropionyl chlorides before separation was 75%. In the preparations reported in this paper (with the exception of acetic acid) the yields of monochlorinated derivatives which were obtained varied between 70 and 90% of the calculated (based on chlorine). Losses were chiefly due to the formation of higher chlorinated compounds and loss of sulfuryl chloride through the condenser.

propionyl chloride (b. p. 51–54° at 100 mm., $n^{20}D$ 1.440) and β-chloropropionyl chloride (b. p. 81–84° at 100 mm., $n^{20}D$ 1.454) were as 45 to 55.

The identities of the products were confirmed by the preparation of the anilides: α-chloropropionanilide, m. p. 91–92°, and β-chloropropionanilide, m. p. 119–120°.

The chlorination of propionyl chloride is a much slower reaction which requires four to six hours for completion.

Isobutyric Acid and Isobutyryl Chloride.—The chlorinations of isobutyric acid and isobutyryl chloride were carried out in a manner similar to those already described. The product first was fractionated under reduced pressure and then refractionated at atmospheric pressure. The analysis and identification of the products was complicated by the fact that the values of the boiling points of the two isomeric chloroisobutyryl chlorides reported in the literature are in error. Michael and Garner[14] report the boiling points of α- and β-chloroisobutyryl chlorides to be 126–127° and 171–172°, respectively. The distillation of the reaction products from our preparations yielded two fractions, b. p. 117–118° ($n^{20}D$ 1.4369) and 151–152° ($n^{20}D$ 1.4542). The lower-boiling of these products was identified as α-chloroisobutyryl chloride by transformation into the acid, m. p. 28–30°, and the preparation of the anilide, m. p. 71–71.5°. The anilide of the higher-boiling fraction, which must be the β-chloro derivative, was prepared; the derivative crystallized from alcohol and water in long prismatic needles, m. p. 109.0–109.5°.

Anal. Calcd. for $C_{10}H_{12}ONCl$: N, 7.1; Cl, 17.98. Found: N, 7.2; Cl, 18.01.

***n*-Butyric Acid and *n*-Butyryl Chloride.**—Both *n*-butyric acid and *n*-butyryl chloride reacted with great ease. The chlorination of 150–200 g. of these compounds was complete in less than one hour. The isomeric chlorinated acids were isolated as the acid chlorides (after treatment with thionyl chloride) by fractionation under reduced pressure. At a pressure of 40 mm., the alpha derivative was collected at 45–50°, the beta ($n^{20}D$ 1.4525) at 65–67°, and the gamma ($n^{20}D$ 1.4631) at 83–85°. The identities of the isomers were confirmed by the preparation of the *p*-toluides.[15]

Trimethylacetic Acid and Chloride.—The β-chlorotrimethylacetic acid was separated from the reaction mixture by fractionation under reduced pressure; the acid was collected at 126–129° at 30 mm. It crystallized from low-boiling ligroin in the form of plates melting at 40–42°. The identity of the product was established by a chlorine determination and the neutralization equivalent.

Anal. Calcd. for $C_5H_9O_2Cl$: Cl, 26.07; neut. equiv., 136.5. Found: Cl, 25.88; neut. equiv., 136.

The amide crystallized from water in the form of plates, m. p. 108–109°.

Anal. Calcd. for $C_5H_{10}ONCl$: N, 10.34. Found: N, 10.42.

The β-chlorotrimethylacetyl chloride, formed by the chlorination of trimethylacetyl chloride, was also isolated from the reaction mixture by fractionation (b. p. 85–86° at 60 mm., $n^{20}D$ 1.4539). The amide was prepared and found to be identical with that obtained from the chlorinated acid.

(14) Michael and Garner, *Ber.*, **34**, 4054–4055 (1901).

(15) Wolffenstein and Rolle, *ibid.*, **41**, 736–737 (1908).

Chlorination of Propionyl Chloride (Effect of Halogen Carriers).—The reaction mixture was made up of 46.3 g. of propionyl chloride (0.5 mole) and 40.5 g. of sulfuryl chloride (0.3 mole). Iodine (0.5 g.) was added, and the mixture heated under reflux for twelve hours. The loss in weight of the reaction mixture was 80% of the calculated amount. Fractionation of the reaction mixture yielded 24.3 g. of material distilling in the range 103–110°. This material was treated with mercury to remove free iodine, and redistilled. The final yield was 22.0 g. of an acid chloride (b. p. 108–109°) which was identified as α-chloropropionyl chloride. The formation of the beta isomer could not be demonstrated.

Catalysts other than iodine were tested. Granulated animal charcoal causes complete dissociation of the sulfuryl chloride in five hours; however, less than 20% of chlorinated acid chloride was formed. Aluminum chloride, which is a very vigorous catalyst for the chlorination of aromatic nuclei with sulfuryl chloride, was unsatisfactory for this reaction. A mixture of iodine and carbon reduces the time required for the reaction to six hours and may therefore have some advantage over the use of iodine alone. In all cases the alpha isomer was the only chlorinated acid chloride which could be isolated.

Sulfonation of Propionic Acid.[16]—A mixture of 78.0 g. of propionic acid (1.0 mole) and 67.5 g. of sulfuryl chloride (0.5 mole) was heated gently under reflux for two hours. During the course of the reaction the flask was illuminated by a 300-watt lamp situated about 5 cm. from the reaction flask. After the reaction was complete, a mixture of ligroin (60–70°) and benzene was added, precipitating a white solid. The mixture was permitted to stand for twenty-four hours at room temperature to ensure complete precipitation. The supernatant liquid was then decanted, and the solid was washed several times with dry ligroin. Finally, the mixture was filtered on a Büchner funnel and the solid quickly transferred to a desiccator containing paraffin and phosphorus pentoxide. The weight of the dry crude product (m. p. 100–102°) was 28.3 g., a yield of 37%.

Its properties and reactions indicate that this substance must be β-sulfopropionic acid. The analysis and identification were rendered difficult by our inability to purify the product by recrystallization: the crude material was insoluble in ligroin, benzene and chloroform, and extremely soluble in water and alcohol to yield strongly acid solutions. The extreme hygroscopic nature of the substance added to the difficulties of analysis. A qualitative analysis showed the presence of sulfur and the absence of halogen.

Anal. Calcd. for $C_3H_6O_5S + {}^1/_2H_2O$ ($HO_3SC_2H_4COOH + {}^1/_2H_2O$): C, 22.09; S, 19.63; H, 4.3; neut. equiv., 81.5. Found: C, 22.11; S, 19.62; H, 4.7; neut. equiv., 80.6.

The water indicated in this analysis is probably not a definite quantity. It was noted that even very short exposures to the atmosphere rapidly increased the water content of the material.

The position of the sulfonic acid group was definitely established by a study of the solubility and composition of the barium salt. The barium salt of α-sulfopropionic

(16) These results are to be considered as a preliminary report; we are continuing the study of this reaction.

acid crystallizes from water with 1.5 moles of water and is soluble to the extent of 7 parts of salt per 100 parts of water. On the other hand, the barium salt of the β-isomer crystallizes with 5.0 moles of water and is less than one-tenth as soluble.

Ten grams of the dried sulfopropionic acid was dissolved in 300 cc. of hot water, and the solution was neutralized with crystalline barium hydroxide. The hot solution was filtered and permitted to cool to room temperature. The crystals which separated (prismatic plates) were collected on a filter and air dried. The filtrate was then concentrated to 100 cc. and the process was repeated. A total yield of 22.1 g. of the air-dried salt was obtained (first crop, 15.8 g.; second crop, 6.3 g.), representing slightly more than 90% of the yield theoretically possible.

Anal. Calcd. for $Ba(C_3H_4O_5S)\cdot 5H_2O$: H_2O, 23.73; Ba, 36.21. Found: H_2O, 23.57; Ba, 36.33.

In the course of the attempts to recrystallize the original product, it was found that treatment with thionyl chloride yielded a crystalline substance which has been tentatively identified as an anhydride of β-sulfopropionic acid.

Three grams of the crude sulfopropionic acid was heated under reflux for three hours with 20 g. of thionyl chloride. Ligroin was added, and the mixture was heated until the solid which at first had precipitated, redissolved. Upon cooling, a solid separated in the form of thin plates. This material was recrystallized from thionyl chloride and ligroin, and placed in a vacuum desiccator over paraffin and freshly fused potassium hydroxide. The substance melted sharply at 76–77°. It contained sulfur, but no chlorine. The neutralization equivalent was found to be 67.4, 68.3; the calculated value for the anhydride is 68.0.

Acids as Catalysts for Sulfonation of Hydrocarbons.[9]—Since the carboxyl group appears to be the active catalyst in this reaction, we studied the photochemical sulfonation of hydrocarbons in the presence of a carboxylic acid. Sulfonation occurs, but the yields are low. The following experiment is typical of the results obtained.

In a flask were placed 42.0 g. of cyclohexane (0.5 mole), 33.8 g. of sulfuryl chloride (0.25 mole) and 1.0 g. of acetic acid. The mixture was heated gently and illuminated for four hours. Upon fractionation, there was obtained 20 g. of cyclohexyl chloride (b. p. 65–70° at 60 mm.) and 2.2 g. of cyclohexane sulfonyl chloride (b. p. 125–135° at 12 mm.). The yield of sulfonyl chloride is but 5% of the calculated.

Summary

1. The action of sulfuryl chloride on acetic, propionic, *n*-butyric, isobutyric, and trimethylacetic acids and the corresponding acid chlorides under various conditions, has been investigated.

2. In the absence of catalysts and light sulfuryl chloride does not react with organic acids and acid chlorides.

3. In the presence of a small quantity of added peroxide, the higher aliphatic acids and acid chlorides react vigorously to form 70 to 90% yields of chlorinated derivatives. On the other hand, acetic acid reacts with difficulty, and acetyl chloride cannot be chlorinated in this way.

4. The yields of the various isomeric chloro derivatives indicate that the alpha position in the carbon chain is substituted with greater difficulty than the beta and gamma positions. That is, *the product consists chiefly of beta or beta and gamma chloro acids (or the corresponding acid chlorides)*. For example, the chlorination of *n*-butyryl chloride yields 15% α-, 55% β-, and 30% γ-chlorobutyryl chloride.

5. If halogen carriers, such as iodine, instead of peroxides are used to catalyze the reaction of sulfuryl chloride with acid chlorides, substitution takes place only at the alpha position. The mechanisms involved in the two reactions must be of two different types; it appears that the peroxide-catalyzed reaction is a chain reaction involving chlorine atoms, while the iodine-catalyzed chlorination is due to another form of active chlorine.

6. Sulfuryl chloride also undergoes a photochemically catalyzed reaction with the higher aliphatic acids to yield sulfonated acids. In this way, a 37% yield of β-sulfopropionic acid readily can be isolated. *n*-Butyric and isovaleric acids also have been sulfonated. Acetic acid does not react.

7. Acetic acid catalyzes the photochemical sulfonation of hydrocarbons with sulfuryl chloride. The yield is small.

8. In the course of this investigation, the following compounds have been prepared and characterized: β-chlorotrimethylacetic acid and the corresponding acid chloride and amide, and the anhydride of β-sulfopropionic acid.

CHICAGO, ILLINOIS RECEIVED DECEMBER 21, 1939

[CONTRIBUTION FROM THE CHEMISTRY LABORATORIES OF THE UNIVERSITY OF IDAHO]

The Viscosities of Arabogalactan Solutions

BY HARRY S. OWENS

Arabogalactan is a water-soluble polysaccharide present in the Eastern, Western and Siberian varieties of the larch. Trimble[1] in 1898 described a water-soluble material extracted from larch wood, but he reported no quantitative data concerning it. Schorger and Smith[2] investigated it further and called it ϵ-galactan, believing that the only monosaccharide residue present in the molecule was galactose. Wise and Peterson,[3] Wise and Unkauf,[4] Nikitin and Soloviev,[5] Barry[6] and Woodruff[7] have shown that arabogalactan contains both arabinose and galactose and that the proportion of sugar residues in the molecule is about one to six, respectively.[8]

As much as 17% of arabogalactan has been reported present in the heartwood of the Western larch,[2] yet little is known of its properties, functions in the tree, or its possible utilization. It seemed desirable to determine some of its physical properties because of this scarcity of information and also because the knowledge obtained could be applied to other problems under way in these Laboratories.

Viscosity measurements were chosen because they offer a means of obtaining some idea of the shape of large molecules in solution, and they may be used to determine the approximate molecular weight of such molecules.

Materials.—The arabogalactan was extracted from shavings taken from the butt of a Western larch tree. A system of counter-current extractions was used in which 400 g. of shavings was placed in a crock with sufficient water to saturate the fibers; then 4 liters of water was added. After four days the extract was poured on a fresh batch of water-soaked shavings while 4 liters of water was added to the extracted shavings. This process was repeated until the initial 4 liters of water had extracted 1600 g. of shavings. The concentrated extract was filtered through a filter bed of filter-aid and charcoal until clear and colorless, then poured into four volumes of 95% alcohol. After drying the precipitate, a white powder was obtained having an ash content of 0.06% and an anhydrogalactose content of 85% (87.7% of theoretical). The product was dissolved in water, and filtered through fritted glass membranes in order to remove filter paper fibers and particles of dust that could not be removed by filtrations through fine filter paper. It was reprecipitated with alcohol and dried at 105°, before using.

The ether, acetone, dioxane, acetic acid and chloroform were analytical reagent grade. The alcohol was 95% U. S. P., and the chloroform was U. S. P. grade. Isobutyl alcohol, ethylenediamine (69.8%), Butyl Carbitol, Cellosolve and monoethanolamine were commercial solvents supplied by the Carbide and Carbon Chemicals Corp. The amyl acetate was a commercial product supplied by Sharples Solvent Corp. Merck activated charcoal was used for all decolorizations. Pfanstiehl Chemical Co. C. P. *d*-lactose and *d*-galactose were used also.

Methods.—An Ostwald viscometer was used throughout this work. The measurements were made in a thermostat kept within 0.1° of the temperature desired.

Densities were determined with a specific gravity bottle of about 50 ml. capacity, and the weights were corrected to readings in vacuum.

Calibrated volumetric flasks were used in making up solutions, and precautions were taken to have the solutions made up to volume at the temperature to be used for measurements.

The tests for solubility of arabogalactan in various solvents were purely qualitative. One-tenth of a gram of the solid was weighed and shaken with 40 to 60 ml. of the solvent. If the solid did not dissolve, the supernatant liquid was decanted and evaporated to dryness and the residue weighed. The solvent acted upon the solid for twenty-four hours at room temperature with intermittent shaking.

Results.—The viscosity measurements made with arabogalactan solutions at 20, 40, and 60° are plotted in Fig. 1. It will be seen that the viscosities of the solutions are directly proportional to the concentration until about 6% is reached. Viscosities of solutions from 6–10% in concentration showed greater and greater deviations from linearity.

Results at 25° with arabogalactan, galactose and lactose solutions are shown in Fig. 2. The viscosity measurements made by Pulvermacher[9] with galactose and lactose are shown for comparison.

The density values for arabogalactan solutions at 25° have been converted to the reciprocals (specific volumes) and are plotted in Fig. 3.

(1) Trimble, *Am. J. Pharm.*, **70**, 152 (1898).

(2) Schorger and Smith, *Ind. Eng. Chem.*, **8**, 494 (1916).

(3) Wise and Peterson, *ibid.*, **22**, 362 (1930).

(4) Wise and Unkauf, *Cellulosechem.*, **14**, 20 (1933).

(5) Nikitin and Soloviev, *J. Applied Chem. (U. S. S. R.)*, **8**, 1016 (1935); through *Chem. Abst.*, **30**, 5563 (1936).

(6) Barry, Thesis, N. Y. State College of Forestry, 1936.

(7) Woodruff, M.S. Thesis, University of Idaho, 1937, under the direction of Dr. E. C. Jahn, now at Syracuse University.

(8) Barry[6] disagrees with this ratio and the significance attached to it. On the basis of specific viscosity measurements of the propionyl and benzoyl derivatives of arabogalactan from various sources and because he was able to fractionate these derivatives, he concluded that arabogalactan is a mixture of araban and galactan.

(9) Pulvermacher, *Z. anorg. allgem. Chem.*, **113**, 141 (1920).

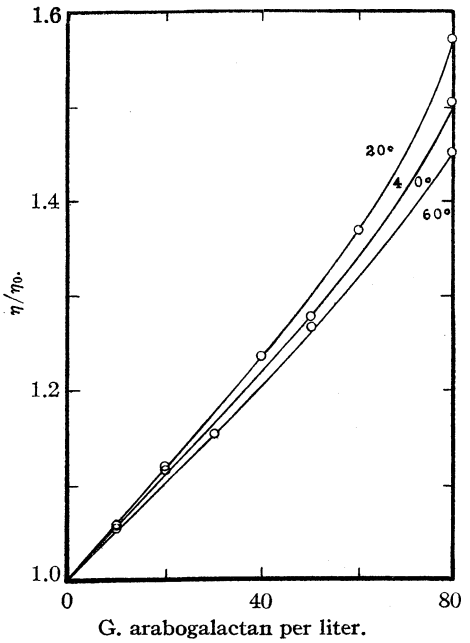


Fig. 1.—Effect of temperature on the relative viscosities of arabogalactan solutions.

By extrapolation to 100% arabogalactan a specific volume is obtained of 0.65 ml. per g.

The tests for solubility indicate that arabogalactan is so difficultly soluble in any of the solvents tried that viscosity measurements were limited to water systems. Arabogalactan was soluble to about a 0.2% solution in carbon tetrachloride,

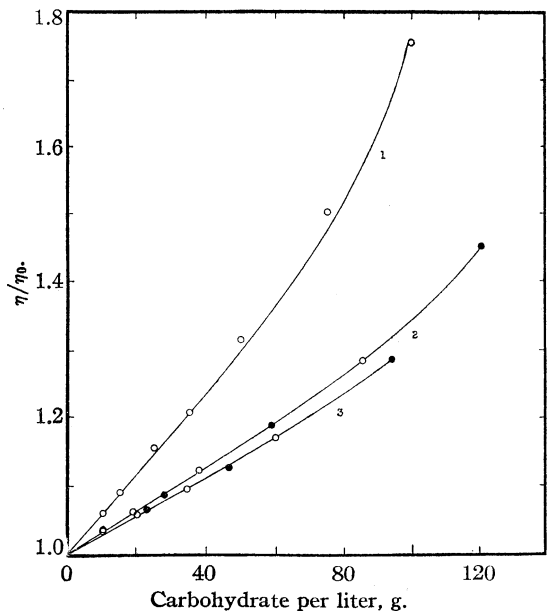


Fig. 2.—Comparison of the relative viscosities of arabogalactan (1), lactose (2), and galactose (3) at 25°; ● Pulvermacher's results.

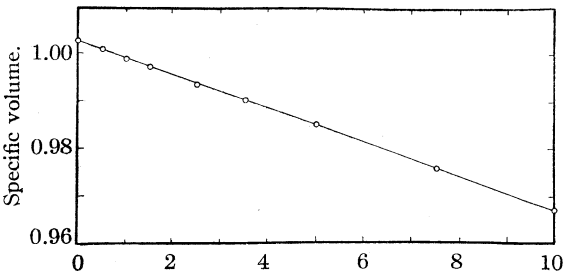


Fig. 3.—Specific volumes of arabogalactan solutions.

ethylenediamine (69.8%) Cellosolve and monoethanolamine. About a 0.1% solution could be formed in Butyl Carbitol. Arabogalactan was insoluble in the other solvents tried.

Discussion

There are several equations available which correlate viscosities and the percentage of the volume of a solution occupied by the dispersed substance. Einstein's[10] equation $\eta/\eta_0 = 1 + 2.5\ \phi$ where η is the viscosity of the solution, η_0 is the viscosity of the pure medium, and ϕ is the fraction of the volume occupied by the dispersed substance, is probably the most widely known. Hatschek's[11] equation $\eta/\eta_0 = 1 + 4.5\ \phi$ has received attention also. A purely empirical equation obtained by Kunitz[12]

$$\eta/\eta_0 = \frac{1 + 0.5\,\phi}{(1 - \phi)^4}$$

probably expresses the facts better than either of the theoretical equations.[13]

The viscosity data have been used in calculating values of ϕ by all three equations. The specific volume also has been calculated by dividing ϕ by the percentage concentration of the arabogalactan solution. The values calculated are shown in Table I.

TABLE I

RELATIVE VISCOSITIES AND PARTIAL VOLUMES OBTAINED FROM VARIOUS VISCOSITY EQUATIONS

		Kunitz		Einstein		Hatschek	
C, g./l.	η/η_0 at 25°	ϕ, %	V, ml./g.	ϕ, %	V, ml./g.	ϕ, %	V, ml./g.
20	1.118	2.50	1.25	4.72	2.36	2.62	1.31
40	1.235	4.68	1.17	9.38	2.35	5.21	1.30
60	1.372	6.90	1.15	14.88	2.48	8.25	1.37
80	1.538	9.20	1.15	21.50	2.69	11.95	1.49
100	1.758	12.00	1.20	30.20	3.02	16.80	1.68

The constancy of the values for the specific volume (V) of arabogalactan to a concentration

(10) Einstein, *Ann. Physik*, **19**, 289 (1906); **34**, 59 (1911).
(11) Hatschek, *Kolloid Z.*, **7**, 30 (1910).
(12) Kunitz, *J. Gen. Physiol.*, **9**, 715 (1925–1926).
(13) Gortner, "Outlines of Biochemistry," John Wiley and Sons, N. Y., 1938, p. 54.

of 60 g. per liter, regardless of the equation used, indicates that the molecule must be spherical. For the entire range of concentrations, the Kunitz equation shows greater constancy for the values of V.

Other evidence indicating a preference for the Kunitz equation comes from the density measurements. The specific volume obtained from those measurements is 0.65 ml. per g., and Fig. 1 indicates that the degree of solvation is low; consequently the lowest figures obtained for the specific volume by means of the viscosity equations should be more nearly correct. The values for V from the Kunitz equation are the lowest reported.

Whether or not the difference between the specific volumes obtained by the viscosity and the density methods represents the amount of water solvated by arabogalactan will require confirmation through measurements of the rate of diffusion of arabogalactan.

Staudinger[14] has devised equations expressing the relation of specific viscosity $\eta_{sp} = (\eta/\eta_0 - 1)$ and the molecular weight. One of these equations can be used for this work. It is $\eta_{sp} = K_m CM/B$ where K_m is a constant determined from viscosity measurements with substances of similar natures of known molecular weights; C is the concentration in g. per liter; B is the "base weight," the molecular weight of the simplest repeating unit in the molecule; M is the molecular weight of the complete molecule.

Galactose was used to determine the value of K_m which was found to be 2.7×10^{-3}. The simplest repeating unit in arabogalactan is $[C_5H_8O_4 \cdot (C_6H_{10}O_5)_6]$, which has a base weight of 1104. Substituting these values in the Staudinger formula yields an average molecular weight of 2300 for arabogalactan.

This value agrees very well with that of Nikitin and Soloviev,[5] who obtained 2208 by chemical methods after they had found that cryoscopic methods were not applicable. (Schorger and Smith[2] report a value of 3286 using cryoscopic methods.) The agreement between the values obtained by Nikitin and Soloviev and the author may or may not be significant. Viscosity measurements of this kind should be made in a medium which will not be solvated by the dissolved material. The search for a solvent having a lower dipole moment than water proved fruitless. However, the greatest source of error in these experiments is the application of the constant, K_m, determined with galactose having a molecular weight of 180. Staudinger and Daumiller[15] working with cellulose triacetates, Fordyce and Hibbert[16] with polyoxyethylene glycols and Kraemer and van Natta[17] with hydroxydecanoic acid derivatives have all shown that the constant, K_m, increases rapidly as the molecular weight of compounds of a homologous series decreases from a value of 2000. K_m is more nearly a true constant with compounds having a molecular weight above 2000. Values for K_m reported in the literature for various types of compounds vary from 0.2 to 2.3×10^{-3}; consequently one can conclude that the molecular weight of arabogalactan is at least 2208 and may be even higher.

Summary

1. The viscosities of arabogalactan solutions having concentrations of from 1–8% have been measured at 20, 25, 40, and 60°.

2. Arabogalactan was found to have a spherical shape when dissolved in water.

3. The molecular weight of arabogalactan is at least 2208, the simplest formula being $(C_5H_8O_4 \cdot (C_6H_{10}O_5)_6)_2$.

MOSCOW, IDAHO RECEIVED FEBRUARY 5, 1940

(14) Staudinger, *Ber.*, **67**, 92 (1934).

(15) Staudinger and Daumiller, *Ann.*, **529**, 219 (1937).

(16) Fordyce and Hibbert, THIS JOURNAL, **61**, 1912 (1939).

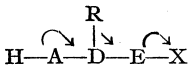
(17) Kraemer and van Natta, *J. Phys. Chem.*, **36**, 3175 (1932).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF DUKE UNIVERSITY]

Elimination and Metathetical Reactions and the Electronic Theory of Rearrangements

BY CHARLES R. HAUSER

Various workers have attempted to formulate general mechanisms for elimination, metathetical and intramolecular rearrangement reactions, which are characteristic of many compounds containing an electronegative atom or group, X (such as halogen or hydroxyl). In 1928 Ingold and Shoppee[1] pointed out that the fundamental type of electronic change underlying a number of apparently diverse rearrangements is the same. They represented these changes according to the following scheme, in which A, D and E are atoms of carbon, nitrogen or oxygen



In 1932 Whitmore[2] formulated a more comprehensive and detailed theory for eliminations, metatheses and intramolecular rearrangements. The essential feature of the theory is that X is removed with a complete octet of electrons, leaving an atom with only a sextet of electrons. The positive fragment thus formed may add an anion, lose a proton or undergo rearrangement (involving the shift of an electron pair together with R attached) to form a new positive fragment which may undergo these changes.

While these generalizations account for the products (both "normal" and rearranged) that are formed in certain reactions effected by acidic reagents[3] or heavy metal salts,[4] it is now recognized that the thory requires modification. Evidence has been presented that at least in certain metatheses[5] and in a pinacol type of rearrangement[6] (in which a molecule of water is eliminated) an atom with an "open" sextet is probably not actually formed as an intermediate.

For the purpose of predicting products it is generally adequate to describe the general courses of reactions, rather than to give detailed mechanisms. The roles of reagents used to effect reactions should be taken into account, and, for convenience, the course may be represented in steps. The courses of eliminations, metatheses and intramolecular rearrangements effected by means of acids, acidic reagents or heavy metal salts (or in certain cases by heat alone) may be described by the generalizations outlined by Whitmore (with the modification that the steps may occur simultaneously). These reactions may be initiated (or facilitated) by an attack of the reagent on X,[7] which is removed with its bonding pair of electrons. The course of elimination of HX involves the removal of X, with or without rearrangement of the molecule, accompanied or followed by the loss of a proton. Metatheses in the presence of these reagents may involve the primary removal of X, or might follow the course outlined in the next paragraph.

Metathetical reactions with basic anions, for example, the alkaline hydrolysis of alkyl halides, may be considered to involve an attack by the anion on the face of the carbon tetrahedron which is opposite X, the addition of the basic anion and the release of X as an anion occurring simultaneously (and being accompanied by the Walden inversion).[8]

Elimination reactions in which HX is removed by bases, probably involve a primary attack on the hydrogen, even when it is attached to a carbon atom. It is obvious that when a base is used to remove HX from a distinct acid, for example, trichloroacetic acid (where X is CCl_3) or a bromoamide, the hydrogen is first withdrawn as a proton, and evidence has been presented by Ingold,[9] Olivier[10] and others[11] that in the elimination of HX from the adjacent atoms of alkyl halides[10] or certain other compounds, the reaction is initiated

(1) Ingold and Shoppee, *J. Chem. Soc.*, 365 (1928); Ingold, *J. Chem. Soc. Annual Reports*, **25**, 133 (1928); also, see Baker, "Tautomerism," Routledge, London, 1934, pp. 276–309.

(2) (a) Whitmore, THIS JOURNAL, **54**, 3274 (1932); (b) Whitmore and Fleming, *J. Chem. Soc.*, 1269 (1934); also, see Wallis in Gilman "Organic Chemistry," John Wiley and Sons, New York, N. Y., 1938, pp. 778–801.

(3) See Whitmore and Langlois, THIS JOURNAL, **54**, 3441 (1932); also, see ref. 2a.

(4) See ref. 2b and Whitmore, Wittle and Popkin, *ibid.*, **61**, 1588 (1939).

(5) See, for example, Johnson in Gilman "Organic Chemistry," John Wiley and Sons, New York, N. Y., 1938, p. 1633.

(6) Bartlett and Pockel, THIS JOURNAL, **59**, 820 (1937); see also Bernstein and Whitmore, *ibid.*, **61**, 1324 (1939).

(7) In this connection, see Roberts and Hammett, *ibid.*, **59**, 1063 (1937); Ayers, *ibid.*, **60**, 2957 (1938); see also ref. 6, p. 821.

(8) For recent references to the Walden inversion see ref. 5 and Bartlett and Knox, *ibid.*, **61**, 3184 (1939).

(9) See especially, Ingold, Hughes and co-workers, *J. Chem. Soc.*, 1177–1291 (1937), and earlier papers; Taylor, *ibid.*, 343, 1962 (1937); Watson, *J. Chem. Soc., Ann. Repts.*, **35**, 226 (1938).

(10) Olivier, *Rec. trav. chim.*, **53**, 1093 (1934).

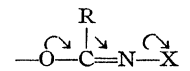
(11) See Hauser, LeMaistre and Rainsford, THIS JOURNAL, **57**, 1056 (1935).

by an attack on the hydrogen atom. The remainder of this paper is devoted to the development of these ideas.

The Removal of HX from Organic Compounds by Means of Bases.—In this paper it is assumed as a working hypothesis that most organic compounds from which HX is removed by means of bases to form unsaturated products (or, in certain cases, cyclic products) function as acids, and that the primary acid–base reaction conditions subsequent changes that may occur. For convenience, the general course of these elimination reactions may be divided into three steps. First, the hydrogen is removed as a proton; second, X is released with a complete octet of electrons (*i. e.*, as an anion); and third, the molecule is stabilized. While intimate mechanisms may differ, most eliminations effected by bases may be considered to follow this general course.[12]

The first step is regarded as an acid–base reaction according to the modern conception of acids and bases. The extent to which this reaction may occur independently of subsequent changes should depend upon the acidic strength of the organic compound, the solvent, and the strength of base used. For a given base and solvent, the equilibrium of the acid–base reaction will of course be determined by the acidic strength of the organic compound. Two extreme types of reaction would be type I, in which the equilibrium of the acid–base reaction is far on the side of corresponding salt, and type II, in which the equilibrium of the acid–base reaction would be far on the side of the original acid and base. An example of type I is the reaction of alkali with a distinct acid, such as trichloroacetic acid, or even a bromoamide, and an example of type II is the reaction of this base with an extremely weak acid, such as an alkyl halide or a compound of the type RCH=NX. Although these types exhibit different kinetics, both may be classified according to the general course outlined above. It should be pointed out that in reactions of type I, steps (2) and (3) may occur simultaneously, while in reactions of type II, all three steps may be simultaneous and dependent on one another.

It has been shown that at least in certain cases reactions of type I exhibit monomolecular kinetics, the reaction measured presumably being the decomposition of the negative organic ion[13] of the salt which is formed by the removal of the proton. The rate of decomposition of the negative organic ion, even though rearrangement occurs, in general appears to be dependent upon the anionic stability (or the "negativity") of X and on the capacity for electron release of the remainder of the molecule. Thus, for example, in the decomposition[14] of negative organic ions of the type



the order of increasing rate (as well as the order of increasing anionic stability of X) when R is phenyl and X is varied is as follows: p-$CH_3OC_6H_4COO$ < HC_6H_4COO < m-FC_6H_4COO < m-$NO_2C_6H_4COO$; while the order of decreasing rate (as well as the order of decreasing capacity for electron release of R) when X is benzoate or bromine and R is varied is as follows: p-$CH_3OC_6H_4$ > HC_6H_4 > m-ClC_6H_4 > m-$NO_2C_6H_4$.

Most reactions of type II, at least when HX is removed from adjacent atoms, exhibit bimolecular kinetics, the rate of elimination of HX being dependent upon the "activity" of the hydrogen and the strength of base used. Thus, hydrogen bromide is removed by alkali two hundred times faster from ethylene dibromide than from ethylidene bromide,[10] and in the series of para substituted benzalchlorimines, $Y—C_6H_4CH=NCl$, the rates of elimination of hydrogen chloride by alcoholic alkali are directly related to the strengths of the corresponding carboxylic acids.[11]

Since the rates of elimination of HX from adjacent atoms of compounds of type II are related to the activities of the hydrogen, it might appear that the removal of the proton is the rate determining step of the reaction,[15] but it might also be possible for the rate determining step to be the release of X as an anion from the negative organic ion that would be formed by the removal of the proton. Since the equilibrium of the acid–base

(12) In certain cases in which the hydrogen is relatively unreactive, and X relatively easily released as an anion, it is possible that X might be removed first followed by the loss of the proton, even in the presence of a base. In this connection see *J. Chem. Soc., Ann. Repts.*, **35**, 226 (1938).

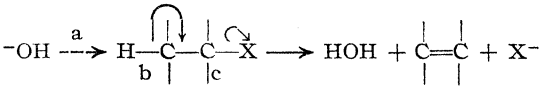
(13) The decomposition of the trichloroacetate ion exhibits monomolecular kinetics. The reaction gives carbon dioxide and presumably the ion $(CCl_3)^-$ which immediately takes up a proton from the solvent forming chloroform; Verhoek, THIS JOURNAL, **56**, 576 (1934).

(14) See Renfrow and Hauser, *ibid.*, **59**, 2308 (1937); Hauser and Renfrow, *ibid.*, **59**, 121 (1937); Bright and Hauser, *ibid.*, **61**, 618 (1939).

(15) The reactions of certain extremely weak acids (in which the acidic hydrogen is attached to carbon) with bases, are slow enough to measure; Conant and Wheland, *ibid.*, **54**, 1212 (1932).

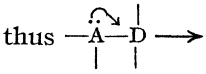
reaction would be far on the side of the original base and extremely weak acid, the concentration of the negative organic ion should be dependent upon the concentrations of both the base and the acid. The fact that the rate is directly related to the activity of the hydrogen rather than the ease of release of X, as in reactions of type I, might be accounted for on the basis that the activating atom or group, for example, the para substituent of a benzalchlorimine, activates the hydrogen relatively more than it retards the release of chloride ion.

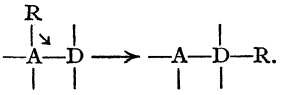
According to the generally accepted view of elimination of HX from the adjacent atoms of many compounds of the type II, the removal of the proton and the release of X are regarded as essentially simultaneous processes. A more detailed mechanism for the elimination of hydrogen halide from alkyl halides may be represented as follows



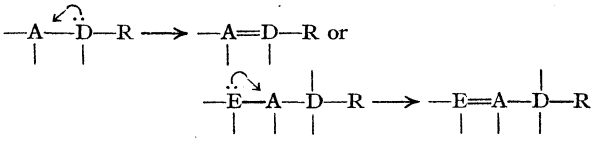
As bond a is being formed, bonds b and c are extended and finally broken simultaneously, the electron pair from bond b shifting at the same time to form the double bond. In this way a minimum of energy would probably be required for the elimination reaction.

Although the complete withdrawal of the proton may be accompanied by the simultaneous release of X as an anion, the alkyl halide may still be regarded as an acid in a broad sense; the elimination appears to involve a primary attack by the base on the "active" hydrogen atom, the shift of the electron pair and the release of X being dependent[16] upon this primary reaction. Regardless of the intimate mechanism involved, the base apparently conditions the reaction so that its course may be described by the steps outlined above.

The second step of the general course, involving the release of X with a complete octet of electrons, would leave an atom with only a sextet of electrons; this makes it possible for an electronic shift to occur within the molecule. If there is a free pair of electrons on an atom adjacent to the one from which X was released, this pair may shift to form a double (or triple) bond between the two atoms, thereby stabilizing the molecule; thus  . But if there is no free pair of electrons on atom A, the deficiency of atom D may be satisfied by a shift of an electron pair together with group R (or hydrogen) attached from atom A to atom D, thus



This rearrangement may involve inversion (Walden) of atom D. The migration of the electron pair (together with R) from atom A to atom D would leave atom A with only a sextet of electrons, a deficiency which may be satisfied by a shift of a free pair of electrons from atom D, or from another atom E, adjacent to atom A, to form a double (or triple) bond thus



From the foregoing discussion one should expect that when the proton is removed by a base, followed by the release of X (with a complete octet of electrons) from an *adjacent* atom, no rearrangement should occur, since the molecule can be stabilized merely by the shift of the free pair of electrons (left by the removal of the proton) to form a double or triple bond[17]; the shift of a free pair of electrons in this manner should take place more readily than a shift of an electron pair together with hydrogen or group R attached from one atom to another. On the other hand, if the proton and X are eliminated from the same atom or from a three atom system, rearrangement may be expected. It is noteworthy that although the removal of the proton cannot in itself bring about a rearrangement, the primary acid–base reaction plays an important role in determining whether or not rearrangement will occur.

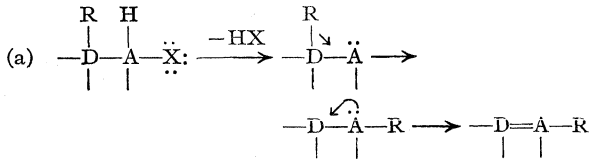
It may be considered that the manner in which the molecule is stabilized, the third step of the general course, depends upon the system from which HX is removed. This is based of course on obvious valency requirements and may be illustrated by the equations listed below, in which A, D and E represent atoms of carbon, nitrogen, or oxygen. Steps (1) and (2) are combined for

(16) The reaction appears to be dependent also on the polarizability of X, since the ease of elimination of hydrogen halide from alkyl iodides, bromides and chlorides decreases in this order. In this connection see Taylor, *J. Chem. Soc.*, 1962 (1937).

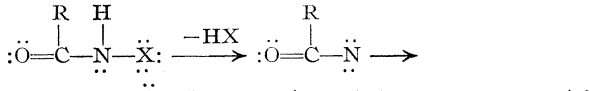
(17) See Hauser and Jordan, THIS JOURNAL, **57**, 2454 (1935).

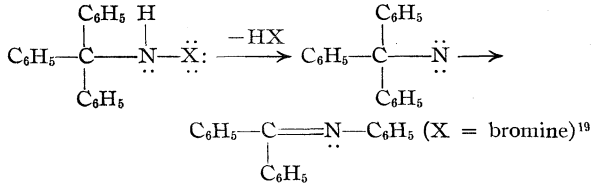
simplicity with step (3) shown separately, but this representation is to be regarded merely as a formal scheme which is an aid in predicting products. It should be noted, also, that as far as the prediction of products is concerned, there need be no distinction between reactions of types I and II.

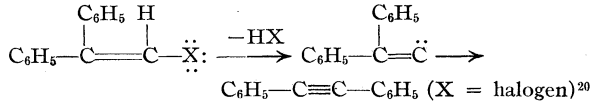
When HX is removed (by a base) from the same atom, the molecule may be stabilized by the formation of unsaturated products (a), by rearrangement, or (b) by dimerization.

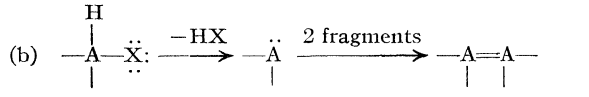


Examples:

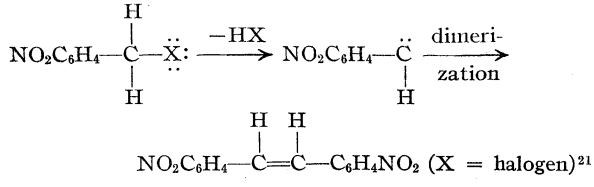




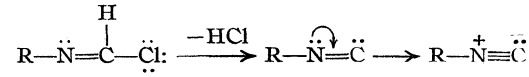




Example:

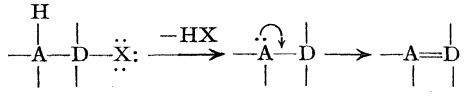


A special case arises when HX is removed from the same atom, adjacent to which there is an atom with a free pair of electrons. Then it is theoretically possible for the molecule to be stabilized, in accordance with the octet rule, merely by a shift of the free electron pair, without involving rearrangement of the molecule; in this case, however, one atom becomes positively, and the adjacent one negatively, charged. This might occur in the formation of isonitriles from primary amines, chloroform and alkali. According to the mechanism frequently assumed for this reaction the intermediate, RN=CHCl, is formed. This could eliminate HCl followed by the shift of the free electron pair on the nitrogen atom, thus:

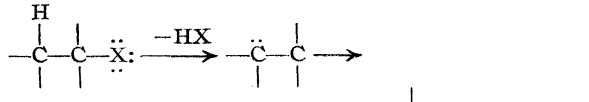


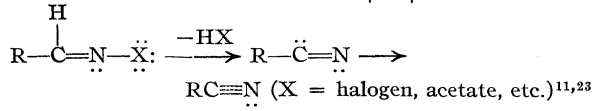
Recent evidence supports this structure for isonitriles. The fact that isonitriles when heated[22] rearrange to nitriles, indicates that the molecule can become more stable by the migration of R together with its electron pair to form the less polar nitrile.

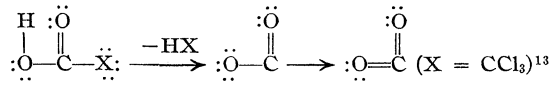
When HX is removed (by a base) from adjacent atoms, the molecule may be stabilized by the formation of unsaturated products without rearrangement; the stabilization involves merely the shift of the free pair of electrons, left by the removal of the proton, to form a double or triple bond; thus



Examples:







When HX is removed (by a base) from a three-atom system the molecule may be stabilized, (a)

(18) In the Hofmann and Lossen reactions HX may be considered to be removed from a one or a three-atom system (see ref. 14).

(19) Stieglitz and Vosburgh, *Ber.*, **46**, 2151 (1913).

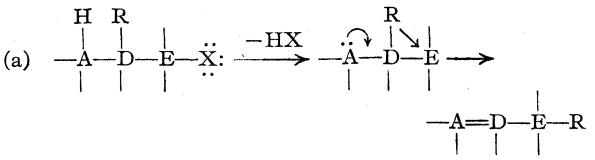
(20) Coleman and co-workers [THIS JOURNAL, **56**, 132 (1934); *ibid.*, **58**, 2310 (1936)] have found that with potassium amide in liquid ammonia diarylhaloethenes give good yields of tolanes.

(21) Ortho and para nitrobenzyl halides with alcoholic alkali give partly the corresponding dinitrostilbenes. See Michael, *ibid.*, **42**, 820 (1920). It should be noted that in these cases rearrangement is not possible.

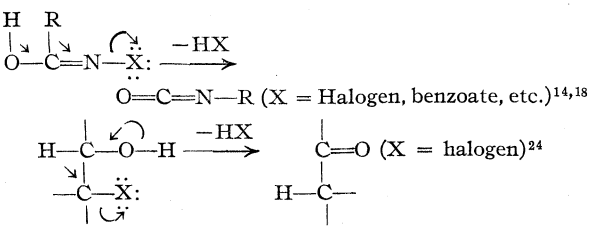
(22) See Hurd, "The Pyrolysis of Carbon Compounds," The Chemical Catalog Co., New York, N. Y., 1929, p. 603.

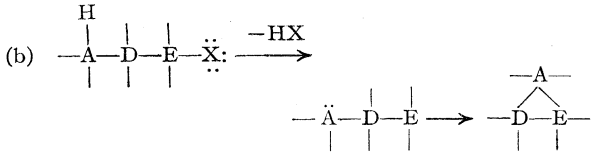
(23) The geometrical configuration of these compounds determines the ease with which the elements of HX will be eliminated, the *anti*-isomers eliminating HX much more readily than the *syn*-isomers (see especially ref. 17).

by the formation of unsaturated products involving rearrangement of the molecule, or (b) by cyclization

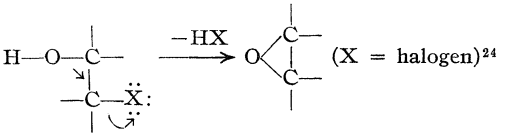


Examples:

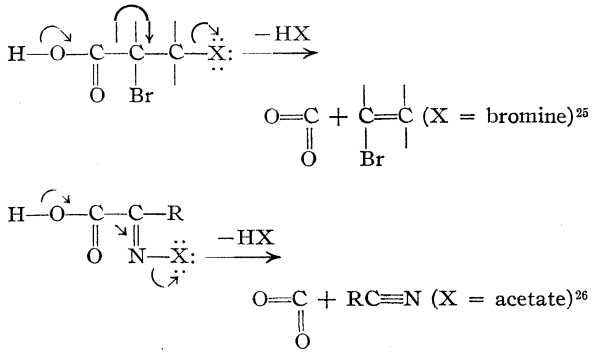


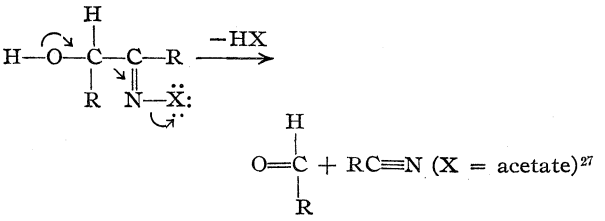


Example:

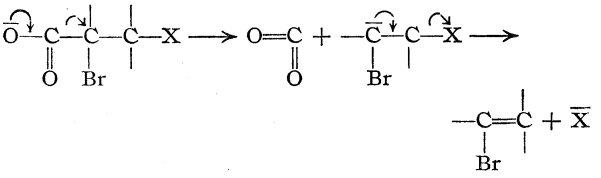


When HX is removed (by a base) from a four-atom system the molecule may be stabilized (a) by the formation of two unsaturated products without rearrangement, or (b) by cyclization. Examples in which two unsaturated products are formed without rearrangement may be represented as follows





These systems might be "double" two atom systems in which case the decomposition of the anion (formed by the removal of the proton) could be represented as follows:



When HX is removed (by a base) from five and six atom systems, the molecules are generally stabilized by cyclization. It should be pointed out that these reactions may or may not involve the primary removal of the hydrogen as a proton. The elimination of HX from acids, for example, γ-bromobutyric acid,[28] in the presence of alkali (where the acid–base reaction is of type I) obviously involves, first, the removal of the hydrogen as a proton to form the alkali salt, followed presumably by the release of bromide ion and cyclization to give γ-butyryl-lactone. But the elimination of HX from weaker acids, for example, 4-bromobutylamine, $BrCH_2CH_2$-$CH_2CH_2NH_2$, in the presence of alkali, apparently does not involve the primary removal of the hydrogen as a proton, since the reaction is not dependent upon the concentration of the base. In these cases the elimination of hydrogen halide is facilitated by the presence of the base apparently because it neutralizes the acid that is formed in the elimination, thereby preventing the reverse reaction (*e. g.*, opening of the ring). The mechanism for these eliminations has been discussed by Salomon.[29]

In the examples listed above and in others, the formation of unsaturated products involves rearrangement of the molecule (except in cases of dimerization) when HX is removed by a base from one or three atom systems, but no rearrangement when HX is removed by a base from two

(24) Apparently, on elimination of HX, *cis*-halohydrins undergo rearrangement, while *trans*-halohydrins cyclize giving ethylene oxide rings. See Suter and Lutz, THIS JOURNAL, **60**, 1360 (1938); Winstein and Lucas, *ibid.*, **61**, 1576 (1939); Bartlett, *ibid.*, **57**, 224 (1935).

(25) See Bachman, *ibid.*, **55**, 4279 (1933).

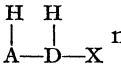
(26) Hantzsch, *Ber.*, **24**, 45 (1891).

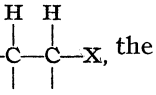
(27) See Blatt and co-workers, THIS JOURNAL, **56**, 1148 (1934); **57**, 1330 (1935).

(28) See Caldin and Wolfenden, *J. Chem. Soc.*, 1239 (1936).

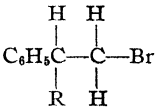
(29) Salomon, *Trans. Faraday Soc.*, **32**, 153 (1936).

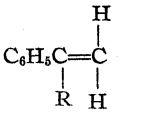
or four atom systems.[30] These facts support the general theory discussed in this paper.[31]

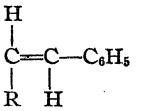
In most of the examples listed above, the organic compound can eliminate the elements of HX only from one particular system of atoms. There are many compounds, however, which might eliminate HX in two or more ways; for example, a compound of the type  might eliminate the elements of HX either from the same atom (accompanied by rearrangement or dimerization) or from adjacent atoms. In these cases it has frequently not been possible to determine with certainty which course is followed,[32] since the same unsaturated product could be formed by either course; thus, the elimination of HX from atom D, accompanied by a shift of the hydrogen (together with its electron pair) from atom A to atom D would give an unsaturated product identical with the one resulting from the elimination of HX from the adjacent atoms A and D.

Most recent workers have assumed that with alkyl halides of the type  , the hydrogen halide is removed by bases from adjacent atoms[33] without rearrangement of the molecule, and although there are statements in the literature to the contrary,[34] it now appears that at least the olefins formed from simple alkyl halides may be accounted for on this basis. Olivier[10] lists a number of alkyl halides and related compounds which, when treated with bases, give unsaturated products that could be formed without rearrangement. Chablay[35] has reported that isobutyl halides with sodamide in liquid ammonia give the expected isobutylene. Recently, Whitmore and co-workers have made a careful search for all products formed from certain alkyl halides and hot alcoholic alkali. They found[36] that *n*-butyl iodide gives butene-1 and *n*-butyl ethyl ether, while isoamyl iodide gives 3-methyl-butene-1 and isoamyl ethyl ether; no other olefins were obtained. The ethers were formed presumably by substitution reactions. Since the olefins may be accounted for on the basis that the elements of hydrogen iodide were eliminated from adjacent carbon atoms, they may be regarded as "unrearranged" products; however, it should be remembered that the same olefins would have resulted if the elements of hydrogen iodide were removed from the same carbon atom, and the elimination accompanied by the shift of a hydrogen from an adjacent carbon atom.

In contrast to the results discussed above, Amagat[37] has reported that certain phenylalkylethyl bromides when heated with sodamide in boiling xylene (b. p. 140°) give rearranged olefins. Under these conditions, bromides of type (I), in which R is methyl, ethyl or isopropyl


(I)


(II)


(III)

were reported to give almost exclusively olefin (III), the formation of which would obviously involve rearrangement of the molecule.

On repeating this experiment in this Laboratory[38] using potassium amide instead of sodamide, we have found that the bromide in which R is ethyl, although giving some of olefin (III), also gives approximately an equal amount of olefin (II). It has been found, furthermore, that when the reaction is carried out with potassium amide in liquid ammonia (b. p. −33°), the bro-

(30) Whether or not this is true in all cases remains of course to be determined by experiment. An apparent exception has been reported by Werner and Piguet, *Ber.*, **37**, 4295 (1904); Werner and Detscheff, *ibid.*, **38**, 69 (1905). These workers reported that β-benzoinoxime or β-benzilmonoxime when heated with benzenesulfonyl chloride and alkali give partly phenyl isocyanide, which is a rearrangement product. Evidence has been obtained in this Laboratory, however, that the rearrangement is effected merely by heat rather than by the action of the base. These results will be published shortly.

(31) Ingold and co-workers have shown that in the decomposition of quaternary ammonium compounds to form unsaturated products, the removal of HNR_3 from the same atom of the positive ion (α-hydrogen elimination) is accompanied by dimerization, and the removal of HNR_3 from a three-atom system (γ-hydrogen elimination) is accompanied by rearrangement; whereas the removal of HNR_3 from adjacent atoms (β-elimination) forms unsaturated compounds without dimerization or rearrangement. See Ingold and Rogers, *J. Chem. Soc.*, 722 (1935).

(32) It is of interest to note that the substitution of certain hydrogen atoms by deuterium might serve to give positive data concerning the course followed. This study is being carried out in this Laboratory.

(33) In this connection see Watson, *J. Chem. Soc., Ann. Repts.*, **35**, 226 (1938); also, see ref. 10.

(34) It has been stated, for example, that isobutyl halides with alcoholic alkali give both *n*-butylene and isobutylene; see Francis, "Notes on Organic Chemistry," Edward Arnold and Company, London, 1935, p. 182.

(35) Chablay, *Compt. rend.*, **156**, 327 (1913); see Bergstrom and Fernelius, *Chem. Rev.*, **12**, 92 (1933).

(36) Whitmore, Wittle and Flinn, reported at the Pittsburgh meeting of the American Chemical Society, September, 1936.

(37) Amagat, *Bull. soc. chim.*, **49**, 1410 (1931).

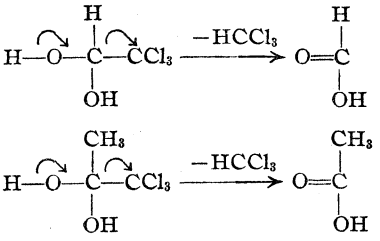
(38) These results were presented by Hauser, Bright and Renfrow before the division of organic chemistry at the Boston meeting of the American Chemical Society, September, 1939. These results will be published soon.

mide (in which R is methyl or ethyl) gives almost entirely olefin (II).[38] The formation of this olefin has been assumed to involve the elimination of hydrogen bromide from adjacent carbon atoms without rearrangement, but it is possible that hydrogen bromide was removed from the same carbon atom, accompanied by the shift of the hydrogen atom.

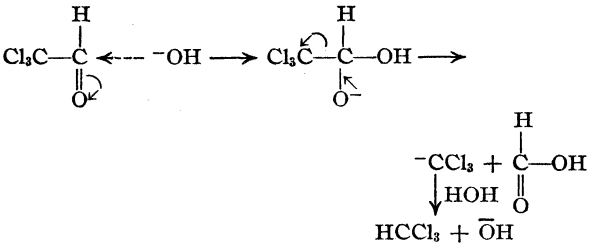
The formation of olefin (III) under the more drastic conditions (at 140°) might have involved the removal of hydrogen bromide from the same carbon atom, accompanied by the shift of the phenyl group or of R; or the reaction might have consisted of a thermal decomposition in which the base functioned merely to neutralize the hydrogen bromide eliminated.

It has been reported[39] that ethylchloroamine when warmed with alcoholic alkali and the mixture treated with excess hydrochloric acid, gives acetaldehyde, formaldehyde and methylamine. While the acetaldehyde could have been formed without rearrangement (by hydrolysis of acetaldehyde-imine which would be formed if the elements of hydrogen chloride were eliminated from adjacent atoms), the formation of formaldehyde and methylamine would necessarily involve a rearrangement of the molecule. These compounds may be accounted for on the basis that the elements of hydrogen chloride were removed from the same atom (nitrogen) and the elimination was accompanied by a shift of the methyl group to give formal-methylamine, which subsequently underwent hydrolysis; the acetaldehyde also could be accounted for on this basis, by assuming the shift of the hydrogen atom. Since the hydrogen attached to the nitrogen of the ethylchloroamine is much more active (acidic) than the hydrogen on the adjacent carbon atom, one might expect that the elements of HX would be removed from the same atom (nitrogen).

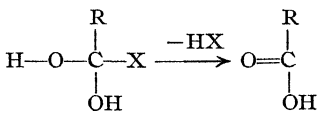
The reactions of bases with compounds containing the carbonyl (or similar) group require special consideration. Simple aldehydes and ketones are relatively stable toward alkali, but negatively substituted derivatives, for example, CCl_3CHO or CCl_3COCH_3, are readily cleaved by this reagent. Since these compounds form hydrates,[40] the reaction with aqueous alkali may be considered to involve the removal of HX, where X is CCl_3, from adjacent atoms of the hydrate; thus



The intermediate negative organic ion that would result if a proton were removed from the hydrate might also be formed by a direct attack of the hydroxyl ion on the carbonyl group of chloral; thus



Represented in this manner the haloform reaction becomes analogous to the hydrolysis of esters, amides, anhydrides, acid chlorides, etc. These compounds may be represented by the general formula $\begin{matrix} R-C=O \\ | \\ X \end{matrix}$ or $\begin{matrix} H-C=O, \\ | \\ X \end{matrix}$ where X is an electronegative atom or group, such as OC_2H_5, NH_2, OCOR, Cl, CCl_3, etc. In the presence of water these carbonyl compounds form hydrates (at least in low concentrations) which may eliminate the elements of HX from adjacent atoms

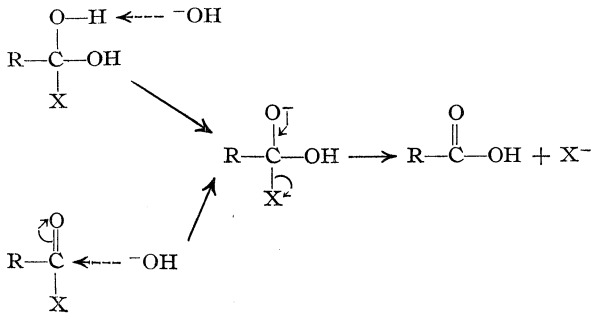


The hydrolysis of compounds of the type $\begin{matrix} R-C=O \\ | \\ X \end{matrix}$ by means of aqueous alkali apparently involves the intermediate formation of a negative organic ion,[41] which may be formed either by the removal of a proton from the hydrate or by a direct attack of the hydroxyl ion on the carbonyl group; thus

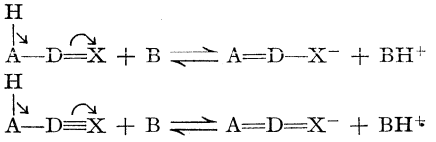
(39) See Franklin, "Nitrogen System of Organic Compounds," A. C. S. Monograph 68, Reinhold Publishing Corp., New York, N. Y., 1935, pp. 182–183.

(40) See Fuson and co-workers, THIS JOURNAL, **52**, 3269 (1930), and later papers.

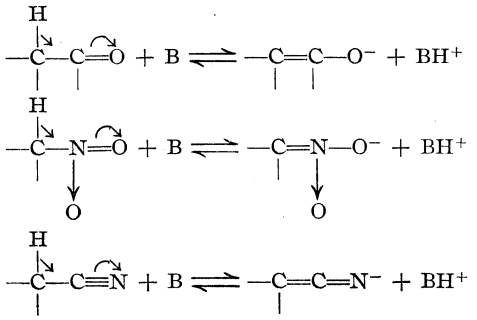
(41) In this connection see Waters and Lowry, "Physical Aspects of Organic Chemistry," D. van Nostrand Company, New York, N. Y., 1936, pp. 236, 267.



In the compounds considered thus far, X is linked by a single bond. In the elimination of the proton and of X as an anion from such compounds, the covalence of X is decreased one unit. It might be expected that certain compounds containing a relatively negative atom or group X joined by a double or triple bond, as for example, the oxygen in the carbonyl group or the nitrogen in the cyanide group, might give up a proton to a base and "partially" release X, in which the covalence of X likewise decreases one unit; the removal of the proton by a base (B) and the "partial" release of X from adjacent atoms may be illustrated as follows:

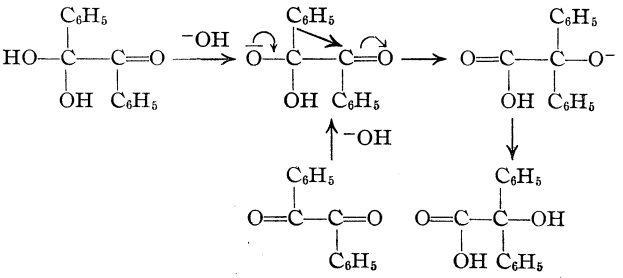


Examples:



Obviously, these are examples of enolizations of the well-known triad systems[42] in the presence of bases. It should be pointed out that the anions formed in these enolizations are resonance structures; consequently, these examples are not strictly analogous to the elimination reactions discussed in this paper.

In the enolizations in the presence of bases represented above there is a removal of the proton and "partial" removal of X from adjacent atoms; therefore, no rearrangement should be expected. Similar processes are known, however, in which there is a removal of a proton and a "partial" removal of X from a three-atom system, and in these cases rearrangement takes place. The benzil–benzilic acid rearrangement belongs to this type.[43] Westheimer[44] and Roberts and Urey[45] have presented evidence recently that this rearrangement in the presence of alkali involves the intermediate formation of a negative organic ion. This might be formed either by loss of a proton from the hydrate of benzil or by a direct attack of hydroxyl on benzil. The formation of the intermediate negative ion and its rearrangement to benzilic acid may be represented as follows



The ideas discussed in this paper are applicable to a number of other apparently diverse eliminations and rearrangements.

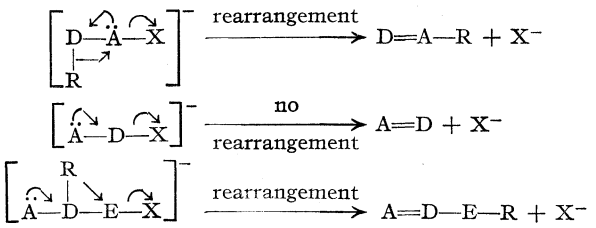
Finally, it should be pointed out that the fundamental change that takes place when the elements of HX are removed from organic compounds by means of bases to give unsaturated products may be considered to involve the decomposition of negative organic ions; the latter may exist for an appreciable time as, for example, in the reaction of a bromoamide with alkali, or may have only transient (or no "actual") existence, as in the reaction of an alkyl halide with this base. The negative organic ion is generally formed by the removal of a proton by the action of a base, but in certain cases may be formed by an attack of a basic ion (hydroxyl) on the carbonyl or similar group, as may occur, for example, in the benzil-benzilic acid rearrangement in the presence of alkali. The products formed on decomposition of the negative organic ions may be predicted readily from a consideration of the relative positions of X and the free pair of electrons carrying the negative charge, as illustrated by the following examples

(42) In this connection see, for example, Gilman, "Organic Chemistry," John Wiley and Sons, New York, N. Y., 1938, pp. 1705, 1707.

(43) For other examples, see especially ref. 1.

(44) Westheimer, THIS JOURNAL, **58**, 2209 (1936).

(45) Roberts and Urey, *ibid.*, **60**, 880 (1938).



These illustrations are of course essentially the same as those given above where it was considered that the products formed depended upon the system from which HX is removed and, as already pointed out, the molecule may be stabilized in certain cases by dimerization or cyclization instead of by rearrangement.

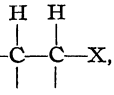
Conclusions and Summary

1. General theories are presented for the classification of eliminations, metatheses and rearrangements of compounds containing X, a relatively electronegative atom or group, such as halogen, hydroxyl, etc.

2. Eliminations, metatheses and intramolecular rearrangements effected by acids, acidic reagents and heavy metal salts (electron acceptors) are initiated by an attack of the reagent on X, which is removed with its bonding pair of electrons. The general courses of reaction are described by the generalizations outlined by Whitmore with the modification that the steps may occur simultaneously.

3. Eliminations effected by bases (proton acceptors) are initiated by an attack of the base on the hydrogen. Two extreme types of reactions are considered; in type I, the equilibrium of the primary acid–base reaction is far on the side of the resulting salt, while in type II, the equilibrium of the acid–base reaction is far on the side of the original acid (extremely weak). The general courses of reaction are described by the following steps: The hydrogen is removed as a proton; X is released with a complete octet of electrons; the molecule is stabilized. In reactions of type I, the second and third steps may be simultaneous processes, while in reactions of type II, all three steps may occur simultaneously. The manner in which the molecule is stabilized depends upon the system from which HX is removed. When HX is removed from the same atom or from a three-atom system, the molecule may be stabilized by rearrangement (or dimerization) giving unsaturated products, whereas when HX is removed from adjacent atoms or a four-atom system, ("double" two-atom system) the molecule may be stabilized by the formation of unsaturated products without rearrangement. When HX is removed from systems containing three or more atoms, the molecule may be stabilized by cyclization.

4. Metathetical (substitution) reactions involving basic anions, for example, the alkaline hydrolysis of alkyl halides, commonly occur side by side with eliminations. In these cases, the anion attacks the carbon at the face of the tetrahedron opposite the position of X, the addition of the anion and the release of X as an anion occurring simultaneously.

5. Certain compounds are considered in which it is possible for HX to be removed by bases in two ways; for example, alkyl halides of the type  , might eliminate the elements of HX either from the same carbon, accompanied by rearrangement or dimerization, or from the adjacent carbon atoms without rearrangement.

6. The reactions of certain carbonyl compounds and their hydrates with bases are discussed in the light of the generalizations presented above.

DURHAM, NORTH CAROLINA
RECEIVED NOVEMBER 24, 1939

[CONTRIBUTION FROM THE LABORATORY OF PHYSICAL CHEMISTRY, UNIVERSITY OF WISCONSIN]

The Physical Chemistry of Secalin. Electrophoresis and Diffusion Constant Studies of the Prolamine of Rye[1]

BY A. C. ANDREWS[2]

Those proteins in the cereal grains which are soluble in 60–80% ethyl alcohol, classified as prolamines, have been found to possess properties that are nearly identical in many respects. The prolamine in the cereal rye (*Secale Cereale*) has been described repeatedly as being identical with the gliadin in wheat. It was this close similarity of properties of these two prolamines that prompted studies of the electrophoretic mobilities and diffusion constant of the rye prolamine, since corresponding properties of the prolamine in wheat are fairly well worked out. The literature on this rye protein is not extensive, and a separate name was not suggested for it until Gortner[3] gave it the name of "secalin." Previous to this it shared with the prolamine from wheat the name of "gliadin."

Experimental

Preparation of Secalin.—Fresh rye grain was ground by a commercial mill into a meal of moderate degree of fineness. About 2000 g. of this rye meal was then placed in a four-liter bottle and covered with enough 70% alcohol to assure an excess present after the meal became thoroughly soaked. This mixture was allowed to stand for forty-eight hours with frequent stirring, filtered by suction, and washed thoroughly with 70% alcohol. The alcohol extract, which was dark red in color, was then poured slowly with constant stirring into a large quantity of iced water containing potassium chloride. Secalin, being insoluble in aqueous solutions, was immediately precipitated and settled out on the bottom of the containing vessel. The yellowish brown, sticky mass of secalin was reprecipitated in like manner several times. About 30–70 g. of impure wet secalin was obtained from the 2000 g. of rye meal.

Purification of Secalin.—The procedure used in purifying secalin was a modification of the method used by Dill and Alsberg[4] in their purification of gliadin from wheat. The alcoholic solution of secalin was placed in a cold room for three days at a temperature of −10°. Because of the large change in solubility with temperature, much of the secalin precipitated upon standing at this temperature. The solid secalin was filtered off and the supernatant liquid was three times subjected for three hours to an acetone–dry-ice bath (about −35°), until all the secalin had been precipitated. In so doing, the coloring matter and fat accumulated in the supernatant liquid. Finally this purified secalin was dissolved in 70% alcohol and twice dialyzed against fresh solvent through cellophane membranes. All dialyses were carried out in tightly stoppered bottles in a refrigerator. The outer liquid from the first dialysis was colored a slight green, but that from the second dialysis remained colorless and was therefore used as solvent for diluting the dialyzed protein when more dilute solutions were required.

An attempt was made to purify secalin by a method similar to that sometimes used in the purification of zein from corn. This method involves the extraction of coloring matter and fatty impurities by repeated shaking out of the impure alcohol extract with an immiscible organic solvent. Great difficulties were encountered in attempting to purify secalin by this method, especially in the selection of the best organic solvent. In the preparation of zein, low boiling point petroleum ether is used; with secalin, this solvent invariably resulted in the precipitation of the dissolved protein. The extent to which this precipitation took place was variable, sometimes great quantities of the protein being precipitated merely by the addition of ether to the extract, without shaking. Other times the protein was precipitated during shaking, resulting in a semi-permanent emulsion. As the emulsion broke and the ether rose, the precipitated protein rose with it, from which it could be separated only with great difficulty. Protein so precipitated was but slowly redissolved, if at all, in 70% alcohol. It had a pure white color while still wet, but rapidly turned gray upon drying and exposure to air. In attempting to find an organic solvent for the extraction of fat and coloring matter, many were tried, and finally carbon tetrachloride was chosen because it had the least precipitating effect upon secalin in 70% alcohol. Even it would at times precipitate secalin, but upon long standing in contact with the alcohol the protein would partially redissolve. Concentrated solutions of this protein in 70% alcohol were reddish-brown in color, becoming light yellow upon addition of more alcohol.

Other organic liquids were used in attempting to find a suitable solvent for the impurities, of which acetone, tetrachloroethane, oleic acid, and dioxane were found to have a precipitating effect. Ethyl oleate, decahydronaphthalene, glycerol, and ethylene glycol showed no precipitating effect. The precipitating reaction produced by acetone was very marked.

The Diffusion Apparatus.—The apparatus used in the determination of the diffusion constant of secalin was similar to that used by Tiselius and Gross,[5] but the concentration gradients were measured by the refractometric

(1) This material comprises a portion of a thesis submitted to the Faculty of the University of Wisconsin in partial fulfilment of the requirements for the degree of Doctor of Philosophy, June, 1938.

(2) Present address, Chemistry Department, Kansas State College, Manhattan, Kansas.

(3) R. A. Gortner, Fifth Colloid Symposium Monograph, A. C. S., 1924.

(4) D. B. Dill and C. L. Alsberg, *J. Biol. Chem.*, **65**, 279 (1925).

(5) A. Tiselius and D. Gross, *Kolloid-Z.*, **66**, 11 (1934).

method developed by Lamm,[6] in which a transparent uniform scale is photographed through the diffusion cell. The refractive index gradient at the diffusion boundary produces a distorted image of the scale, in which the displacement of the scale lines is proportional to the concentration gradient, provided the refractive index is a linear function of the concentration. The arrangement of the apparatus was similar to that described by Lamm and Polson.[7] The diffusion cell was nearly identical to the one used and described in detail by them, and by Svedberg.[8] The internal diameter of the diffusing solution arm was 1 cm. The linear scale was a photographic reduction of a large scale to a length of 53 mm., consisting of 200 divisions, every tenth being numbered. The source of illumination was a sodium vapor lamp. The final line displacement caused by the blurring of the boundary was read by means of a Gaertner micro-comparator. These line displacements were then plotted against the undeviated scale, and the curve so obtained was used in calculation of the diffusion constant.

The Electrophoresis Apparatus.—The apparatus used in obtaining the electrophoretic mobility was similar to that in general use, which employs the moving boundary method and is described in detail by Tiselius.[9] It consisted of a "U" tube having an inside diameter of 1 cm., accurately ground and polished cylindrical inside each arm. The electrode vessels that made connection to the top of each arm of the "U" tube had a combined capacity of 450 cc. The protein solution made connection at the bottom of the "U" through a three-way stopcock, in which the boundary was formed and from which it was moved into position in the two arms of the "U." The apparatus was immersed in the same water-bath at 25° and the same optical system was used as in the diffusion constant determinations. The movements of the boundaries were followed by the refractometric method developed by Lamm. Silver–silver chloride electrodes were used with an electrolyte solution of magnesium chloride in 70% alcohol. Currents between 2–3 milliamperes were used and the value taken was the mean of the current strength at the beginning and end of a time interval.

The protein solutions were prepared from purified secalin in 70% alcohol in concentrations from 0.4 to 1%. The solvent used for the solutions in electrophoresis was 62.9% by weight of ethyl alcohol solution, made 0.02 molar with respect to sodium acetate. The buffers were then made by adding varying amounts of acetic acid to this sodium acetate–alcohol–water solvent, in concentrations from 0.0022 to 0.18 *M*. The resulting *p*H values of all solutions and solvents were determined by means of the glass electrode after dialysis. Dialysis was carried out similarly to that described previously, the protein solution being dialyzed against buffers of the same concentration as that used as solvent. The outer liquid from the last dialysis served as the solvent into which the protein moved during electrophoresis. All conductivity measurements on solutions and solvents were made in a conductivity cell of the type designed by Washburn, using a Leeds and Northrup Jones conductivity bridge at 25°.

Calculations.—The distance between the scale divisions of the developed photographic plates was read to a thousandth of a millimeter. The normal undeviated scale, photographed through the solvent was computed and used as a reference scale. The differences between corresponding scale divisions of the deviated and "deviated" scale, called "*Z*" values, were plotted against the deviated scale. The curve so produced should approach the normal Gaussian or probability curve for a homogeneous dispersed substance.

In the calculation of the diffusion constant the equation used was

$$Dt = \frac{A^2}{4\pi H_{max.}^2}\left(\frac{l-b}{l}\right)^2$$

Here D is the diffusion constant, t the time in seconds, A the area under the Gaussian curve, determined with a planimeter, $H_{max.}$ the maximum ordinate of the curve, l the optical distance from the scale to the objective lens, and b the optical distance from the center of the diffusion cell to the scale. Zero time was chosen as that time at which the boundary first became visible in the cylindrical portion of the tube. The diffusion constants are expressed as $D \times 10^7$ cm.^{2} per sec.

In the calculation of the electrophoretic mobility, the Gaussian curves were not nearly as symmetric as the diffusion curves, being more irregular and jagged in outline. In an electrophoresis experiment there would be one such Gaussian curve from each scale picture taken corresponding to each interval of time, the difference between the pictures being mainly that of a displacement of the maximum ordinate along the scale in a direction depending upon the direction and time of flow of the current. Accumulated percentages of the areas under each curve for each 0.5 cm. abscissa interval were then calculated and plotted against the deviated scale, giving a series of "*S*" curves, one for each picture. The differences in the "*S*" curves would be a shift along the millimeter scale abscissa by an amount corresponding to the direction of current flow, to the velocity of migration and to charge on the protein particle. The value of u(cm.^{2} sec.$^{-1}$ volt^{-1}) was then calculated by $u = qkd/it = d/Ft$, where $F = i/qk$. In this equation, q is the cross sectional area of the "U" tube, k, the conductivity of the solution, t, the time in seconds, i, the mean current during the interval between photographic exposures, and d, the magnitude of the displacement in cm. of the 50% point in the "*S*" curves.

Results

Diffusion Constant.—The general law of linear diffusion was stated first by Fick in 1855 in two mathematical laws that bear his name. Fick's second law, $\partial c/\partial t = D\partial^2 c/\partial x^2$, defining the linear diffusion constant, allows of experimental verification. This partial differential equation and the corresponding theory are completely re-

(6) O. Lamm, "Measurements of Concentration Gradients in Sedimentation and Diffusion by Refraction Methods," Dissertation, Upsala, Sweden, 1937.

(7) O. Lamm and A. G. Polson, *Biochem. J.*, **30**, 528–541 (1936).

(8) T. Svedberg, "Colloid Chemistry," A. C. S. Monograph Series 16, The Chemical Catalog Co., New York, N. Y., 1928.

(9) A. Tiselius, Inaugural Dissertation, University of Upsala, Upsala, Sweden, 1930, pp. 14–18.

viewed in many places [Williams and Cady[10]] and has for our problem a solution

$$C = C_0/2 + \frac{C_0}{2\sqrt{\pi Dt}} \int_0^{\frac{x}{2\sqrt{Dt}}} e^{-(\alpha - x)^2/4Dt}\, d\alpha$$

Here the integral is of the form of the well-known probability integral and so can be evaluated from experimental results, provided it is assumed that the refractive index is exactly proportional to the concentration for all concentration ranges used. In Fig. 1 are shown four experimental typical curves obtained by plotting "Z" against the deviated scale. They are actually those obtained in diffusion experiment no. 4. The

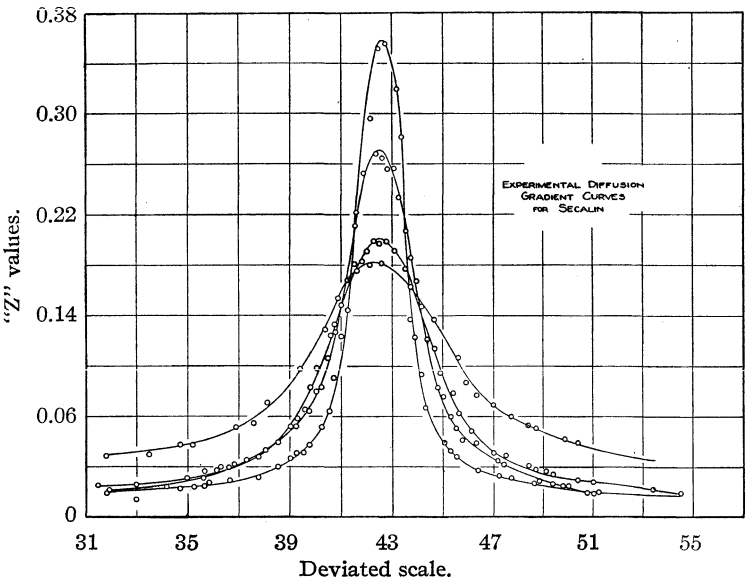


Fig. 1.—Experimental diffusion curves, showing the decrease in maximum ordinate with time as the boundary blurs.

curves are symmetrical about the maximum ordinate, and the experimental points lie nicely on the smooth curve. In Table I are given the constants obtained from all such curves. The areas under the curves of Fig. 1 show a maximum deviation from the average area of 3%. In Table I the results tabulated are those obtained for secalin from the two described methods of preparation. The first three experiments were made on a solution containing 1.035 g. of secalin per 100 cc. of solution and prepared by the use of an organic solvent; the other experiments used secalin obtained by the method of low temperatures in concentration of 0.695 g. per 100 cc. of solution. Secalin obtained by either method gave nearly identical diffusion constants.

(10) J. W. Williams and L. C. Cady, *Chem. Rev.*, **14**, 171 (1934).

The values of the diffusion constant decreased with the elapsed time of diffusion. Such a variation in diffusion constant with time seems to be inherent with the experimental method, probably explained in a large part by the mechanical inability to form a perfectly static boundary. Other investigators apparently have noticed this, because in nearly all cases the values are reported for those in which the elapsed time was sufficient for D to become fairly constant. In Table I the value of D for secalin decreases rapidly for the first 40,000 seconds and then in some cases becomes very nearly constant. Extrapolation of the diffusion constant–time curve to very large time intervals gives $D_{25} = 1.84 \times 10^{-7}$. An average of all such values for times 50,000 seconds or greater gives $D^{\text{av.}}{}_{25} = 1.91 \times 10^{-7}$. The curve obtained by the method of least squares for the combined values in experiments 1, 2, and 4 gives $D_{25} = (1.8 \pm 0.2) \times 10^{-7}$, when extrapolated to large time intervals. The value of the diffusion constant of secalin calculated to water solution at 25° by use of the equation $D^{H_2O}{}_{25} = D^{\text{alc.}}{}_{25}\, \eta^{\text{alc.}}{}_{25}/\eta^{H_2O}{}_{25}$, where $D^{H_2O}{}_{25}$ and $D^{\text{alc.}}{}_{25}$ are the diffusion constants in water and alcohol, and $\eta^{H_2O}{}_{25}$ and $\eta^{\text{alc.}}{}_{25}$ are their viscosities, gives $D^{H_2O}{}_{25} = 4.78 \times 10^{-7}$. For 20° the value is $D^{H_2O}{}_{20} = 4.3 \times 10^{-7}$.

This value of D for secalin compares favorably with the values of diffusion constants for gliadin, hordein, and zein. Williams and Watson[11] report the diffusion constants (20°) for three rather arbitrary fractions of zein as $D^{H_2O}{}_{20} = 3.0 \times 10^{-7}$, $D^{H_2O}{}_{20} = 4.0 \times 10^{-7}$, and $D^{H_2O}{}_{20} = 5.2 \times 10^{-7}$, in which the second fraction was present in the greatest amount. Lamm and Polson[7] report diffusion constants for three fractions of gliadin as $D^{H_2O}{}_{20} = 4.86 \times 10^{-7}$, $D^{H_2O}{}_{20} = 5.85 \times 10^{-7}$ and $D^{H_2O}{}_{20} = 6.72 \times 10^{-7}$. Quensel and Svedberg[12] report a diffusion constant for hordein from barley of 6.5×10^{-7}.

Sedimentation constants have been reported for zein by Williams and Watson of $s_{20} = 1.9 \times 10^{-13}$ for the predominant zein fraction, and

(11) J. W. Williams and C. C. Watson, Cold Spring Harbor Symposia on Quantitative Biology, VI, 208 (1938).

(12) O. Quensel and T. Svedberg, *Compt. rend. trav. Lab. Carlsberg, Ser. chim.*, **22**, Vol. jubilaire S. P. L. Sørensen, 442–448 (1938).

TABLE I

EXPERIMENTAL DATA OBTAINED IN THE DETERMINATION OF DIFFUSION CONSTANT

Expt.	Time, sec.	$H_{max.} \times 10^2$	Area, $A \times 10^{-2}$ cm.^{2}	Diff. constant, $D \times 10^7$
1	8,980	8.81	2.88	6.70
	15,950	7.36	2.66	4.61
	22,975	6.39	2.58	3.98
	30,280	5.92	2.33	2.88
	37,070	5.15	2.26	2.93
	43,940	4.90	2.16	2.49
	76,650	4.00	2.17	2.15
	82,960	3.82	2.16	2.18
	101,960	3.66	2.20	2.01
	129,500	3.29	2.11	1.79
	163,690	3.18	2.22	1.69
	170,610	3.06	2.20	1.72
2	18,020	7.52	2.18	2.62
	92,830	3.66	2.10	2.24
	97,292	3.54	2.11	2.06
	117,165	3.25	2.10	2.00
	131,995	3.07	2.10	2.00
	172,125	2.90	2.16	1.81
3	20,145	5.24	1.94	3.85
	67,005	3.25	1.58	1.98
	79,815	2.94	1.56	1.99
	98,410	2.72	1.60	1.96
	116,175	2.48	1.53	1.83
	149,570	2.30	1.45	1.50
4	11,272	3.76	1.25	5.62
	21,312	3.22	1.26	4.34
	32,260	2.83	1.29	3.70
	107,712	2.09	1.23	1.85
	120,272	1.95	1.23	1.92
	132,485	1.85	1.19	1.80
	150,192	1.77	1.18	1.71
	159,217	1.72	1.30	2.07
5	40,930	3.52	1.37	2.14
	48,430	3.05	1.23	1.94
	59,520	2.94	1.31	1.92
	67,310	2.60	1.26	2.01
	76,515	2.60	1.34	2.01
	122,507	2.10	1.27	1.72
	131,705	2.08	1.34	1.80
	143,400	1.99	1.32	1.75
	152,805	1.89	1.29	1.76

Krejci and Svedberg[13] give one for gliadin of 2.10×10^{-13}. Until secalin is actually centrifuged, its sedimentation constant can be assumed to lie between that of zein and gliadin, as does the diffusion constant. Then an approximate molecular weight can be calculated by the use of the formula $M = RTs/D(1 - Vd)$. Here M is the molecular weight of the sedimenting molecule, R, the gas constant, T, the absolute temperature, D, the diffusion constant, V, the partial specific volume of the protein, and d, the density of the solvent. The quantity V is taken as 0.722 (see Krejci and Svedberg[13]), and s is assumed to be 2.0×10^{-13}. Using these values for secalin gives an approximate molecular weight of 40,500. Lamm and Polson[7] calculated a value 27,500 for gliadin, while a value of 26,750 was reported by the use of the equilibrium centrifuge. Quensel and Svedberg[12] similarly calculated a molecular weight of 27,000 for hordein. Ultracentrifugal determinations with zein reported by Williams and Watson[11] give 40,000 for the molecular weight of this prolamine.

(13) L. Krejci and T. Svedberg, THIS JOURNAL, 57, 946 (1935).

Electrophoresis.—The electrophoretic mobility of a protein particle varies with the *p*H of the solution, the ionic strength of the medium, etc. In general there is a certain *p*H for which the mobility becomes zero. This *p*H, which is called the isoelectric point, is definite for each protein as long as the ionic strength of the system is kept low and constant. The mobility of the particle increases as the *p*H is changed from the isoelectric point, but the direction of movement is opposite on the two sides of this point. Secalin shows its greatest mobility in the more acid solutions, and the mobility gradually decreases as the *p*H of the solutions increases, becoming zero at *p*H (in alcohol) of 6.67 ± 0.1. Further decrease in acidity produces a movement of protein particles again, but in a direction opposite to that of the original.

Two representative curves are plotted in Fig. 2, one for the change in mobility as current goes "up" on the right as one faces the "U" tube, and "down" as the current goes in the reverse direction. The mobilities are not exactly the same in both directions. The slope of the "up" curve is 1.30 and of the "down" curve is 1.47; thus the protein migrated about 11% faster in "up" direction than in "down." Zero mobility in the "up" direction is at a *p*H (alc.) of 6.74, and in the "down" direction of 6.60. The average of these two values gives an isoelectric point for the protein secalin at a *p*H (alc.) of 6.67. Practically all the experimental mobilities in Table II lie well within a range of ±0.1 of a *p*H unit from the curves of Fig. 2. Also practically any other straight line that reasonably could be drawn will have a zero mobility within ±0.1 *p*H unit of 6.67. The notation *p*H as used here for expressing hydrogen-ion concentration in alcohol–water solutions is defined in the same manner

TABLE II

ELECTROPHORETIC EXPERIMENTS WITH SECALIN

Expt.	pH (alc.)	Time, sec.	d/l (mm./sec.) $\times 10^3$	Current (milliamps.) (i)	Sp. cond. (K)	Mobility ($U = u \times 10^5$)
			"Up" Direction			
I-R	5.25	5875	0.638	2.05	3.615×10^{-4}	0.885
		5015	.737	2.05		1.008
		5315	.638	2.05		0.885
I-L		5845	.623	2.05		.865
		5275	.618	2.05		.856
II-R		6005	.760	2.15		1.005
		5700	.737	2.15		0.976
III-R	5.99	6165	.354	2.085	3.942×10^{-4}	.526
		5510	.333	2.075		.498
		5910	.324	2.070		.486
III-L		4320	.582	2.085		.866
		5480	.463	2.075		.693
IV-R	6.2	5170	.178	2.080	3.571×10^{-4}	.240
		4745	.200	2.070		.272
		5707	.219	2.070		.297
IV-L		5726	.279	2.070		.279
		4797	.371	2.070		.503
		5944	.267	2.105		.356
V-R	7.18	5287	− .187	2.050	3.605×10^{-4}	− .263
V-L		5257	− .196	2.050		− .278
		6615	− .112	2.050		− .158
		5690	− .165	2.050		− .232
VI-R		4920	− .228	2.380		− .271
		6591	− .220	2.400		− .260
		6309	− .185	2.400		− .219
VI-L		4910	− .126	2.385		− .150
		6630	− .330	2.400		− .390
		6240	− .228	2.400		− .269
VII-L		3262	− .270	2.105		− .362
		5223	− .436	2.090		− .589
		4870	− .448	2.100		− .601
			"Down" Direction			
I-R	5.25	5600	−0.735	2.055	3.615×10^{-4}	−1.016
		10245	− .437	2.070		−0.600
I-L		5560	− .570	2.055		− .788
II-R		5885	− .901	2.150		−1.192
		5390	− .683	2.150		−0.903
II-L		5930	− .773	2.160		−1.016
		5450	− .690	2.170		−0.905
III-R	5.99	4830	− .475	2.075	3.942×10^{-4}	− .710
		6100	− .493	2.095		− .732
		6005	− .233	2.115		− .342
III-L		6110	− .164	2.095		− .243
		5990	− .351	2.115		− .515
IV-R	6.2	5906	− .312	2.105	3.571×10^{-4}	− .416
IV-L		5095	− .259	2.075		− .350
		6063	− .231	2.090		− .311
V-L	7.18	6346	.260	2.050	3.605×10^{-4}	+ .366
		4417	.351	2.050		+ .495
		6080	.280	2.050		+ .394
VI-R		5460	.311	2.450		+ .360
		7515	.297	2.500		+ .339
		6975	.324	2.500		+ .367
VI-L		7514	.426	2.050		+ .482

as Haugaard and Johnson,[14] namely: "a water–alcohol mixture has the same hydrogen-ion activity as an aqueous solution when they both have the same potential difference against the hydrogen electrode."

In comparing this value of the isoelectric point with other investigators' results, it is necessary to convert all such data to an alcohol–water basis. Gortner[3] gives an isoelectric point for secalin at a *p*H of 5.43 (in water) obtained by methods of acid and base combining ratios. This value calculated to the alcohol basis by use of the tables of Haugaard and Johnson[14] gives an isoelectric point at a *p*H of 6.75, which is about the value obtained from these mobility experiments. Czonka, Murphy, and Jones[15] tabulated the results of isoelectric points obtained by a method similar to the critical precipitation method for a large number of proteins. The isoelectric point of secalin is given at a *p*H of 6.2, but no statement is made as to whether it was on the water or alcohol–water basis.

Gortner[3] gives isoelectric points for zein and gliadin at 6.29 and 7.11, respectively, calculated to the water–alcohol basis. Similarly, Williams and Watson give isoelectric points for their three fractions of zein, calculated to alcohol–water basis, at *p*H of 6.29, 7.16, and 6.95. Thus it would seem that the isoelectric points of the prolamines from the cereals so far studied lie within the same *p*H region.

Miscellaneous Experiments

Dielectric Constant and the Time of Relaxation.—A series of preliminary experiments was made in which the dielectric dispersion curve was determined for secalin over a frequency range of 24.2 kilocycles to 24.2 megacycles. The secalin used in these preliminary experiments was especially purified by electrodialysis at 10 milliamperes and 110 volts until the conductivity of the solution became equal to that of the solvent; the concentration of this solution was 0.204 g. of protein per 100 cc. of solution. The ratios of the dielectric constant change in the solution to that of solvent were plotted against the logarithms of their frequencies. The midpoints of the curves showing anomalous dispersion give as provisional values times of relaxation of $\tau_1 = 7.4 \times 10^{-7}$ sec., and $\tau_2 = 7.0 \times 10^{-8}$ sec., for the rotations about short and long axes. These figures, corrected to a process taking place in pure water at 25°, are 29×10^{-8} sec. and 2.7×10^{-8} sec., respectively. The ratio of major to minor axis from these times of relaxation is about ten to one for the secalin molecule. Details of similar experimental work and calculations for the protein zein are given in a recent article.[16]

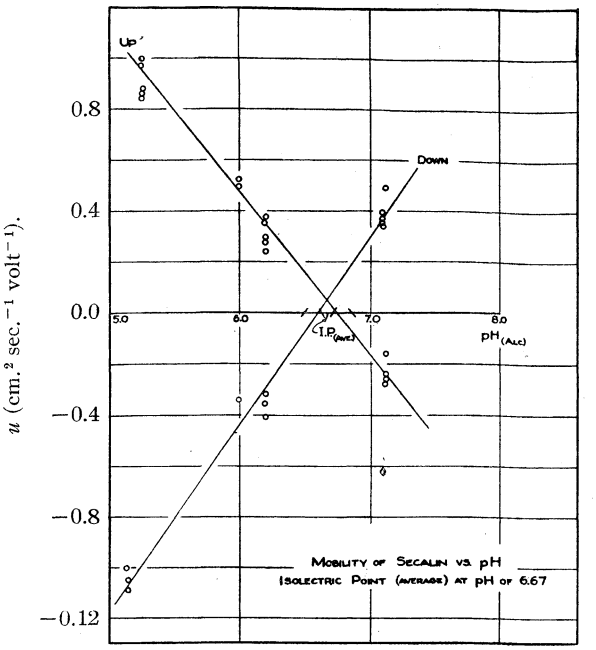


Fig. 2.—The effect of acidity upon the mobility of secalin in alcohol solution. The mobility becomes zero at *p*H of 6.67.

Optical Rotation and Refractive Index Increment.—The optical rotation for solutions containing 0.6950 and 0.5260 g. of secalin per 100 cc. of solution, respectively, gave specific rotations of −66.2 and −69.3° for an average of −67.7° at 25°. The refractive index increment ($\Delta\eta$ /g./100 cc.) was determined by the use of an immersion refractometer, giving an average refractive index increment of 1.51×10^{-3}.

The author wishes to express his thanks for the helpful advice of J. W. Williams throughout the course of this work. Grateful acknowledgment is also made to the Wisconsin Alumni Research Foundation for a scholarship which helped to make it possible to perform the work herein described.

Summary

The prolamine of rye grain was prepared and

(14) G. Haugaard and A. H. Johnson, *Carlsberg Laboratory Reprints*, Vol. 18, No. 2.

(15) F. A. Czonka, J. C. Murphy and D. B. Jones, THIS JOURNAL, **48**, 766 (1926).

(16) M. A. Elliott and J. W. Williams, *ibid.*, **61**, 718 (1939).

purified by two different methods and certain of its physical constants were determined.

The diffusion constant calculated to the water basis at 25° was found to be 4.78×10^{-7} cm.^{2} per sec. (At 20°, $D = 4.3 \times 10^{-7}$ cm.^{2}/sec.)

A calculation by means of sedimentation methods, using this value of "D" and an estimated value of the sedimentation constant, gave a molecular weight for secalin of approximately 40,000. Thus the predominant constituent of secalin seems to belong in the egg albumin molecular weight class of molecules.

The ordinary isoelectric point for secalin as determined by electrophoretic mobilities was found to be at pH 6.67.

MADISON, WIS. RECEIVED JANUARY 6, 1940

[CONTRIBUTION FROM THE BAKER CHEMISTRY LABORATORY OF CORNELL UNIVERSITY]

Fluorochloroethanes as Solvents for the Cryoscopic Determination of Molecular Weights

BY JACK BERNSTEIN AND WILLIAM T. MILLER

The purpose of this paper is to call attention to the suitability of fluoropentachloroethane, *sym*-difluorotetrachloroethane and *unsym*-difluorotetrachloroethane for use as solvents for the determination of molecular weights. These substances have large molecular freezing point depressions, are chemically inert and melt within convenient working ranges. Their solvent action is in general very good for non-associated substances. A representative list of qualitative solubilities of organic compounds in *sym*-difluorotetrachloroethane has been reported by Booth.[1]

Fluoropentachloroethane.—Fluoropentachloroethane was found to work particularly well as a molecular weight solvent using a semimicro procedure modeled after the Rast procedure as modified by Munster.[2] A sealed tube is necessary for the melting point determinations because of the high vapor pressure of this substance near its melting point. Small thin-walled "micro boiling point tubes" were used (4.5 × 60 mm.), and the fluoropentachloroethane was added by rolling it into small pellets which were dropped into the tube. In each case the ratio of the weight of the solute to the weight of the solvent was such as to give a depression of the freezing point between 9 and 15°.

From the observed values of the depression of the freezing point values of the freezing point constant k as calculated by the usual formula $k = \Delta TSM/s1000$ were obtained. The concentrations varied from 3–10%, and the values listed are the mean values of at least two determinations with an average deviation from the mean of about 0.1, except where otherwise indicated: benzyl bromide, 41.5; benzyl ether, 42.1; decachlorobutane, 42.6; *p*-dichlorobenzene, 42.1; 4,4′-difluorodiphenyl, 42.8; isoamyl acetate, 41.3; methyl benzoate, 41.1; naphthalene, 42.1; acetone, s/S = 0.0201, 0.0221, k = 31.5, 32.3; benzoic acid, s/S = 0.0230, 0.0483, 0.0682, k = 24.5, 22.0, 21.3; benzyl alcohol, s/S = 0.0485, 0.0691, k = 26.7, 23.6; *n*-butyl alcohol, s/S = 0.0304, 0.0512, k = 28.7, 23.5; butyraldehyde, s/S = 0.0149, 0.0220, 0.0226, 0.0379, k = 31.3, 33.5, 33.2, 27.7; α-naphthol, s/S = 0.0241, 0.0482, k = 38.3, 32.9; nitrobenzene, s/S = 0.0392, 0.0429, k = 35.8, 36.7, respectively.

Acetanilide, aniline and dimethylaniline were sparingly soluble in fluoropentachloroethane and hexachloroethane formed a crystalline solid phase of higher melting point. For the measurements in which there was complete solubility and no apparent association or compound formation, the average value of k was 42.0.

The fluoropentachloroethane used in this work was prepared by fluorinating pentachloroethane[3] and melted at 99.9° after purification by distillation. This substance also may be prepared readily from hexachloroethane and antimony trifluoride.[1,4]

***sym*- and *unsym*-Difluorotetrachloroethane.**—These compounds do not work well with the semimicro procedure because of the difficulty of observing crystallization in the small tubes. However, their large freezing point depressions and convenient melting temperatures may be utilized in the usual macro procedure,[5] and their use for precise cryoscopic measurements is indicated. The constant k for *sym*-difluorotetrachloroethane was determined as 37.7 and for *unsym*-difluorotetrachloroethane as 38.6, using naphthalene and *p*-dichlorobenzene.

Naphthalene, s/S = 0.00140, 0.00140, 0.00127, k = 37.1, 36.7, 37.4; *p*-dichlorobenzene, s/S = 0.00129, 0.00121, 0.00134, k = 38.1, 38.0, 38.8; naphthalene, s/S = 0.000660, 0.00113, k = 38.2, 37.9; *p*-dichlorobenzene, s/S = 0.000794, 0.000863, 0.000919, k = 38.2, 39.4, 39.3, respectively.

The *sym*-difluorotetrachloroethane was prepared by adding fluorine to tetrachloroethylene[3] and melted at 24.7°. It also may be prepared from hexachloroethane and antimony trifluoride.[1,4] No direct methods for the preparation of *unsym*-difluorotetrachloroethane have appeared in the literature although it has been character-

(1) Booth, Mong and Burchfield, *Ind. Eng. Chem.*, **24**, 328 (1932).

(2) Gattermann and Wieland, "Laboratory Methods of Organic Chemistry," The Macmillan Co., New York, N. Y., 1937, p. 86.

(3) Miller, THIS JOURNAL, **62**, 341 (1940).

(4) Locke, Brode and Henne, *ibid.*, **56**, 1726 (1934).

(5) Reilly and Rae, "Physico-Chemical Methods," Methuen and Co., Ltd., London, 1933, p. 439.

ized.[4] However, it was found possible to obtain this material directly from trifluorotrichloroethane ($CF_2ClCFCl_2$)[6] and aluminum chloride.[7]

Summary

Fluoropentachloroethane, *sym*-difluorotetrachloroethane and *unsym*-difluorotetrachloroethane were shown to be good cryoscopic solvents for non-associated substances. Their large molecular freezing point depressions, chemical inertness and convenient melting temperatures recommend their use.

(6) "Freon 113" of Kinetic Chemicals Inc., Carney's Point, N. J.
(7) Miller, THIS JOURNAL, **62**, 993 (1940).

ITHACA, N. Y. RECEIVED DECEMBER 28, 1939

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

Solubility and Molecular Rotation of Certain Tetra-, Penta- and Hexa-Substituted Benzenes

BY CHARLES P. SMYTH AND GEORGE L. LEWIS

In a discussion by Baker and Smyth[1] of the process of fusion, it has been pointed out that the gain of entropy by a solid through the setting in of molecular rotation in the crystal tends to raise the melting of the solid to a temperature much higher than that at which it presumably would have melted in the absence of such rotation. In view of the close relation between the processes of solution and fusion, it has seemed desirable to investigate the influence of molecular rotation in a solid upon its solubility. Recent dielectric constant measurements by White, Biggs and Morgan[2] have shown that the molecules of many penta- and hexa-substituted benzenes have rotational freedom in the plane of the benzene ring. Dr. Morgan has very kindly made a number of pure samples of these substances available to us for solubility and dipole moment measurements, the latter of which are discussed elsewhere.[3] In addition, the solubilities of hexamethylbenzene and hexachlorobenzene obtained from the Eastman Kodak Company have been measured. Benzene was used as a solvent which would dissolve adequate quantities of the least soluble of the substances investigated. It was purified in the usual manner.[4]

Experimental Method

The solubility measurements were carried out at four different temperatures in a thermostat. An excess of the substance, the solubility of which was to be measured, was added to the benzene in a test-tube mounted on a mechanical shaker in a water-bath and shaken at a temperature of about 48° until the solution was thought to be saturated, some of the solid still remaining undissolved. The temperature of the bath was then lowered to 41.88° where it was held fixed for at least forty-five minutes. The formation of new crystals was used as the criterion of saturation. Part of the saturated solution was withdrawn by means of a completely water-jacketed pipet, in which the temperature of the water was higher than that of the solution, and run into a weighing bottle. After this sample of solution had been weighed, the solvent was evaporated at about 40° in a current of warm, dry air, and the solute remaining as a residue in the bottle was weighed. The concentrations of the saturated solutions at three lower temperatures were successively determined in the same way, an ordinary pipet being used for temperatures below that of the room. The probable error in the solubilities thus determined was 2%.

(1) Baker and Smyth, THIS JOURNAL, **61**, 1695 (1939).
(2) White, Biggs and Morgan, *ibid.*, **62**, 16 (1940).
(3) Smyth and Lewis, *ibid.*, **62**, 721 (1940).
(4) Smyth and Walls, *ibid.*, **54**, 1854 (1932).

Experimental Results

The solubilities expressed as the mole fraction N of solute in the saturated solution are listed in Table I for the four different temperatures at which they were determined. The substances are designated by letters in the first column, which are used in place of the long names of the substances in Table II and in Fig. 1. The solubilities may be examined with the aid of a slightly modified equation given by Hildebrand[5] $\log N = -\Delta E_f (T_m - T)/4.575\, T_m T$, in which ΔE_f is the latent heat of fusion of the solute and T_m its melting point on the absolute scale. According to this equation which represents the ideal solubility, the plotting of $\log N$ against $1/T$ should give a nearly straight line with slope $-\Delta E_f/4.575$ and upper limit with $N = 1$ at the melting point of the solute. As the latent heats of fusion of the substances under consideration here have not been determined, the ideal solubility curves cannot be drawn, but, in Fig. 1, the values of $\log N$ plotted against $1/T$ for each substance are

(5) Hildebrand, "Solubility," Reinhold Publishing Corporation, New York, N. Y., 1936, p. 34.

TABLE I

MOLE FRACTIONS OF POLYSUBSTITUTED BENZENES IN SATURATED SOLUTION IN BENZENE

	Solute	t, °C. = 8.77	19.92	29.93	41.88
		N			
A	Hexachlorobenzene	0.0077	0.0102	0.0147	0.0209
B	Hexamethylbenzene	.0277	.0382	.583	.0814
C	1,3,5-Trimethyl-2,4,6-trichlorobenzene	(.007)	.0136	.0190	.0270
D	1,2,5-Trimethyl-3,4,6-trichlorobenzene	.0111	.0147	.0217	.0319
E	Pentachlorotoluene	.0083	.0112	.0153	.0224
F	Tetrachloro-*o*-xylene	.0077	.0110	.0150	.0217
G	1,2,3,4-Tetramethyl-5,6-dichlorobenzene	.0188	.0253	.0370	.0475
H	Pentamethylchlorobenzene	.0349	.0488	.0737	.1010
I	Pentachlorobenzene	.157	.184	.242	.334
J	4,5-Dichloro-*o*-xylene	.152	.213	.305	—
K	Ethylpentachlorobenzene	—	(22.12°) .468	(32.36°) .645	(42.57°) .851
L	3,4,5-Trichloro-*o*-xylene	—	(17.46°) .483	(27.83°) .526	(37.45°) .809

TABLE II

TEMPERATURES OF ROTATION AND MELTING, HEATS AND ENTROPIES OF FUSION, AND DIPOLE MOMENTS

Solute	t_r, °C.	t_m, °C.	ΔE_f, kcal./mole	ΔS_f, e. u./mole	μ ($\times 10^{18}$)
A		226	5.4	10.8	0
B		166	5.6	12.8	0
C		205	5.7	11.9	0
D	−44	210	5.8	12.0	1.83
E	11	224	5.4	10.8	1.55
F	−26	228	5.4	10.8	2.65
G	−74	193	5.1	11.0	2.93
H	−47	154	5.5	12.9	1.85
I		86	4.2	11.7	0.88
J	—	76	5.5	15.7	3.01
K	—	56	5.4	16.3	1.50

found to lie very close to a straight line drawn through the melting point at log $N = 0$. Several substances are omitted from Fig. 1 because their curves are very close to those shown and the curve for 3,4,5-trichloro-*o*-xylene is omitted because of the somewhat unsatisfactory character of the three values which were determined at different temperatures from the others. The slopes of similar curves plotted on a larger scale without reference to the melting points are used to calculate approximate values of the heats of fusion ΔE_f given in Table II, which, in turn, are used to calculate the entropies of fusion, $\Delta S_f = \Delta E_f/T_m$, given in Table II. The probable errors in these two quantities calculated from the slopes of the curves would appear to be about 5% but may more safely be set at 10%. Table II also lists the melting points t_m in °C. and the temperatures t_r determined by White, Biggs and Morgan below which rotation ceases or, more correctly speaking, at which rotation is so hampered that the imaginary part ϵ'' of the dielectric constant reaches a maximum for a frequency of 100 kc. A dash in this column indicates the absence of rotation in the solid. The dielectric constant of the solid would fail to give information as to the rotation of the symmetrical molecules of the first three substances listed and is not conclusive as to pentachlorobenzene. The last column gives the dipole moments found for the substances.[3]

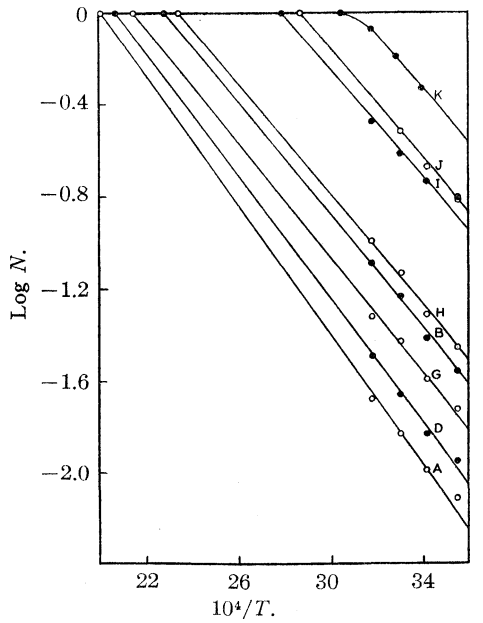


Fig. 1.—Solubilities of substituted benzenes in benzene.

Discussion of Results

Certain simple and expected relations are apparent in the data of Tables I and II and certain seeming anomalies occur. The hexamethylbenzene molecule with its hydrocarbon surface[6] is about four times as soluble in benzene as the hexachlorobenzene molecule with its less similar chlorine surface, and the melting point of the substance is correspondingly lower. Trichloromesitylene, sub-

(6) See Langmuir, "Third Colloid Symposium Monograph," The Chemical Catalog Company, Inc., New York, N. Y., 1925, p. 3.

stance C, is not half-way between hexachlorobenzene and hexamethylbenzene in solubility but is much closer to the former in solubility and melting point. The interchange of position of a chlorine and a methyl group to give the unsymmetrical 1,2,5-trimethyl-3,4,6-trichlorobenzene molecule with a considerable dipole moment has only a very small effect upon the solubility and melting point. Increase of the number of chlorines in the hexasubstituted molecule to four and five reduces the solubilities and raises the melting points a little so that they are hardly distinguishable from those of hexachlorobenzene, although tetrachloro-*o*-xylene possesses a particularly large dipole moment. The solubility curves for this substance and pentachlorotoluene are omitted from Fig. 1 because of their practical coincidence with that for hexachlorobenzene, A. Increase in the number of methyl groups in the hexa-substituted molecule increases the solubility until pentamethylchlorobenzene has a solubility about 25% greater than that of hexamethylbenzene together with a slightly lower melting point. These eight hexa-substituted benzenes may be grouped roughly as having relatively low solubilities and high melting points. Their dipole moments vary from 0 to 2.93 without having any apparent effect upon the solubility. The last five of them, D-H, have been found[2] to possess freedom of molecular rotation in the crystal and thus possess additional entropy in the solid, which raises their melting points according to the relation observed by Baker and Smyth[1] and lowers their solubilities. The first three substances, A–C, fit so well into this group that one would certainly expect their molecules also to possess freedom of rotation in the crystal. Also, it is difficult to see how the five somewhat less symmetrical hexa-substituted benzenes can rotate if these do not. However, Lonsdale[7] has interpreted careful X-ray analyses of hexamethyl- and hexachlorobenzene at room temperature on the basis of non-rotation of the molecules and Brockway and Robertson[8] have done the same with hexamethylbenzene. The results of White, Biggs and Morgan[2] indicate that molecular rotation should occur in hexachlorobenzene, but possibly only above the temperature employed in the X-ray investigation. The rotation of hexamethylbenzene might be expected to begin at a lower temperature and it seems possible that its transition at $-165°$, which produces a change in the slope of the specific heat–temperature curve and involves an entropy of transition of 2.28 e. u. per mole,[9] may mark the acquisition of rotational freedom in the plane of the ring. At any instant of time, most of the molecules would be executing rotational oscillation about potential energy minima which would occur at angular intervals of 60°. As location of the molecule in any one of these six minima would be indistinguishable from that in any other, it appears possible that the results of the X-ray analysis may correspond to that given by nearly stationary molecules in spite of the existence of rotational freedom. It appears possible, therefore, tentatively to regard the eight substances, which have been grouped because of low solubilities and high melting points, as possessing freedom of molecular rotation in the plane of the ring.

The dielectric constant results for pentachlorobenzene communicated to the authors by Dr. Morgan suggest a restricted rotation of the molecule somewhat like that in isopropyl bromide,[1] which apparently raises the melting point of the latter some 20 or 30°. The solubility and melting point of pentachlorobenzene are nearer to those of the non-rotating substances, although the melting point is somewhat raised as in the case of isopropyl bromide.

4,5-Dichloro-*o*-xylene and ethylpentachlorobenzene, which are definitely shown by their low dielectric constants[2] to possess practically no rotational freedom, have low melting points and high solubilities. The solubilities of pentachlorobenzene and 4,5-dichloro-*o*-xylene differ but slightly from each other, while the dipole moments are very different. Ethylpentachlorobenzene has a solubility more than twice as large as those of the other two and a dipole moment intermediate between theirs. 3,4,5-Trichloro-*o*-xylene has a solubility close to that of ethylpentachlorobenzene and a higher moment, 2.46. Its high solubility and fairly low melting point would lead one to expect non-rotation in the solid, but the dielectric constant determinations[2] show a rotational transition at 15–20°. This constitutes the only definitely established exception among these substances to the rule that molecular rotation in a solid tends to give the solid lower solubility than it would have in the absence of rotation, but the answer to the question of molecu-

(7) Lonsdale, *Proc. Roy. Soc.* (London), **A123**, 494 (1929); **A133**, 536 (1931).

(8) Brockway and Robertson, *J. Chem. Soc.*, 1324 (1939).

(9) Huffman, Parks and Daniels, THIS JOURNAL, **52**, 1547 (1930).

lar rotation is only tentatively indicated and not positively settled in the cases of three of the twelve substances.

It must be remembered that, at the temperature of a rotational transition, the solubility of the low-temperature form of a solid in equilibrium with the high-temperature form must be the same as that of the latter. The difference in slope of the solubility curves above and below the transition depends primarily upon the heat of transition. Although the substances under consideration here do not show sharp, reversible transitions, it is not unreasonable to suppose that solubilities measured not far from the temperatures at which molecular rotation ceases may well be either high or low as determined by factors other than molecular rotation, but, in a great majority of the cases here investigated, molecular rotation reduces the solubility.

The curves in Fig. 1 and those omitted from it show that the solubilities of these highly-substituted benzenes in benzene are close to the ideal. The curve for ethylpentachlorobenzene is the only one which does not pass through the melting point, partly, at least, because its points are so near the melting point that a slight adjustment in its slope cannot make it reach the melting point. A melting point only 10° lower, but still 10° higher than the apparently incorrect[2] value given in Beilstein, would fall on the line.

The entropies of fusion of all but the last two substances, J and K, in Table II lie between 10.8 and 12.9 units, differing from a mean value by no more than their possible errors. The last two substances, 4,5-dichloro-*o*-xylene and ethylpentachlorobenzene, which are the only two definitely proved to have no molecular rotation in the solid, have entropies of fusion four or five units higher, as they acquire degrees of rotational freedom on melting which most, at least, of the other substances have already acquired in the solid. The entropies of fusion of the rotating substances are higher than those found previously for substances with smaller molecules rotating in the solid, but are much lower than the value 22.1 found for the long molecule of cetyl alcohol,[10] which, because of molecular rotation around the long axis, is little more than half of that found for non-rotating hydrocarbons of about the same length. The values for the hexa-substituted benzenes with rotating molecules are close to those for the lighter molecules of the xylenes and dichlorobenzenes, which do not have freedom of molecular rotation in the solid. The value for hexamethylbenzene is lower than that calculated empirically by Huffman, Parks and Daniels[9] without allowance for rotation by about the amount which rotation might cause. In other words, the two substances, which have been definitely shown not to rotate, have reasonable values for their entropies of fusion, and the other substances in Table II have values lower by an amount which can arise from their possession of rotational freedom in the solid.

In conclusion, it may be said that, in the case of these similarly shaped molecules, the dipole moment of the molecule as a whole has no detectable effect upon the solubility of the substance in the non-polar solvent, benzene. The solubilities of these substituted benzenes are almost ideal and tend to be lower when the molecules possess freedom of rotation in the solid, although other factors occasionally predominate over this tendency. In view of the relations between molecular rotation and melting point and between melting point and solubility, an at least approximate relation between molecular rotation and solubility follows almost inevitably and from the same fundamental cause.

The writers wish to express their gratitude to Dr. S. O. Morgan of the Bell Telephone Laboratories for the loan of the substances upon which these measurements have been made as well as for information concerning them.

Summary

The solubilities in benzene of twelve tetra-, penta-, and hexa-chlorine and methyl substituted benzenes have been measured at four temperatures. The solubilities are approximately ideal and are independent of the dipole moments of the molecules. The heats and entropies of fusion have been calculated from the slopes of the solubility curves. In accordance with the relation previously observed between molecular rotation in the solid and melting point, the solubilities and entropies of fusion tend to be low and the melting points high when the molecules possess freedom of rotation in the solid.

(10) Baker and Smyth, THIS JOURNAL, **60**, 1229 (1938).

PRINCETON, NEW JERSEY RECEIVED JANUARY 30, 1940

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, No. 215]

The Reactivity of Atoms and Groups in Organic Compounds. XX. The Effect of Substituents on the Relative Reactivities of the Hydroxyl Group in Derivatives of Benzoic Acid

BY JAMES F. NORRIS AND ARTHUR E. BEARSE[1]

Some time ago a report was given of the study of the influence of substituents on the relative reactivities of the hydrogen atom of the carboxyl group in a number of derivatives of benzoic acid.[2] It appeared of interest to determine the relative reactivities of the hydroxyl group in the acids previously studied to discover the influence of the substituents on the carbon–oxygen bond. Comparisons between the effects on the two bonds linked to oxygen gave information in regard to the influence of substituents on reactivity through a chain of atoms; it also furnished evidence in regard to the theory of alternating strong and weak bonds put forward by Flürscheim.[3]

Among the acids studied were several which contained one or two substituents in the *ortho* position. These were studied with the expectation that the results would be helpful in a fuller understanding of the so-called "diortho effect."

The velocity constants of the reactions between the acids and thionyl chloride were determined: $RCOOH + SOCl_2 = RCOCl + HCl + SO_2$. The course of the reaction was followed by determining, from time to time, the pressure produced by the two gases as they were formed in a closed system of constant volume. Since thionyl chloride and the gases formed are corrosive, a new type of all-glass apparatus was designed; it is described in the experimental part of this paper. A large excess of thionyl chloride served as the solvent.

The results of the experiments are given in Table I.

TABLE I

Column I, substituents present in benzoic acid; Column II, average first order velocity constants at 25° of the reaction $RCOOH + SOCl_2 = RCOCl + HCl + SO_2$, time in minutes; Column III, relative values of the constants compared with benzoic acid taken as 1; Column IV, relative reactivities of the acidic hydrogen atoms, when known, benzoic acid taken as 1.

I	II	III	IV[a]
2,6-Dimethoxy	Too fast to measure	...	...
4-Methoxy	0.065 (0.0629–.0677)	9.8	...
2,4,6-Trimethyl	.055 (0.560–.0541)	8.2	...
2,4,6-Triethyl	.051 (.0509–.0501)	7.6	...
2-Methoxy	.026 (.0265–.0260)	3.9	0.04
4-Methyl	.026 (.0257–.0254)	3.8	...
3-Methyl	.011 (.0112–.0111)	1.7	.6
2-Methyl	.0074 (.00735–.00746)	1.1	.4
Benzoic	.0067 (.00661–.00656) (.00672–.00682)	1	1
2-Chloro	.0011 (.00106–.00104)	0.16	16.5
3-Chloro	.00062 (.00062–.00062)	.09	9.6
2,6-Dichloro	.00056 (.00053–.00059)	.08	...
2-Chloro-6-nitro	.00047 (.00047–.00046)	.07	...
2-Nitro	.00021 (.00017–.00024)	.03	83
3-Nitro	Too slow to measure		

[a] Norris and Strain, ref. 2.

A comparison of the figures in Column III shows that the relative reactivities of the hydroxyl group in all the acids which contain CH_3, C_2H_5 or CH_3O groups are greater than the reactivity of the hydroxyl group in benzoic acid. The presence of two of these groups in the ortho positions greatly increases reactivity. It has been shown[4] that the acyl chlorides prepared from these diortho substituted acids react so rapidly with ethyl alcohol at 0° that the rates of the reaction could not be measured. The hydroxyl groups in the acids which contained Cl and NO_2 were less reactive than the hydroxyl group in benzoic acid. The presence of two of these substituents in the ortho positions greatly reduced reactivity. The acyl chlorides of these acids reacted so slowly at 0° with ethyl alcohol that the rates of the reactions could not be measured. These facts will be helpful in arriving at a satisfactory interpretation of steric hindrance. The effect on the reduction of reactivity of the hydroxyl group by Cl and NO_2 was greater in the meta than in the ortho position; the same conclusion was drawn from the relative reactivities of the acyl chloride with alcohol.

In the preparation of acyl chlorides from acids and thionyl chloride, a molecular quantity of pyridine has been used to assist the reaction.[5] L. F. Fieser and M. Fieser[6] prepared the acyl

(1) From the thesis submitted by Arthur E. Bearse in partial fulfilment of the requirements for the degree of Doctor of Philosophy, 1936.

(2) Norris and Strain, THIS JOURNAL, **57**, 187 (1935).

(3) Flürscheim, *J. Chem. Soc.*, **95**, 718 (1909); *Phil. Mag.*, **47**, 569 (1924).

(4) Norris and Young, THIS JOURNAL, **57**, 1420 (1935); Norris and Ware, *ibid.*, **61**, 1418 (1939).

(5) Carre and Libermann, *Compt. rend.*, **199**, 1422 (1934).

(6) L. F. Fieser and M. Fieser, THIS JOURNAL, **57**, 782 (1935).

chloride of a derivative of butyric acid by treating the latter, dissolved in ether, with thionyl chloride and a trace of pyridine. The effect of pyridine and its concentration on the rates at which certain of the acyl chlorides were formed was investigated to discover to what extent the substituent in the acid affected the rates. The effect of concentration of the catalyst was studied in the case of benzoic acid. When equal molecular quantities of the acid and of pyridine were used the rate of the reaction at 25° was 97 times that of the uncatalyzed reaction; with 12.5 moles of acid to 1 of pyridine the rate was 82 times; with 25 moles 64, and with 50 moles 36 times. It was evident that pyridine acted as a catalyst and not as a reagent to remove hydrogen chloride. This conclusion was strengthened by the fact that when 12.5 moles of benzoic acid was treated with a large excess of thionyl chloride and 1 mole of N,N-dimethylcyclohexylamine, the rate was increased 91 times and when an equivalent quantity of the hydrochloride of the amine was used the rate increased 67 times. Dimethylaniline in the same concentration increased the rate with benzoic acid only 14 times.

The reactions were carried out in the way used in the case of the uncatalyzed reactions. The results are given in Table II.

TABLE II

Column I, substituent in benzoic acid; Column II, first order velocity constant of catalyzed reaction at 25°; mole conc. of acid to pyridine 12.5 to 1, time in min.; Column III, ratio of constant of catalyzed reaction to constant of uncatalyzed reaction; Column IV, relative rates of catalyzed reactions with benzoic acid = 1; Column V, relative rates of uncatalyzed reactions, benzoic acid = 1.

I	II	III	IV	V
2-Nitro	0.35–0.30	1520	0.6	0.03
2-Chloro	.63	600	1.1	.16
2-Methyl	.66	89	1.2	1.1
Benzoic acid	.54– .55	82	1	1
3-Chloro	.048	77	0.09	0.09
2,6-Dichloro	.042	75	.08	.08
3-Methyl	.67	60	1.2	1.7
4-Methyl	.67	26	1.2	3.8
3-Nitro	.0011	..	0.002	..

The figures in Column III show the great effect of the catalyst in increasing the rate of the reaction between the acids and thionyl chloride. The effect was greatest in the case of the acids containing a substituent in the *ortho* position. From Column V it is seen that the two acids most affected were those that had low reactivity when measured by the uncatalyzed reaction. Columns IV and V show that the relative reactivities measured by the catalyzed and by the uncatalyzed reactions are not the same. The three methyl derivatives are more reactive than benzoic acid when measured in either way and the halogen and nitro derivatives, with the exception of the 2-chloro compound, are less reactive than benzoic acids.

The practical application of these results is evident, namely, the use of pyridine or dimethylcyclohexylamine as a catalyst in preparing acyl chlorides by means of thionyl chloride. Hans Meyer[7] who applied the reaction to a large number of acids, without a catalyst, reported that certain acids required heating the mixture for several hours. The acid chloride was obtained by removing the excess of thionyl chloride by distillation. In our experiment the catalyzed reaction was complete at 25° in the case of benzoic acid in about ten minutes; the 3-chloro acid required about one hour for complete reaction.

Details of Experiments

The Apparatus Used.—This is sketched in Fig. 1. The vessel in which the reaction took place (A, side view at left) had two arms, 8 cm. long and 3 cm. in diameter and a no. 20 ground glass joint. It was connected through the joint to a tube, attached to a shaking device, and flexible glass bends to the stopcock B. The apparatus up to the cock was placed in a thermostat at 25 ± 0.02°. A tube from B led to cock C and a closed spiral tube (18 turns 2.5 cm. in diameter) to which was sealed a small mirror. The tube and mirror were enclosed in a jacket which was connected with cocks as indicated and a manometer, having two arms, in which the pressure could be adjusted. When the pressure in the reaction vessel increased the spiral would cause the mirror to change its position. The position of the mirror was indicated by a beam of light reflected from it onto a screen. In order to determine the increased pressure in the partially evacuated apparatus, the pressure outside of the spiral was adjusted roughly by letting air in through the cocks, and a final adjustment was made by raising the vessel containing mercury attached to the manometer until the spot of light from the mirror returned to the original zero position. The pressure added to balance the inside pressure was measured on the manometer. This method of measuring the pressure of a corrosive gas was used successfully by Johnson[8] in measuring the vapor pressure of ammonium chloride at high temperatures and by workers in the Research Laboratory of Inorganic Chemistry of this Institute.

In using the apparatus the desired weight of the solid acid was introduced into the weighed reaction vessel A held so that one tube was vertical and the other horizontal. Through a short piece of glass tubing placed in the opening

(7) Hans Meyer, *Monatsh.*, **22**, 415, 477 (1901). See also McMaster and Ahmann, THIS JOURNAL, **50**, 145 (1928), and Clark and Ball, *Trans. Roy. Soc. Can.*, III, **27**, 97 (1933).

(8) Johnson, *Z. physik. Chem.*, **61**, 457 (1907).

was introduced a smaller tube carrying the acid. By tapping the tube the required amount of acid could be dropped into the vertical tube. The reaction vessel A was again weighed. The weight of acid introduced could be determined to 1 mg. The reaction vessel was connected with the rest of the apparatus by means of the ground glass joint which had been treated with "lubriseal," and water was added to the thermostat which was brought to approximately 25°. Enough of the water was then drawn off to permit the removal of the reaction vessel after it had been wiped dry. By means of a calibrated pipet exactly 10 cc. of thionyl chloride was added to the leg of the reaction vessel which did not contain the acid. The reaction vessel was again connected with the apparatus, care being taken to prevent the thionyl chloride from coming in contact with the acid. The water was returned to the thermostat and the shaker and water pumps connected at C and F were started. The system was evacuated until the pressure on the two sides of the spiral manometer was about 140 mm. This required about one and one-half minutes. The cocks C and E were then closed. Shaking was continued for ten minutes to allow the system to come to equilibrium; during this time the temperature of the thermostat was brought to 25 ± 0.02°. The shaker was stopped, the cock B was closed and the reactants were mixed by rotating the reaction vessel through 90 degrees. The time was recorded as zero time. The pressure was measured by adjusting the pressure in the outside of the spiral manometer so that the spot of light reflected from the mirror returned to the zero position. The cock B was opened and the shaker started.

Readings of pressure were made at intervals of time that depended on the rate at which the reactions were taking place. When a reading was made the cock B was closed and the shaker stopped. In order to avoid a possible leak in the apparatus, the two sides of the glass joint that connected the reaction vessel with the rest of the apparatus were held in position during the shaking by a wire around projections sealed to the two parts of the joint. Shaking was continuous during the first hour except when pressure readings were made; thereafter the shaker was run only for ten minutes preceding a reading. The adjustments in the outside pressure were made through the three-way cock F; air was either withdrawn by the pump or admitted through the cock.

Calculation of the Velocity Constants.—The constants were calculated from the formula

$$K = \frac{2.303}{t} \log \frac{P}{P - p}$$

in which P is the final pressure and p is the pressure at time t. By plotting the log terms against t a straight line was obtained up to a high percentage conversion in the case of most of the acids. The slope of the line is a measure of the constant. In certain cases the line did not cut the axis of time at zero and the time correction, determined in the usual way, was used in calculating the constant.

The method of calculation required the determination of the pressure when the reaction was complete (P). This value was determined in the case of benzoic acid and the acids more reactive than benzoic. It was found to be nearly constant since equivalent weights of the acids were used. In the case of the less reactive acids the experimental values found with benzoic acid were used for P.

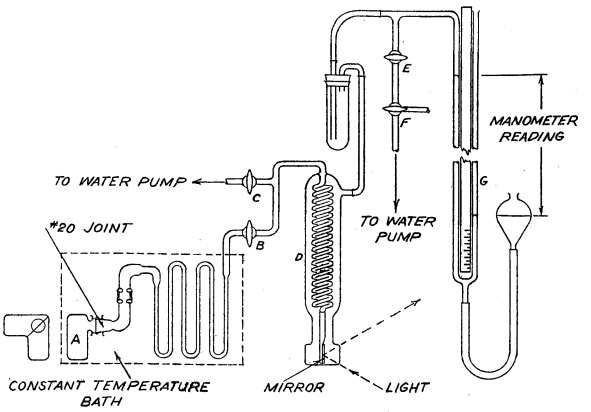


Fig. 1.—Apparatus for measuring pressure increase.

In the case of certain of the inactive acids the following formula was used as a check

$$K = \frac{2.303}{t_2 - t_1} \left(\log \frac{P}{P - P_2} - \log \frac{P}{P - P_1} \right)$$

Control experiments in which thionyl chloride without an acid was used showed that a pressure was developed slowly. This probably was due to the slow diffusion of the chloride into the parts of the apparatus outside the thermostat. In order to correct for this added pressure four runs were made; they agreed well and furnished average values to be used in calculating the real increase in pressure due to the reaction. The correction increased from 1 mm. to 10 mm. at the end of three hundred minutes. In the case of benzoic acid and the acids that were more reactive, the correction was a small percentage of the observed pressure; the constants were calculated from times less than one hundred and forty minutes. In the case of the very inactive acids the correction amounted to from 10 to 30 % of the observed reading.

The Reagents Used.—The acids were purified by crystallization until the melting points were constant and checked closely the best values in the literature. They were dried in an oven and finally in a vacuum desiccator over activated aluminum for at least twelve hours before use.

The 2,6-dichlorobenzoic acid was prepared from 2,6-dichlorotoluene by a convenient method which has not

been described. The method is given in detail because we were unsuccessful in preparing the acid by the direct oxidation of the toluene derivative with potassium permanganate.[9] Attempts to prepare the acid by oxidation of the toluene derivative with alkaline or acid permanganate, chromic acid and sulfuric acid in acetic acid, and potassium dichromate and sulfuric acid did not give satisfactory results.

Twenty grams of 2,6-dichlorotoluene was placed in a 300-cc. flask having two necks to which were attached a reflux condenser and a separatory funnel the end of which was just above the liquid. The flask was heated in an oil-bath at 170° and 19.8 g. of bromine was added slowly through the funnel at such a rate that no bromine escaped. When the reaction was complete and the flask was cold, the contents were transferred to a 1-liter flask fitted with a mercury seal stirrer, and a reflux condenser. A solution of 6 g. of sodium hydroxide in 500 cc. of water was added and the mixture heated to boiling with the stirrer running. Powdered potassium permanganate was added in small portions through the condenser and washed down with a little water. When the color disappeared more permanganate and small amounts of a solution of sodium hydroxide to keep the mixture alkaline were added. After 24.8 g. of the permanganate had been used during about two hours the color persisted. This was removed by alcohol and the mixture was distilled with steam; about 0.7 cc. of the chlorotoluene was recovered. The material in the flask was filtered and the solid washed with water. The filtrate was concentrated to about 150 cc. and enough hydrochloric acid added to precipitate the 2,6-dichlorobenzoic acid. The acid was digested with water, dried and crystallized from a mixture of equal volumes of benzene and ligroin. The yield of pure acid which melted at 143–144° was 57% of the theoretical amount calculated from the 2,6-dichlorotoluene used. A similar method could be applied probably to other hydrocarbon derivatives which resist ordinary oxidizing agents.

The method was based on information from the du Pont Company, that 2-chloro-6-nitrotoluene could be brominated readily in the side chain at 170°, whereas a higher temperature is required for chlorination and the resulting yield is very small.

In an attempt to prepare 2-chloro-6-nitrobenzoic acid from the corresponding aldehyde by means of the Cannizzaro reaction, it was found that the aldehyde group was removed and nearly the theoretical yield of *m*-chloronitrobenzene was obtained.

Purification of Thionyl Chloride.—The material used (Eastman Kodak Company, No. 246, b. p. 75–76°) was fractionally distilled in an all glass apparatus with a Davis column. The several fractions were used in test experiments with benzoic acid. The value of the velocity constant for the reaction varied from 0.0103 to 0.0131. It was evident that a small amount of impurity was present which increased the rate and could not be removed by fractionation. A portion of the original sample (50 cc.) was treated with 1 g. of benzoic acid and allowed to stand twelve hours. The excess of thionyl chloride was then distilled off, fractionated, and tested by determining the velocity constant of the reaction with benzoic acid. This was found to be less than before treatment. Four such treatments, followed by fractionation, caused a marked decrease in the constant. Four additional treatments caused only a slight decrease. Four more treatments changed the constant only within the experimental error of the process. All determinations were made with thionyl chloride that had been subjected to twelve treatments with benzoic acid and subsequent fractionation in which the first part of the distillate was rejected. Two separate preparations gave products which yielded constants that checked within less than 3%. The purification did not appreciably affect the boiling point of the thionyl chloride. The samples used boiled at 74.8–75.6° (751 mm.). The recorded boiling point is 75° (746 mm.).[10]

(9) Claus and Stanenhagen, *Ann.*, **269**, 224 (1892). Cohen and Dakin, *J. Chem. Soc.*, **79**, 1132 (1901), report failure with this method.

Summary

1. The relative reactivities of the acidic hydroxyl groups of a number of derivatives of benzoic acid have been determined by measuring the rates at which the acids react with thionyl chloride.

2. The results show that the acids which have the more reactive hydroxyl groups have the less reactive acidic hydrogen atoms.

3. Acids which have methyl, ethyl or methoxy groups in the two positions ortho to the carboxyl group have very reactive hydroxyl groups; the acids having chlorine or the nitro group in these positions have very inactive hydroxyl groups.

4. A study of the effect of pyridine and of N,N-dimethylcyclohexylamine on the rates of the reaction showed that the latter were greatly increased by the catalysts. The acids which contained the substituent in the ortho position were most affected; the rate with *o*-nitrobenzoic acid was increased 1520 times, *o*-chlorobenzoic acid 600 times, and *o*-methylbenzoic acid 87 times when the concentration of the catalyst was 1 mole to 12.5 moles of the acid.

CAMBRIDGE, MASS. RECEIVED JANUARY 6, 1940

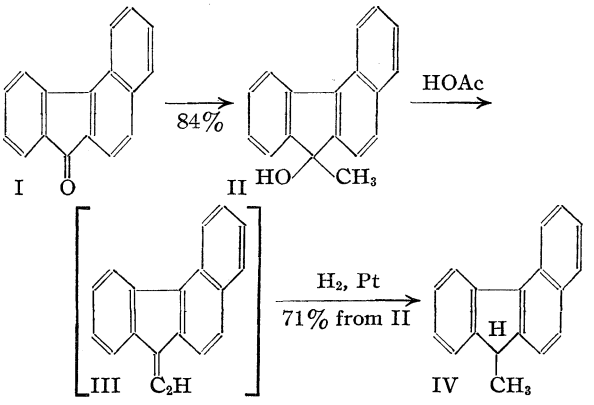
(10) Arri, *Chem. Abs.*, **24**, 277 (1930).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

9-Methyl-3,4-benzfluorene

BY LOUIS F. FIESER AND LLOYD M. JOSHEL[1]

Because of the marked carcinogenic activity of 10-methyl-1,2-benzanthracene,[2] it seemed of interest to synthesize and test the somewhat analogous 9-methyl-3,4-benzfluorene (IV). 3,4-Benzfluorenone-9 (I) was prepared from 1-phenyl-2,3-naphthalic anhydride by the method of Schaarschmidt[3] but with the introduction of modifications which raised the over-all yield to 83%. Condensation of the ketone with methyl-



magnesium chloride gave the crystalline carbinol II in good yield, and it was found that this substance is readily dehydrated by short boiling in glacial acetic acid solution. On attempting to isolate the 9-methylene compound III only polymeric material was obtained, for the hydrocarbon appears to be a labile substance resembling 9-methylenefluorene (dibenzofulvene).[4] By heating the carbinol in acetic acid and shaking the resulting solution with hydrogen and Adams catalyst it was possible to obtain the desired hydrocarbon IV without difficulty.

Experimental Part[5]

3,4-Benz-9-fluorenone-1-carboxylic acid[3] was prepared by adding 100 g. of powdered aluminum chloride rapidly (less than five minutes) to a stirred suspension of 91.7 g. of 1-phenyl-2,3-naphthalic anhydride in 500 cc. of dry benzene, refluxing for two hours, and decomposing the cooled mixture with 200 cc. of 20% hydrochloric acid. The solvent was steam distilled and the scarlet red precipitate was washed with hot dilute hydrochloric acid and with hot water, affording 91 g. (99%) of material sintering at 293° and melting at 295–296°. Treatment of the anhydride with hydrogen fluoride at room temperature for twenty-four hours resulted in only partial conversion to the fluorenone derivative.

For decarboxylation to **3,4-benzfluorenone-9** the acid (20 g.) was heated with basic copper carbonate (0.5 g.) in a bath at 310–320°. As soon as the acid melted carbon dioxide was evolved vigorously and the reaction was over in about five minutes. The product was distilled at the pressure of the water pump and crystallized from acetone, giving 13.1 g. of the ketone in the form of orange prisms, m. p. 159–160.5°, and 1.0 g., m. p. 158–160° (84%).

9-Methyl-3,4-benzfluorenol-9 (II).—A solution of 5 g. of the ketone in benzene was treated with excess methylmagnesium chloride in ether and after refluxing for two hours the mixture was decomposed with 25% ammonium chloride solution. The organic layer was washed, dried, and evaporated and the product then crystallized from ether–ligroin in small, colorless needles, m. p. 116–118°; yield 4.5 g. (84%). This material was sufficiently pure for the subsequent steps. A sample recrystallized for analysis melted at 117.8–118.6°.

Anal. Calcd. for $C_{18}H_{14}O$: C, 87.77; H, 5.73. Found: C, 87.72; H, 6.01.

Dehydration.—A solution of the crude carbinol from 1 g. of ketone in 10 cc. of acetic acid was refluxed for one hour, diluted with water and extracted with benzene. Evaporation of the dried solution left an oily residue which when rubbed with alcohol gave an amorphous, almost colorless solid which sintered and darkened at about 200° and completely melted to a deep red liquid at 275–280°; yield 0.7 g. (71%). A similar polymer resulted on distillation of the crude carbinol with a crystal of iodine, followed by passage of a benzene solution of the distillate through a tower of alumina.

Anal. Calcd. for $(C_{18}H_{12})_x$: C, 94.70; H, 5.30. Found: C, 94.40; H, 5.59.

9-Methyl-3,4-benzfluorene (IV).—A solution of 0.60 g. of the carbinol in 25 cc. of acetic acid was refluxed for one hour, cooled, and at once transferred to a hydrogenation flask and shaken with 25 mg. of Adams catalyst and hydrogen. The absorption of one mole of gas was complete in twenty minutes. The product was collected and distilled in vacuum, and crystallization from benzene–ethanol afforded 0.4 g. (71%) of light yellow blades, m. p. 80–81° (a little polymeric material was removed by filtration of the solution). Recrystallization gave material melting constantly at 80.8–82.0°. The color was not removed by treatment with Norite or by passage through a tower of alumina.

Anal. Calcd. for $C_{18}H_{14}$: C, 93.87; H, 6.13. Found: C, 93.63; H, 6.27.

(1) Fellow of the Finney-Howell Research Foundation.

(2) For summary, see Fieser, *Am. J. Cancer*, **34**, 37 (1937).

(3) Schaarschmidt, *Ber.*, **48**, 1826 (1915); **49**, 1444 (1916); Schaarschmidt and Georgeocopol, *ibid.*, **51**, 1082 (1918).

(4) Sieglitz and Jassoy, *ibid.*, **55**, 2032 (1922); Wieland, Reindel and Ferrer, *ibid.*, **55**, 3313 (1922); Wieland and Probst, *Ann.*, **530**, 274 (1937).

(5) All melting points are corrected. Microanalyses by Lyon Southworth.

In a larger run using a more concentrated solution the yield was poorer and more polymer was encountered. In another experiment the preliminary refluxing was omitted and the solution of the carbinol in acetic acid was shaken with catalyst and hydrogen in a vessel equipped with a sealed-in steam coil. No polymer was formed, but the yield of saturated hydrocarbon was lower.

The **picrate** crystallized from ethanol as reddish-orange needles, m. p. 128–128.5°, with slight previous sintering.

Anal. Calcd. for $C_{24}H_{17}O_7N_3$: N, 9.15. Found: N, 8.72.

Summary

9-Methyl-3,4-benzfluorene has been synthesized for comparison with the actively carcinogenic 10-methyl-1,2-benzanthracene.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASSACHUSETTS

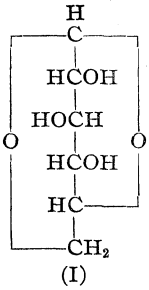
RECEIVED FEBRUARY 24, 1940

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

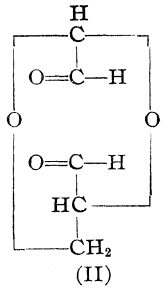
The Cleavage of the Carbon Chain of Levoglucosan by Oxidation with Periodic Acid[1]

BY ERNEST L. JACKSON AND C. S. HUDSON[1]

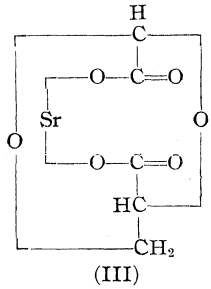
The structure of levoglucosan (I) has been established by methylation methods[2] and by its relationship to the structure of β-methylglucopyranoside.[3] A compound having this structure should be oxidized by periodic acid to produce the dialdehyde (II).



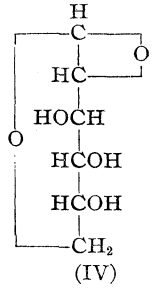
(I)
Levoglucosan



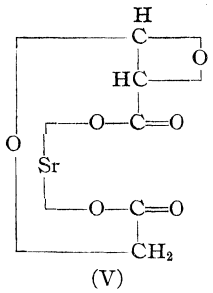
(II)
L′-Oxy-D-methylene-diglycolic aldehyde[4]



(III)
Strontium L′-oxy-D-methylene-diglycolate



(IV)



(V)

The oxidation of levoglucosan with periodic acid or sodium metaperiodate yields a sirupy product which is doubtless L′-oxy-D-methylene-diglycolic aldehyde (II). Oxidation of this product by bromine water kept neutral with strontium carbonate produces in good yield a crystalline strontium salt of a dibasic acid and, under the conditions employed, smaller amounts of strontium oxalate and strontium D-glycerate. The strontium salt of the dibasic acid was proved to be strontium L′-oxy-D-methylene-diglycolate (III) by oxidizing it with bromine water in the presence of strontium carbonate to produce strontium oxalate and strontium D-glycerate. The structure of the dialdehyde (II) follows from that of the strontium salt (III). The formation of strontium oxalate and strontium D-glycerate during the oxidation of the dialdehyde (II) to the strontium salt (III) with bromine water and strontium carbonate evidently is due to the oxidation of some strontium L′-oxy-D-methylene-diglycolate. These results prove levoglucosan to have structure (I); the beta configuration for carbon atom 1 is required by the accepted stereo configurations of the α- and β-forms of D-glucopyranose.[5]

Levoglucosan, upon oxidation by periodic acid or sodium metaperiodate, consumes two moles of the oxidant and produces one mole of formic acid.[6] These figures agree with formula (I). The same data could fit a compound having structure (IV), but (IV) is excluded since the corresponding strontium salt (V) could not yield strontium D-glycerate by oxidation with bromine water and strontium carbonate.

L′-Oxy-D-methylene-diglycolic acid, which is a cyclic acetal having as its two components glyoxylic and D-glyceric acids, could not be hydrolyzed by hot 2.5 *N* hydrochloric acid. This

(1) Publication authorized by the Surgeon General, U. S. Public Health Service. Presented in part before the Division of Organic Chemistry, at the Boston meeting of the American Chemical Society, Sept. 11–15, 1939. (Not copyrighted.)

(2) Irvine and Oldham, *J. Chem. Soc.*, **119**, 1744 (1921); Charlton, Haworth and Herbert, *ibid.*, 2855 (1931).

(3) Josephson, *Ber.*, **62**, 313 (1929).

(4) The dialdehyde is named according to the plan previously adopted by Jackson and Hudson, THIS JOURNAL, **59**, 994 (1937).

(5) See F. Micheel, "Chemie der Zucker und Polysaccharide," Akademische Verlagsgesellschaft m. b. H., Leipzig, 1939, p. 153.

(6) *Cf.* Jackson and Hudson, THIS JOURNAL, **61**, 1530 (1939).

acetal, like the chloraloses[7] and trichloroethylidene glycerol,[8] is exceptional in its stability in the presence of acids.

These oxidation reactions can be employed in the study of the structure of other sugar anhydrides. Strontium L′-oxy-D-methylene-diglycolate serves as a reference compound for the determination of the ring structure of any aldohexose anhydride, the two rings of which are of the α-1,5 and the β-1,6 type. An application of this method to the study of the structure of D-altrosan is shown in the following article.[9]

Experimental

Oxidation of Levoglucosan with Periodic Acid.—To 25 ml. of 0.542 *M* aqueous periodic acid solution (2.1 molecular equivalents) was added a solution of 1.0432 g. of pure levoglucosan in water. The solution, diluted with water to 50 ml. at 20° and kept in a 20–21° room, showed $[M]_D \times 10^{-2}$: −98.2 (4.3 min.); −92.5 (7.6 min.); −84.4 (13.8 min.); −71.9 (27.1 min.); −60.5 (50.7 min.); −48.4 (90.3 min.); −40.3 (145 min.); −33.6 (236 min.); −28.9 (357 min.); −19.5, constant (24 hrs.). The specific rotation of L′-oxy-D-methylene-diglycolic aldehyde, calculated from the final $[M]_D$ value of the oxidation solution, is −15.0°. After twenty-four hours an analysis of 5 ml. of the solution showed an excess of 0.14 molecular equivalent of periodic acid, the consumption of the oxidant thus being 1.96 molecular equivalents.

For the preparation of strontium L′-oxy-D-methylene-diglycolate, the oxidation of 10.4 g. of levoglucosan with 500 ml. of 0.271 *M* aqueous periodic acid solution was carried out as described above. Upon completion of the reaction, the solution was neutralized cautiously to phenolphthalein with hot strontium hydroxide solution. L′-Oxy-D-methylene-diglycolic aldehyde was isolated as a colorless sirup by the procedure described in a previous paper[4] for the methoxydiglycolic aldehydes from the methyl-pentopyranosides, with the exception that the solvent for extraction of L′-oxy-D-methylene-diglycolic aldehyde from the strontium salts was absolute methanol. To a solution of the dialdehyde in 2500 ml. of water were added 190 g. of strontium carbonate and 15 ml. of bromine. After the bromine had been dissolved, the mixture was kept in the dark at 25° for fifteen hours with frequent shaking during the first hour. Excess bromine was removed by aeration, and excess strontium carbonate was filtered off and washed with water. The solution, freed from bromine ions with silver carbonate and from excess silver with hydrogen sulfide, was concentrated *in vacuo* (bath, 50–55°) to 300 ml., filtered and the concentration continued to about 100 ml., when prismatic needles of strontium L′-oxy-D-methylene-diglycolate usually had started to separate. After the addition of 10–15% of ethanol, the mixture was left in the refrigerator to complete crystallization; yield[10] calculated as $C_5H_4O_6Sr$,[11] 7.2 g. (45%). The mother liquor contained strontium D-glycerate. The strontium L′-oxy-D-methylene-diglycolate, after one or two recrystallizations from water, was pure; it crystallizes from water at 20° or at refrigerator temperature as long prismatic needles of its pentahydrate; at 30° or above as small compact clusters of short needles of its monohydrate, which is less soluble in water than the pentahydrate. In preparing the solution of the strontium salt in water for crystallization, the less soluble monohydrate may be precipitated during the process of dissolving the pentahydrate, if a minimum amount of water and steam-bath temperature are employed. The procedure adopted, therefore, was to dissolve the strontium salt in a large excess of warm water, then concentrate the solution *in vacuo* (bath, 45–50°) to a relatively small volume and filter it quickly to remove any crystals that might be present. Thereafter, crystallization was allowed to proceed at a temperature selected to yield the desired hydrate of the strontium salt. For analysis and determination of the rotation of strontium L′-oxy-D-methylene-diglycolate, crystals of the pure pentahydrate were dried to constant weight at 100° *in vacuo*. The anhydrous strontium salt showed a specific rotation[12] of +37.5° in water (*c*, 0.45; *l*, 2). Upon exposure to the air at 20–25° the anhydrous salt soon showed an increase in weight in excess of the amount calculated for the water content of the monohydrate.

Anal. Calcd. for $C_5H_4O_6Sr$: C, 24.23; H, 1.63; Sr, 35.38. Found: C, 24.19, 23.99; H, 1.77, 1.49; Sr, 35.32, 35.16.

The monohydrate of strontium L′-oxy-D-methylene-diglycolate was prepared both by crystallization of the strontium salt from water, preferably at 45° which yields homogeneous crystals, and by efflorescence of the pentahydrate. Crystals of the pentahydrate, exposed to comparatively humid air at about 30°,[13] showed no appreciable change in composition during ten to fifteen days, but thereafter effloresced in the course of several weeks to produce the monohydrate. The monohydrate is characterized by its pronounced stability at high temperature. It lost weight only slowly at 145–150° *in vacuo*, but at 175° *in vacuo* was converted to an anhydrous strontium salt. The specific rotation in water of samples of the monohydrate obtained under three different conditions were: (from water at 30°) +36.9° (*c*, 0.38; *l*, 4); (from water at 45°) +36.8° (*c*, 0.39; *l*, 4); (from efflorescence) +36.4° (*c*, 0.47; *l*, 4).

Anal. Calcd. for $C_5H_4O_6Sr \cdot H_2O$: H_2O, 6.78; C, 22.60; H, 2.28; Sr, 32.98. Found: (from water at 45°) H_2O,

(7) Hanriot and Richet, *Compt. rend.*, **117**, 734 (1893); Pictet and Reichel, *Helv. Chim. Acta*, **6**, 621 (1923); White and Hixon, THIS JOURNAL, **55**, 2438 (1933).

(8) Hibbert, Morazain and Paquet, *Can. J. Research*, **2**, 131 (1930).

(9) Richtmyer and Hudson, THIS JOURNAL, **62**, 961 (1940).

(10) The yield was only 25% in an experiment carried out under the same conditions, with the exception that the time for the oxidation of the dialdehyde was twenty-nine hours instead of fifteen hours.

(11) The water content of the crystals varies with the conditions of time, temperature and humidity under which they are dried. It was at first believed that the salt had crystallized as a trihydrate (*cf.* the accompanying article[9]), but a careful study has revealed with certainty only a mono and a pentahydrate.

(12) Except where otherwise stated, all rotations in this article are specific rotations at 20° for sodium light; *c* = g. per 100 ml. of solution; *l* = length in dm.

(13) Crystals of the pentahydrate, exposed to the air simultaneously at 20°, were stable as shown by the result of an analysis at the end of forty-five days. Calcd. for $C_5H_4O_6Sr \cdot 5H_2O$: H_2O, 26.67; Sr, 25.94. Found: H_2O, 26.71, 26.51; Sr, 25.80, 25.61.

6.77, 6.85; C, 22.45, 22.64; H, 2.28, 2.43; Sr, 32.85, 32.81; (from water at 30°) Sr, 32.85, 32.72; (from water at 95–100°) Sr, 32.84; (from efflorescence) Sr, 32.79, 32.95.

Strontium D-glycerate, which is produced during the oxidation of L′-oxy-D-methylene-diglycolic aldehyde with bromine water and strontium carbonate, was isolated as well-formed octahedral prisms of the dihydrate[14] by concentrating the filtrate from the crude strontium L′-oxy-D-methylene-diglycolate pentahydrate *in vacuo* to about 10 ml.; air-dried; yield of the crude dihydrate, 3 g. After purification by recrystallization from about three parts of water, the dihydrate melted at 136–137° (uncor.) and rotated +15.2° in water (*c*, 0.5; *l*, 2). The pure dihydrate is stable at 100° *in vacuo*, but at 125° *in vacuo* it loses approximately the weight calculated for two moles of combined water and becomes slightly colored. A specimen of calcium D-glycerate dihydrate, prepared from the strontium salt, rotated +15.5° in water (*c*, 0.6; *l*, 2) and melted at 142–143° (uncor.) alone or mixed with authentic calcium D-glycerate dihydrate.

Anal. Calcd. for $C_6H_{10}O_8Sr \cdot 2H_2O$: H_2O, 10.80; Sr, 26.26. Found: H_2O (dried at 125° *in vacuo*), 11.20, 11.30; Sr, 26.24, 26.08.

Oxalic acid was produced in the course of these oxidation reactions, as shown by the isolation of strontium oxalate from the excess strontium carbonate, which was recovered from the oxidation of L′-oxy-D-methylene-diglycolic aldehyde. A solution of the excess strontium carbonate in hydrochloric acid was boiled to expel carbon dioxide, cooled and neutralized with ammonium hydroxide solution. From the precipitate of strontium oxalate monohydrate (yield, 1.8 g.) was prepared oxalic acid dihydrate, which was characterized by usual methods.

L′-Oxy-D-methylene-diglycolic Acid.—The specific rotation of L′-oxy-D-methylene-diglycolic acid, obtained by liberating it from its pure anhydrous strontium salt in aqueous solution with an equivalent of hydrochloric acid, was +8.0° (*c*, 1.3; *l*, 2). The acid was isolated in crystalline condition, and was shown to be stable in hot aqueous solution. A solution of 2 g. of pure strontium L′-oxy-D-methylene-diglycolate in 80 ml. of hot water was cooled to 25°. After the addition of the calculated amount of *N* sulfuric acid solution and 90 ml. of absolute ethanol, the strontium sulfate was filtered off and the filtrate was concentrated *in vacuo* (bath, 50°) to a colorless sirup, which was made up to 50 ml. of solution in water. The rotation of this solution was unchanged by heating it in a stoppered flask on the steam-bath for five and one-half hours. The solution was then concentrated *in vacuo* to a sirup, which crystallized as needles during evacuation of the flask at room temperature to remove the last traces of solvent. The crystalline acid is readily soluble in acetone and in ether, but practically insoluble in petroleum ether. That the acid was unchanged by the heating of its aqueous solution and the subsequent operations was proved by neutralization of its solution in water with strontium hydroxide and isolation of strontium L′-oxy-D-methylene-diglycolate, which in the anhydrous condition rotated +37.5° in water (*c*, 0.4). Calcd. for $C_5H_4O_6Sr$: Sr, 35.38. Found: Sr, 35.28. The acid was not hydrolyzed by hot 2.5 *N* hydrochloric acid solution. To a suspension of 0.3 g. of pure strontium L′-oxy-D-methylene-diglycolate in water was added sufficient 5 *N* hydrochloric acid to balance the strontium ions and make the concentration of the hydrochloric acid approximately 2.5 *N* after the solution had been diluted with water to 25 ml. The rotation of this solution was unchanged by heating it in a stoppered flask on the steam-bath for four hours.

L′-Oxy-D-methylene-diglycolic aldehyde, likewise, seemed resistant to acid hydrolysis. A solution of the dialdehyde, prepared from 2.67 g. of levoglucosan as previously described, in 100 ml. of 0.1 *N* hydrochloric acid showed only a minor change in rotation when it was heated on the steam-bath for seven hours; the rotation, measured in a 1-dm. tube, changed from α_D −0.31° to α_D −0.24°; full hydrolysis to glyoxal and D-glyceric aldehyde would be expected to cause reversal of the sign of rotation.

Strontium D-Glycerate and Strontium Oxalate from the Oxidation of Strontium L′-Oxy-D-methylene-diglycolate.—Five grams of pure strontium L′-oxy-D-methylene-diglycolate, containing about 15% of combined water as indicated by its specific rotation of +31.9°, was dissolved in approximately 1500 ml. of water. After the addition of 90 g. of strontium carbonate and 7 ml. of bromine, the mixture was shaken until the bromine had dissolved and, thereafter, shaken occasionally while it was kept in the dark at room temperature. The rotation of the solution, measured in a 4-dm. tube, decreased during forty-two hours from α_D +0.39° to α_D +0.05°. Excess bromine was then removed by aeration, and excess strontium carbonate was filtered off and washed with water. The excess strontium carbonate was dissolved in hydrochloric acid, the solution was boiled to expel carbon dioxide and neutralized with ammonium hydroxide, which precipitated 1 g. (about 30% yield) of strontium oxalate monohydrate. Oxalic acid dihydrate, prepared from the strontium oxalate, was characterized by customary methods. The filtrate from the excess strontium carbonate, after being freed from bromine ions with silver carbonate and from excess silver with hydrogen sulfide, was concentrated *in vacuo* to 75 ml., filtered and the concentration continued to about 10 ml. The solution, which was somewhat acid, was neutralized to litmus paper with strontium hydroxide solution and then concentrated to a thin sirup to which ethanol was added to turbidity. After being seeded with crystals of strontium D-glycerate dihydrate, the solution yielded at room temperature 0.7 g. of crystals rotating +9.9° in water. From the mother liquor was obtained, by concentration and dilution with ethanol, 0.4 g. of crystals rotating +7.3° in water. The first crop gave by two recrystallizations from water about 0.1 g. of prisms, which resembled crystals of strontium D-glycerate dihydrate; air-dried; m. p. 131–132° (uncor.); rotation, +14.3° in water. Calcd. for $C_6H_{10}O_8Sr \cdot 2H_2O$: Sr, 26.26. Found: Sr, 26.70, 27.01. After another recrystallization from a mixture of water and ethanol, the crystals melted at 134–135° (uncor.) and showed no depression when mixed with authentic strontium D-glycerate dihydrate.

There were indications that another substance, as yet unidentified, may be formed in this oxidation reaction.

(14) *Cf.* Frankland and Appleyard, *J. Chem. Soc.*, **63**, 300 (1893).

The rotation of the crude product, which was a mixture not readily separable into its constituents with a small quantity of material, was considerably lower than that of both strontium D-glycerate and strontium L′-oxy-D-methylene-diglycolate. After several recrystallizations from mixtures of water and ethanol, crystals of doubtful purity containing 30.8% of strontium were isolated; specific rotation, +7.0° in water.

Oxidation of Levoglucosan with Sodium Metaperiodate.—A solution of 0.3488 g. of pure levoglucosan in water was mixed with 10 ml. of 0.453 *M* aqueous sodium metaperiodate solution (2.1 molecular equivalents). The solution, after being diluted with water to 25 ml. at 20° and kept in a 20° room for twenty hours, showed $[M]_D \times 10^{-2} = -19.1°$. The specific rotation of L′-oxy-D-methylene-diglycolic aldehyde, calculated from the final $[M]_D$ value of the oxidation solution, is −14.7°; this value is in good agreement with the specific rotation of −15.0° calculated from the end rotation of the periodic acid oxidation solution. After twenty hours an analysis of 5 ml. of the solution showed an excess of 0.11 molecular equivalent of sodium metaperiodate; the consumption of the oxidant was thus 1.99 molecular equivalents. The acidity of the reaction solution at the end of twenty hours corresponded to the production of 1.00 molecular equivalent of formic acid (5 ml., diluted with 300 ml. of water and neutralized to methyl red, required 4.30 ml. of 0.1 *N* sodium hydroxide; calcd. 4.30 ml.).

We express our thanks to Drs. A. E. Knauf and W. D. Maclay for a supply of levoglucosan and to Dr. W. T. Haskins for carrying out the microanalyses.

Summary

Levoglucosan yields, by oxidation with periodic acid or sodium metaperiodate, L′-oxy-D-methylene-diglycolic aldehyde, which is oxidized by bromine water kept neutral with strontium carbonate to produce, under specified conditions, crystalline strontium L′-oxy-D-methylene-diglycolate in 45% yield and smaller amounts of strontium oxalate and strontium D-glycerate. The structure of strontium L′-oxy-D-methylene-diglycolate was proved by its oxidation with bromine water in the presence of strontium carbonate to produce strontium oxalate and strontium D-glycerate. These results show the levoglucosan molecule to have two rings, one of which is of the pyranoid and the other of the septanoid type. This confirmation of the generally accepted ring structure of levoglucosan demonstrates the applicability of these oxidation reactions to the structural study of the sugar anhydrides.

L′-Oxy-D-methylene-diglycolic acid, which could not be hydrolyzed by hot 2.5 *N* hydrochloric acid, is one of the few acetals possessing such stability.

WASHINGTON, D. C. RECEIVED FEBRUARY 26, 1940

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

The Ring Structure of D-Altrosan[1]

BY NELSON K. RICHTMYER AND C. S. HUDSON

A few years ago we reported[2] that "crystalline D-altrose is converted by hot hydrochloric acid from $[\alpha]_D^{20}$ +34 to −98°; this is accompanied by partial loss of reducing power presumably due to the formation of an anhydro-D-altrose to the extent of 57% at equilibrium." Independently, Robertson and Griffith[3] found that the removal of the glycosidic methoxyl group from certain partially methylated α-methyl-altrosides by hydrolysis with 4–8% hydrochloric acid "leads to the production of an anhydro-derivative in equilibrium with a small amount of a reducing sugar." They cited also the case of the "methyl epiglucosamine" of Fischer, Bergmann and Schotte[4]; this substance, which is probably a 3-amino methylaltroside,[5] undergoes acid hydrolysis with the formation of an anhydro compound from the liberated sugar and consequent loss of reducing power.[6] Robertson and Griffith suggested that the anhydro-linkage in these compounds must involve position 4 or 6, since only these positions are available in the case of the 2,3-dimethylaltrose which forms an anhydride. The suggestion was confirmed later[7] by the fact that 4,6-dimethyl-α-methylaltroside is hydrolyzed in normal fashion to a reducing sugar without anhydride formation.

Hudson,[8] in 1938, presented conclusive evidence that sedoheptulosan, the anhydride which is formed spontaneously from sedoheptulose (D-altroheptulose) in acid solution, possesses the

(1) Publication authorized by the Surgeon General, U. S. Public Health Service. Presented in part before the Division of Organic Chemistry, at the Boston meeting of the American Chemical Society, Sept. 11–15, 1939. (Not copyrighted.)

(2) Richtmyer and Hudson, THIS JOURNAL, **57**, 1721 (1935).

(3) Robertson and Griffith, *J. Chem. Soc.*, 1196 (1935).

(4) Fischer, Bergmann and Schotte, *Ber.*, **53**, 541 (1920).

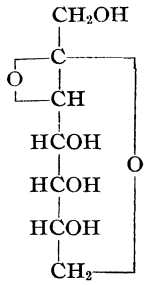
(5) K. Freudenberg, Burkhart and Braun, *ibid.*, **59**, 715 (1926).

(6) Levene and Meyer, *J. Biol. Chem.*, **55**, 224 (1923).

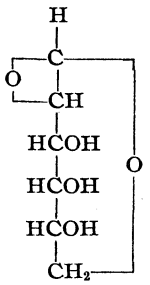
(7) Robertson and Dunlop, *J. Chem. Soc.*, 474 (1938).

(8) Hudson, THIS JOURNAL, **60**, 1241 (1938).

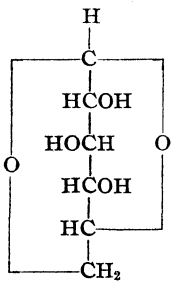
unusual combination of an ethylene oxide and a septanoid ring (I).



Sedoheptulosan
I



D-Altrosan (?)
II

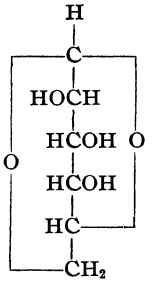


Levoglucosan
III

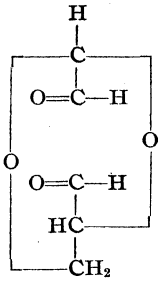
Because of the identical configurations of the asymmetric carbon atoms in sedoheptulose and D-altrose, and because of the ease with which these two sugars undergo anhydride formation in the presence of acids, it did not seem unreasonable to suggest that a similar structure II might be written for D-altrosan rather than a <1,5> <1,6> ring system like that which had been established previously for levoglucosan (III). It was emphasized, however, that formula II for D-altrosan rested solely upon the apparent analogy to sedoheptulosan (I), and that additional experimental data would be necessary to answer the question.

In a recent Communication[9] we announced the successful crystallization, after three years, of a sample of D-altrosan which had been prepared by removing the D-altrose component from the altrose–altrosan equilibrium mixture by oxidation with bromine water. With the additional crystalline material now available we are continuing our study of D-altrosan, and are reporting at this time a proof of its ring structure. To this end we have utilized the periodic acid method of oxidation developed by Jackson and Hudson,[10] especially as described in the preceding article.[11]

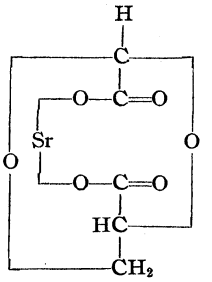
The oxidation of D-altrosan with periodic acid or with sodium metaperiodate has been shown to consume two equivalents of oxidizing agent, and to liberate one equivalent of formic acid. The resulting aldehyde upon further oxidation with bromine water produced a dibasic acid, readily isolated as a crystalline strontium salt of the composition $C_5H_4O_6Sr \cdot 5H_2O$. Of the many ring combinations possible for D-altrosan, $C_6H_{10}O_5$, only two could fulfill the requirements of reacting with two moles of periodic acid, with the elimination of one carbon atom as formic acid, and the subsequent formation of a dibasic acid containing the other five carbon atoms. These two possibilities are the <1,2> <1,6> formula II already suggested, and the <1,5> <1,6> formula IV analogous to that of levoglucosan (III).



D-Altrosan
IV



Dialdehyde
V



Strontium salt
VI

The actual decision between formulas II and IV for D-altrosan was relatively simple after the pioneer work reported in the preceding paper. Thus the rotation[12] $-14.7°$ for the dialdehyde V in the periodic acid solutions was in close agreement with the value recorded for L′-oxy-D-methylene-diglycolic aldehyde obtained from levoglucosan under comparable conditions. The crystalline strontium salt VI was found to agree in its rotation in water, its rotation in acid, in the conversion of the pentahydrate to the monohydrate (which is the stable form in air at room temperature), in its solubility in water, and by a determination of mixed solubilities,[13] with strontium L′-oxy-D-methylene-diglycolate from levoglucosan.

Since a compound with structure IV would be expected to produce the same dialdehyde V and the same strontium salt VI as are obtained from levoglucosan (III), whereas a compound with structure II could not, and since the proof of structure of the strontium salt from levoglucosan is in complete harmony with the structure III established previously for that compound, therefore D-altrosan must have the same ring system as levoglucosan, and accordingly may be designated[14] D-altrosan α<1,5>β<1,6>.

Experimental

D-Altrosan.—The reactions by which lactose is converted to D-altrosan have been described previously.[2,9] Briefly,

(9) Richtmyer and Hudson, THIS JOURNAL, **61**, 214 (1939).
(10) Jackson and Hudson, *ibid.*, **59**, 994 (1937).
(11) Jackson and Hudson, *ibid.*, **62**, 958 (1940).

(12) Throughout the article the rotations are specific rotations at 20° for sodium light; *c* designates concentration in grams per 100 cc. of solution.
(13) Montgomery and Hudson, THIS JOURNAL, **52**, 2105 (1930).
(14) The name altrosan (or altrose anhydride), rather than anhydroaltrose, is used to indicate anhydride formation involving the glycosidic hydroxyl group. This system of nomenclature is in accord with the proposal of M. Bergmann (*Ber.*, **58**, 2647, 2650 (1925); see also F. Micheel, "Chemie der Zucker und Polysaccharide," Akademische Verlagsgesellschaft m. b. H., Leipzig, 1939, p. 151).

lactose octaacetate was chlorinated and rearranged to acetochloroneolactose by the action of aluminum chloride and phosphorus pentachloride. The acetochloroneolactose[15] was hydrolyzed by six hours' boiling with water to hydrochloric and acetic acids, galactose and altrose; at the same time about 60% of the altrose was converted to altrosan. The acids were removed in the usual manner, the galactose by fermentation, the altrose by oxidation with bromine water and subsequent separation as calcium altronate, and the remaining altrosan was crystallized. From 1132 g. of acetochloroneolactose was obtained 75 g. of crystalline D-altrosan,[16] and from the mother liquors by acetylation was obtained 51 g. of crystalline 2,3,4-triacetyl-D-altrosan and 14 g. of altrose α-pentaacetate.[17]

Oxidation of D-Altrosan with Sodium Metaperiodate.—To 0.6173 g. of altrosan in 25 cc. of water was added 20 cc. of 0.419 *M* aqueous sodium periodate (2.2 equivalents of $NaIO_4$), and the solution left at 20° for forty-five hours. The volume was adjusted with water exactly to 50 cc. The specific rotation, calculated as the dialdehyde V, was −14.4° as compared with the value −14.7° obtained by Jackson and Hudson[11] for the dialdehyde formed in the same way from levoglucosan. The titration of an aliquot for excess periodate indicated the consumption of 1.97 equivalents of oxidizing agent. Titration of another aliquot with aqueous sodium hydroxide, using methyl red as indicator, showed the formation of 0.97 equivalent of acid, presumably formic acid.

Oxidation of D-Altrosan with Periodic Acid.—Since a preliminary experiment indicated that the reaction of altrosan with periodic acid proceeded almost instantaneously at 20°, with considerable evolution of heat, subsequent oxidations were carried out at a lower temperature. Thus, to 5.469 g. of D-altrosan, dissolved in 75 cc. of water and cooled in an ice-bath, were added six 25-cc. portions of 0.495 *M* aqueous periodic acid (2.2 equivalents of HIO_4) at ten-minute intervals. The solution was left overnight at 20°, and its volume adjusted to 250 cc. with water. The specific rotation, calculated as the dialdehyde V, was −14.5°, and in a second experiment −14.9°; these values are in good agreement with the rotation of −15.0° obtained by Jackson and Hudson from their similar oxidation of levoglucosan. The titration of an aliquot for excess periodic acid revealed that 1.96 equivalents of oxidizing agent had been consumed.

Isolation of the Dialdehyde V and Oxidation to the Strontium Salt VI.—The solutions from the oxidation of altrosan with periodic acid were combined, neutralized to phenolphthalein with strontium hydroxide, filtered, and the filtrate concentrated *in vacuo* to a small volume in the presence of 1 g. of strontium carbonate. The solution was filtered into a smaller flask and concentrated *in vacuo* practically to dryness. The dialdehyde was extracted readily with absolute methyl alcohol, and was left behind as a colorless sirup upon removal of the alcohol *in vacuo*. A concentrated aqueous solution of this sirup was estimated, from its rotation, to contain 4.95 g. of the dialdehyde, derived from 7.35 g. of D-altrosan.

For oxidation, the solution of dialdehyde was diluted with water to 1900 cc., and 145 g. of strontium carbonate and 7 cc. of bromine added. The mixture was shaken frequently during the first hour, then left fourteen hours more at room temperature (25°). Excess bromine, insoluble strontium salts and strontium bromide were removed by aeration, filtration and treatment with silver carbonate, respectively. The filtrate was freed from dissolved silver with hydrogen sulfide, and the solution concentrated *in vacuo*. The strontium salt which crystallized spontaneously during the distillation weighed 5.8 g. Twice recrystallized from water, and air-dried for two days, it had the composition of a pentahydrate.

Anal. Calcd. for $C_5H_4O_6Sr \cdot 5H_2O$: Sr, 25.94; H_2O, 26.67. Found: Sr, 25.94; H_2O, 25.91.

Identification of the Strontium Salt as Strontium L'-Oxy-D-methylene-diglycolate VI.—Inasmuch as the strontium salt derived from levoglucosan was found at first by Jackson and Hudson to crystallize apparently as a trihydrate, and the strontium salt from D-altrosan had crystallized as a pentahydrate, a careful comparison of the two substances was made. The pentahydrate rotated +28.1° in water, equivalent to +38.3° calculated as the anhydrous strontium salt (*c*, 0.45), as compared with +37.5° reported by Jackson and Hudson for their anhydrous strontium salt (*c*, 0.45). Dissolved in an excess of aqueous hydrochloric acid, the pentahydrate showed a rotation of +7.9° calculated as the free organic acid (*c*, 1.3), as compared with the rotation +8.0° for the L'-oxy-D-methylene-diglycolic acid (*c*, 1.5) liberated by Jackson and Hudson from their anhydrous strontium salt.

Further comparison was made directly between the strontium salt from D-altrosan and the strontium salt from levoglucosan prepared by the same procedure. Thus, the latter salt also was obtained as a pentahydrate by the concentration of its aqueous solution *in vacuo* with the bath temperature about 40°. This salt was filtered, washed with cold water, and a portion of it placed on a watch glass in a room kept at 20° ± 1°. Overnight the strontium salt lost its adsorbed moisture, then remained constant in weight for two days. A sample removed at that time showed it to be a pentahydrate.

Anal. Calcd. for $C_5H_4O_6Sr \cdot 5H_2O$: Sr, 25.94. Found: Sr, 25.92.

The remainder of this portion kept at 20° soon began to lose weight, slowly at first and then more rapidly as shown in Fig. 1, until a total of 3.85 molecular equivalents of water had been lost in thirty days. From another sample at 30°, the loss of water was complete in four days, and the final stage of the strontium salt monohydrate was reached.

Anal. Calcd. for $C_5H_4O_6Sr \cdot H_2O$: Sr, 32.98. Found: Sr, 32.79 (salt from levoglucosan), 32.82 (salt from D-altrosan, air-dried at 30° for twenty-four days).

The concluding proof of identity of the strontium salts from levoglucosan and D-altrosan was obtained through a study of their solubilities. In 5 cc. of aqueous solution,

(15) It is unnecessary to isolate the acetochloroneolactose except in preliminary experiments designed to ensure favorable yields. Instead, the mixture of acetochloro derivatives may be used, and the lactose component removed by the regular hydrolysis and fermentation operations.

(16) The rotation in water (*c*, 2.5) of a carefully purified sample of D-altrosan has been determined as −213.0 ± 0.6°, or slightly lower than the −215° reported in our preliminary Communication.

(17) These compounds and some of their transformation products will be described in a future publication.

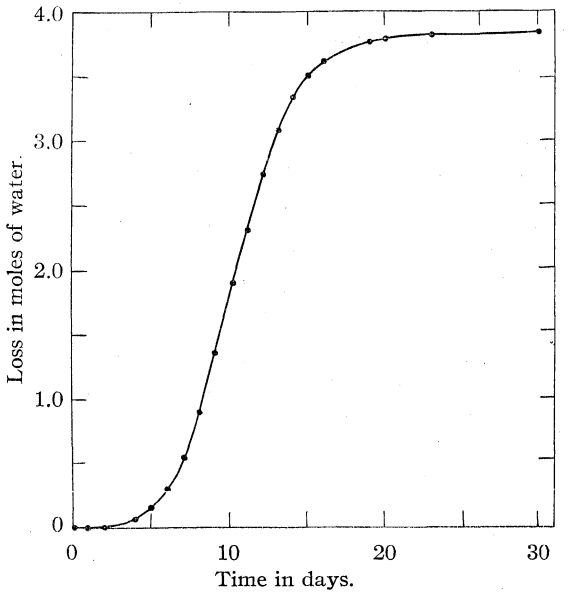


Fig. 1.—Conversion of strontium salt pentahydrate to monohydrate in air at 20°.

saturated by shaking five days at 20° with an excess of the solid strontium salt from levoglucosan, there was contained 40.6 mg. of the strontium salt monohydrate. In 5 cc. of a similar solution from D-altrosan there was 40.2 mg. To a portion of the solution saturated with the salt from levoglucosan then was added solid strontium salt from D-altrosan, and the mixture shaken five days at 20°; the filtered solution contained 40.2 mg. of the monohydrate in 5 cc. A similar value for the solubility, 40.6 mg. in 5 cc., was reached from supersaturation, by shaking the strontium salt from levoglucosan first at 30° (44.8 mg. soluble in 5 cc.), and then at 20°.

One of the authors (N. K. R.) desires to thank the Chemical Foundation of New York for a Research Associateship, and the American Academy of Arts and Sciences for a grant from the Cyrus M. Warren Fund. The authors also express their indebtedness to Dr. W. T. Haskins for carrying out the microanalyses, and to Dr. A. E. Knauf for the sample of levoglucosan which was oxidized.

Summary

The oxidation of D-altrosan with periodic acid, followed by bromine water and strontium carbonate, to the same strontium L′-oxy-D-methylenediglycolate which is obtained from levoglucosan, has shown that D-altrosan possesses the same ring system as levoglucosan, and accordingly is to be designated D-altrosan $\alpha<1,5>\beta<1,6>$.

WASHINGTON, D. C. RECEIVED FEBRUARY 26, 1940

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Ketene Acetals. IV. Polymers of Ketene Diethylacetal[1]

BY PAUL R. JOHNSON,[2] HARRY M. BARNES[3] AND S. M. MCELVAIN

One of the first chemical properties of ketene acetal to be noticed was its readiness to polymerize. The polymer appeared as a thin, white deposit on the interior of the flasks and condensers in which ketene acetal had been distilled and also as a semi-solid gum which settled out of distilled samples of ketene acetal after a few days of standing. It soon was noted that distillation apparatus that had been cleaned with the ordinary chromic acid–sulfuric acid mixture before the distillation of ketene acetal acquired an excessive amount of the polymer on the inner glass surfaces. If, however, the interior of the apparatus were washed with an aqueous alkali solution after the use of the acid cleaning solution, and then rinsed and dried in the usual manner, the amount of polymer formed during the distillation of ketene acetal was scarcely noticeable. Similarly, dusting the interior of the containers in which ketene acetal was kept with sodium or potassium *t*-butoxide practically eliminated the polymerization of the acetal on standing.

Although acidified glass surfaces cause some polymerization of ketene acetal, this catalyst is not efficient enough to allow for the preparation of the polymer in quantity. In the first paper of this series[4] it was reported that heat caused polymerization of the acetal. It is now believed that the polymerization then noted was due to the acidity of the inner surface of the container in which the acetal was heated, since later experiments have shown that ketene acetal may be heated at 190–240° for six hours in *new* Pyrex tubes without any perceptible polymerization. Also, a sample of ketene acetal sealed in a new soft-glass container and kept in diffuse sunlight has remained clear and mobile after three years.

(1) The third paper of this series is Magnani and McElvain, THIS JOURNAL, **60**, 2210 (1938). This work was supported in part by the Wisconsin Alumni Research Foundation.

(2) du Pont Post-doctorate Research Assistant, 1938–1940.

(3) Wisconsin Alumni Research Foundation Scholar, 1935–1936, Research Assistant, 1937–1938.

(4) Beyerstedt and McElvain, THIS JOURNAL, **58**, 529 (1936).

A search for other catalysts for this polymerization showed that benzoyl peroxide, which is such an efficient catalyst for the polymerization of many vinyl compounds, has no appreciable effect on ketene acetal, but that a number of metallic chlorides are very powerful catalysts for its polymerization. Barium, mercury and calcium chloride are least effective. In the order of increasing effectiveness as catalysts to transform ketene acetal into an immobile gel are the chlorides of nickel, cobalt, cadmium, zinc, iron, and aluminum. The cobalt and cadmium chlorides cause eventual polymerization to a white solid, but the cobalt polymer becomes discolored after twelve to twenty-four hours. The polymers obtained from nickel, zinc, iron, and aluminum are pasty products which rapidly turn brown or red. The most satisfactory polymer is that obtained with cadmium chloride, and all of the work which is now reported was done with this polymer.

The addition of a trace (6 mg. per 10 g. of acetal) of cadmium chloride to ketene acetal transforms it in a few hours, without any marked thermal effect, into a white, wax-like solid which contains about 45% of unpolymerized ketene acetal. The removal of the monomer by heating (100°) under reduced pressure (0.5 mm.) leaves the polymer as a perfectly dry, white powder. The carbon and hydrogen content of this polymer is practically the same as for ketene acetal; the ethoxyl value is slightly lower than that found for the monomer. The polymer is insoluble in all organic solvents, although ketene acetal and the aromatic hydrocarbons produce a noticeable swelling. The dry polymer is quite stable to heat, showing no evidence of decomposition at temperatures up to 200°. It is completely stable to alkali and is recovered without any apparent change after treatment with boiling 10% sodium hydroxide solution. The polymer is, however, very sensitive to acids. It slowly turns to a brownish-red powder when allowed to stand in the laboratory air for twenty-four hours. Dilute acids at room temperature convert it at once to a red oil which is insoluble in water. Refluxing the polymer with dilute acid converts it to a reddish-black oil which solidifies, on cooling, to a brittle glass. Both of these red polymers are alkali-soluble but are quite insoluble in other solvents. The difference between them appears to be in the extent to which ethoxyl groups have been removed by hydrolysis.

It seemed likely from previous work on unsymmetrically substituted ethylenes[5] that ketene acetal would polymerize in a "head to tail" manner. This supposition was supported by the properties of the red product obtained from the acid hydrolysis of the polymer. The color and alkali solubility of this product indicate a poly-1,3-diketone in an enolic, and hence highly conjugated, form. An unsuccessful attempt to obtain such a poly-1,3-diketone from poly-dichloroethylene has been reported.[6] This type of polyketone was undoubtedly obtained by Marvel and Denoon[5a] as the oxidation product of polyvinyl alcohol with dichromate. Although they did not isolate the polyketone they did obtain acetone from the alkaline hydrolysis of it.

The simplest representations of the white and red polymers from ketene acetal, on the basis of a "head to tail" union, are I and IV. In I and the

$$CH_3C(OEt)_2[-CH_2C(OEt)_2]_n-CH_2C(OEt)_3 \xrightarrow{H^+ + H_2O}$$

I

$$CH_3CO[-CH_2CO]_n-CH_2COOEt \longrightarrow$$

II

$$CH_3CO\left[-CH=\overset{\displaystyle OH}{\overset{|}{C}}-\right]_n-CH_2COOEt \longrightarrow$$

III

$$CH_3CO\left[-CH=\overset{\displaystyle OH}{\overset{|}{C}}-\right]_n-CH_3 + CO_2$$

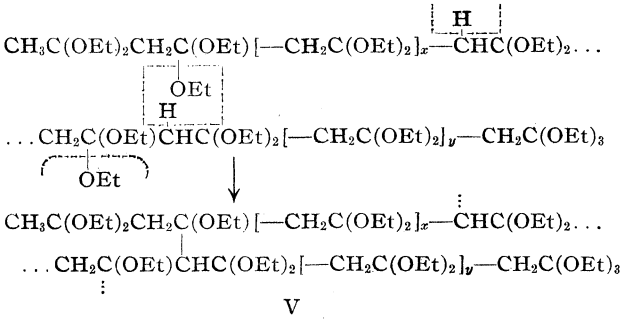
IV

intermediate compounds, II and III, the ends of the chain are shown completed by the addition of a molecule of alcohol. It is seen that I has a saponifiable end-group, but attempts to estimate n by saponification equivalents were unsatisfactory. The values of the equivalents obtained ranged from 1600 to 3000 and this, together with the fact that the polymer remained insoluble in alcoholic alkali, indicated that adsorption of varying amounts of alkali on the polymer, rather than saponification, had occurred. However, the values obtained from the amount of carbon dioxide evolved during the acid hydrolysis of I to the polyketone (IV) were quite consistent and indicated a molecular weight of 2600–2700 for I. Such molecular weights show n in formula I to be 20–21. Since linear polymers in this range of polymerization are generally soluble in some of the organic solvents, the value of n as determined from the carbon dioxide evolved from the hydrolysis of I

(5) Marvel and co-workers, (a) THIS JOURNAL, **60**, 280, 1045 (1938); (b) *ibid.*, **61**, 1682, 3156, 3234, 3241, 3244 (1939); (c) *ibid.*, **62**, 45 (1940).

(6) Staudinger and Feistt, *Helv. Chim. Acta*, **13**, 832 (1930).

must be considered as a measure of the average length of unit chains that have undergone cross-linking. The nature of this cross-link has not been determined, but it is quite likely that it results from inter-unit loss of alcohol in some such manner as



V

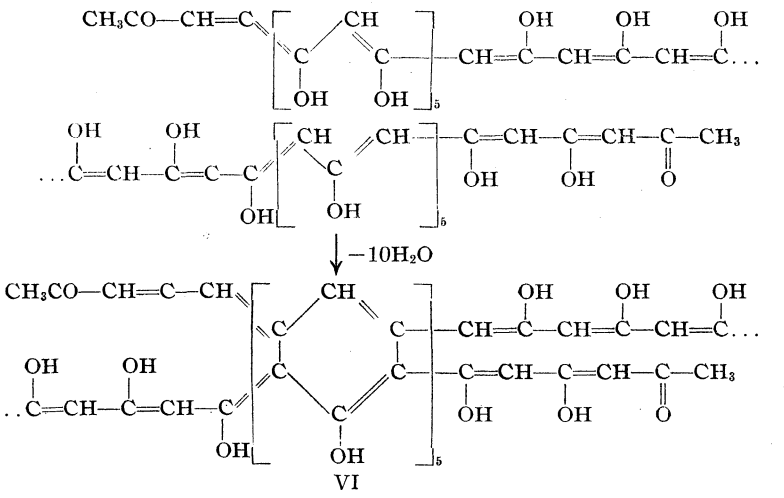
The amount of cross-linking per unit chain is not known but it cannot be very extensive because the ethoxyl content of the polymer (V) is very little lower than that of ketene acetal itself.

Approximate confirmation of the molecular weight of I as calculated from its yield of carbon dioxide was obtained from the other hydrolysis product, the red polymer. The carbon and hydrogen analyses of this polymer suggest an empirical formula of $C_{45}H_{38}O_{17}$, instead of $C_{45}H_{48}O_{22}$ which IV would have if n is 21. This indicates that the red polymer is composed of units of IV cross-linked by bonds resulting from the loss of an average of five molecules of water per unit of IV as in VI. It is unlikely that the end methyl groups in IV are involved in this cross-linkage. If this is the case, the red polymer would yield, on vigorous oxidation, two molecules of acetic acid for each unit of IV and for each molecule of carbon dioxide that had been obtained from the white polymer. On the basis of the empirical formula, $C_{45}H_{38}O_{17}$, 425 g. of the red polymer would be expected to produce 1 mole of acetic acid.

An alkaline solution of the red polymer was attacked rapidly by potassium permanganate and completely oxidized (to a permanent permanganate color) at 100°. On acidification 80% of the carbon of the polymer was evolved as carbon dioxide. Determinations of the acetic acid formed in a number of these oxidations gave values between 558 and 645 as the number of grams of polymer necessary to produce 1 mole of acetic acid. Considering the experimental errors involved in the determination, these results represent maximum values and are sufficiently close to the theoretical value of 425 to lend support to the molecular weight of I as determined by hydrolytic decarboxylation.

Attempts to obtain a neutral equivalent of the red polymer were unsuccessful. The usual colorimetric methods, of course, were not applicable and a potentiometric titration of an alkaline solution of the polymer using an antimony–antimony-oxide electrode gave a titration curve which showed no definite break except at the point of complete precipitation of the polymer.

The red polymer that was obtained by the hydrolysis and decarboxylation of I was very resistant to further hydrolysis. Heating in a bomb at 200° in 10% sulfuric acid for seven hours gave a trace of acetone and some acetic acid. When it was heated with 5% aqueous sodium hydroxide at 240° for twenty-two hours, acetone together with a considerable quantity of acetic acid was obtained. Acidification of the alkaline solution gave a reddish-black precipitate, the analysis of which showed an increase in the ratio of carbon to hydrogen and oxygen over that present in the original red polymer.



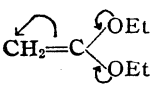
VI

The formation of acetone and acetic acid together with the higher ratio of carbon to hydrogen and oxygen in the polymer remaining after the drastic alkaline hydrolysis of VI suggest that this hydrolysis involves the cleavage of side chains from the cyclic nuclei of VI.

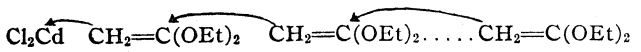
That the color of the red polymer is due to its high conjugation, which is most simply illustrated by the cross-linking of two chains of IV in VI, is shown by the fact that the color can be removed by hydrogenation. This hydrogenation was carried out on an alkaline solution of the polymer, with Raney nickel as the catalyst, at 225° and under 200 atmospheres of pressure. After an initial absorption of hydrogen the reduction stopped due to a coating of a tarry material on the catalyst. The red color of the solution remained but it was finally removed by separating the deactivated catalyst and continuing the reduction with fresh Raney nickel. Acidification of the resulting alkaline solution gave a tan-colored precipitate which amounted to about 12% of the weight of the red polymer taken for hydrogenation. From the filtrate ethyl alcohol and acetic acid could be distilled. Evaporation of the solution left a dark, viscous, alcohol-soluble oil which was not investigated further.

The results described above leave no doubt that, in the main, the ketene acetal polymers are built up by a "head to tail" linking of the monomer. This is further substantiated by the fact that nitric acid completely oxidizes the red polymer without leaving a trace of residue, a fact that shows there is no "head to head, tail to tail" linkage present, since this type of structure would be expected to leave succinic acid on such oxidation.

The mechanism by which ketene acetal undergoes polymerization is suggested by its structure. It is an unusual hetero-enoid system[7] in that two very effective hetero atoms, oxygen, are attached to the same unsaturated carbon atom. The anionoid center which is built up on the methylene carbon by the electromeric shifts from the hetero atoms, thus



is very powerful as is shown by the readiness with which ketene acetal adds compounds of the type of water, alcohol, acids, etc., which are capable of furnishing such a cationoid addendum as a proton. If the negative portion of the addendum (*e. g.*, :OH, :OEt, :Br, RCOO:, etc.) is sufficiently mobile it will add to the carbon atom that carries the hetero atoms. If, however, there is no mobile anion (as in the case of the acidified glass surfaces) or if the highly polarized methylene group of the acetal can coördinate with a metal, such as cadmium chloride, a chain reaction may be initiated and propagated in the following manner[8]:



Addition of the proton and the ethoxyl group from a molecule of alcohol to the ends of the polymer chain would release the catalyst from the methylene group and saturate the carbon atom at the other end of the chain.

The Dimer and Trimer of Ketene Diethylacetyl.—When ketene acetal was polymerized with a larger amount of catalyst (36 mg. per 10 g. of acetal) the reaction was very vigorous and the temperature rose sufficiently to cause refluxing of the acetal. The polymer so obtained was a soft gel from which a number of products were removed by distillation under diminished pressure. Up to 100° (0.5 mm.) a mixture of ketene acetal and ethyl orthoacetate, representing 8–15% of the weight of the starting material, distilled. Between 100–130° (0.5 mm.) a product, amounting to about 13% of the starting material and which proved to be a dimer of ketene acetal, came over. At 150–160° (0.5 mm.) another liquid product, amounting to about 20% of the original ketene acetal distilled; also a small amount of ethyl alcohol collected in a cold trap during the distillation of this higher boiling product. The residual polymer is a dry, light tan solid, the properties of which were quite similar to those of the white polymer described above.

The dimer of ketene acetal could not be obtained analytically pure. Although fractionation yielded a product with a constant boiling point and refractive index, the ethoxyl content was generally 2–3% lower than the theoretical value for VII. Work with this dimer was hampered by its tendency to lose alcohol on standing.[9] Freshly prepared samples showed molecular weights of 207–212 as determined by the freezing point of benzene (theoretical for VII, 232) and saponification equivalents of 217–239. Hydrolysis of the dimer by dilute acid yielded acetone and treatment with 95% alcohol containing a trace of hydrochloric acid, converted it, practically quantita-

(7) Robinson, "Outline of an Electrochemical (Electronic) Theory of the Course of Organic Reactions," Institute of Chemistry of Great Britain and Ireland, London (1932); Gilman, "Organic Chemistry," Vol. II, John Wiley and Sons, New York, 1938, p. 1679.

(8) Only one chain of ketene acetal molecules is shown coördinated with cadmium chloride; obviously two such chains would be required to give the metal a complete octet of electrons.

(9) For example, one sample showed an ethoxyl content of 74.2% immediately after distillation, but a month later this sample contained only 63.0% ethoxyl.

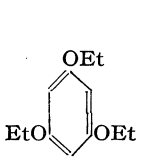
tively, into acetoacetic ester. It absorbed bromine rapidly. All of these properties are readily explained by structure VII.[10]

$CH_3C(OEt)_2CH{=}C(OEt)_2$

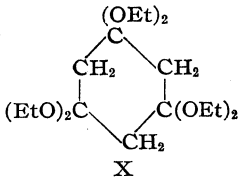
VII

$CH_3C(OEt)_2CH_2{-}C(OEt)_2CH{=}C(OEt)_2$

VIII



IX



X

$CH_3COCH_2COCH_2COOEt$

XI

The fraction boiling at 150–160° (0.5 mm.) proved to be a mixture of the open chain trimer (VIII) and at least one other product. Fractionation failed to give a product with a constant refractive index although the product boiled over a rather narrow range. Ethoxyl determinations showed that successive fractions had approximately the same composition as ketene acetal. Cryoscopic methods and saponification equivalents gave widely varying values for the molecular weight. When a portion of this fraction was heated with 5% sulfuric acid, a small amount of a solid steam distilled. This product was shown to be 1,3,5-triethoxybenzene (IX). It seems likely that it was formed by the loss of alcohol from the cyclic trimer 1,1,3,3,5,5-hexaethoxycyclohexane (X) during the distillation of the trimer fraction, since alcohol appeared in the cold trap as this fraction was collected. The possibility that IX is formed by cyclization of the open chain trimer (VIII) was shown to be unlikely by the fact that fractions which were known to contain at least 50% of this trimer could not be converted to IX by heating for two hours at 180°.

When the trimer fraction was treated with 95% alcohol containing a trace of acid it was converted into ethyl γ-acetoacetoacetate (XI), which was characterized as the copper derivative and as the lactone of γ-acetoacetoacetic acid. An estimate of the amount of the trimer VIII that was present in the fraction was obtained by distillation under atmospheric pressure of the ethyl acetoacetoacetate formed from the trimer. Acetylacetone was formed by this distillation and the amount collected indicated that the trimer fraction was at least 50% of the open chain trimer VIII.

It should be mentioned that the dimer and trimer of ketene acetal are formed concurrently with the polymer and are not pyrolysis products of it. This is shown by the fact that the polymer prepared from a trace of cadmium chloride may be heated at 155° and under 0.5 mm. pressure for several hours without yielding any distillate. It is believed that the higher temperatures produced by the rapid polymerization of ketene acetal interrupt some of the reaction chains so that considerable amounts of the dimer and trimer are formed along with the polymer.

Substituted Ketene Acetals.—In contrast to the ease with which ketene acetal undergoes polymerization, the halogenated ketene acetals[11] do not polymerize. Samples of these compounds stored in ordinary glass bottles in diffuse daylight are, after eighteen months, clear and mobile. Neither the mono- or dichloro-ketene acetals nor the corresponding bromo compounds showed any tendency to polymerize with cadmium, cobalt or iron chloride. A sample of chloroketene acetal was heated with cadmium chloride at 110° for seventy hours without any apparent change. Another sample of this acetal, after heating for eighteen hours with benzoyl peroxide, still reacted as vigorously with water as did the original material. Boron trifluoride and the boron trifluoride–ether complex react with chloroketene acetal to produce a mobile red oil, but no material of a high polymer nature could be obtained by prolonged heating with this catalyst.

Experimental

Ketene Diethylacetal.—The ketene acetal used in this work was prepared by the action of potassium *t*-butoxide on bromoacetal[12] instead of iodoacetal which was used in the first paper[4] of this series. To 550 g. of *t*-butyl alcohol in a 1-liter round-bottom flask, with a small side tube and reflux condenser fitted with a calcium chloride tube, was added 39 g. (1 atom) of potassium. The alcohol was refluxed until all of the potassium had dissolved (about twelve hours). Then 198 g. (1 mole) of bromoacetal was added to the *t*-butyl alcohol solution and the resulting solution refluxed for about five hours. Without attempting to remove the precipitated potassium bromide, the reaction mixture was fractionated through an 18-in. (46-cm.) Vigreux column, equipped with a total-reflux, partial take-off distilling head and the *t*-butyl alcohol slowly distilled from an oil-bath at a reflux ratio of about 8:1.

(10) The possibility of this dimer being 1,1,3,3-tetraethoxycyclobutane was considered, but the marked unsaturation of the dimer and the apparent tendency of the cyclic trimer to lose alcohol seemed to support the open chain formula (VII).

(11) Beyerstedt and McElvain, THIS JOURNAL, **59**, 2266 (1937); Magnani and McElvain, *ibid.*, **60**, 2210 (1938).

(12) Filachione, *ibid.*, **61**, 1705 (1939).

When the alcohol ceased distilling at a bath temperature of 125° the pressure was lowered to 200 mm. and the remainder of the alcohol removed at 50–52°. A small amount of intermediate was followed by the distillation of ketene acetal at 83–85° (200 mm.). When an ebullition tube was used during the distillation nitrogen, rather than laboratory air, was drawn through it. The yield of ketene acetal amounted to 70 g. (60% of the theoretical).

Determination of Ethoxyl in Ketene Acetals.—In the past, attempts to apply the Viebock ethoxyl technique to ketene acetals have not been very successful. The results not only have been low, but have varied over a wide range. With ketene acetal and compounds derived from it satisfactory results were never obtained, while with the halogenated ketene acetals it was only by the most careful manipulation that acceptable analyses were made. The difficulty appeared to be due to the rapid hydrolysis of the acetals by the hydriodic acid and loss of ethyl alcohol before it was converted into ethyl iodide. The suggestions of Elek[13] improved the results somewhat but consistently accurate analyses could not be obtained even with these refinements in technique.

It was found necessary to redesign the apparatus so that any alcohol produced by the rapid hydrolysis of the sample could not escape from the reaction chamber without passing through boiling hydriodic acid. The apparatus that was found to give the best results is shown in Fig. 1. Flask A (25 ml.) was charged with 10 ml. of hydriodic acid (sp. g. 1.7), a few crystals of phenol, and about 40 mg. of red phosphorus; flask B (25 ml.) was charged with 2 ml. of hydriodic acid and 20 mg. of red phosphorus; a 5% cadmium sulfate–sodium thiosulfate solution was used in the scrubber C; in the absorption tube D was placed 10 ml. of a 10% solution of sodium acetate in acetic acid, to which 15–30 drops of bromine (approximately 20 drops for every 15 mg. of ethoxyl in the sample) had been added; in the tube E was placed 5 ml. of the acetate–acetic acid solution and about 5 drops of bromine. Before the start of the determination the acid in flask B was heated to gentle refluxing, and a slow stream of carbon dioxide allowed to pass through the system. The sample (15–30 mg.) was weighed into a small glass cup with ground in stopper and dropped into the reaction flask A at room temperature. The flask was reconnected to the apparatus as quickly as possible, and then slowly heated to gentle refluxing. Heating was continued for thirty minutes with a slow stream of carbon dioxide, and for fifteen to thirty minutes with a faster flow of the gas to carry the last traces of the ethyl iodide into the absorbent. The tubes D and E were then removed and their contents washed into an Erlenmeyer flask for the iodometric titration.

This apparatus has been found to give very satisfactory results with compounds related to ketene acetal. However, ketene acetal itself gave consistent values of 76.6% ethoxyl (77.6% is theoretical) regardless of the method of preparation of the compound or wide variations in technique of the determination.

Polyketene Diethyl Acetal.—To 83 g. of freshly distilled ketene acetal was added 50 mg. of powdered cadmium chloride and the polymerization allowed to proceed

(13) Elek, *Ind. Eng. Chem., Anal. Ed.*, **11**, 174 (1939).

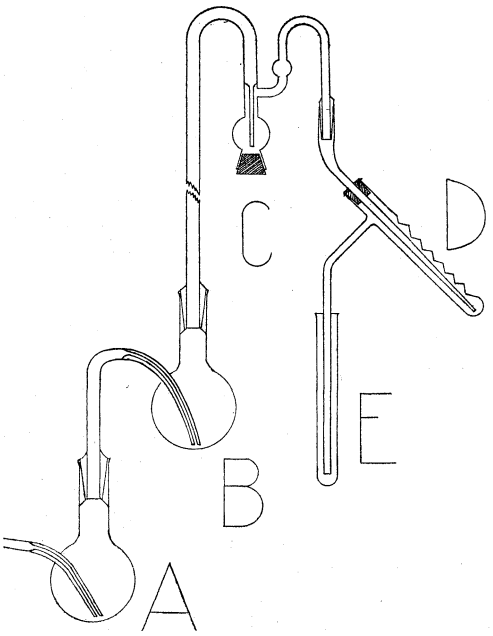


Fig. 1.

with occasional shaking. Several hours were required to reach the gel stage, after which the polymer was stirred to distribute the catalyst through the gel. After standing overnight the polymer was a waxy white solid. It was transferred to a distilling flask and heated in an oil-bath at 100° (0.5 mm.) for two hours. During this time 37 g. of ketene acetal collected in a carbon dioxide snow–acetone trap. The remaining polymer was a white powder

Anal. Calcd. for $(C_6H_{12}O_2)_x$: C, 62.02; H, 10.41; OC_2H_5, 77.6. Found: 62.19, 9.85, 76.3.

That the large recovery of ketene acetal is not due to depolymerization is shown by the fact that the monomer could be recovered from the polymer just as well by extraction in a soxhlet extractor with ether as by heating under diminished pressure. Also, heating the remaining polymer for one hour at 155° (0.5 mm.) gave no distillate, while heating at 210° (0.5 mm.) for one and one-half hours gave only a small amount of ethyl alcohol as a distillate.

When the dry polymer was heated at 250° (0.5 mm.) a fairly rapid decomposition took place and ethyl alcohol amounting to 27% of the weight of the original polymer was obtained as a distillate. The material remaining in the flask after this pyrolysis was an acetone-soluble, viscous, red tar.

The white ketene acetal polymer is insoluble in all of the common organic solvents including aniline, anisole, nitrobenzene, acetal and ketene acetal. The latter liquid and the aromatic hydrocarbons caused a noticeable swelling of the polymer. It is remarkably stable to alkali, remaining apparently unchanged after refluxing with a 10% aqueous solution of sodium hydroxide. It is, however, extremely sensitive to acids, being converted into a red oil immediately by aqueous acids. Refluxing with acid gives the red polymer described below.

Hydrolytic Decarboxylation of Polyketene Acetal.—A weighed sample of the polymer was placed in a 50-ml.

flask having a side arm and attached through a reflux condenser to a carbon dioxide absorption train. To the polymer was then added 25 ml. of a carbon dioxide-free 5% aqueous solution of sulfuric acid and the acid refluxed, with a stream of nitrogen passing through the system, until the ascarite tube in the absorption train attained constant weight. The unit weight of the polymer was calculated on the basis that one polymer unit would produce one molecule of carbon dioxide. Table I shows the data from two representative runs.

TABLE I

Sample, g.	CO_2, g.	Unit wt. of polymer calcd.
3.0464	0.0510	2628
3.1919	0.0515	2727

Hydrolysis of Polyketene Acetal. The Red Polymer.—Polyketene acetal (30 g.) was refluxed for half an hour in 50 ml. of 0.3 *N* sulfuric acid. The mixture was then cooled and the supernatant liquid poured from the viscous red precipitate. The precipitate was treated with 100 ml. of distilled water and the water refluxed for a few minutes, after which it was decanted into the original sulfuric acid solution. After cooling and solidifying the red polymer was ground to a fine powder, washed onto a filter and dried. The yield amounted to 8.9 g.

The aqueous acid solution, obtained by the two decantings, contained some of the red polymer in colloidal suspension. This solution was distilled until 100 ml. of distillate had been collected. The density of this distillate indicated that it contained about 24 g. of ethyl alcohol (theoretical for the amount of polyketene acetal used, 23.3 g.). The distillation of the alcohol caused the suspension of the red polymer to precipitate. By filtration an additional 1.1 g. of this product was obtained, which brought the total yield to 10 g. (theoretical, 11.4 g.).

Anal. Calcd. for $(-CH_2CO-)_x$: C, 57.2; H, 4.76. Found: C, 63.6; H, 4.49. Calcd. for $C_{45}H_{38}O_{17}$: C, 63.5; H, 4.47.

The red polymer is sufficiently soluble in alcohol and acetone to give a light red solution, but it is insoluble in ether, chloroform and benzene. It dissolves readily in dilute alkali to give a deep red, almost black solution from which it is not precipitated by saturation with carbon dioxide. Acidification of the alkaline solution precipitates the polymer as a gelatinous brownish-red precipitate. When heated to 60–70° the red polymer softens and changes to a viscous, dark red oil.

Oxidation of the Red Polymer.—A weighed sample of the solid red polymer was dissolved in 50 ml. of 0.1 *N* sodium hydroxide and carefully washed into a reaction flask which was connected through a reflux condenser to a carbon dioxide absorption train. The solution was heated to boiling and then a 1 *N* solution of potassium permanganate was added in portions from a buret until a permanganate color at 100° persisted for fifteen minutes. The oxidation required about ninety minutes. The mixture then was cooled and 50 ml. of 10% sulfuric acid added. The acidified solution was boiled to expel the carbon dioxide while the system was swept out with nitrogen. The acidified solution was centrifuged and the supernatant liquid decanted from the manganese dioxide which was washed with water and recentrifuged until the washings were neutral to litmus. The washings and original solution were combined and distilled until only 50 ml. remained. The distillate was titrated with standard alkali. Portions of water were added to the residue from the distillation and distilled out until negligible titration was obtained. Acetic acid was shown to be the acid present in the distillate by its Duclaux numbers and the melting point of its *p*-toluidide. Table II shows the results of two such oxidations.

TABLE II

Sample g.	1 *N* $KMnO_4$ used, ml.	CO_2, g.	Millimoles of acetic acid	Polymer per mole acetic acid, g.
0.6836	105	1.2898	1.2238	558
0.4442	68	0.8734	0.6879	645

A 2-g. sample of the white polyketene acetal was hydrolyzed by boiling with 50 ml. of 1% nitric acid. The alcohol formed was removed by distilling out one-half of the solution. The remainder of the solution which contained the red polymer was treated with 5 ml. of concentrated nitric acid and evaporated to dryness on a steam-bath. The black residue was treated with concentrated nitric acid until its color was destroyed. At this point no residue whatsoever remained.

Hydrolysis of the Red Polymer.—After heating the polymer in a sealed tube with 10% sulfuric acid at 200° for seven hours, 85% of it was recovered. The acid solution contained a trace of acetone and some acetic acid. Alkaline hydrolysis was much more satisfactory. A solution of 2 g. of the polymer in 60 ml. of 5% sodium hydroxide was placed in a steel bomb and heated at 240° for twenty-two hours. The hydrolysis solution then was washed into a distilling flask and about one-third of its volume distilled out. Acetone was determined quantitatively in this distillate as the 2,4-dinitrophenylhydrazone, and also by the procedure of Marasco.[14] The two procedures checked and showed the total yield of acetone from the hydrolysis to be 0.08 g.

Acidification of the reddish-black solution, remaining after the removal of the acetone, with dilute sulfuric acid precipitated 1.0 g. of a black substance which contained 73.9% of carbon and 4.6% of hydrogen. The acid solution was distilled, as described above, until all of the acetic acid had been removed. Titration with standard alkali showed that the distillate contained 0.35 g. of acetic acid. It was further identified as the *p*-toluidide.

Hydrogenation of the Red Polymer.—A solution of 11 g. of the red polymer in 100 ml. of 1% sodium hydroxide was refluxed for a short time over Raney nickel, which had been freed from the alcohol under which it was stored by several washings with distilled water. After cooling, the solution was decanted from the nickel and made up to 250 ml. with water that had been used to wash the nickel. This solution, together with 3 g. of washed Raney nickel, was placed in a bomb and shaken with hydrogen under 3500 lb. (233 atm.) pressure at 225° for five and one-half hours. During this time 26 (±2) moles of hydrogen were absorbed on the basis of a molecular weight of 850 (calcd. for $C_{45}H_{38}O_{17}$). The alkaline solution was still red in color

(14) Marasco, *Ind. Eng. Chem.*, **18**, 701 (1926).

and the catalyst was coated with about 1.2 g. of an acetone-soluble tar. This deactivated catalyst was replaced with fresh catalyst and the hydrogenation continued under the same conditions for another five hours. A small amount of additional hydrogen was absorbed, and the alkaline solution was no longer red, but was yellow with a green fluorescence. From this alkaline solution 0.8 g. of ethyl alcohol was distilled. Acidification of the remaining solution gave a precipitate of 1.4 g. of a tan-colored solid. This product was not investigated further. From the acidified solution 0.54 g. of acetic acid was removed by distillation. After removal of the acetic acid the solution was evaporated at 200 mm. and the residue extracted with alcohol. This alcoholic solution on evaporation left 0.8 g. of a dark, viscous oil.

The Dimer and Trimer of Ketene Acetal.—To 74 g. of freshly distilled ketene acetal was added 300 mg. of cadmium chloride. Polymerization was very rapid and the temperature of the reaction was sufficient to cause refluxing of the ketene acetal. In fifteen minutes after the addition of the catalyst the acetal became a moist solid. After standing overnight, the flask containing the polymer was attached, through a condenser, receiver and cold trap, to a vacuum pump and heated in an oil-bath under 0.5 mm. pressure. The fractions were collected at the bath temperature, in the amounts and in the places as shown in Table III.

TABLE III

Fraction	Bath temp., °C.	Wt., g.	Collected in
1	to 25°	2.4	Trap
2	102–108	3.65	Trap
3	102–108	4.35	Receiver
4	108–130	5.35	Receiver
5	152–159	1.80	Trap
6	152–159	15.00	Receiver

Fractions 1 and 2 were mixed and fractionated and shown to be a mixture of ketene acetal and ethyl orthoacetate. Fraction 3 was fractionated through an 8-in. (21-cm.) Stedman column and yielded 2.45 g. of material boiling at 61–62° (0.5 mm.). By a similar fractionation 2.75 g. of material of the same boiling point was obtained from fraction 4. This material contained the dimer of ketene acetal, the characterization of which is described below. Fraction 5 proved to be ethyl alcohol. Fraction 6, after the removal of a small amount of impure dimer and an intermediate fraction, yielded 12 g. of a product boiling at 91–92° (0.1 mm.) which is discussed below.

The fraction that boiled at 61° (0.5 mm.) showed an ethoxyl content of about 75% (the ethoxyl content of ketene acetal and its dimer (VII) is 77.6%); $n^{25}D$ 1.4258 for the first and last portions of the fractions; d^{25}_4, 0.9441; mol. wt. (freezing point of benzene), 207, 212; saponification equivalents varied from 217 to 239 (calcd. value for VII, 232). A sample of this fraction that had been opened from time to time was found, after a month, to have an ethoxyl content of 63%. This lower ethoxyl value may be due to intramolecular loss of alcohol or partial hydrolysis of an acetal group by moisture from the air. No attempt was made to ascertain which of these processes is responsible for the instability of the dimer fraction. Hydrolysis of a portion of this fraction with aqueous 5% sulfuric acid yielded acetone which was characterized as the 2,4-dinitrophenylhydrazone.

A 0.86-g. sample of this fraction was treated with 2 ml. of 95% alcohol containing a trace of hydrochloric acid and the resulting solution heated on a steam-bath under a reflux for ten minutes. The alcohol was removed under diminished pressure and the remaining acetoacetic ester (0.39 g.) was characterized as the semicarbazone, m. p., 129–130°.[15] The dimer does not add absolute alcohol. A 1.0-g. sample of it was allowed to stand with 2 ml. of absolute ethyl alcohol for forty-eight hours. After evaporation of the alcohol under diminished pressure and with a stream of dry nitrogen passing through the liquid, the remaining oil had the same refractive index and ethoxyl content as the starting material. Repetition of the experiment with a trace of hydrogen chloride in the alcohol led to the same results.

The fraction boiling at 91–92° (0.1 mm.), which was obtained from fraction 6 above, had an ethoxyl content of 76% (the ethoxyl content of ketene acetal and its trimer (VIII) is 77.6%). However, the refractive indices of the first and last portions of this fraction varied between 1.4414 and 1.4400. When 2.8 g. of this fraction was refluxed with 3% sulfuric acid for thirty minutes and the resulting mixture distilled, an oily substance, which crystallized on cooling in an ice-bath, came over with the aqueous distillate. After filtration and recrystallization from alcohol, the solid weighed 0.1 g., melted at 43.5°, and contained 64.2% ethoxyl. It was shown to be 1,3,5-triethoxybenzene (% ethoxy, 64.3) by comparison with an authentic specimen prepared by the method of Will and Albrecht.[16]

A 3.2-g. sample of the fraction boiling at 91–92° (0.1 mm.) was treated with 7 ml. of 95% alcohol containing a trace of hydrochloric acid. After standing overnight the excess alcohol was removed under diminished pressure and the remaining oil distilled. It boiled at 87–90° (0.4 mm.) and showed an ethoxyl content of 40.0%. A 0.3-g. portion of this distillate was boiled for a few minutes in 0.3 *N* sulfuric acid and then poured into a saturated solution of copper acetate. The copper derivative which formed immediately was filtered off and dried. It weighed 0.1 g. This blue derivative was suspended in boiling benzene for a few minutes, then filtered and dried. It melted at 183–184°[17] and contained 22.6% ethoxyl (calcd. for the copper derivative of γ-acetoacetoacetic ester, $Cu{\cdot}C_{16}H_{22}O_8$: 22.2%).

Six drops of the trimer fraction were added to 0.5 ml. of 70% sulfuric acid and the mixture warmed to 80° for five minutes. After standing without further heating, for an additional fifteen minutes, an equal volume of water was added. Cooling precipitated the lactone of γ-acetoacetoacetic acid which, after recrystallization from water, melted at 185–187°.[18]

A 1.95-g. portion of the trimer fraction boiling at 91–92° (0.1 mm.) was refluxed with 0.3 *N* sulfuric acid for twenty minutes. After cooling, the mixture was extracted with ether and the ether layer separated and dried. The ether

(15) Thiele and Stange, *Ann.*, **283**, 29 (1894).
(16) Will and Albrecht, *Ber.*, **17**, 2107 (1884).
(17) Sproxton, *J. Chem. Soc.*, **89**, 1187 (1906).
(18) Collie, *ibid.*, **59**, 609 (1891).

was removed by distillation and the remaining brown liquid heated with a free flame, under atmospheric pressure, until it distilled. Decomposition accompanied the distillation of a yellow oil which came over at 130–140°. The yield of this oil amounted to 0.25 g. and it was shown to be acetylacetone by its conversion to 1-(2,4-dinitrophenyl)-3,5-dimethylpyrazole, m. p. 121–122°, and the comparison of this derivative with an authentic specimen.[19] The 0.25 g. yield of this diketone indicates that the trimer fraction contained at least 50% of the straight chain trimer VIII.

The boiling point of the trimer fraction as well as its content of 1,3,5-triethoxybenzene remained unchanged after a sample of this fraction had been heated at 180° under atmospheric pressure for two hours.

Summary

1. Evidence is presented to show that ketene acetal is converted by cadmium chloride into a white polymer composed of chains having, on an average, 22–23 ketene acetal molecules joined in a head to tail manner. The insolubility of the polymer suggests cross-linking of these chains.

2. The white polymer is converted by acid hydrolysis into an alkali soluble red polymer composed of cross-linked poly-1,3-diketone units which exist in a highly conjugated, enolic form. Molecular weight estimation of this polymer from an end group corresponds fairly well with a similar estimation of the molecular weight of the white polymer.

3. Rapid polymerization of ketene acetal by larger amounts of cadmium chloride produces an open chain dimer and trimer together with 1,3,5-triethoxybenzene. The latter product probably is formed from the cyclic trimer, 1,1,3,3,5,5-hexaethoxycyclohexane.

4. Halogenated ketene acetals cannot be caused to polymerize.

5. An improved method for the preparation of ketene acetal from bromo-acetal is described.

6. The construction and operation of a new apparatus for the determination of the ethoxyl content of the types of acetals encountered in this work are described.

(19) Brady, *J. Chem. Soc.*, 758 (1931).

MADISON, WISCONSIN RECEIVED FEBRUARY 23, 1940

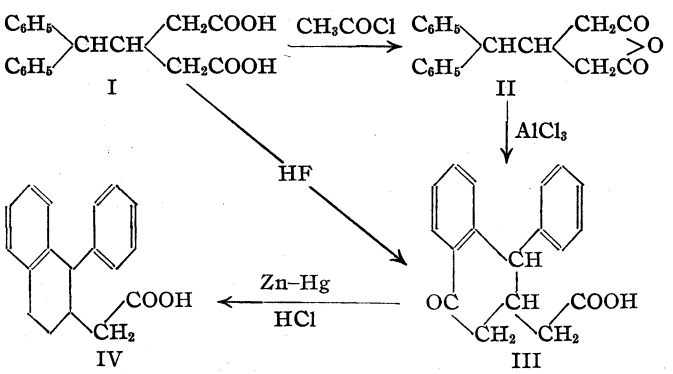
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

The Synthesis of 2-Methyl-3,4-benzphenanthrene

BY MELVIN S. NEWMAN[1] AND LLOYD M. JOSHEL[2]

Because of the interest in 3,4-benzophenanthrene as a structure possessed of carcinogenic activity, the previously reported synthesis[3] has been modified so that 2-substituted derivatives may be prepared. In this paper is described the synthesis of 2-methyl-3,4-benzphenanthrene[4] and 2-ethyl-3,4-benzphenanthrene.

In the earlier synthesis,[3] β-benzohydrylglutaric acid, I, after conversion to its acid chloride, was cyclized to 1,2,9,10,11,12-hexahydro-2,9-diketo-3,4-benzphenanthrene from which 2,9-disubstituted derivatives were prepared. The present modification consists in treating the anhydride, II, of β-benzohydrylglutaric acid with aluminum chloride whereby 1,2,3,4-tetrahydro-4-keto-1-phenyl-2-naphthaleneacetic acid, III, was isolated in 63% yield. The same keto-acid was obtained more easily in 89% yield by treatment of the acid, I, with anhydrous hydrogen fluoride.[5] By reduction III was converted into 1,2,3,4-tetrahydro-1-phenyl-2-naphthaleneacetic acid, IV.[4]



The remaining steps required for the synthesis of 2-methyl-3,4-benzphenanthrene and 2-ethyl-

(1) The Elizabeth Clay Howald Scholar at The Ohio State University, 1939–1040.

(2) This material was largely contained in a Dissertation presented by L. M. J. to The Ohio State University in partial fulfillment of the requirements for the Ph.D. degree, June, 1938. Completing experiments were conducted by L. M. J. at Harvard University under tenure of a Finney-Howell Research Fellowship.

(3) Newman and Joshel, THIS JOURNAL, **60**, 485 (1938).

(4) Hewett, *J. Chem. Soc.*, 596 (1936).

(5) Fieser and Hershberg, THIS JOURNAL, **61**, 1272 (1939).

3,4-benzphenanthrene are similar to those carried out by Hewett.[4]

In conclusion it seems of interest to point out that while 2-methyl-3,4-benzphenanthrene is a very potent carcinogenic agent when tested by painting on the skin,[6] it has proved to be only very slightly active when tested by the injection technique.[7] This finding serves to emphasize the differences in carcinogenic activity of hydrocarbons when estimated by the painting technique as compared to the injection technique. The present instance is one in which the compound is less active when tested by injection whereas in the case of 10-methyl-1,2-benzanthracene,[8] the activity measured by injection was greater than that measured by painting.[9] The following 3,4-benzphenanthrene derivatives have proved inactive when tested by injection[7]: 2,9-dimethyl-[3], 2,9-diethyl-[3], 6,7-dimethyl-[10] and 2-isopropyl-8-methyl-.[11]

Experimental[12]

β-Benzohydrylglutaric Acid, I.—After considerable experimentation the following procedure was found to yield the most consistent results. A solution of 50 g. of diphenylacetaldehyde in 150 cc. of ethyl cyanoacetate was treated with 5 cc. of diethylamine and allowed to stand in a stoppered flask for twelve hours at room temperature. The mixture was then heated for twelve hours on the steam-bath with the further addition of two 5-cc. portions of diethylamine. The resulting cloudy suspension was refluxed for sixty-two hours with a solution of 125 cc. each of water and concentrated sulfuric acid in 350 cc. of acetic acid. The organic acid fraction thus produced was isolated, decarboxylated by heating to 200°, and esterified with methanol and dry hydrogen chloride. A portion of the ester fraction, b. p. about 180° at 2 mm. was crystallized from aqueous methanol yielding colorless needles, m. p. 73.4–74.2°.

Anal. Calcd. for $C_{20}H_{22}O_4$: C, 73.60; H, 6.79. Found: C, 73.91; H, 6.90.

The remaining ester was saponified and 13.4 g. (17.6%) of acid, I, m. p. 172–175°, suitable for use in the next step, was obtained. The pure acid melted at 177.6–178.2°.[3]

1,2,3,4 - Tetrahydro - 4 - keto - 1 - phenyl - 2 - naphthaleneacetic Acid, III.—Twelve grams of the above acid was treated in a metal flask with 150 g. of anhydrous hydrogen fluoride[5] for nine hours at room temperature. The solution was poured on ice and the solids collected. The filtered carbonate extract of this material was acidified and the acid crystallized from benzene–ligroin to yield 9.3 g. of colorless needles, m. p. 115.4–116.2°, and 0.7 g., m. p. 113.0–114.5° (total 89%). The sample for analysis was crystallized from benzene and melted, after thorough heating *in vacuo*, at 115.4–116.2°.

Anal. Calcd. for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75; neut. equiv., 280. Found: C, 77.43; H, 5.84; neut. equiv., 279.

The same acid was prepared in 63% yield from β-benzohydrylglutaric anhydride[3] using aluminum chloride in *sym*-tetrachloroethane solution.

1,2,9,10,11,12 - Hexahydro - 2 - keto - 3,4 - benzphenanthrene.—This compound was prepared either by Hewett's method[4] using *sym*-tetrachloroethane as solvent or by the use of anhydrous hydrogen fluoride,[5] the latter offering no advantage over the former.

1,2,3,4 - Tetrahydro - 1 - phenyl - 2 - naphthaleneacetic Acid, IV.—The keto acid, III, was converted in 74% yield into IV using Martin's modification of the Clemmensen reduction. Our purest sample melted at 140.2–140.8° (lit.[4] 138–139°).

2-Methyl-3,4-benzphenanthrene.—A solution of 1.9 g. of the above ketone in dry benzene was refluxed with an ether solution of methylmagnesium chloride for two and one-half hours. The crude alcohol was heated with 0.2 g. of palladium charcoal[13] for two hours at 290–320° (77% of the theoretical hydrogen collected). By crystallization of the picrate followed by chromatographic adsorption on alumina, there was isolated 1.11 g. (60%) of 2-methyl-3,4-benzphenanthrene, m. p. 69.6–71.0°. The hydrocarbon was recrystallized from benzene–methanol, separating as almost colorless needles, m. p. 70.4–71.0° (lit.[4] leaflets, m. p. 69.5–70.0°). The picrate formed bright orange-red needles, m. p. 141.8–143.2°, from benzene–alcohol.

Anal. Calcd. for $C_{25}H_{17}O_6N_3$: C, 65.93; H, 3.76; N, 9.23. Found: C, 66.11; H, 3.99; N, 9.35.

2-Ethyl-3,4-benzphenanthrene.—A benzene solution of 1.0 g. of 1,2,9,10,11,12-hexahydro-2-keto-3,4-benzphenanthrene was refluxed with an excess of ethylmagnesium bromide, the alcohol thus produced dehydrated by heating with a crystal of iodine, and the tetrahydro derivative aromaticized by heating with 0.26 g. of sulfur at 230° for forty minutes. The distilled crude hydrocarbon was treated with 1 g. of picric acid in benzene–alcohol. A total of 1.00 g. (51%) of picrate, m. p. 78.4–80.0°, was obtained. A portion recrystallized for analysis melted at 80.0–81.0°.

Anal. Calcd. for $C_{26}H_{19}O_7N_3$: C, 64.33; H, 3.95; N, 8.66. Found: C, 64.31; H, 3.78; N, 8.38.

By chromatographic adsorption on alumina, the hydrocarbon was obtained and distilled. Considerable difficulty in crystallization was encountered but by cooling a methanol solution with solid carbon dioxide, seed crystals were obtained. **2-Ethyl-3,4-benzphenanthrene** crystallized from alcohol in colorless needles, m. p. 50.4–51.2°, and had a blue–violet fluorescence in ultraviolet light.

Anal. Calcd. for $C_{20}H_{16}$: C, 93.71; H, 6.29. Found: C, 93.57; H, 6.16.

(6) Bachmann, Cook, *et al.*, *Proc. Roy. Soc.*, **B123**, 343 (1937).

(7) Private communication from Dr. M. J. Shear.

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

(9) Shear, *Am. J. Cancer*, **33**, 510 (1938). See also Cook, Robinson and Goulden, *J. Chem. Soc.*, 393 (1937), and reference 6.

(10) Fieser, Fieser and Hershberg, THIS JOURNAL, **58**, 1463 (1936).

(11) Private communication from Professor M. T. Bogert. See Adelson and Bogert, *ibid.*, **59**, 1776 (1937).

(12) All melting points corrected. The authors are indebted to H. S. Clark and J. H. Walker for analyses and to O. Woolfolk for the preparation of a quantity of pure diphenylacetaldehyde. The assistance of Messrs. Walker and Woolfolk was made possible through the Ohio State W. P. A. project No. 65-1-42-89.

(13) Zelinsky and Turowa-Pollak, *Ber.*, **58**, 1295 (1925).

The *sym*-**trinitrobenzene derivative** formed yellow-orange needles from benzene–alcohol, m. p. 105.6–106.6°.

Anal. Calcd. for $C_{26}H_{19}O_6N_3$: C, 66.52; H, 4.08; N, 8.95. Found: C, 66.37; H, 3.77; N, 9.19.

Summary

The preparation of 1,2,3,4-tetrahydro-4-keto-1-phenyl-2-naphthaleneacetic acid by ring closure of β-benzohydrylglutaric anhydride using aluminum chloride or by direct cyclization of β-benzohydrylglutaric acid using anhydrous hydrogen fluoride is described. The keto group of this keto acid was reduced by the Clemmensen method and the reduced acid cyclized to 1,2,9,10,-11,12-hexahydro-2-keto-3,4-benzphenanthrene. By reaction with the appropriate Grignard reagents followed by dehydration and dehydrogenation 2-methyl-3,4-benzphenanthrene and 2-ethyl-3,4-benzphenanthrene were prepared from the above hexahydroketone.

COLUMBUS, OHIO RECEIVED FEBRUARY 26, 1940

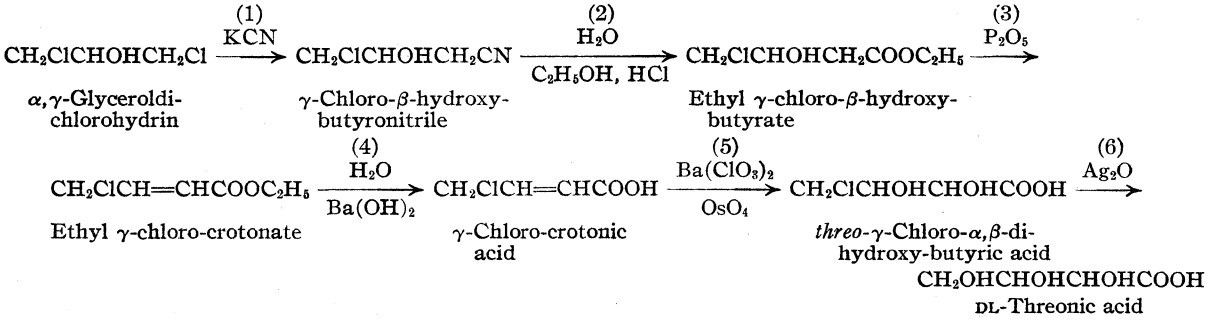
[CONTRIBUTION FROM THE KENT AND GEORGE HERBERT JONES CHEMICAL LABORATORIES, UNIVERSITY OF CHICAGO]

Improvements in the Preparation of DL-Threonic and DL-Erythronic Acids

BY J. W. E. GLATTFELD AND EDWARD RIETZ[1]

The reason for the interest in the two acids mentioned in the title of this article has been recorded several times.[2,3] Briefly, the acids are possible sources of the DL-aldotetroses. These are needed for a proposed study of the saccharinic acid rearrangement of the tetroses which it is hoped to make in these laboratories. Because of the availability of DL-erythronic lactone, definite progress has been made in devising a procedure for its transformation into DL-erythrose.[2] The difficulty of the preparation of DL-threonic acid, however, has prevented corresponding progress with this substance. The main object of the work reported below, therefore, was the simplification and improvement of the known procedure for the preparation of DL-threonic acid.[4] Incidentally, the method of preparation of DL-erythronic lactone was also much improved by the use of vinylacetic acid, an intermediate in the preparation of DL-threonic acid.

DL-Threonic Acid.—The only recorded synthesis of DL-threonic acid is that of Braun.[4b,c]



This process was carried out several times, but great difficulty was experienced at first in inducing the DL-threonic acid sirup to crystallize. The acid is converted into the lactone much more readily, apparently, than Braun's paper[4b] would indicate. To succeed in crystallizing the sirup obtained by concentration of a water solution of the acid, the evaporation must be discontinued before all of the water is removed, that is, while the residue is still a *thin* sirup. If the evaporation is continued at 40° and 2 mm. for four hours after nearly all of the water has been removed, as Braun recommends, the residue will be largely lactone and will not crystallize. That the acid is converted into lactone was demonstrated by the subjection of a sample of crystalline acid to distillation at 3 mm. The distillate, which titration indicated consisted of 87% lactone and 13% free acid, could not be induced to crystallize even when seeded with crystals of DL-threonic acid.

After having succeeded in producing crystalline acid by Braun's procedure, attention was turned

(1) This article is condensed from a dissertation presented by Edward Rietz in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the University of Chicago.

(2) Glattfeld and Kribben, THIS JOURNAL, **61**, 1720 (1939).

(3) Glattfeld and Lee, *ibid.*, **62**, 354 (1940).

(4) Géza Braun, *ibid.*, **52**, (a) 3167, (b) 3176 (1930), (c) **54**, 1133 (1932).

to improvements in the process. These consisted in producing the intermediate, ethyl γ-chlorocrotonate in a 20% yield (calculated from allyl alcohol) by a much simpler method than that used by Braun. The steps involved in the new procedure are

$$CH_2{=}CHCH_2OH \xrightarrow[HCl]{(1)\ Cu_2(CN)_2} CH_2{=}CHCH_2CN \xrightarrow[HCl]{(2)\ H_2O} CH_2{=}CHCH_2COOH \xrightarrow[HCl]{(3)\ C_2H_5OH}$$

Allyl alcohol — Allyl cyanide (75%) — Vinylacetic acid (60%)

$$CH_2{=}CHCH_2COOC_2H_5 \xrightarrow{(4)\ Cl_2} CH_2ClCHClCH_2COOC_2H_5 \xrightarrow{(5)\ C_2H_5ONa} CH_2ClCH{=}CHCOOC_2H_5$$

Ethyl vinylacetate (70%) — Ethyl β,γ-dichlorobutyrate (not isolated) — Ethyl γ-chlorocrotonate (65%)

The feasibility of the procedure was first established by the preparation of the corresponding bromo derivative, which was obtained in 23.4% yield calculated from allyl alcohol. The ester was hydrolyzed to γ-bromocrotonic acid, which in turn was oxidized to *threo*-γ-bromo-α,β-dihydroxybutyric acid. The procedure for the preparation of the bromo ester was then successfully applied to the preparation of the corresponding chloro ester, which in turn was transformed by Braun's procedure (steps 4–6) into DL-threonic acid. This was obtained in 5.3% yield calculated from the allyl alcohol.

DL-Erythronic Acid.—The best source of DL-erythronic acid at present is the lactone of γ-hydroxy-isocrotonic acid, which is obtained by treatment of glycerolmonochlorohydrin with sodium cyanide, followed by hydrolysis of the nitrile so produced.[5] The amount of the unsaturated lactone formed varies greatly, the yield (average 23%) sometimes being as high as 30% and sometimes being almost negligible. It is oxidized to DL-erythronic acid, the lactone of which was obtained by Braun[6] in 75% yield. It was found that vinylacetic acid could be transformed into isocrotonolactone in 21% yield as follows

$$CH_2{=}CHCH_2COOH \xrightarrow[OsO_4]{(1)\ Ba(ClO_3)_2}$$

Vinylacetic acid

$$CH_2CHOHCH_2C{=}O \xrightarrow{(2)\ P_2O_5} CH_2CH{=}CHC{=}O$$

β-Hydroxybutyrolactone — Isocrotonolactone

Although the new procedure does not give the isocrotonolactone in larger yield than the old one at its best, it has definite advantages. It eliminates the uncertainty in the production of the lactone, is less time consuming, avoids the use of sodium cyanide, and permits the use of larger quantities in a run.

A few remarks concerning the oxidation of vinylacetic acid and the dehydration of β-hydroxybutyrolactone should be recorded. When the osmic acid was used in comparatively large amount, the reaction became violent. Furthermore, perfectly pure vinylacetic acid was found to be essential for good results. The pure acid obtained by extraction of the impurities from a solution of the sodium salt gave markedly better yields and required less catalyst than the acid purified by mere fractionation. The dehydration of β-hydroxybutyrolactone has been studied quite extensively in these laboratories. Glattfeld and Stack[7] observed that dehydration occurs (yield of unsaturated lactone 59%) when an absolute alcohol solution of the lactone containing a little sulfuric acid is heated for seventy-five hours in the presence of calcium sulfate. It was found that the use of more vigorous dehydrating agents shortened the time required for dehydration; phosphorus pentoxide was found to be the most satisfactory. By its use yields of the unsaturated lactone as high as 50% were obtained.

Experimental Part

I. Threonic Acid

Allyl Cyanide.—This was prepared in 75% yield (boiling range 115–120° at atmospheric pressure) by heating allyl alcohol and a slight excess of cuprous cyanide and concentrated hydrochloric acid under reflux according to the method of Brekpot.[8]

γ-Bromo-crotononitrile.—Although this material was found to be unsuitable for the preparation of threonic acid, the procedure by which it was prepared is described here because it is new to the literature and because the yield is much higher (55%) than that which the authors obtained by the older method of Lespieau and Brule.[9,10]

(5) Glattfeld, Leavell, Spieth and Hutton, THIS JOURNAL, **53**, 3164 (1931).

(6) Géza Braun, *ibid.*, **51**, 235, 246 (1929).

(7) Glattfeld and Stack, *ibid.*, **59**, 753 (1937).

(8) Brekpot, *Bull. soc. chim. Belg.*, **39**, 466 (1930).

(9) Lespieau, *Bull. soc. chim.*, [3] **33**, 55 (1905).

(10) Brule, *ibid.*, [4] **5**, 1019 (1909).

One mole (67 g.) of allyl cyanide is dissolved in a mixture of 90 cc. of tertiary butyl alcohol and 450 cc. of medium boiling ligroin. One mole of bromine (160 g.) dissolved in 100 cc. of tertiary butyl alcohol is added dropwise to the vigorously-stirred solution of the nitrile. A mercury seal is used to prevent contact with atmospheric moisture. The temperature is maintained within the range 15–25°. The solution is allowed to stand for fifteen to thirty minutes to ensure complete absorption of the bromine. It is then cooled to 0° and a solution of 23 g. of sodium in the minimum amount of absolute ethyl alcohol necessary to effect solution is added dropwise to the vigorously-stirred solution. The solution is filtered (hood) and the solvent removed under reduced pressure at a maximum temperature of 45°. The residue is fractionated and the fraction boiling at 80–85° at 12 mm. is collected. This weighs 80 g. (55%).

Care is necessary in working with this material. It is a powerful vesicant and lachrymator.

Vinylacetic Acid.—This acid of boiling range 66–69° at 10 mm. was prepared in 60% yield by the hydrolysis of allyl cyanide according to the method of Falaise and Frognier.[11] During the distillation of this compound, a considerable amount of unchanged nitrile is recovered in a carbon dioxide–acetone cooled trap placed between the receiving flask and the pump. When this recovered nitrile is taken into account, the yield of vinylacetic acid approaches 75%.

Ethyl Vinylacetate.—The ester was prepared from vinylacetic acid, ethyl alcohol and hydrogen chloride according to the directions of Falaise and Frognier.[12] The yield of the fraction boiling at 119–124° at atmospheric pressure was 70%.

Ethyl γ-Bromo-crotonate.—The procedures for the preparation of this compound and of ethyl γ-chlorocrotonate are new to the literature and are therefore given in detail.

One fifth of a mole (23 g.) of ethyl vinylacetate is dissolved in 90 cc. of tertiary butyl alcohol, the solution is cooled to 15–25°, and a solution of one-fifth of a mole of bromine (32 g.) in 90 cc. of tertiary butyl alcohol is added dropwise to the well-stirred solution which is contained in a flask equipped with a mercury seal to prevent the access of atmospheric moisture. The solution is then allowed to stand for one-half hour to ensure complete absorption of the bromine, after which it is cooled to 0°. A solution of sodium ethoxide, prepared by the addition of sufficient absolute ethyl alcohol to effect solution of 4 g. of sodium, is added dropwise to the vigorously-stirred solution. The solution is filtered and the solvent removed under reduced pressure at a maximum temperature of 45°. The residue is fractionated and the fraction of boiling range 78–82° at 2 mm. is collected. A yield of 23 g. (60% is obtained. The over-all yield calculated on the basis of the allyl alcohol is 23.4% as compared with Braun's yield of 1.7% calculated on the basis of glycerol.

The material was hydrolyzed and the γ-bromo-crotonic acid was oxidized to *threo*-γ-bromo-α,β-dihydroxybutyric acid as described by Braun. Both compounds melted at the temperature noted by Braun. As the last-named acid is quite difficult to prepare, however, it is not a practical material for the preparation of threonic acid. It was found to be much easier to prepare threonic acid from ethyl γ-chlorocrotonate, the preparation of which is described in the next section.

Ethyl γ-Chloro-crotonate.—Three moles of ethyl vinylacetate (342 g.) is dissolved in 600 cc. of dry carbon tetrachloride, and dry chlorine is passed into the cool (10–20°) well-stirred solution. When the theoretical amount of chlorine (213 g.) has been absorbed (determined by increase in weight of the reaction mixture) the solution is allowed to stand at room temperature for one-half hour to ensure complete absorption of chlorine. The dichloro ester is unstable and loses hydrogen chloride. The mercury seal is not removed, therefore, while the mixture is attaining room temperature. The solution is then cooled to about −5° and a solution of 62 g. of sodium (90% of theory), dissolved in the quantity of absolute alcohol necessary to effect solution, is added dropwise to the vigorously-stirred solution. The temperature is maintained below 0° because of undesirable side reactions which occur at higher temperatures. After the ethoxide has been added, the sodium chloride which has precipitated is removed by filtration or by the use of the centrifuge. Filtration is frequently quite difficult, but the centrifuge has always given a satisfactory separation. The "centrifuging" is best accomplished by the use of four 250-cc. centrifuge tubes, emptying the contents, and repeating the operation until the solid material has been removed from the entire liquid. The solvent is removed under reduced pressure with the water pump, and the residue fractionated. The fraction of boiling range 72–80° at 10 mm. weighs 290 g. (65%).

Threonic Acid.—The procedure for the preparation of threonic acid from this point was essentially that of Braun. Ethyl γ-chloro-crotonate was hydrolyzed to γ-chlorocrotonic acid (78–80°, 60%) which in turn was oxidized to *threo*-γ-chloro-α,β-dihydroxybutyric acid (97–98°, 75%) by means of osmic acid-activated barium chlorate.

Forty-seven grams of *threo*-γ-chloro-α,β-dihydroxybutyric acid was treated according to Braun[4c] and yielded 23 g. of DL-threonic acid, m. p. 98°, 59% yield calculated from the *threo*-γ-chloro-α,β-dihydroxybutyric acid used.

II. Erythronic Acid

While the vinylacetic acid of boiling range 66–69° at 10 mm. is sufficiently pure for the threonic acid synthesis, a higher degree of purity is necessary for the preparation of erythronic acid. This substance was obtained by the procedure of Falaise and Frognier.[13] The pure acid was recovered from the salt in 90% yield and boiled at 71° at 13 mm.

β-Hydroxy-butyrolactone.—Thirty-five grams of pure vinylacetic acid is added to 90 cc. of water containing 25 g. of barium chlorate and 5 cc. of a 0.2% solution of osmium tetroxide. The temperature is kept below 35° by occasional cooling. After one day, an additional 5 cc. of 0.2% osmium tetroxide solution is added. At the end of the third day, the reaction mixture is subjected to distillation under reduced pressure at a maximum temperature of 50°. The lactone is extracted from the residue with absolute

(11) Falaise and Frognier, *Bull. soc. chim. Belg.*, **42**, 433 (1933).

(12) Falaise and Frognier, *ibid.*, p. 438.

(13) Falaise and Frognier, *ibid.*, p. 436.

alcohol, the solution is filtered free from inorganic material, and subjected to complete distillation under reduced pressure at 40°. The residue is fractionated. The fraction boiling between 135–160° at 2–5 mm. consists chiefly of the hydroxy-lactone. It weighs 14 g. (35%). Fractionation at reduced pressure yields the pure lactone which boils at 145–148° at 2–4 mm.

Preparation of Isocrotonolactone.—Seventy-one grams of phosphorus pentoxide is added, 10 to 20 g. at a time, to a solution of fifty grams of β-hydroxybutyrolactone in 200 cc. of dioxane. The mixture is allowed to stand for an hour (in one experiment the mixture stood overnight without ill effect). The dioxane solution is then decanted into a Claissen flask. The residue is extracted twice with absolute alcohol, the alcohol extracts being added to the dioxane solution. The solvent is removed under reduced pressure (10–15 mm. with water-bath at 70–80°), and the residue is distilled at 7 mm. The boiling range of 22 g. of material obtained in this way was 80–86° (53%).

Anal. Calcd. for $C_4H_4O_2$: H, 4.78; C, 57.1. Found: H, 5.16; C, 57.05.

The lactone was then transformed into DL-erythronic lactone by the procedure of Braun. From 78 g. of the unsaturated lactone of boiling range 82–86° at 7 mm. there was obtained 49 g. of crude DL-erythronic lactone, m. p. 88–90°; a yield of 45%.

Summary

1. New procedures which shorten the time of preparation and increase yields have been devised for the preparation of the following compounds: ethyl γ-bromo-crotonate, ethyl γ-chlorocrotonate, γ-bromo-crotononitrile, β-hydroxy-butyrolactone, and isocrotonolactone.

2. Braun's synthesis of DL-threonic acid has been greatly modified. The over-all yield by the new procedure is 5.3% (calculated from allyl alcohol) as against 2.2% (calculated from glycerol dichlorohydrin) by Braun's procedure.

3. The preparation of β-hydroxy-butyrolactone and isocrotonolactone from vinylacetic acid as reported in this article is a much more dependable process than the procedure in which these substances are made from glycerol monochlorohydrin.

CHICAGO, ILLINOIS RECEIVED JANUARY 26, 1940

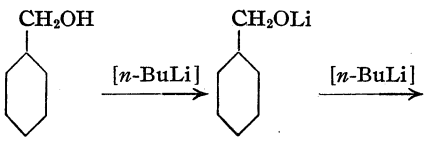
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Metalation of Alcohols and Amines

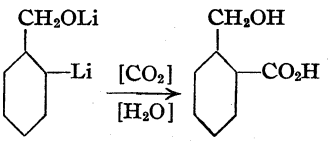
BY HENRY GILMAN, G. E. BROWN, F. J. WEBB AND S. M. SPATZ

Halogen-metal interconversion reactions have been noted in a great variety of reactions, and are of particular interest with polyfunctional compounds.[1] Hydrogen-metal interconversion reactions or metalations are also very common, but because they generally take place at a somewhat slower rate than halogen-metal interconversion reactions there is a greater opportunity for secondary reactions with polyfunctional compounds.

We are now reporting preliminary observations on the metalation of some selected simple alcohols and amines, and will report later on polyfunctional compounds having alcohol and amino groups. Metalation takes place with all the chief types of aromatic alcohols and amines: primary, secondary and tertiary. An illustration is the metalation of benzyl alcohol.



(1) Gilman, "Metalation and Related Interconversion Reactions," Eighth National Organic Chemistry Symposium, St. Louis, Dec. 30, 1939. See also recent papers in THIS JOURNAL on interconversion reactions with organometallic compounds.



In accordance with the general rules postulated for interconversions with organometallic compounds,[1] metalation occurs *ortho* to the group containing the hetero element. The only exception now known is the metalation of dibenzothiophene by phenylcalcium iodide, where metalation takes place in the 3- and not in the 4-position.[2,3]

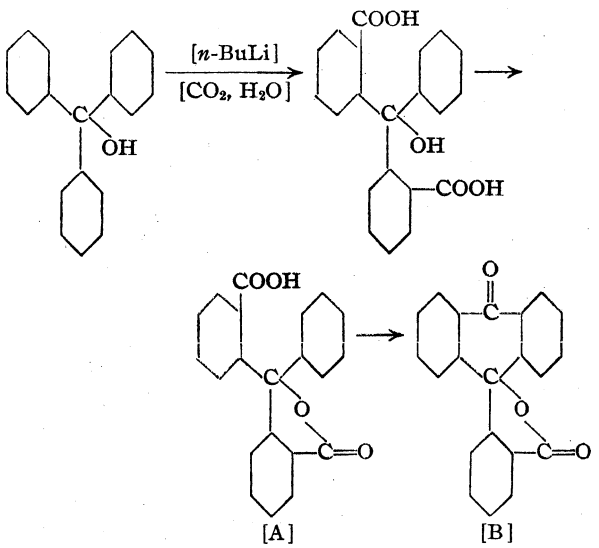
Poly-metalation is to be expected with the more reactive organometallic compounds, and was observed earlier in the dibenzofuran series.[4] It may be stated that, in general, halogen-metal interconversions, hydrogen-metal interconversions as well as the numerous other interconver-

(2) Gilman, Jacoby and Pacevitz, *J. Org. Chem.*, **3**, 120 (1938).

(3) Under generally drastic conditions of high temperature and pressure, Houben and co-workers [*Ber.*, **37**, 3978 (1904); **42**, 3729, 4488, 4815 (1909); **46**, 3833 (1913)] have obtained predominantly *para*-amino acids by interaction of carbon dioxide with the complexes derived from various secondary and tertiary amines with Grignard reagents. Under corresponding conditions they did not isolate acidic material from primary aromatic amines.

(4) Gilman and Young, THIS JOURNAL, **56**, 1415 (1934); **57**, 1121 (1935).

sions involving organometallic compounds can be correlated with the relative reactivities of organometallic compounds.[5] A case of dimetalation is reported now with triphenylcarbinol.



The acid isolated was the lactone of triphenylcarbinol-2,2′-dicarboxylic acid [A], which was characterized by dehydration to the oxanthrone [B]. It is of interest that this dimetalation took place with a quantity of *n*-butyllithium sufficient to react with but one of the three phenyl groups in triphenylcarbinol.

Metalation is probably one of the oldest reactions in organic chemistry. Davy[6] in 1837, incidental to attempts to obtain improved yields of his newly discovered potassium, fused potassium tartrate with carbon and obtained a highly reactive substance which yielded acetylene when treated with water. It is quite likely that an ethynylpotassium was formed as an intermediate. The halogen-metal interconversion reaction is also quite old, and an early reference is the work of Kalle on the reaction between benzenesulfonyl chloride and diethylzinc to yield zinc benzenesulfinate and ethyl chloride.[7]

Experimental Part

Benzyl Alcohol.—A solution of 10.8 g. (0.1 mole) of benzyl alcohol was added dropwise to a cold, stirred solution of approximately 0.2 mole of *n*-butyllithium in 400 cc. of ether. After refluxing for forty-two hours, the mixture was carbonated by pouring jet-wise on crushed carbon dioxide; acidified with iced dilute hydrochloric acid; and extracted with ether. Extraction of the ether layer with sodium bicarbonate solution, followed by acidification, yielded 1.5 g. of a yellow solid melting in the range 65–115°. This was evidently a mixture of phthalide[8] and *o*-carboxybenzyl alcohol[8] since heating with sodium hydroxide solution and then acidification gave 1.3 g. of *o*-carboxybenzyl alcohol, m. p. 120.5–121.5°, in a yield of 8.7%, or 21.5% based on the benzyl alcohol which had reacted.

Anal. Calcd. for $C_8H_8O_3$: neut. equiv., 152. Found: neut. equiv., 150.4.

On resolidification, the compound melted at 73–74°, showing the conversion to phthalide. Oxidation with alkaline permanganate gave phthalic acid which was identified by comparison with an authentic specimen.

From the neutral fraction there was recovered 6.5 g. or 60% of benzyl alcohol.

Benzyl Methyl Ether.—An orienting experiment showed that ethers of alcohols can also be metalated. A diethyl ether solution of 0.1 mole *n*-butyllithium and 12.2 g. (0.1 mole) of benzyl methyl ether was refluxed for twenty hours, then carbonated and worked up in a customary manner. The acid obtained, probably *o*-carboxybenzyl methyl ether, melted at 94–95° after recrystallization from petroleum ether (b. p., 60–68°).

Anal. Calcd. for $C_9H_{10}O_3$: neut. equiv., 166. Found: neut. equiv., 166.

Benzohydrol.—The usual initial vigorous reaction (due to replacement of active hydrogen by lithium) took place when 0.1 mole of *n*-butyllithium was filtered into an ether solution of 9.2 g. (0.05 mole) of benzohydrol. Ether was added to bring the total volume to 250 cc. The solution gradually turned brownish-red and after several hours became deep red. After refluxing for forty-six hours carbonation was effected by solid carbon dioxide. The yield of 2-phenylphthalide[9] (formed by lactonization of the *o*-carboxybenzohydrol) was 1.95 g. or 18.6%. This product melted at 114.5°, and was oxidized by alkaline potassium permanganate to *o*-benzoylbenzoic acid[9] (m. p., 126.5°).

Triphenylcarbinol.—The suspension resulting from mixing 13 g. (0.05 mole) of triphenylcarbinol with slightly more than 0.1 mole of *n*-butyllithium was stirred, and refluxed for forty-eight hours prior to carbonation. The alkaline extract of the hydrolyzate yielded 1.2 g. of a product melting at 187–215°. Recrystallizations from acetic acid raised the melting point to 240°.

Inasmuch as a first experiment with triphenylcarbinol gave no acid, the reaction was repeated using 0.5 g. of copper bronze as a catalyst. It was shown earlier that various catalysts can be used to retard and accelerate organometallic reactions.[10] The catalyst not only improved the yield (to 2.3 g.), but also gave a purer acid. It is now known that the interconversion reactions are affected not only by catalysts, but also by solvents, concentration of reactants, time and temperature. Apropos the first negative experiment with triphenylcarbinol, it should be recalled that the formation of organolithium

(5) See pp. 435–439 in Gilman, "Organic Chemistry," John Wiley and Sons, New York, N. Y., 1938.
(6) Davy, *Ann.*, **23**, 144 (1837).
(7) Kalle, *ibid.*, **119**, 153 (1861).
(8) Hessert, *Ber.*, **10**, 1445 (1877).
(9) Rotering and Zincke, *ibid.*, **9**, 631 (1876).
(10) Gilman, St. John, St. John and Lichtenwalter, *Rec. trav. chim.*, **55**, 577 (1936).

compounds is a little more erratic[11] than that of the corresponding Grignard reagents, and that one advantage to the use of carbonation in these preliminary studies is to get the extra check afforded by the odor of *n*-valeric acid formed by carbonation of the slight excess of *n*-butyllithium.

The acid melting at 240° was shown to be the lactone of triphenylcarbinol-2,2′-dicarboxylic acid,[12] and was characterized by conversion to 9-phenyl-9-hydroxanthr-10-one-2′-carboxylic acid lactone[12] melting at 234°. The yield of pure lactone-acid was 0.8 g. or 4.85%; or 52.5% if allowance be made for the recovery of 11.8 g. of triphenylcarbinol.

Aniline.—A mixture of 4.6 g. (0.05 mole) of aniline and slightly more than 0.15 mole of *n*-butyllithium was refluxed for fifty hours and then carbonated to yield 4.2% of anthranilic acid. Characterization was completed by diazotization and coupling with β-naphthol to the red 1-(*o*-carboxyphenylazo)-2-naphthol melting at 271°, using the method of mixed melting points with an authentic specimen.[13] There was recovered 2.9 g. of aniline, and the yield of anthranilic acid on the basis of aniline not recovered is 13.7%.

The larger than usual excess of *n*-butyllithium was used here to take care, if necessary, of the two active hydrogens attached to the nitrogen. It is quite likely that experiments now in progress will reveal the possibility of first replacing such hydrogens by metals other than lithium or by the use of organometallic compounds other than those of lithium.

Diphenylamine.—An ether solution of 13.5 g. (0.08 mole) of diphenylamine and 0.16 mole of *n*-butyllithium was stirred and refluxed for eighteen hours. Carbonation, followed by hydrolysis, yielded 1.85 g. or 10.9% of N-phenylanthranilic[14] acid melting at 182°. Recrystallization from a hot methanol–water mixture gave 1.45 g. or an 8.5% yield of the pure compound melting at 183.5°. The yield of N-phenylanthranilic acid based on the quantity of diphenylamine actually reacting was 30.3%.

In a second experiment the yield was somewhat improved by a longer period of refluxing. When the reactants were refluxed for twenty-four hours, the yield was 14.7%, or 38.2% based on the diphenylamine actually reacting.

N-*n*-Butylaniline.—Fifteen grams (0.1 mole) of freshly distilled N-*n*-butylaniline was heated for twenty hours with a slight excess over two equivalents of *n*-butyllithium in 275 cc. of ether. Subsequent to carbonation and hydrolysis, there was isolated a 2% yield of N-*n*-butylanthranilic acid.

N-*n*-Butylanthranilic Acid.—A solution prepared from 10 g. (0.073 mole) of anthranilic acid and 5 g. of potassium carbonate was refluxed for sixteen hours with 10 g. (0.073 mole) of *n*-butyl bromide. After cooling, the precipitate was dissolved in potassium hydroxide, and the oily material extracted with benzene. Neutralization of the alkaline layer precipitated the N-*n*-butylanthranilic acid which after crystallization from dilute methanol melted at 80–81° and weighed 6.4 g.

Anal. Calcd. for $C_{11}H_{15}O_2N$: N, 7.25. Found: N, 7.36.

A mixed melting point with the acid isolated from the metalation of N-*n*-butylaniline showed no depression.

Triphenylamine.—A reaction mixture of 12.25 g. (0.05 mole) of triphenylamine, 0.1 mole of *n*-butyllithium and 0.5 g. of copper bronze was stirred and refluxed for forty-five hours prior to carbonation. The yield of acidic material was 2.16 g. In addition, 9.6 g. or 78.5% of the triphenylamine was recovered. The mixture of acids has not as yet been resolved.

Piperidine.—An ether solution of 17 g. (0.2 mole) of piperidine and 0.42 mole of *n*-butyllithium was refluxed for twenty hours. On working up by customary procedures, subsequent to carbonation, there was obtained 21.6 g. or an 89% yield of piperidine hydrochloride in addition to a small quantity of an as yet unidentified oil. It is quite likely that more reactive organometallic compounds can effect such secondary reactions on piperidine as dehydrogenation[15] and cleavage.

Acknowledgment.—The authors are grateful to F. W. Moore and W. Harber for assistance.

Summary

It is shown that *n*-butyllithium metalates some typical primary, secondary and tertiary aromatic amines and some typical primary, secondary and tertiary aromatic alcohols.

AMES, IOWA RECEIVED JANUARY 29, 1940

(11) Gilman, Zoellner and Selby, THIS JOURNAL, **55**, 1252 (1933).

(12) Scholl and Donat, *Ann.*, **512**, 24 (1934); Cook, *J. Chem. Soc.*, 65 (1928).

(13) Anschütz and Schmidt, *Ber.*, **35**, 3469 (1902).

(14) N-Phenylanthranilic acid was characterized by conversion to N,N-diphenylanthranilic acid in accordance with the directions of Goldberg and Nimerovsky, *ibid.*, **40**, 2448 (1907).

(15) Gilman and Bradley, THIS JOURNAL, **60**, 2333 (1938).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Triphenylgallium[1]

BY HENRY GILMAN AND R. G. JONES

Trimethylgallium and triethylgallium have been examined in recent years,[2] but nothing is known of their behavior with a simple organic functional group like carbonyl. For purposes of comparison with other phenyl-metallic compounds, we have prepared triphenylgallium in adequate quantities from the expensive metal to permit examination of sufficient reactions to warrant broad correlations with related organometallic compounds. Triphenylgallium (m. p. 166°) is conveniently prepared in satisfactory yields (82%) by interaction of diphenylmercury with gallium.

The expected reaction with benzaldehyde was observed: namely, formation of benzohydrol. Inasmuch as H. D. Gooch[3] has shown that, in general, benzalacetophenone has a reactivity close to that of benzaldehyde and acetophenone, reaction was expected with the conjugated system in benzalacetophenone. 1,4-Addition did take place, and an 85% yield of β,β-diphenylpropiophenone resulted. There was no evidence of 1,2-addition, and this finding is in accordance with the generalization[4] that only extremely reactive RM compounds add 1,2; that moderately reactive RM compounds add 1,4; and that RM compounds of intermediate reactivity, like phenyllithium, add both 1,2 and 1,4.

Series of Relative Reactivities of Functional Groups.—On the basis of the series of relative reactivities of functional groups prepared by Entemann and Johnson[5] from their studies with phenylmagnesium bromide, benzonitrile is quite low in reactivity. Accordingly, it was not surprising to find that benzonitrile did not react with triphenylgallium under the selected conditions. Inasmuch as groups like the azo and anil linkages are of lesser activity than the nitrile group, reactions were not attempted with compounds like azobenzene and benzophenone-anil.

Again,[3] an inconsistency was observed with benzoyl chloride and benzophenone. Both of these compounds are of approximately equal reactivity with phenylmagnesium bromide. However, with triphenylgallium only benzoyl chloride and not benzophenone reacted under customary conditions. These results together with others[3,6] reported recently demonstrate rather conclusively that the order of reactivity of benzophenone and benzoyl halides with RM compounds that are less reactive than Grignard reagents is unlike the order established with phenylmagnesium bromide. Under unusual conditions, a liberal excess of triphenylgallium and extensive refluxing in xylene, reaction did take place with benzophenone, but the product isolated in 35% yield was triphenylmethane. Benzyl chloride and triphenylgallium gave undoubtedly diphenylmethane, for the oil resulting yielded benzophenone on oxidation.

Color Test.—The most surprising result was the absence of a color test[7] under usual conditions inasmuch as a color test has always been noted with those organometallic compounds sufficiently reactive to add to the carbonyl group in benzaldehyde and to the conjugated system in benzalacetophenone. Undoubtedly, the absence of a color test under customary conditions is associated in part with the pronounced tendency of gallium compounds to form coördinate linkages. For example, Dennis and Patnode[2a] have shown that the simple triethylgallium reacts violently with water, the etherate vigorously, and the ammine only very slowly. It is quite probable that the dimethylamino groups in the Michler ketone used in the color test may have tied up some of the triphenylgallium in the form of the less reactive ammine. Also, the carbonyl group in Michler ketone and in benzophenone may have participated in the formation of coördinate complexes. In any event, a color test was obtained by heating with an excess of triphenylgallium in benzene for about fifteen minutes. It is significant that the color tests were much weaker than those observed with triphenylthallium,[3] which is less prone to form coördinate linkages.

(1) Paper XXIX in the series of "Relative Reactivities of Organometallic Compounds." The preceding paper, XXVIII, is THIS JOURNAL, **62**, 344 (1940).

(2) (a) Dennis and Patnode, THIS JOURNAL, **54**, 182 (1932). (b) Renwanz, *Ber.*, **65B**, 1308 (1932). (c) Kraus and Toonder, *Proc. Natl. Acad. Sci. U. S.*, **19**, 292, 298 (1933) [*C. A.*, **27**, 2646 (1933)]; THIS JOURNAL, **55**, 3547 (1933).

(3) Gilman and Jones, *ibid.*, **61**, 1513 (1939).

(4) Studies by R. H. Kirby; see p. 89 of paper by Gilman and Bailie, *J. Org. Chem.*, **2**, 84 (1937).

(5) Entemann and Johnson, THIS JOURNAL, **55**, 2900 (1933).

(6) Gilman and Nelson, *ibid.*, **61**, 743 (1939).

(7) Gilman and Schulze, *ibid.*, **47**, 2002 (1925).

Relative Reactivities of Triphenylgallium and Triphenylthallium.—In preceding studies on the relative reactivities of organometallic compounds, the color test has been found most convenient. The necessity of using an excess of triphenylgallium for a color test precluded its use in a comparison with triphenylthallium. However, the relative reactivities of these two R_3M compounds was established by an indirect procedure involving benzaldehyde, which reacts with each of them. Under parallel conditions, a solution of known concentration of benzaldehyde was added separately to each of the R_3M compounds, and the periodic removal of samples on which tests were made for benzaldehyde showed that triphenylgallium is more reactive than triphenylthallium. The rate studies were carried out at room temperature to avoid the thermal conversion noted earlier[3] of triphenylthallium to the highly reactive phenylthallium.

The 79% yield of benzophenone based on interaction of one mole of triphenylgallium with three moles of benzoyl chloride shows that with some reactants all three phenyl groups are available. With triphenylthallium, only one R group enters into reaction and an invariable product is a diphenylthallium salt.

Experimental Part

Preparation of Triphenylgallium.—A mixture of 1 g. (0.0143 g. atom) of gallium metal and 5.45 g. (0.0153 mole) of diphenylmercury was heated in a Schlenk tube which had been thoroughly flushed out with nitrogen. Heating was effected at 130° in an oven, and after fifty hours the molten diphenylmercury had given place to a white crystalline mass. The tube was opened under nitrogen and 10 cc. of dry chloroform was added. After warming the chloroform to dissolve all of the solid, the solution was filtered and then subjected to distillation (under nitrogen) until crystals began to appear in the hot solution, about 4 cc. of which remained. The mass of shiny needle-like crystals which separated on cooling were filtered off on a sintered glass plate, and washed with petroleum ether (b. p. 65–68°). The product was redissolved in 3 cc. of hot chloroform, and the crystals which separated on cooling were again filtered, washed with petroleum ether, and dried under nitrogen. The triphenylgallium (1.85 g.) melted at 166°; the clear colorless melt quickly solidified on cooling and remelted at the same temperature.

Anal.[8] Calcd. for $C_{18}H_{15}Ga$: Ga, 23.18. Found: Ga, 23.27 and 23.38.

Better yields of triphenylgallium were obtained when the theoretically required quantities of gallium and diphenylmercury were used. Thus, from 1.92 g. (0.0275 g. atom) of gallium and 14.5 g. (0.0405 mole) of diphenylmercury, heated at 130° for seventy-five hours, 6.68 g. or an 82% yield was obtained of triphenylgallium which melted at 165–166° without recrystallization.

On short exposure, dry air appeared to have little effect on triphenylgallium. However, in the presence of any moisture the compound quickly decomposed, and one of the products was benzene. Complete solution of triphenylgallium in warm dilute sulfuric acid, incidental to analysis, required about twenty-four hours.

Benzaldehyde.—A solution of 0.83 g. (0.00277 mole) of triphenylgallium and 0.294 g. (0.00277 mole) of benzaldehyde in 20 cc. of benzene was refluxed for ten hours. After hydrolysis with 25 cc. of 2 *N* hydrochloric acid, the benzene layer was separated and washed with 40% sodium bisulfite solution. Removal of the benzene by distillation left an oil which crystallized on cooling to give a 70% yield of benzohydrol, melting at 65-66° after two crystallizations from petroleum ether (b. p. 60–68°). Identification was completed, as was done by all solids described in this paper, by the method of mixed melting points with an authentic specimen.

Benzalacetophenone.—A solution of 1.1 g. (0.00365 mole) of triphenylgallium and 0.76 g. (0.00365 mole) of benzalacetophenone in 20 cc. of benzene was refluxed for eight and one-half hours. Subsequent to hydrolysis by hydrochloric acid and then working up by customary procedures there was obtained 0.88 g. or an 85% yield of β,β-diphenylpropiophenone.

Benzoyl Chloride.—A solution of 1.44 g. (0.00478 mole) of triphenylgallium and 2.01 g. (0.0143 mole) of benzoyl chloride in 25 cc. of benzene was refluxed (under nitrogen, as usual) for eleven hours. The yield of benzophenone was 2.05 g. or 79%.

In another experiment, a mixture of 1.06 g. (0.0035 mole) of triphenylgallium suspended in 25 cc. of petroleum ether (b. p. 65–68°) containing 1.47 g. (0.0105 mole) of benzoyl chloride was heated for nine hours. The ketone was isolated in this case as benzophenone oxime, the yield of which was 1.4 g. or 68.4%.

It is interesting to note that generally satisfactory yields of ketones are obtainable from organometallic compounds of group III metals in their reactions with acid halides and acid anhydrides. This applies in a noteworthy extent to the organoaluminum halides. In most of these reactions of ketone formation, the acid anhydrides are superior to acid halides, both with RM compounds in group III and RM compounds like those of cadmium in group II.

Benzophenone.—After refluxing for twenty-four hours a solution of 1.00 g. (0.0033 mole) of triphenylgallium and 1.82 g. (0.01 mole) of benzophenone in 20 cc. of xylene, 94.5% of the benzophenone was recovered as the oxime, and no triphenylcarbinol was isolated. The experiment was repeated with xylene as the solvent, and also with benzene as the solvent. In the latter case, 95.5% of the benzophenone was recovered as the oxime.

An additional experiment was carried out with an excess of triphenylgallium. A solution of 1.51 g. (0.0050 mole) of triphenylgallium and 0.3 g. (0.00167 mole) of benzophenone in 15 cc. of xylene was refluxed for twenty-

(8) The analytical procedure was that used by Dennis and Bridgman, THIS JOURNAL, **40**, 1546 (1918).

four hours. A small quantity of white amorphous precipitate formed. After cooling, the reaction mixture was shaken with 25 cc. of dilute hydrochloric acid and 25 cc. of benzene. The aqueous layer was separated and the benzene–xylene layer was washed with dilute hydrochloric acid and then with water. The residue from the organic extract was subjected to steam distillation subsequent to removal of the solvents. The steam distillate yielded an oil which partially solidified on standing, and when crystallized from a mixture of 1 cc. of 95% ethanol and 1 cc. of petroleum ether (b. p. 60–68°) gave a 35% yield of triphenylmethane.[9]

Benzyl Chloride.—To a suspension of 1.36 g. (0.0045 mole) of triphenylgallium in 25 cc. unsaturate-free petroleum ether (b. p. 65–68°) contained in a conventional three-necked flask provided with a mechanical stirrer, was added slowly a solution of 1.71 g. (0.0135 mole) of benzyl chloride in 25 cc. of petroleum ether. There was no evidence of reaction until about one-third of the benzyl chloride solution had been added, when suddenly a large quantity of red, tarry precipitate appeared accompanied by some heat of reaction. Subsequent to hydrolysis, the oily residue remaining after removal of the organic solvents was oxidized by potassium dichromate and sulfuric acid to give 0.1 g. or a 9% yield of benzophenone, isolated and characterized as the oxime.

Color Test.—In preliminary tests, about 0.05 g. of solid triphenylgallium was added to about 1 cc. portions of benzene containing Michler ketone. Both saturated and 1% Michler ketone solutions were used. In every case the test was negative, even when the mixtures were heated at 70° out of contact with air or moisture for as long as two and one-half hours prior to hydrolysis.

A mixture of 0.57 g. (0.0019 mole) of solid triphenylgallium and 0.1 g. (0.00038 mole) of solid Michler ketone was placed in a flask containing nitrogen. Next 12.5 cc. of dry benzene was added, the time noted, and 1-cc. samples were removed periodically and tested by hydrolyzing and adding the acetic acid–iodine solution.[7] The test was negative after four hours at room temperature. The mixture was then heated on the water-bath at 65–75°, and after one hour a 1-cc. sample gave a good color test.

The experiment was repeated using 0.43 g. (0.00143 mole) of triphenylgallium, 0.13 g. (0.00048 mole) of Michler ketone and 16 cc. of benzene. The solution was heated immediately on the water-bath at 70°. A faint positive test was obtained in fifteen minutes; a better test in thirty minutes; and a good test in one hour. In all cases, the colors given in triphenylgallium tests were weaker than the color of a positive test for triphenylthallium.

Relative Reactivities of Triphenylgallium and Triphenylthallium.—In parallel experiments, a solution was prepared by mixing quickly benzaldehyde and R_3M compound in benzene, so that the initial concentration of benzaldehyde was 0.16 molar and that of R_3M was 0.20 molar. The solution was stirred constantly at room temperature, and at regular intervals 1-cc. samples were withdrawn and tested for benzaldehyde.[10] The end-point of the reaction was taken when three samples (removed within a period of ten minutes) no longer gave positive tests for benzaldehyde. The times in two experiments with triphenylgallium were eleven and fourteen hours; and the times in corresponding experiments with triphenylthallium were forty and fifty hours.

Summary

Triphenylgallium (m. p. 166°), prepared from gallium and diphenylmercury, reacts normally with benzaldehyde, benzalacetophenone and benzoyl chloride. Because of the probable formation of coördinate compounds with Michler ketone and benzophenone, there is no color test and no reaction with benzophenone under customary conditions. Extended heating with an excess of triphenylgallium gives a color test with Michler ketone, and benzophenone reacts to give triphenylmethane. Rate studies with benzaldehyde show triphenylgallium to be more reactive than triphenylthallium.

AMES, IOWA RECEIVED JANUARY 29, 1940

(9) Schorigin, *Ber.*, **41**, 2723 (1908), obtained triphenylmethane from a reaction between phenylsodium and carbon dioxide.

(10) Barlet and Vandier, *Ann. chim. anal. chim. appl.*, **1**, 325 (1896), [*Chem. Zentr.*, **68**, II, 226 (1897)].

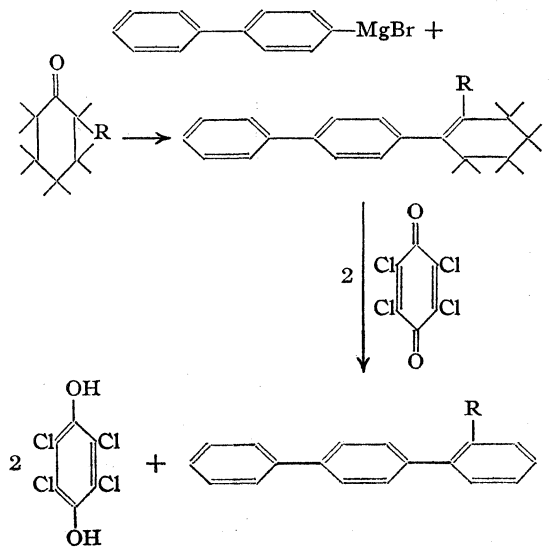
NOTES

Low Temperature Dehydrogenations. II

By Richard T. Arnold, Clair Collins and Wm. Zenk

In an introductory report[1] it was shown that several different types of hydroaromatic compounds can be dehydrogenated at comparatively low temperatures by making use of chloranil or other quinones with high oxidation potentials.

This method has now been extended to reactions leading to the preparation of unsymmetrical biphenyl, terphenyls, etc., according to the scheme



Of course, the synthesis of substituted cylohexenes in the first step here is limited to those molecules which do not have groupings present which will react rapidly with the Grignard reagent. However, these groups (—NO_2, etc.) are not affected in the dehydrogenation reaction with chloranil as they are when sulfur or selenium is used.

A convenient and cheap synthesis of chloranil has been described[2] and confirmed in this Laboratory. It makes use of the action of concentrated hydrochloric acid on benzoquinone in the presence of hydrogen peroxide (30%). This preparation practically eliminates the cost of these dehydrogenations, especially when it is realized that three-fourths of the hydroquinone which results can be recovered and converted quantitatively to the quinone by nitric acid.

(1) Arnold and Collins, This Journal, **61**, 140 (1939).
(2) M. Gallatti, *Ann. chim. applicata*, **22**, 602 (1932).

It has been demonstrated recently[3] that sulfur can be used to prepare certain unsymmetrical biphenyls in satisfactory yields, but in the terphenyl and phenylnaphthalene series the classical dehydrogenations are disappointing.[4,5] The procedure described in this paper gives very satisfactory yields (50–70%) in all of these cases.

Thermal rearrangements have been found to be commonplace in alkyl and arylnaphthalenes in the region of 300.[6] The use of low temperature dehydrogenation here is obvious.

Recently, the classical synthesis of terphenyls by the reaction between nitrosoamines and hydrocarbons has been extended to new cases and the conditions of the synthesis greatly improved.[7] While this method is very general, the yields reported are not comparable with those obtained in our investigations. The results obtained are summarized in Table I.

Table I

Compound	Product	Yield, %
1-*p*-Biphenylcyclohexene	Terphenyl	47
1-*p*-Biphenyl-2-methylcyclohexene	2-Methylterphenyl	72
1-α-Naphthylcyclohexene	α-Phenylnaphthalene	67
1-β-Naphthylcyclohexene	β-Phenylnaphthalene	72
1-*o*-Tolylcyclohexene	2-Methylbiphenyl	72

At present we are investigating the efficacy of chloranil as a dehydrogenating agent for straight chain hydrocarbons.

Experimental

1-*p*-Biphenyl-2-methylcyclohexene.—Ninety-five cubic centimeters of a Grignard solution (prepared from 100 g. of 4-bromobiphenyl, in 500 cc. of ether) was treated with 12 cc. of 2-methylcyclohexanone in an equal volume of benzene. The reaction mixture was decomposed with dilute sulfuric acid. Dehydration was accomplished by heating for one hour with 20% oxalic acid. The benzene layer was fractionated and the residue distilled in a sausage flask; yield 6.75 g.

2-Methylterphenyl.—A solution containing 3.58 g. of the above cyclohexene derivative, 7.3 g. of chloranil and 25 cc. of commercial xylene was refluxed for ten hours, cooled, and filtered, giving 4.55 g. of chloranilhydroquinone. The filtrate was diluted with an equal quantity of ether,

(3) Sherwood, Short and Stansfield, *J. Chem. Soc.*, 1832 (1932).
(4) Von Braun, Irmisch and Nelles, *Ber.*, **66**, 1472 (1933).
(5) Fieser and Hershberg, This Journal, **60**, 940 (1938).
(6) Mayer and Schiffner, *Ber.*, **67**, 67 (1934).
(7) France, Heilbron and Hey, *J. Chem. Soc.*, 1283 (1939).

washed with dilute alkali, dried, and fractionated. The residue was distilled in a small sausage flask and yielded 2.53 g. of the methylterphenyl which melted at 91–92° after recrystallization from methanol.[7]

Anal. Calcd. for $C_{19}H_{16}$: C, 93.34; H, 6.60. Found: C, 92.97; H, 6.58.

Terphenyl.—A sample (1.46 g.) of *p*-biphenylcyclohexene, 3.3 g. of chloranil and 18 cc. of dry xylene were refluxed and the reaction worked up as described in the preceding section; yield of terphenyl 0.63 g. The product melted at 210–211.5°. The identity of the substance was checked by preparing the nitro derivative; melting point 275°.[7]

α-Phenylnaphthalene.—Five grams of α-naphthylcyclohexene prepared as described in the literature[8] was refluxed with 11.8 g. of chloranil in 20 cc. of xylene for five hours. The reaction mixture was cooled, diluted with an equal volume of petroleum ether (30–60°) and filtered, yielding 8.4 g. of chloranil hydroquinone. The remainder was removed by basic extraction. The resulting fractionation yielded 3.33 g. of α-phenylnaphthalene. The structure was checked by the formation of its nitro derivative which melted at 129–130°. The literature reports 132°.[8]

β-Phenylnaphthalene.[5]—Following the same procedure as given above, β-naphthylcyclohexene was dehydrogenated to give β-phenylnaphthalene in a yield of 72%. The constitution of this molecule was proved by direct oxidation to β-phenyl 1,4-naphthoquinone; melting point 108–109°.[9]

2-Methylbiphenyl.—This substance was obtained by refluxing a solution containing 12 g. of *o*-tolylcyclohexene, 36 g. of chloranil, and 115 cc. of xylene. The yield of pure product obtained by fractionation was 8.5 g. (72.6%).[3]

(8) Weiss and Waidich, *Monatsh.*, **46**, 456 (1925).
(9) Chattaway and Lewis, *J. Chem. Soc.*, **65**, 873 (1894).

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Catalytic Action of 8-Hydroxyquinoline on the Oxidation of *p*-Phenylenediamine

BY FREDERICK BERNHEIM AND PHILIP HANDLER[1]

8-Hydroxyquinoline can, under certain conditions, catalyze the oxidation of cysteine to cystine.[2] It has now been shown that it has a catalytic effect on the oxidation of *p*-phenylenediamine and certain related substances. Figure 1 shows this effect on *p*-phenylenediamine recrystallized from water and from alcohol. The oxygen uptake was measured at 37° in the Warburg apparatus. Successive recrystallizations of the diamine have no effect on the catalysis, showing that the 8-hydroxyquinoline is not simply removing an antioxidant. Addition of metal ions such as the cupric, ferric and vanadate does not enhance the catalytic effect which is, therefore, probably not due to a metal-8-hydroxyquinoline complex. The catalysis is not affected by 0.02 *M* cyanide or pyrophosphate. It has an optimum *p*H at about 6.5 and the rate falls off rapidly in alkaline solutions. The oxidation product is deeply colored, which is characteristic of the polymer of the quinone diamine and which can be reduced by hydrosulfite. On isolation and hydrolysis with acid it gives free ammonia. From the oxygen uptake figures a small percentage of further oxidation products must be formed which have not been isolated.

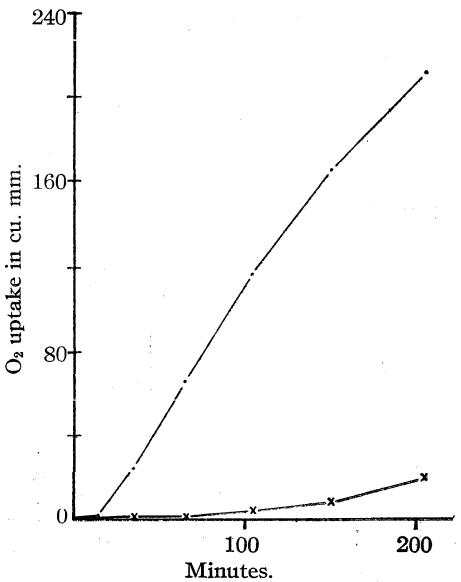

Fig. 1.—The oxygen uptake of 3.0 mg. of *p*-phenylenediamine in 2.0 cc. of water at *p*H 6.7: ×—×, control; ·—·, with 0.05 mg. of 8-hydroxyquinoline. The short latent period is characteristic.

8-Hydroxyquinoline has no effect on the oxidation of *o*-phenylenediamine, catechol or hydroquinone in acid or alkaline solutions. It has a comparatively small effect on the oxidation of *p*- and *o*-aminophenols in alkaline solutions (*p*H 7.8). 2-Hydroxyquinoline and certain other quinoline derivatives are without catalytic action.

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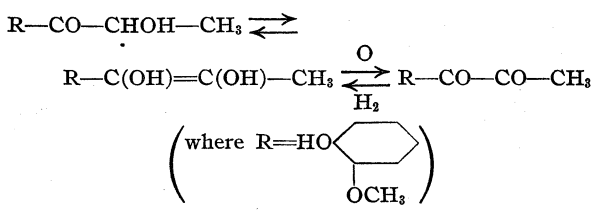
(1) One of us (P. H.) is indebted to the Markle Foundation for its support during this work.
(2) F. Bernheim and M. L. C. Bernheim, "Symposia on Quantitative Biology," Vol. VII, 1939, in press.

The Mechanism of Plant Respiration

BY HAROLD HIBBERT

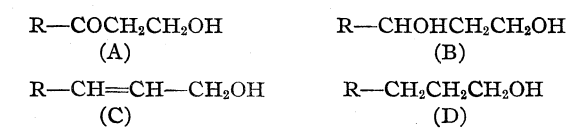
The discovery (see following note) in the ethanolysis products from spruce wood of methyl guaiacyl diketone alongside the previously re-

ported α-hydroxypropiovanillone[1] raises a question of considerable biochemical significance. The latter product, in its ene–diol form, is evidently the "donator" in a new oxidation–reduction system, the newly discovered diketone being the "acceptor."



Such a system with its presumptive accompanying dioxypropylene guaiacolase is thus closely related to the ene–diol catechol, –ascorbic acid and –dioxymaleic acid systems shown recently by Szent-Györgyi and co-workers[2] to form an integral part of the cycle of changes involved in plant (and presumably animal) respiration. The wide occurrence of this new oxidation–reduction system in various forms of higher plant life[1,3] and the fact that both methyl guaiacyl diketone and α-hydroxypropiovanillone apparently are derived from methyl glyoxal provide additional support for the author's theory of plant synthesis[4] in which this intermediate of carbohydrate metabolism appears to play such an extraordinarily important role.

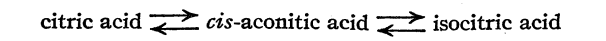
In the suggested new system of plant respiration the roles of oxalacetic, malic, fumaric, and succinic acids are taken by (A), (B), (C) and (D), respectively



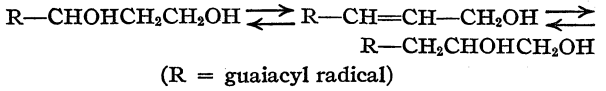
(R = guaiacyl radical)

Of these, coniferyl alcohol (C) is known to be a very widely distributed plant product.

It may also be pointed out that in this new conception the important biological system[5] known to function in intermediary metabolism



has its counterpart in that of

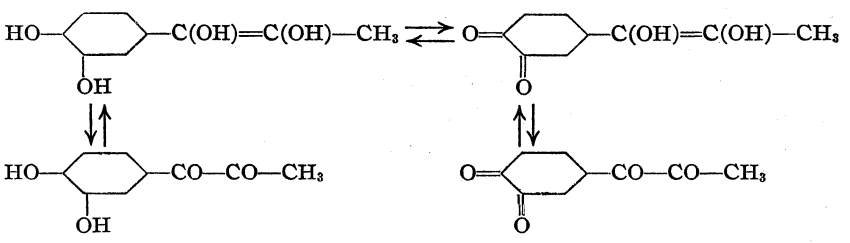


(R = guaiacyl radical)

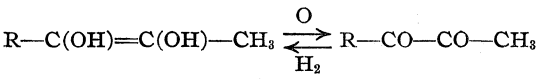
these last three products having a close biochemical relationship to the above ene–diol form.

Obviously the same considerations apply to the case of the corresponding syringyl compounds obtained in the ethanolysis of hard woods.[3]

Since in the early stages of plant growth the phenolic substances present are unmethoxylated, presumably the above new oxidation–reduction mechanism is represented there by a *di*-ene–diol system



in which not only the catechol ⇄ orthoquinone portion can function, but also the side chain grouping, as indicated by the changes



Such a combination is quite unique in cell oxidation systems and presumably is intimately related to the very much slower rate of reduction–oxidation changes involved in plant, as contrasted with animal, cell respiration.

It seems very probable that the above oxidation–reduction phenomena are intimately associated with (a) the very marked change in color taking place when chlorine and other oxidizing agents are brought into contact with unbleached pulps, and (b) the discoloration of newsprint and other papers in the presence of light and air.

Experiments with this new system on plant and animal tissues are to be undertaken and a full discussion of the subject is to appear in a forthcoming publication wherein the role of the ene–diol oxidation–reduction system as the almost certain forerunner of lignin synthesis is to be discussed comprehensively.

(1) Cramer, Hunter and Hibbert, THIS JOURNAL, **61**, 509 (1939).
(2) For review see *Ber.*, **72**, 53 (1939).
(3) (a) Hunter, Cramer and Hibbert, THIS JOURNAL, **61**, 516 (1939); (b) Brickman, Pyle and Hibbert, *ibid.*, **61**, 523 (1939).
(4) Hibbert, *ibid.*, **61**, 725 (1939).
(5) Martius and Knoop, *Z. physiol. Chem.*, **242**, 1 (1936); Martius, *ibid.*, **247**, 104 (1937); **257**, 29 (1938); Krebs and Johnson, *Enzymologia*, **4**, 148 (1937); Johnson, *Biochem. J.*, **33**, 1046 (1939).

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RECEIVED JANUARY 11, 1940

Structure of the Ethanolysis Products from Spruce and Maple Wood

BY LEO BRICKMAN, J. J. PYLE, W. L. HAWKINS AND HAROLD HIBBERT

A re-investigation of the "aldehyde fraction" obtained in the ethanolysis of maple and spruce wood[1] has shown that two of the constituents previously identified (incorrectly) as syringoyl- and vanilloyl-acetaldehydes are, in reality, 1,2-diketones, namely, the benzil derivatives, methyl-4-hydroxy-3,5-dimethoxyphenyl diketone (C_6H_3-(OH)$(OCH_3)_2$-CO-CO-CH_3) (A) and methyl guaiacyl diketone (C_6H_2(OH)(OCH_3)-CO-CO-CH_3) (B), respectively. Proof of this has been found in the synthesis of the benzils by oxidation of the corresponding benzoins, namely, α-hydroxypropiovanillone and α-hydroxypropiosyringone, by means of copper sulfate and pyridine. The monosemicarbazone of (A) melts at 213° and its disemicarbazone at 240°, while the mono-2,4-dinitrophenylhydrazone of (B) melts at 226–227° and its monosemicarbazone at 214–215°. No depression in melting point was found on admixture with the corresponding products isolated from the ethanolysis products.

The mistake in identity arose as a result of the aldehyde-like properties possessed by these 1,2-diketones.

A full account of the supporting chemical evidence is to be given in a forthcoming publication.

(1) Pyle, Brickman and Hibbert, THIS JOURNAL, **61**, 2198 (1939).

DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY
MCGILL UNIVERSITY
MONTREAL, CANADA RECEIVED JANUARY 11, 1940

Purification of High Molecular Weight Fatty Esters

BY LORAN O. BUXTON AND ROLAND KAPP

In the course of our research it became necessary to prepare relatively large quantities of substantially acid-free high molecular weight fatty esters. We have found that the following process is more satisfactory for removing substantially all of the unreacted fatty acids than the usual methods.

The procedure most suitable is as follows. The unreacted alcohol is distilled from the esterification mass, and the residual mixture of free fatty acids, crude ester, and catalyst is dissolved in 2 to 5 parts by weight of a solvent such as ethylene dichloride to 1 part of ester. A convenient sample (10 to 20 g.) of the solvent solution of the crude ester is dissolved in an alcohol–ether mixture, and titrated with standard 0.5 *N* alcoholic potassium hydroxide. On the basis of this titration value an equivalent weight of concentrated aqueous potassium hydroxide, preferably of 38% strength, is added slowly with constant stirring to the solvent solution of the ester mixture. In a relatively short time the potassium soap of the unreacted fatty acids will rise to the surface as a flocculent aggregate, and any mineral acid present as catalyst will also precipitate out as the potassium salt. The solvent solution is filtered without suction, and the soap mass is washed with a small amount of fresh ethylene dichloride to remove traces of neutral ester, and the filtrate distilled. It is not necessary to dry the filtrate.

By this process we have been able to obtain quantitatively the yields of methyl and ethyl esters of lauric, oleic, linoleic, stearic and ricinoleic acids, from the original esterified mass prepared with the respective crude acids. The process also has been applied successfully to the preparation of relatively pure mono- and di-naphthenates of diethylene glycol. The esters obtained in this manner have acid values from 0.5 to 1.0 and can be purified further by vacuum distillation. Relatively large amounts of ester can be purified in this manner without the formation of troublesome emulsions and without the hazards hitherto inherent in the use of ether.

NOPCO LABORATORIES
NATIONAL OIL PRODUCTS COMPANY
HARRISON, NEW JERSEY RECEIVED FEBRUARY 20, 1940

Lupine Studies. XVI.[1] The Isolation of Nonalupine from *Lupinus andersonii* Wats

BY JAMES FITTON COUCH

The isolation of nonalupine from *Lupinus sericeus* has been reported recently.[1] In that species this alkaloid is associated with spathulatine first isolated from *L. marianus*.[2] Nonalupine has now been isolated from *L. andersonii*, a perennial, Pacific States lupine, which has not previously been examined chemically. Spathulatine was not found in the last named species.

Experimental

Material.—The plant used in this investigation was collected by the writer on the south road, Crater Lake Mt.,

(1) Previous paper, No. XV, THIS JOURNAL, **62**, 554 (1940).
(2) J. F. Couch, *ibid.*, **46**, 2507 (1924).

Oregon, on August 24, 1930. At that time the plant was just beginning to bloom. The plants were dried and shipped to Washington, D. C. The whole plant with the exception of the roots was used.

Isolation of the Alkaloid.—The finely ground plant (7.415 kg.) was moistened with alcohol containing 75 g. of acetic acid and then extracted with alcohol. The alkaloid was recovered by the process previously described.[3]

The crude alkaloid weighed 130.4 g. or 1.76% of the plant material. It was negative to the modified Grant test for sparteine, practically insoluble in petroleum ether, slightly soluble in ethyl ether, and completely soluble in cold acetone. On standing the sirupy alkaloid solidified to a mass of crystals embedded in a thick sirup.

The mass was washed with cold ethyl acetate, which removed most of the sirup. The crystals were then recrystallized several times from hot ethyl acetate with the addition of a little norit and finally from methyl isobutyl ketone. The melting point was constant at 91–92° (cor.). Mixed with nonalupine from *L. sericeus* there was no alteration in the melting point. The substance was dried to constant weight for analysis.

Anal. Calcd. for $C_{15}H_{24}ON_2$: C, 72.50; H, 9.74; N, 11.28. Found: C, 72.37, 72.39; H, 9.55, 9.57; N, 11.28, 11.20.

The alkaloid was similar in all chemical and physical respects with nonalupine.

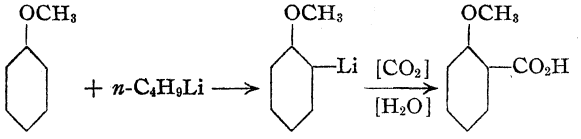
(3) J. F. Couch, THIS JOURNAL, **56**, 2434 (1934).

PATHOLOGICAL DIVISION
BUREAU OF ANIMAL INDUSTRY
WASHINGTON, D. C. RECEIVED JANUARY 26, 1940

Lateral Metalation of Methyl Phenyl Sulfide

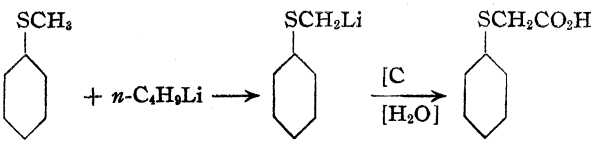
BY HENRY GILMAN AND F. J. WEBB

Metalation by organometallic compounds of a great variety of ethers invariably involves hydrogen situated *ortho* to the hetero element. Some of the types examined are: aryl alkyl ethers, diaryl ethers, and cyclic ethers like furan, benzofuran and dibenzofuran. The following reaction with anisole is typical.



The same general reaction takes place with the sulfur analogs of the diaryl ethers and the cyclic ethers mentioned, with but one exception. Metalation of dibenzofuran by a variety of organometallic compounds involves the 4-position (*ortho* to the hetero element); however, the exceptional case has been noted with the related heterocycle, dibenzothiophene. Although metalation of dibenzothiophene by organolithium and organopotassium compounds also involves the 4-position, metalation by phenylcalcium iodide introduces the metal in the 3-position, or *meta* to the hetero element.[1]

We now find that metalation of methyl phenyl sulfide proceeds quite unlike the related anisole, and instead of giving an *ortho* nuclear metalation product[2] yields exclusively a lateral metalation product.



There is a possibility that nuclear metalation may have occurred initially, and that the lithium then migrated to the methyl group. This remains to be established. In this connection, it is interesting to note that *o*-, *m*- and *p*-tolylsodiums rearrange laterally to benzylsodium.[3] The metalation of other sulfur and related types is being examined, together with some syntheses of these new reactive compounds such as the bridging of the 1- and 9-positions in dibenzofuran types by hetero elements and groups.

Experimental

A solution containing approximately 0.2 mole of *n*-butyllithium was divided into two equal parts. To one portion was added 12.4 g. (0.1 mole) of methyl phenyl sulfide in 30 cc. of ether; and to the other portion was added 10.8 g. (0.1 mole) of anisole in 30 cc. of ether. Each of the mixtures was stirred and refluxed for fifteen hours, and then carbonated by solid carbon dioxide. By means of the usual procedures, there was isolated from the reaction with methyl phenyl sulfide, 7.32 g. (43.5%) of phenylmercaptoacetic acid (m. p., 61–63°). This compound was identified by comparison with an authentic specimen prepared from thiophenol and chloroacetic acid in accordance with the directions of Gabriel.[4] In addition, there was recovered 3.7 g. or 29.8% of methyl phenyl sulfide, which raises the yield of phenylmercaptoacetic acid to 62% on the basis of methyl phenyl sulfide not recovered.

The reaction with anisole gave 4.92 g. or 32.4% of *o*-methoxybenzoic acid; 0.65 g. or 5.37% of 2,2′-dimethoxybenzophenone; and 1.9 g. or 17.6% of recovered anisole. All solids were identified by the method of mixed melting points.

From a check experiment with methyl phenyl sulfide there was obtained 5.9 g. or 35.2% of phenylmercaptoacetic acid (m. p. 61–63°) and 4.5 g. or 36.3% of recovered methyl phenyl sulfide.

(1) Gilman and Jacoby, *J. Org. Chem.*, **3**, 108 (1938); Gilman, Jacoby and Pacevitz, *ibid.*, **3**, 120 (1938).

(2) Phenoxathiin and N-ethylbenzothiazole are known to metalate *ortho* to a hetero element, and with the former compound *ortho* to the oxygen linkage.

(3) Gilman and Pacevitz, THIS JOURNAL, **62**, 873 (1940); Gilman, Pacevitz and Baine, *ibid.*, **62**, May (1940).

(4) Gabriel, *Ber.*, **13**, 1389 (1870).

We have just observed that *ethyl* phenyl sulfide with *n*-butyllithium gives *o*-ethylmercaptobenzoic acid.

DEPARTMENT OF CHEMISTRY
IOWA STATE COLLEGE
AMES, IOWA RECEIVED FEBRUARY 26, 1940

Hydrogenation of Wood

BY H. P. GODARD, JOSEPH L. MCCARTHY AND HAROLD HIBBERT

Studies on hydrogenation of lignin and other plant materials at high pressures have now shown that maple and spruce wood meals readily undergo hydrogenation. The two latter products were first freed from resin, fats, etc., by the customary preliminary extraction treatment with alcohol–benzene, alcohol, and water in the order named, then dried, suspended in anhydrous dioxane, the copper–chromium oxide catalyst added and the mixture then subjected to the action of hydrogen at around 250 to 280° at a pressure of 5000–6000 pounds per square inch (333–400 atm.) for periods of twelve to sixteen hours.

The main products isolated were (a) 4-*n*-propylcyclohexanol-1, b. p. 92–95° (7 mm.), refractive index $n^{25}D$ 1.4633, and (b) 4-*n*-propylcyclohexanediol-1,2, b. p. 107–110° (1 mm.), refractive index $n^{25}D$ 1.4808; some higher boiling oils also were obtained. These substances undoubtedly originate from the lignin present in the wood, the combined yields of (a) and (b) in the preliminary work, when calculated on the total (Klason) lignin present originally, amounting to around 60 to 70% in the case of maple and about 35 to 40% in the case of the spruce meal. Similar results were obtained using wood meal previously extracted with cold 5% alkali, although in these cases the yields were somewhat lower.

Presumably other suspending media such as tetralin, decalin, cyclohexane, as well as the above solvents (a) and (b), can be used in place of dioxane, and these are being actively investigated.

It is of considerable interest that the accompanying carbohydrate–polysaccharide components also undergo simultaneous hydrogenation and hydrogenolysis as indicated by the large absorption of hydrogen (about 3.2 moles of hydrogen per 100 g. of wood meal). The nature of these reactions and of the resulting products are also under investigation.

DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY
MCGILL UNIVERSITY
MONTREAL, CANADA RECEIVED FEBRUARY 12, 1940

The Effect of Chlorine Substitution on the Fungistatic Properties of Acetic and Propionic Acids

BY CHARLES HOFFMAN, T. R. SCHWEITZER AND GASTON DALBY

In a recent paper the fungistatic properties of β-iodopropionic acid were reported in connection with a study of a series of normal, branched-chain, and substituted fatty acids.[1] It was shown that β-iodopropionic acid had remarkable fungistatic properties which apparently depended to some extent on the nature of the iodine atom itself. The effect of substituents is also of interest from the point of view of the relationship of molecular structure to fungistatic power. Monochloroacetic, α-chloropropionic, and β-chloropropionic acids are readily available and their fungistatic curves illustrate the effect of the introduction of a single chlorine atom in all possible positions.

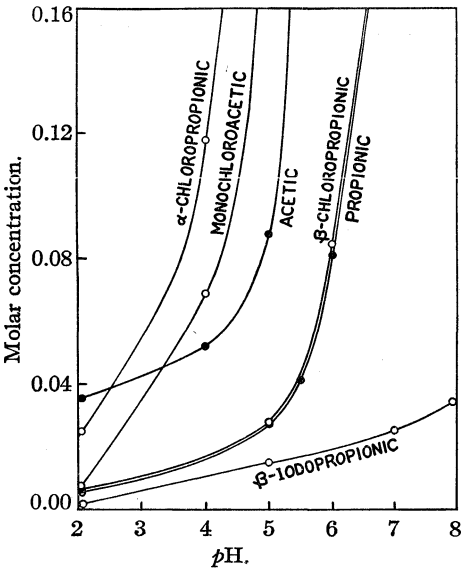


Fig. 1.—Molar concentrations of the indicated acids at various *p*H values necessary to inhibit mold for forty-eight hours at 37.5°.

The method used was as previously reported.[1] β-Chloropropionic acid has a curve practically identical with that of propionic acid itself and is markedly different from the β-iodopropionic acid curve which is indicated on the graph for comparison. The introduction of chlorine on the alpha carbon of propionic acid sharply decreases its fungistatic properties. Monochloroacetic acid is also much less effective than acetic acid except

(1) Hoffman, Schweitzer and Dalby, *Food Research*, 4, 539 (1939).

in the very high *p*H ranges. A chlorine atom on the carbon next to the carboxyl affects the fungistatic properties of the acid, whereas the same substituent on the beta carbon atom has no effect. Constitutional factors are therefore of considerable significance on the biological effect of fatty acids.

Langmuir[2] pointed out that halogen substitution had an appreciable effect on the dissociation constant of a fatty acid. The theory[3] is rather widely held that the biological activity of an acid is dependent on the dissociation constant; that is, the less ionized the acid, the more powerful its biological effect. The relative fungistatic properties of acetic and monochloroacetic, and of propionic and α-chloropropionic acids, when compared with their respective dissociation constants are in agreement with this theory. In the case of propionic and β-chloropropionic acids, however, the fungistatic properties are not so closely related to the dissociation constants. Propionic acid has a dissociation constant of 1.33×10^{-5}, and β-chloropropionic acid 8.59×10^{-5},[2] but the two acids have essentially identical fungistatic properties.

(2) Langmuir, *Chem. Rev.*, **6**, 465 (1929).

(3) (a) Tekelenburg, *Nederland. Tijdschr. Hyg. Microbiol. Serol.*, **2**, 176 (1927); (b) Bach, *Bull. sci. pharmacol.*, **39**, 7 (1932).

WARD BAKING COMPANY
NEW YORK, N. Y. RECEIVED JANUARY 17, 1940

The Preparation of Aurin Tricarboxylic Acid*

BY DUNCAN A. HOLADAY

Recent work in this Laboratory required the use of pure aurin tricarboxylic acid. Several methods of preparing this compound were tried, including those of Scherrer and Smith,[1] Heisig and Lauer,[2] and Caro.[3] A product satisfactory for use in the determination of aluminum was obtained by each of these methods, but in no instance did the product contain more than 70% aurin tricarboxylic acid based on the air-dried material. The content of dye was determined by titration with titanium trichloride solution.[4]

In the course of the work it was observed that the material prepared by Caro's method would undergo a further reaction on treatment with a second portion of the oxidizing mixture (sodium nitrite–sulfuric acid solution). A study of this reaction developed the following modification of Caro's procedure which has several advantages over previously described preparations and yields a product of high purity. The methods of Heisig and Lauer, and of Scherrer and Smith, require that the temperature be kept below 5°. In the following procedure the reaction is not highly exothermic, and therefore no rigid temperature control is necessary. Caro recommends a purification with sodium bisulfite, which is difficult to perform and in the author's hands does not yield a pure product. In the modified procedure no purification of the reaction product is necessary except the removal of inorganic salts.

Experimental Part

Five grams of finely powdered sodium nitrite was added slowly and with vigorous stirring to 36 cc. of sulfuric acid, avoiding evolution of oxides of nitrogen. To this solution an intimate mixture of 10 g. of methylene-disalicylic acid[5] and 5 g. of salicylic acid was added in small portions with vigorous stirring. After addition of all of the solid material, the mixture was allowed to stand for an hour with occasional stirring. It was then poured into a solution of 5 g. of sodium nitrite in 36 cc. of sulfuric acid, stirred, and allowed to stand overnight. The reaction mixture was added slowly to one liter of cold water, allowed to stand for an hour, and filtered on a Büchner funnel. The precipitate was suspended in one liter of warm water (50°) and filtered. This suspension and filtration was repeated, the free water removed by drawing air through the funnel, and drying was completed in a vacuum oven at 70°. The yield of dry product was 10.5 g. It titrated 97% aurin tricarboxylic acid.

(5) Vanino, "Präparative Chemie," Vol. II, 1937, p. 585.

FOOD DIVISION
U. S. FOOD AND DRUG ADMINISTRATION
WASHINGTON, D. C. RECEIVED DECEMBER 15, 1939

Type III Surface Tension Curves with Minimum in Dilute Solution in Pure Hydrocarbons

BY M. E. L. MCBAIN AND L. H. PERRY

Many properties of colloid systems in water are usually explained in terms of free ions, so that it becomes interesting to examine non-ionizing solvents to see in how far similar behavior is to be found where free ions are almost or quite lacking. One very striking property of many colloidal electrolytes in water is that in very dilute solution they lower the surface tension to about one-third that of water. The surface tension is then at a minimum and thereupon rises to a flat maximum in slightly less dilution. Some non-electrolytic detergents likewise similarly lower the surface

* Not copyrighted.

(1) Scherrer and Smith, Bureau of Standards Res. Paper RP1118.

(2) Heisig and Lauer, *Org. Syntheses*, **9**, 8 (1929).

(3) Caro, *Ber.*, **25**, 941 (1892).

(4) Evenson and Nagel, *J. Ind. Eng. Chem., Anal. Ed.*, **3**, 167 (1931).

tension of water to an almost equal extent in very dilute solution, but it then remains constant on further concentration. The existence of these type III curves has been thoroughly established[1] and they are of special interest because the positive adsorption actually observed by a number of methods does not accord with the requirements of the Gibbs theorem as ordinarily applied to surface tension measurements.

Using hydrocarbons as solvents, we have found that type III curves with minima do actually occur in non-ionizing media. This is shown in Fig. 1 for pure lauryl sulfonic acid dissolved in

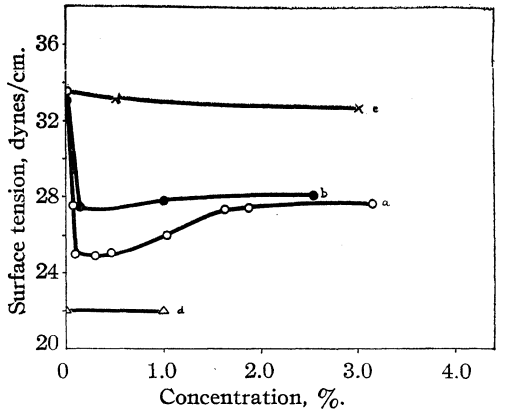


Fig. 1.—Surface tension curves in hydrocarbon solutions: Type III curves for lauryl sulfonic acid in (a) Nujol and (b) mineral oil; Type I curves for (d) lauryl sulfonic acid in *n*-heptane and (e) butyric acid in Nujol.

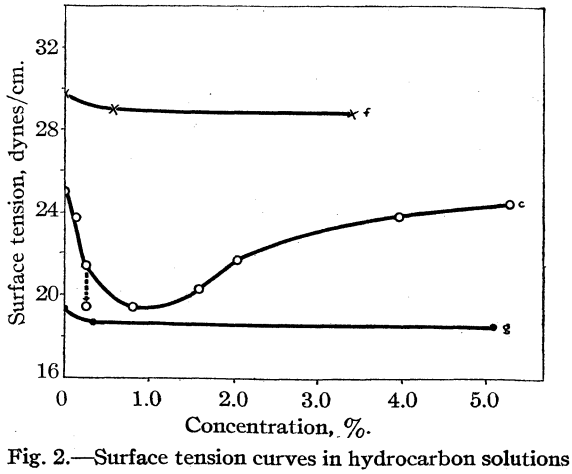


Fig. 2.—Surface tension curves in hydrocarbon solutions of lauryl sulfonic acid: Type I curves for (f) benzene and (g) iso-octane; Type III curve for (c) hydrogenated tetraisobutylene, showing with vertical dashed line the time effect in lowering of surface tension in very dilute solutions only.

(1) McBain and Mills, Reports on Progress in Physics, **5**, 30 (1939); McBain, Vinograd and Wilson, THIS JOURNAL, **62**, 244 (1940); McBain and Wood, *Proc. Roy. Soc.*, **174A**, in press (1940); McBain, Mills and Ford, THIS JOURNAL, **62** in press (1940).

(a) Nujol, (b) mineral oil, and, in Fig. 2, (c) hydrogenated tetraisobutylene. The results were obtained with the DuNoüy ring tensiometer at 27°, first sweeping the surface to remove contamination. These solutions unlike most of the others to be mentioned leave a film within the ring.

On the other hand, lauryl sulfonic acid in solvents such as iso-octane, xylene, benzene and heptane scarcely lowers the surface tension. For iso-octane the value 19.3 dynes/cm. falls steadily with concentration to 18.5 in 5% solution (type I curve). For benzene the value 29.7 of the pure solvent becomes 28.7 for 3.4%, and for *n*-heptane the value of 22.2 is not changed when 1% of acid is added. These results are summarized in Table I.

TABLE I

SOLUTIONS OF $C_{12}H_{25}SO_3H$ IN HYDROCARBONS SHOWING SURFACE TENSION OF SOLVENT, σ_0; OF 1% SOLUTION, σ_1; AT MINIMUM, $\sigma_{min.}$, IF ANY; AND TYPE OF SURFACE TENSION CURVE

Solvent	σ_0	σ_1	$\sigma_{min.}$	Type
Nujol	33.5	25.9	24.8 at 0.2%	III
Mineral oil	33.0	27.8	27.4 at 0.18%	III
Benzene	29.7	29.3	none	I
Xylene	27.8	27.3	none	I
Tetraisobutylene	25.3	22.5	22.3 at 0.15%	III
Hydrogenated tetraisobutylene	25.0	19.5	19.4 at 0.8%	III
Decane	23.7	22.3	none (?)	I, III (?)
Heptane	22.2	22.2	none	...
Iso-octane	19.5	19.2	none	I

It is interesting to compare a surface tension curve in Nujol and in the similar mineral oil with that in water,[1] where the surface tension at the minimum is the same in all three cases, though that of water is as high as 72 dynes. The first thought, that solvents whose own surface tension is already as low as this minimum could not be lowered, is negatived by the result in hydrogenated tetraisobutylene, where it drops from 25 dynes to 19.4. However, the two intervening solvents, benzene and xylene, are not similarly affected by lauryl sulfonic acid. They are lowered but slightly and yield no minimum, showing that surface tension of the solvent is no sufficient guide.[2] Decane appears to be on the borderline among saturated hydrocarbons.

Polar compounds are not enough. For example, nonyl glucoside and another excellent detergent, a polyethylene oxide derivative, scarcely

(2) Interesting contrasts between spreading behavior of hexane and benzene on mica surfaces have been reported by Bangham, Mosallam and Saweris, *Trans. Faraday Soc.*, **34**, 554 (1938); *Nature*, **140**, 237 (1937).

lower the surface tension of Nujol or hydrogenated tetraisobutylene. The measurements are hampered, however, by low solubility and a tendency to separate on cooling. In water, Woo's unpublished measurements show that they lower the surface tension from 72 to 31 dynes in extreme dilution, namely, 0.02 and 0.2% solutions, respectively, thereafter remaining constant up to 1% solution.

The sulfated sodium naphthenic or petroleum soaps supplied by the Sherwood Petroleum Company are oil-soluble, not water-soluble. They actually raise the surface tension of *n*-hexane from the value 20.2 to 20.4 or 20.5 for 10% solution and to 22.3 for 50% solution, thus giving a type II curve.

A number of especially interesting solutes of different types could not be tested on account of their insolubility, but a non-electrolytic detergent showed no appreciable lowering in Nujol although 14 and 24% solutions gave the small lowerings of 0.5 and 2.0 dynes. Butyric acid likewise is ineffective, the lowering being 0.5, 0.9 and 2.0 dynes for 1, 9 and 20% solutions, respectively. Lauric acid in 3% solution gave the distinctly greater lowering of 2 dynes. Triethanolamine oleate in 0.5 and 9% gave a lowering of 1 dyne and 2 dynes; thymotic acid in 1% solution 0.8 dynes; and stearic acid gave 1 dyne lowering for 0.7%. Calcium and zinc stearates have practically no effect.

It is evident that appreciable lowering and the production of a type III curve in these hydrocarbons require such a degree of polarity that the solute forms a strong electrolyte or colloidal electrolyte in water.

The only explanation to account for the minimum found in a type III curve is that put forward by McBain[3] based upon the electrical double layer. Now in the present non-ionizing solvents this would have to be a condensed Helmholtz double layer of the classical type instead of the partly diffuse type existing in water. However, the Helmholtz double layer is adequate for explaining lowering of surface or interfacial tension.

These novel observations evidently should suggest many other approaches and experiments to investigators in this field and are significant as a guide to other phenomena in hydrocarbon systems.

DEPARTMENT OF CHEMISTRY
STANFORD UNIVERSITY
STANFORD UNIV., CALIF.

RECEIVED JANUARY 19, 1940

(3) McBain, Ford and Wilson, *Kolloid. Z.*, **78**, 1 (1937).

Alkanolamines. VIII. Reaction of Ethanolamines on *p*-Nitrobenzoic Acid

BY M. MELTSNER, DANIEL GREENFIELD AND HARRY ROSENZWEIG

In some of the previous papers of this series[1,2,3,4] it was shown that alkanolamines, but not their salts, may reduce an aromatic nitro group and that the unreduced and reduced compounds may form addition compounds with the alkanolamines. This is now confirmed by the following experiment on the action of ethanolamines on *p*-nitrobenzoic acid.

Experiment I.—One mole of ethanolamine and one mole of *p*-nitrobenzoic acid were heated at 100° for four hours. The brown solid residue, after extraction with ether and chloroform, was crystallized from alcohol. A white compound of m. p. 168° was obtained. An ether extraction of this substance from dilute hydrochloric acid yielded *p*-nitrobenzoic acid while the hydrochloric acid layer on evaporation gave a white solid, m. p. 82°, corresponding to ethanolamine hydrochloride. The white compound was therefore an addition product, $NO_2C_6H_4COOH\cdot NH_2CH_2CH_2OH$.

Similarly diethanolamine yielded $NO_2C_6H_4COOH\cdot NH(CH_2CH_2OH)_2$, m. p. 138°, and triethanolamine yielded $NO_2C_6H_4COOH\cdot N(CH_2CH_2OH)_3$, m. p. 116°.

Experiment II.—One mole of ethanolamine was refluxed with one mole of *p*-nitrobenzoic acid in an oil-bath for two hours. The reaction mixture was treated several times with cold water and filtered. The filtrate was evaporated to dryness on the water-bath and the residue extracted with alcohol. Evaporation of the alcohol gave a solid identified as *p*-aminobenzoic acid by its positive test for the amino group, its melting point (186°) and the melting point of the dinitrobenzoate (195°). The dry residue, insoluble in alcohol, was recrystallized from hot water and gave $NO_2C_6H_4COOH\cdot NH_2CH_2CH_2OH$.

The residue, insoluble in cold water, was extracted with chloroform to isolate some more *p*-aminobenzoic acid and then recrystallized from hot water. There was obtained in large amounts a pale yellow compound, m. p. 130°, which was identified as the addition product of two moles of ethanolamine and one mole of azoxybenzoic acid: N calcd., 13.72; found, 13.64. The compound can be reduced to yield *p*-aminobenzoic acid. Hydrolysis of the compound with alkali gave *p,p'*-azoxybenzoic acid which was identified by means of its ethyl ester. Hydrolysis of the compound with hydrochloric acid yielded monoethanolamine hydrochloride.

Experiment III.—Four moles of diethanolamine and one mole of *p*-nitrobenzoic acid were heated for two hours at 180°. The reaction mixture was washed with chloroform, extracted with hot water and filtered. On cooling, yellow crystals are obtained and identified as *p*-aminobenzoic acid.

(1) Meltsner, *et al.*, THIS JOURNAL, **57**, 2554 (1935).
(2) Kremer, *ibid.*, **59**, 1681 (1937).
(3) Kremer and Kress, *ibid.*, **60**, 1031 (1938).
(4) Meltsner, *et al.*, *ibid.*, **60**, 1236 (1938).

The authors wish to express their thanks to Mr. Jack Riseman for assistance in connection with Experiment II.

DEPARTMENT OF CHEMISTRY
THE CITY COLLEGE
COLLEGE OF THE CITY OF NEW YORK
NEW YORK, N. Y. RECEIVED JANUARY 27, 1940

The Oxidation–Reduction Potential of Vitamin K_1

BY BYRON RIEGEL, PERRIN G. SMITH[1] AND CARL E. SCHWEITZER

Because of the increasing physiological importance of oxidation–reduction systems, the oxidation–reduction potential of pure synthetic vitamin K_1 has been determined. Such potentials are also important for elucidating the structures of quinones and for this reason, at the suggestion of Professor L. F. Fieser, we first measured the potential of the vitamin in potent alfalfa concentrates. This value, 358 mv., in conjunction with the C-H analysis and the absorption spectrum first published by Dam, Karrer, *et al.*,[2] provided strong evidence that vitamin K_1 was a 2,3-dialkyl-1,4-naphthoquinone. This was evident from the values of Table I.

TABLE I

	E_0 in mv.
1,4-Naphthoquinone	484[a]
2-Methyl-1,4-naphthoquinone	408[a] 422[b]
2,3-Dimethyl-1,4-naphthoquinone	340[a]

[a] L. F. Fieser and M. Fieser, THIS JOURNAL, 57, 491 (1935).

[b] J. W. H. Lugg, A. K. Macbeth and F. L. Winzor, *J. Chem. Soc.*, 1457 (1936).

This information together with other known facts led to the prediction of the first specific structure[3] for vitamin K_1 which later proved to be correct.

Karrer and colleagues[4] have reported the oxidation–reduction potential $E_m = +5$ mv. for vitamin K_1. It is not absolutely clear, from their experimental data, how their value compares with other quinone potentials because they did not use the customary method. However, from a consideration of the pH of the solvent used it seems that their value of the oxidation–reduction potential E_0 is about 400 mv. This estimation does not take into account a possible junction potential.

In the fractionation of alfalfa extracts it was found that a stock solution of 3% vitamin K_1 concentration had the best keeping qualities and gave the most reliable potentials over a period of time. More highly refined concentrates showed considerable variation in both bioassay and potential upon storage. Because of these variations and the occasional presence of other substances which affected the oxidation–reduction curve it seemed advisable to delay publication until the determination could be made on the pure vitamin.

The length of time required to establish equilibrium (in some instances twenty-four hours for the complete titration) in the case of the refined concentrates made it necessary to employ a stable reference electrode. The Ag–AgCl electrode was found to be very suitable for this purpose since it is stable for at least several weeks.

The oxidation–reduction potential of pure vitamin K_1 was found to be 363 mv. at 20°.

Experimental

The preparation of the vitamin K active concentrates[5] from alfalfa has been described. The synthetic vitamin K_1 used in this work was prepared according to the method of Fieser.[6]

In the solvent used, 95% ethanol 0.2 N in hydrochloric acid and 0.2 N in lithium chloride, the positive potential of the Ag–AgCl electrode against the hydrogen electrode in the same solvent was approximately 200 mv. This value varies somewhat in different lots of the same solvent depending on the exact chloride ion concentration. However, it is necessary to determine the potential against the hydrogen electrode only once for any one lot of solvent. In the solvent used for the determination of the potential of the pure vitamin the Ag–AgCl electrode gave a value of +203 mv. against the hydrogen electrode. The solubility of the vitamin at room temperature was found to be about 5 mg. per ml. in the above solvent. This same solvent was used to prepare the very dilute solution of titanium trichloride used in the potentiometric titrations. Both platinized and bright platinum electrodes were used and gave the same results although the platinized electrodes seemed to reach equilibrium more rapidly.

Two independent determinations, checking within 1 mv., gave a potential of +160 mv. for the vitamin against the Ag–AgCl electrode. Thus the vitamin potential, E_0, against the hydrogen electrode is 363 mv. All measurements were made at 20°.

CHEMICAL LABORATORIES
NORTHWESTERN UNIVERSITY
EVANSTON, ILLINOIS RECEIVED FEBRUARY 23, 1940

(1) Abbott Research Fellow.

(2) H. Dam, A. Geiger, J. Glavind, P. Karrer, W. Karrer, E. Rothschild and H. Salomon, *Helv. Chim. Acta*, **22**, 310 (1939).

(3) L. F. Fieser, D. M. Bowen, W. P. Campbell, M. Fieser, E. M. Fry, R. N. Jones, B. Riegel, C. E. Schweitzer and P. G. Smith, THIS JOURNAL, **61**, 1925 (1939).

(4) P. Karrer and A. Geiger, *Helv. Chim. Acta*, **22**, 945 (1939).

(5) B. Riegel, C. E. Schweitzer and P. G. Smith, *J. Biol. Chem.*, **129**, 495 (1939).

(6) L. F. Fieser, THIS JOURNAL, **61**, 3467 (1939).

The Preparation of *unsym*-Difluorotetrachloroethane

BY WILLIAM T. MILLER

No very convenient methods for the preparation of *unsym*-difluorotetrachloroethane have appeared in the literature, although it has been synthesized by the chlorination of difluorotrichloroethane [$CHCl_2CF_2Cl$].[1] In this work, it was found possible to obtain the desired compound satisfactorily from trifluorotrichloroethane[2] [CF_2Cl-CCl_2F] and aluminum chloride. The simplicity of the experimental procedure and cheapness of the starting materials make the product readily available for the first time.

This reaction is not entirely a simple replacement of fluorine by chlorine as some gaseous products are formed[3] and too long heating leads to the formation of hexachloroethane. It was probably for this last reason that Henne and Newman[4] obtained little of the difluoro compound after refluxing trifluorotrichloroethane with aluminum chloride for forty-eight hours.

Experimental

Two hundred cc. of trifluorotrichloroethane[2] and 40 g. of finely powdered aluminum chloride were refluxed on a steam-bath for five hours. The surface of the aluminum chloride turned dark during this period. Distillation of the product through a 50 × 1 cm. column packed with glass helices yielded 51 g. of *unsym*-difluorotetrachloroethane, b. p. 90–91°, m. p. 40–41°, and a very small residue composed principally of hexachloroethane. The lower boiling material distilled almost entirely below 48° but was shown by freezing to contain appreciable amounts of CF_2ClCCl_3. Longer periods of reaction yielded increased quantities of hexachloroethane.

(1) Locke, Brode and Henne, THIS JOURNAL, **56**, 1726 (1934).
(2) "Freon 113" of Kinetic Chemicals, Inc., Carney's Point, N. J.
(3) Compare U. S. Patent 1,994,035 (*C. A.*, **29**, 2974 (1935)).
(4) Henne and Newman, THIS JOURNAL, **60**, 1697 (1938).

DEPARTMENT OF CHEMISTRY
CORNELL UNIVERSITY
ITHACA, N. Y.
RECEIVED FEBRUARY 19, 1940

Some Addition Compounds of Phthaleins and Metallic Salts*

BY GEORG SACHS AND LILI RYFFEL-NEUMANN

K. H. Meyer and A. Hantzsch in 1907[1] described some compounds produced by addition of metallic salts to phenolphthalein, its lactoid dimethyl ether and its quinonoid dimethyl ether ester in non-aqueous solvents. No compound of this kind seems to have been prepared since except a zinc chloride addition compound of the hexamethyl ether of phloroglucin-phthalein.[2] It is surprising that these compounds are all colored, although the organic component might be colorless or even, as, *e. g.*, in the case of dimethoxyphenolphthalein, incapable of assuming a quinonoid structure.

By extending the Meyer and Hantzsch method to other phthaleins we found a number of definite types of addition compounds. As metallic salts we used stannic chloride and antimony pentachloride. Besides phenolphthalein and its dimethyl ether, the phthaleins we dealt with were 3,6-dimethylfluoran, fluorescein and the lactoid dimethyl ether of fluorescein. All addition compounds we obtained were colored. It may be pointed out that all phthaleins mentioned above give colored addition products with acids also and that there is a certain connection between those two series of addition compounds.

The substances were prepared by mixing the component solutions in the manner adopted by Meyer and Hantzsch, a deep tint indicating the formation of an addition compound. In several cases the metal chloride was added without solvent, or cooling was necessary. If the resulting substance did not separate by itself, it was precipitated by a second liquid.

The substances formed differed widely in their stability toward water. Those derived from dimethylfluoran were the most stable. Some of them were, because of their extreme sensitivity to moisture, obtainable only in a closed apparatus. A few substances were so unstable that they could not be weighed for testing and the analysis had to be limited to the determination of the proportion of some constituents. In such cases the addition of indifferent molecules of the solvent could not be controlled.

The compounds we prepared are collected in Table I. The compounds prepared by Meyer and Hantzsch from the same components are inserted and denoted by "M. and H."

The compound (4) mentioned by Meyer and Hantzsch could not be obtained. Instead compound (5) resulted, but, whereas Meyer and Hantzsch claim that the substance was formed slowly, (5) precipitated at once.

Except substance (9) which has a more complicated formula and substance (11) which is a salt

(*) Contribution from the 2nd Chemical Institute of the University of Vienna.
(1) K. H. Meyer and A. Hantzsch, *Ber.*, **40**, 3479 (1907).
(2) H. Lund, *Chem. Zentr.* **102**, II, 2695 (1931).

TABLE I

REACTANTS, PROPERTIES AND ANALYSES OF THE ADDITION COMPOUNDS

No.	Phthalein	Metal chloride and mole ratio to one of phthalein	Solvent (and precipitant)	Description: Color and crystal form	M. p., °C.	Formula P = phthalein	Analyses (M. and H. = analyzed by Meyer and Hantzsch) * indicates atomic ratio rather than % analysis: Metal, % Calcd.	Metal, % Found	Chlorine, % Found	Calcd.	Found
1		1 $SnCl_4$	Nitrobz. (CS_2)	Red	78–79	P·$SnCl_4$·$BzNO_2$				M. and H.	
2	Phenol	1 $SnCl_4$	Anisole (CCl_4)	Pale red		P·$SnCl_4$·BzOMe	Sn, 17.28	17.36			
3		1 $SnCl_4$	Benzonitrile (CCl_4)	Pale red		P·$SnCl_4$·BzCN	Sn, 0.83*	0.77*	1.00*	1.00*	OCH_3, 4.52 N, 0.10*
4	Phenol	1 $SnCl_4$	Nitrobz. (CS_2)	Red	128	P·$SnCl_4$				M. and H	4.28 0.11*
5	dimethyl	1 $SnCl_4$	Nitrobz. (CS_2)	Pink		2P·$SnCl_4$	Sn, 12.46	11.67	14.89	15.18	
6	ether[a]	2 $SbCl_5$	CCl_4	Carmine		P·$SbCl_5$	Sb, 0.69*	0.69*	1.00*	1.00*	OCH_3, 0.35* 0.33*
7		1 $SnCl_4$	CCl_4	Yellow		P·$SnCl_4$	Sn, 20.16	21.35	21.28	24.10	24.39 24.01
8		1 $SnCl_4$	Anisole	Red rhombic and prism		P·$SnCl_4$·BzOMe	Sn, 17.03	17.88	17.59	20.36	20.50 20.30 Anisole, 15.51 15.24
9	3,6-Dimethyl-	20 $SnCl_4$	Anisole	Irregular lamina	139, dec.	2P·3$SnCl_4$·2BzOMe	Sn, 21.53	22.53	23.51	25.73	25.17 Anisole, 13.07 14.50
10	fluoran[b]	1 $SbCl_5$	CCl_4	Yellow	203	P·$SbCl_5$	Sb, 19.42	19.80		28.27	29.32
11		2 $SbCl_5$	CH_3COOH	Or.-yel. needles recryst. from MeCO or $CHCl_3$	203	P·$SbCl_5$·HCl·AcH	Sb, 16.82	17.27	17.02	29.42	29.43 29.37 Ac, 5.95
12		0.5 $SnCl_4$	Nitrobz. (CCl_4)	Yel.-brown		2P·$SnCl_4$	Sn, 12.84	12.27	11.96	15.34	16.58
12a	Fluorescein	1 $SnCl_4$	Nitrobz. (CCl_4)	Yel.-brown		2P·$SnCl_4$	Sn, 12.84	11.75		15.34	16.33
13	Fluorescein di-	0.5 $SnCl_4$	CCl_4	Yellow		P·$SnCl_4$	Sn, 19.13	18.95		22.86	23.61
13a	methyl ether[c]	1 $SnCl_4$	CCl_4	Yellow		P·$SnCl_4$	Sn, 19.13	19.24		22.86	

[a] E. Grande, *Gazz. chim. ital.*, **26**, I, 222 (1896); R. Meyer and O. Spengler, *Ber.*, **38**, 1328 (1905). [b] F. Kehrmann and J. Knop, *ibid.*, **44**, 3510 (1911). [c] H. v. Liebig, *J. prakt. Chem.*, **88**, 26 (1913).

of the acid, $HSbCl_6$, all the compounds listed are included in four different classes: (A) $SnCl_4$·2P, substances (5), (12); (B) $SnCl_4$·P, substances (4), (7), (13); (C) $SnCl_4$·P·Solvent, substances (1), (2), (3), (8); (D) $SbCl_5$·P, substances (6), (10).

The chemical nature of the classes A, C and D seems to be clear. They are complex compounds of coördinated hexavalent tin or antimony, one molecule of the phthalein occupying a single coördination valence. The substances of class B may be interpreted by the hypothesis that the phthalein occupies two coördinated valences or they may be considered as bimolecular compounds with two coördination centers. They are mostly less deeply colored and are mainly formed if solvents lacking secondary valences are used.

GLASGOW, SCOTLAND RECEIVED SEPTEMBER 22, 1939

The Condensation of Phenol and Ethylene Oxide

BY RICHARD A. SMITH

The monophenyl ether of ethylene glycol was first prepared by the reaction between phenol and ethylene oxide in a sealed tube.[1] In this way, by heating at 180° for eight hours, we obtained an 85% yield based on the phenol.

More frequently, however, it has been prepared by the reaction of ethylene chlorohydrin with a phenol salt.[2] We find that using this latter method and refluxing the mixture for eight hours gives, after distillation through a 6-foot column and collection within 0.5°, 1.10 moles of phenoxy glycol (b. p. 165° at 80 mm.), or a 55% yield, from 2 moles of phenol. This same reaction, carried on in a sealed tube for eight hours, gives a 62.5% yield of the same purity.

We now find that by heating, without rocking, molar equivalents of phenol and ethylene oxide in an autoclave charged with hydrogen at tank pressure for four hours until the temperature reaches 200°, the pressure at that time being in excess of 2500 pounds per sq. in., and then allowing it to cool and redistilling the product in a vacuum, a yield of 94% of phenoxy glycol of the same purity is obtained.

WASHINGTON SQUARE COLLEGE
NEW YORK UNIVERSITY
WASHINGTON SQUARE, NEW YORK CITY
RECEIVED NOVEMBER 24, 1939

(1) Roithner, *Monatsh.*, **75**, 674 (1894).

(2) Bentley, Haworth and Perkin, *J. Chem. Soc.*, **69**, 164 (1896); Smith and Niederl, THIS JOURNAL, **53**, 808 (1931); Bellman, U. S. P. 1,841,431 (1932).

The Physical Constants of Pentanol-3

BY FRANK C. WHITMORE AND J. D. SURMATIS

Pure pentanol-3 was required in large quantity for work in progress in this Laboratory. Since the physical constants for the carbinol reported in the literature[1] show wide disagreement, a study was made on the purity of material synthesized in the laboratory and that obtained from Sharples Solvents Corporation.

Propionaldehyde, b. p. 48.0° at 736 mm., $n^{20}D$ 1.3636, was prepared by dehydrogenation of *n*-propyl alcohol with a copper catalyst. It was treated in four 8-mole lots with ethylmagnesium chloride in anhydrous ethyl ether. The crude product obtained in 67% yield after distillation through a column of approximately 25 theoretical plates, was refractionated through a column, 2 × 260 cm. of the total condensation partial take-off type, having approximately 85 theoretical plates. From this distillation a yield of 90% of constant boiling and constant index material resulted. The boiling point was determined in a laboratory Cottrell apparatus, with a thermometer calibrated against one checked by the Bureau of Standards; the refractive index was determined by a Valentine refractometer: b. p. 114.4° at 740 mm., $n^{20}D$ 1.4104, d^{20}_4 0.8218.

Approximately 2800 g. of Sharples pentanol-3 was distilled through a column of approximately 16 theoretical plates, and then refractionated twice through the 85-plate column described above. Of the starting material 27% was obtained with the physical constants: b. p. 114.3–114.5° at 741.5 mm., $n^{20}D$ 1.4102–1.4104, d^{20}_4 0.8203.

SCHOOL OF CHEMISTRY AND PHYSICS
PENNSYLVANIA STATE COLLEGE
STATE COLLEGE, PENNA. RECEIVED DECEMBER 26, 1939

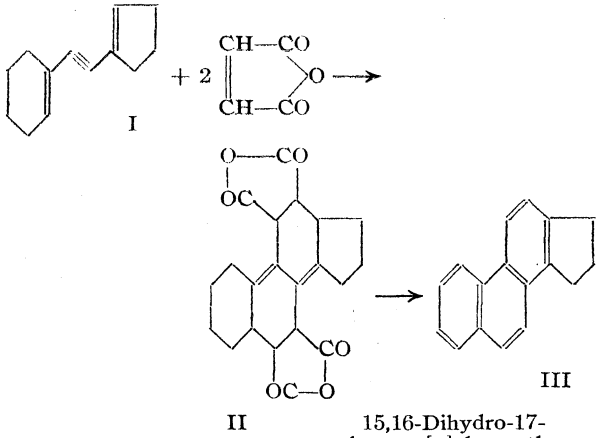
(1) Brunel, THIS JOURNAL, **45**, 1334 (1923); Lucas and Moyse, *ibid.*, **47**, 1460 (1925); Morris and Cortese, *ibid.*, **49**, 2644 (1927); Sherrill Otto and Pickett, *ibid.*, **51**, 3027 (1929); Timmermans and Hennaut-Roland, *J. chim. phys.*, **29**, 529 (1932); Clark and Hallonquist, *Trans. Roy. Soc. Can.*, [3] **24**, 115 (1930); Lauer and Stodola, THIS JOURNAL, **56**, 1216 (1934); Brooks, *ibid.*, **56**, 1998 (1934); Packendorff, *Ber.*, **67**, 905 (1934).

COMMUNICATIONS TO THE EDITOR

THE TOTAL SYNTHESIS OF A NON-BENZENOID STEROID[1]

Sir:

We reported in the last paper[2] that a derivative of hexahydronaphthalene results from the addition of maleic anhydride to 2,5-dimethyl-1,5-hexadiene-3-yne. It has now been found that an analogous reaction occurs when the hydrocarbon I[3] is heated with one mole of maleic anhydride at 130° without solvent. The crystalline product, from ethyl acetate or benzene, has m. p. 249–251° (cor.) with decomposition, and is converted in low yield to 15,16-dihydro-17-cyclopenta[a]phenanthrene (III), m. p. 132–133° (cor.), by heating with palladium–charcoal. This hydrocarbon did not depress the m. p. of an authentic specimen[4] kindly furnished by Dr. Erich Mosettig. *Anal.*[5]



15,16-Dihydro-17-cyclopenta[a]phenanthrene

Calcd. for $C_{21}H_{20}O_6$: C, 68.5; H, 5.5. Found: C, 68.7; H, 5.6. Calcd. for $C_{17}H_{14}$: C, 93.5; H, 6.5. Found: C, 93.5; H, 6.5. Structure II is tentatively assigned to the compound $C_{21}H_{20}O_6$ on the basis of analogy with the hexahydronaphthalene previously[2] described and the absorption curve of the solution in ethanol, λ max. 2555 Å., ε 19,000. It is suggested that a compound of this

(1) This work is supported by Bankhead-Jones funds. (Not subject to copyright.)

(2) Butz, Gaddis, Butz and Davis, *J. Org. Chem.* (recently submitted for publication). The present communication is the fourth paper in the series "Synthesis of Condensed Ring Compounds."

(3) Pinkney, Nesty, Wiley and Marvel, THIS JOURNAL, **58**, 972 (1936).

(4) Burger and Mosettig, *ibid.*, **59**, 1307 (1937).

(5) By Arlington Laboratories, Arlington, Virginia.

structure be called 8(14),9-steradiene-6,7,11,12-tetracarboxylic-6,7,11; 12-dianhydride.

BUREAU OF ANIMAL INDUSTRY
UNITED STATES DEPARTMENT OF AGRICULTURE
BELTSVILLE, MARYLAND
LEWIS W. BUTZ
ADAM M. GADDIS
ELEANORE W. J. BUTZ
RUSSELL E. DAVIS

RECEIVED MARCH 18, 1940

FURTHER COMPOUNDS HAVING ANTI-HEMORRHAGIC ACTIVITY

Sir:

In an investigation involving the synthesis and assay of a number of additional naphthoquinones and derived or related products, considerable data have been accumulated on the problem of correlating vitamin K activity and structure which will be presented after completion of adequate assays on the entire series of compounds synthesized in the two Laboratories. In the meantime we wish to report certain observations from the synthetic work and give some indication of the potencies of the new compounds.

The method developed by one of us for the synthesis of vitamin K_1 [Fieser, THIS JOURNAL, **61**, 2559, 3467 (1939)] has been found capable of wide application. By using 1,4-naphthohydroquinone as one component 2-geranyl, 2-farnesyl, and 2-phytyl-1,4-naphthoquinone have been synthesized in good yield. The phytyl compound [yellow oil, found: C, 82.82; H, 10.31] is the most active member of the series and gives a full response in the chick assay at 50 γ. Similarly the 3-farnesyl derivative of 2-methyl-1,4-naphthoquinone [found: C, 82.97; H, 8.98] is more potent than the 2-geranyl derivative but somewhat less active than vitamin K_1. The synthesis is also applicable in the benzohydroquinone series. 2,3,5-Trimethyl-6-phytyl-1,4-benzoquinone [yellow oil, found: C, 81.04; H, 11.00, hydroquinone diacetate, m. p. 56°] shows no vitamin K activity but it provides a new route to a vitamin E factor. By treatment with stannous chloride in acetic–hydrochloric acid the quinone was converted smoothly into α-tocopherol, identified through the allophanate, m. p. 175–176°, and *p*-nitrophenylurethan, m. p. 130°. Butadiene-toluquinone condenses with phytol under the usual conditions but at the reflux temperature, giving rise to 2-methyl-3-phytyl-5,8-dihydro-1,4-naphthoquinone [found: C, 82.27; H, 10.86], which is active at a level of 5–6 γ. By hydrogenating synthetic vitamin K_1 and purifying the products in the form of the solid hydroquinones, the β,γ-dihydride (active at 6 γ, hydroquinone diacetate, m. p. 57–58°) and $\beta,\gamma,5,6,7,8$-hexahydride (slight activity, diacetate derivative, m. p. 53°) have been obtained in analytically pure form. Both butadiene-toluquinone and 2-methyl-5,8-dihydro-1,4-naphthohydroquinone show marked activity, the latter at dosages as low as 8 γ.

A by-product of the vitamin K_1 synthesis, characterized as a ketonic substance of the formula $C_{31}H_{48}O_2$ [found: C, 82.38; H, 10.65; maxima at 253 and 300 mμ; 2,4-dinitrophenylhydrazone m. p. 107–108°], shows moderate vitamin K activity (50 γ). The Zerewitinoff determination indicates the presence of one active hydrogen and one carbonyl group. Aluminum isopropylate reduction gives a diol, probably $C_{31}H_{52}O_2$ [found: C, 81.52; H, 11.48], and pyrolysis of the by-product gives rise to small amounts of vitamin K_1. The isomeric naphthotocopherol [found: C, 82.30; H, 10.69; maxima at 246 and 320 mμ; *p*-nitrobenzoate, m. p. 84–85°] is active at a higher level (300 γ); on oxidation it yields a yellow hydroxyquinone [found: C, 79.19; H, 10.17].

CONVERSE MEMORIAL LABORATORY
HARVARD UNIVERSITY, CAMBRIDGE, MASS. L. F. FIESER
RESEARCH LABORATORIES, MERCK AND CO., INC., AND MERCK INSTITUTE FOR THERAPEUTIC RESEARCH M. TISHLER
W. L. SAMPSON
RAHWAY, NEW JERSEY

RECEIVED MARCH 20, 1940

THERMAL DECOMPOSITION OF ACETONE CATALYZED BY IODINE

Sir:

Several investigators[1] have shown that small amounts of iodine sensitize the thermal decomposition of various organic compounds. In the case of acetone, Bairstow and Hinshelwood[1a] have reported that the decomposition was not appreciably affected by the presence of iodine. However, Rice and Weiler[2] observed that the decomposition of acetone containing methyl iodide was appreciably faster than the rate for pure acetone. Moreover it was found that the addition of approximately 1% of ethyl iodide enormously increased the rate of decomposition of acetone at 526°.[3] When a small amount of ethyl iodide was allowed to decompose completely in the reaction vessel first and then the acetone added, a large increase in the rate also was observed. This

(1) (a) Bairstow and Hinshelwood, *J. Chem. Soc.*, 1147 (1933); (b) P. A. K. Clusius, *ibid.*, 2607 (1930); (c) Faull and Rollefson, THIS JOURNAL, **58**, 1755 (1936); Rollefson and Garrison, *ibid.*, **62**, 588 (1940).

(2) Weiler, Dissertation, Johns Hopkins University, 1930.

(3) Rice and Walters, unpublished results.

indicated that the iodine which was present in the decomposition products from ethyl iodide[4] was responsible for a large part of the promoting effect.

In the present investigation, we have found that small amounts of pure iodine actually do accelerate the decomposition of acetone in the neighborhood of 500°. The apparatus for this work is of the usual type and includes a Bodenstein valve and a click gage.

Temp., °C.	P_0, mm.	%, I_2	$(\Delta P/P_0)$ % 20–0 min.
506	168	0.00	7.5
506	178	3.60	57.6
493	215	0.00	3.3
493	207	1.55	29.5

(4) Ogg, THIS JOURNAL, **56**, 526 (1934).

From the Table it can be seen that addition of 2–3% of iodine causes the pressure change for the first twenty minutes of the reaction to increase by a factor of eight. The temperature at which Bairstow and Hinshelwood attempted the catalysis of acetone was not given, so that their failure to observe any catalysis may have been due to the fact that they were working in a different temperature range.

We are actively engaged in completing this investigation of acetone and intend to study other ketones such as diethyl and ethyl methyl ketones.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF ROCHESTER
ROCHESTER, NEW YORK
G. M. GANTZ
W. D. WALTERS

RECEIVED MARCH 16, 1940

NEW BOOKS

May's Chemistry of Synthetic Drugs. By PERCY MAY, D.Sc. (Lond.), F.I.C., Consulting Chemist and Chartered Patent Agent, and G. MALCOLM DYSON, Ph.D., F.I.C., A.M.I. Chem.E., Chief Chemist, Genatosan Ltd. Fourth Edition, revised and rewritten. Longmans, Green and Company, Inc., 114 Fifth Avenue, New York, N. Y., 1939. xii + 370 pp. Illustrated. 14 × 22.5 cm. Price, $6.00.

During the past two decades there has been a steadily increasing demand for books which would adequately set forth in clear and concise fashion the salient facts dealing with the relations between the chemical constitution and physiological action of medicinal products and related substances. Despite this evident need there have been surprisingly few ventures into this field of scholarly activity.

May's "Chemistry of Synthetic Drugs," published some thirty years ago (the third edition appeared seventeen years ago), has deservedly had wide popularity. It has given readers an insight into the fundamental concepts of the field, without being handbook in nature. Indeed it was apparently never designed to serve in the role of a monograph which would point the way to new fields of research for the specialist. Rather it has been useful to young chemists who have desired a broad viewpoint of the field of medicinal products, without being compelled to delve into a maze of technical chemical and physiological information.

This, the fourth edition, has arisen from the joint efforts of Percy May and G. Malcolm Dyson. The general plan of the older editions has been followed, but a large amount of new material has been added. It has also been modernized by the inclusion of information on such subjects as hormones, vitamins, steroids, cardiac glucosides, and anthelmintics. Among the sections which have been enlarged are those dealing with hypnotics, mercurials, antiseptics, local anesthetics, analgesics, and alkaloids.

American readers, specialists in the field, will doubtless find cause for real criticism in the rather British and Continental flavor of the book, for it passes over lightly, or not at all, some of the fine developments which have come from the academic and industrial laboratories of this country. Nevertheless the authors have made a real contribution, and the book will unquestionably continue to play the important role which it has played since it was first written by Dr. May.

ARTHUR J. HILL

Plant Viruses and Virus Diseases. By F. C. BAWDEN, M. A., Virus Physiologist, Rothamsted Experimental Station. Chronica Botanica Company, P. O. Box 8, Leiden, Holland, and G. E. Stechert and Company, 31 East 10th Street, New York, N. Y., 1939. 272 pp. 37 figs. 16.5 × 25 cm. Price, Dutch guilders 7, or about $4.00.

Chemists have never been over-modest in their ideas as to the role of chemistry in the scheme of things. Bancroft, for example, has argued eloquently that all the natural sciences are mere provinces of the Chemical Empire. The developments of science in the past few years have certainly favored this *Weltanschauung*. Nevertheless, until very recently even chemists might have hesitated to designate as chemical a book on viruses, *i. e.*, living organisms defined as "obligate parasitic pathogens with at least one dimension less than 200 μ."

Today even this hesitation is unnecessary. Stanley's isolation in 1935 of the virus of the mosaic disease of tobacco as a crystalline protein established this virus as a definite though complicated chemical substance. This certainly makes a review of a book on viruses entirely appropriate for a journal of chemistry.

The contents of the present book justify this chemical allocation. After an introductory survey and chapters on the symptomatology of viruses, their transmission, strains and serological reactions, there follow chapters on their purification, size, optical properties, chemical nature, origin and multiplication. The occurrence of these viruses and the economic importance of the diseases which they produce are also set forth.

It appears from the careful and discriminating discussion in this book that the conclusions of Stanley as to the virus of the mosaic disease of tobacco have been confirmed by subsequent workers, although it has been shown not to be a globulin but a nucleoprotein. The viruses of several other similar diseases also have been isolated in crystalline form and their distinguishing properties ascertained.

The great question which interests every reader, as to whether these apparently inanimate crystalline proteins are alive or capable of living in a suitable environment, is not given a categorical answer. It is shown, however, that the uncertainty is not so much as to whether these viruses are proteins, but rather as to whether viruses are indeed alive. On the one hand, they are certainly small, discrete bodies which resemble bacteria in their behavior, are able to multiply with extreme rapidity in a favorable environment and retain their characteristics tenaciously throughout this multiplication. On the other hand, they have not as yet been successfully cultivated in the absence of living cells, and it may be that this is a decisive distinction which demonstrates them really to be inanimate. However, to the innocent bystander with the history of our knowledge of the enzymes in mind, this seems a somewhat frail barrier to serve as a last defence of vitalism.

ARTHUR B. LAMB

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JOURNAL OF THE
AMERICAN CHEMICAL SOCIETY

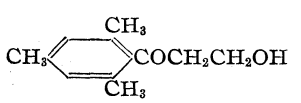
VOLUME 62 MAY 6, 1940 NUMBER 5

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

The Condensation of Paraformaldehyde with Acetomesitylene

BY REYNOLD C. FUSON AND C. H. MCKEEVER[1]

When acetomesitylene is condensed with paraformaldehyde in the presence of potassium carbonate and methanol the principal product is a liquid which was identified as the monomethylol derivative (I). Treatment with hydrochloric acid converted this compound into a substance which was thought to be the corresponding chloride (II).[2] However, subsequent work showed that these structures were open to question. The methylol derivative, made later by the action of formaldehyde on the bromomagnesium derivative of acetomesitylene,[3] proved to be different from that reported previously. The chloride was synthesized by adding hydrogen chloride to vinyl mesityl ketone (III).[4] The compound produced in this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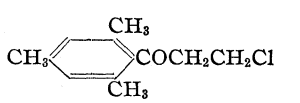
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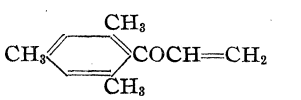
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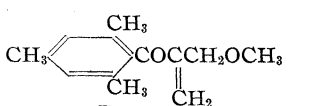
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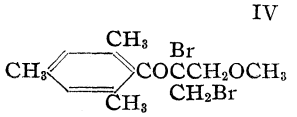

V

manner was entirely different from that first reported. These observations made it necessary to reëxamine the product from acetomesitylene and paraformaldehyde.

By careful refractionation of this oil it was found that the main portion was a compound somewhat richer in carbon than the liquid which was described earlier. It proved to be *an unsaturated ether* having the structure represented by formula IV. The evidence for this structure is conclusive. The compound reacts with bromine to give a stable dibromide (V) from which it is regenerated by treatment with sodium iodide. Catalytic hydrogenation converts the unsaturated ether to isobutyromesitylene. Zeisel determinations show that one methoxyl group is present. Structure IV is the only one which will explain all of these facts.

The formation of the unsaturated ether (IV) by the action of paraformaldehyde on acetomesitylene might be explained by the following steps[5]

$$C_9H_{11}COCH_3 + CH_2O \longrightarrow C_9H_{11}COCH_2CH_2OH \quad (1)$$

$$C_9H_{11}COCH_2CH_2OH \longrightarrow C_9H_{11}COCH{=}CH_2 + H_2O \quad (2)$$

$$C_9H_{11}COCH{=}CH_2 + CH_3OH \longrightarrow C_9H_{11}COCH_2CH_2OCH_3 \quad (3)$$

$$C_9H_{11}COCH_2CH_2OCH_3\ (VI) + CH_2O \longrightarrow C_9H_{11}COCCH_2OCH_3\ (IV) \quad (4)$$
$$\qquad\qquad\qquad

companied by dehydration to the corresponding vinyl ketone (step 2). The addition of methanol to vinyl mesityl ketone (step 3) was found to take place in the presence of potassium carbonate. From the methoxypropiomesitylene (VI) so formed the unsaturated ether (IV) was obtained readily by treatment with paraformaldehyde (step 4). The unsaturated ether was made also by combining the last two steps, *i. e.*, by treating vinyl mesityl ketone with paraformaldehyde in the presence of methanol and potassium carbonate.

Experimental

Preparation of β-Mesitoylethyl Alcohol (I).—To 0.15 mole of the bromomagnesium enolate of acetomesitylene[3] in 300 cc. of absolute ether was added with stirring at 0° 0.3 mole of gaseous formaldehyde. The formaldehyde was produced by heating paraformaldehyde to 170–200° and was introduced into the reaction mixture through a large inlet tube. The mixture was stirred for ten hours at room temperature, then poured into 600 cc. of water which had been acidified with 30 cc. of concentrated hydrochloric acid. The ether layer was separated, washed three times with very dilute hydrochloric acid, twice with water and dried over calcium chloride. The ether was removed and the residue distilled *in vacuo*. There were obtained 6 g. of acetomesitylene, 14 g. of an almost colorless liquid boiling at 135–138° (4 mm.) and 3 g. of residue.

Ten grams of the liquid when redistilled yielded 5 g. of vinyl mesityl ketone, b. p. 95–96.5° (3 mm.), and 5 g. of β-mesitoylethyl alcohol, b. p. 121–123° (2 mm.); $n^{20}D$ 1.5340. The pure compound could not be distilled without appreciable loss, presumably due to dehydration.

Anal.[6] Calcd. for $C_{12}H_{16}O_2$: C, 74.94; H, 8.41. Found: C, 75.20; H, 8.37.

The low-boiling compound was proved to be vinyl mesityl ketone by a mixed melting point of the dibromo derivative with α,β-dibromopropiomesitylene. In one experiment, the crude β-mesitoylethyl alcohol decomposed completely when redistillation was attempted. Vinyl mesityl ketone was obtained in a yield of more than 90%.

Action of Concentrated Hydrochloric Acid on Mesitoylethyl Alcohol.—A mixture of 3 g. of the crude alcohol and 100 cc. of concentrated hydrochloric acid was stirred for forty-eight hours. The reaction mixture was poured into 500 cc. of water and extracted with ether. The ether extracts were washed several times with water, dried and the ether was removed by an air blast. The viscous yellow residue was cooled and induced to solidify by scratching the sides of the container. The chloride separated from low-boiling petroleum ether as colorless plates, m. p. 46–46.5°. The yield was 2.5 g. A mixed melting point with β-mesitoylethyl chloride (II)[4] showed no depression.

Preparation of 3-Methoxyisopropenyl Mesityl Ketone (IV).[2]—A mixture of 81 g. of acetomesitylene, 45 g. of paraformaldehyde, 5 g. of potassium carbonate and 200 cc. of methyl alcohol was shaken at room temperature for four days. The solution was poured into water, acidified with dilute hydrochloric acid and extracted with several small portions of benzene. The benzene extracts were washed thoroughly, the benzene was removed and the residue fractionally distilled at diminished pressure. The following fractions were obtained: (1) 16 g., b. p. 95–122° (4 mm.); (2) 56 g., b. p. 123–129° (4 mm.); (3) 6 g., b. p. 130–136° (4 mm.); (4) 20 g., residue. Fraction 2 was redistilled three times. The 3-methoxyisopropenyl mesityl ketone was a colorless oil, b. p. 110.5–111° (1.5 mm.); $n^{20}D$ 1.5208; d^{20}_{20} 1.0101.

Anal. Calcd. for $C_{14}H_{18}O_2$: C, 77.02; H, 8.31; —OCH_3, 14.22. Found: C, 76.86, 76.76; H, 8.58, 8.50; —OCH_3, 13.85, 14.12.

Preparation of the Dibromo Derivative (V).—A solution of 5.8 g. of bromine in 15 cc. of carbon tetrachloride was added dropwise with stirring to a mixture of 7.8 g. of the ketone and 50 cc. of carbon tetrachloride. The reaction mixture was washed thoroughly with water, dried for one hour over calcium chloride, filtered and the carbon tetrachloride removed by an air blast. A small amount of low-boiling petroleum ether was added to the oil, the solution cooled to 0° and the walls of the vessel were scratched. The mixture solidified almost completely. The dibromide was recrystallized from low-boiling petroleum ether, then methyl alcohol, m. p. 50.5–51.2°; yield 11.5 g.

Anal. Calcd. for $C_{14}H_{18}O_2Br_2$: C, 44.47; H, 4.80. Found: C, 44.49; H, 4.84.

Reaction of Sodium Iodide with the Dibromide.—To 11 g. of the dibromide dissolved in 150 cc. of acetone was added a water solution of 13.5 g. of sodium iodide. The solution darkened immediately. It was allowed to stand overnight at room temperature, poured into 500 cc. of water to which had been added 10 g. of sodium thiosulfate, and extracted with ether. The ether extracts were washed with dilute sodium thiosulfate, then with water, the ether was removed and the residue distilled. There was obtained 4 g. (62% of the theoretical amount) of a liquid boiling at 118° (3 mm.). To remove a trace of iodine this liquid was dissolved in ether and the solution washed with dilute sodium thiosulfate solution. After the solvent was removed the residue was twice distilled, b. p. 114° (2 mm.); $n^{20}D$ 1.5211.

Anal. Calcd. for $C_{14}H_{18}O_2$: C, 77.02; H, 8.31. Found: C, 76.76; H, 8.42.

It could be reconverted to the dibromide.

Catalytic Reduction of 3-Methoxyisopropenyl Mesityl Ketone.—A mixture of 10.2 g. (0.046 mole) of the ketone, 150 cc. of methyl alcohol and 0.5 g. of Raney nickel was reduced under a pressure of two atmospheres. About 0.085 mole of hydrogen was absorbed. The mixture was filtered, poured into water and extracted with ether. The ether extracts were washed with water, dried and distilled. After the ether had been removed, there was obtained a very small amount of low-boiling material, 5 g. of colorless oil, b. p. 120–123° (10 mm.), 3 g. of light yellow oil, b. p. 116–125° (6 mm.) and a small amount of residue. The large fraction was redistilled, b. p. 120–121° (10 mm.);

(6) The analyses reported in this paper are microanalyses and were carried out by Mr. L. G. Fauble and Mr. W. H. Taylor.

$n^{20}D$ 1.5098. A second redistillation produced no change in the boiling point or refractive index. Isobutyromesitylene prepared from isobutyryl chloride and mesitylene by the Friedel–Crafts method boils at 120–121° (10 mm.) and has a refractive index $n^{20}D$ 1.5095. Nitration of this reduction product yielded a compound melting at 125–132°. After several recrystallizations from ethyl alcohol it crystallized in white plates, m. p. 135–138°. The mixed melting point with an authentic sample of dinitroisobutyromesitylene was 135–139°.

Preparation of β-Methoxypropiomesitylene (VI).—A solution of 10 g. of vinyl mesityl ketone, 100 cc. of methyl alcohol and 2 g. of potassium carbonate was shaken for thirty-six hours at room temperature. It was then poured into 300 cc. of water, acidified with dilute hydrochloric acid and extracted with ether. The ether extracts were washed and dried over calcium chloride. The ether was removed and the product distilled. There was obtained 7 g. (60% of the theoretical amount) of β-methoxypropiomesitylene, b. p. 117–117.5° (2.5 mm.); $n^{20}D$ 1.5110; d^{20}_{20} 1.0106, and 3.5 g. of residue.

Anal. Calcd. for $C_{13}H_{18}O_2$: C, 75.69; H, 8.79. Found: C, 75.50; H, 8.86.

If fifteen drops of concentrated hydrochloric acid were used as the catalyst[7] and the reaction mixture refluxed for one hour, the yield of β-methoxypropiomesitylene was increased to 95%.

Bromination of β-Methoxypropiomesitylene.—To a solution of ten drops of the ketone and 3 cc. of carbon tetrachloride was added a 25% bromine–carbon tetrachloride solution until hydrogen bromide was evolved. The excess bromine and carbon tetrachloride were removed by an air blast. A small amount of low-boiling petroleum ether was added and the mixture cooled. It solidified almost completely. The solid recrystallized from methyl alcohol in the form of long white needles, m. p. 78–79.5°. A mixed melting point with α,β-dibromopropiomesitylene showed no depression.

Action of Paraformaldehyde on β-Methoxypropiomesitylene.—To 10 g. of the ketone was added 90 cc. of methyl alcohol, 3 g. of paraformaldehyde and 0.5 g. of potassium carbonate. The reaction mixture was shaken for four days. It was worked up as described above in the preparation of 3-methoxyisopropenyl mesityl ketone. There was obtained 7 g. of light yellow oil, b. p. 115–120° (2.5 mm.); $n^{20}D$ 1.5193, and 3 g. of residue. The oil was redistilled, b. p. 113.5–114° (2 mm.); $n^{20}D$ 1.5207. Bromination of this oil yielded a solid, m. p. 50–51°. The mixed melting point with the dibromo derivative of 3-methoxyisopropenyl mesityl ketone was 50–51°.

Reaction of Paraformaldehyde with Vinyl Mesityl Ketone.—A mixture of 17.4 g. of vinyl mesityl ketone, 6 g. of paraformaldehyde, 100 cc. of methyl alcohol and 2 g. of potassium carbonate was shaken at room temperature for four days. The reaction mixture was worked up as described in the preparation of 3-methoxyisopropenyl mesityl ketone. There was obtained by distillation 12.5 g. of liquid, b. p. 117.5–118.5 (2.5 mm.); $n^{20}D$ 1.5198, and from the residue 2.2 g. of white plates, m. p. 105–107°. A mixed melting point of this solid with a sample of 2,4-dimesitoyl-2,4-pentadiene[2] showed no depression.

A small portion of the liquid was brominated. The solid isolated from the reaction melted at 50–51° and proved to be identical with the bromination product of 3-methoxyisopropenyl mesityl ketone.

Summary

The monomethylol derivative of acetomesitylene ($C_9H_{11}COCH_2CH_2OH$) has been synthesized by condensing the bromomagnesium derivative of acetomesitylene with formaldehyde.

The corresponding chloride ($C_9H_{11}COCH_2CH_2Cl$) has been prepared by the action of hydrochloric acid on either the monomethylol derivative or vinyl mesityl ketone.

Attempts to prepare the methylol derivative by treating acetomesitylene with paraformaldehyde in the presence of potassium carbonate and methanol have been found to yield a complex ether, $C_9H_{11}COCCH_2OCH_3$ (with CH_2 double-bonded to the carbon).

A mechanism is presented for the formation of this ether.

URBANA, ILLINOIS RECEIVED FEBRUARY 21, 1940

(7) Kohler, *Am. Chem. J.*, **42**, 375 (1909).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

The Action of Phosphorus Pentachloride on β-Phenylbenzalacetophenone

BY CHARLES R. CONARD*

When phosphorus pentachloride acts on acetone or other ketones of the type R_2CO, a ketochloride is formed

$$R_2CO + PCl_5 \longrightarrow R_2CCl_2 + POCl_3$$

Straus and others[1] tried this reagent on α,β-unsaturated ketones and found the resulting compounds to be very different from the ketochlorides of the saturated ketones. Straus[2] found, for example, that one of the halogen atoms is much more easily replaced than the other, and obtained the monochloromethoxyl derivatives of many of his unsaturated compounds by boiling their methyl alcohol solutions. He proved the structure of the unsaturated products by ozonization. Typical reactions may be represented as

$$C_6H_5CH{=}CH{-}CO{-}CH{=}CHC_6H_5 \xrightarrow{PCl_5} C_6H_5CHCl{-}CH{=}CCl{-}CH{=}CHC_6H_5$$

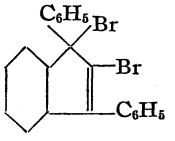
$$C_6H_5CH{=}CH{-}CO{-}C_6H_5 \xrightarrow{PCl_5} C_6H_5CHCl{-}CH{=}CCl{-}C_6H_5$$

$$C_6H_5CH(Cl){-}CH(Cl){-}C{=}C{-}C_6H_5 \xrightarrow{CH_3OH} C_6H_5CH(OCH_3){-}CH(Cl){-}C{=}C{-}C_6H_5$$

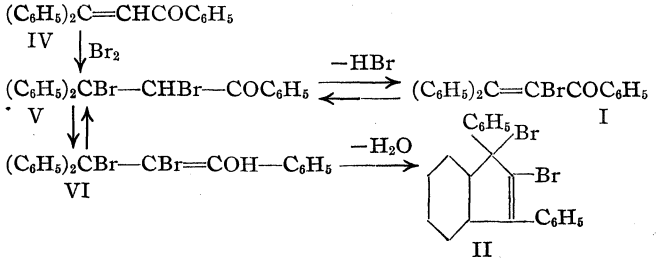
Although several α,β-unsaturated ketones react in this manner, it could not be assumed that β-phenylbenzalacetophenone would give a similar product, since the presence of a second phenyl group on the β-carbon atom may prevent a chlorine atom from attaching itself there. The surprising difference in the action of the β-phenyl derivative as compared to the benzalacetophenone itself is well illustrated by the work of Barre and Kohler,[3] who brominated β-phenylbenzalacetophenone and isolated both α-bromo-β-diphenylpropiophenone and 1,2-dibromo-1,3-diphenylindene. In the light of the above facts it appeared that the action of phosphorus pentachloride on the phenylated ketone would be of interest and this has been tried experimentally.

The β-phenylbenzalacetophenone was treated with phosphorus pentachloride in a manner very similar to that employed by Straus, and the product was handled at reduced temperature to avoid the hydrolysis of any chloro derivatives that might be formed. The product obtained was not a ketochloride; an ethoxy group was easily introduced by boiling in ethyl alcohol, yet the compounds did not correspond to the products isolated by Straus.

The product of the reaction is 1,2-dichloro-1,3-diphenylindene which reacts rapidly with ethyl alcohol to give 1-ethoxy-2-chloro-1,3-diphenylindene. Barre and Kohler have already shown that the halogen in the 1-position is unusually active since it is on a carbon joined to two benzene rings and a double bond.



The above results show that the phosphorus pentachloride is a chlorinating agent acting in a manner similar to the bromine used by Barre and Kohler. In their experiments, however, the conditions of the bromination and the method of handling the product could be used to control the nature of the substance isolated. They offer the following supposition concerning the nature of the reaction. "First the unsaturated ketone (IV)



would be expected to react with a molecule of bromine to form a dibromide (V). This dibromide (V) which contains a bromine atom linked to a carbon atom which also holds the two phenyl groups is very unstable and loses hydrogen bromide very easily. The loss of hydrogen bromide from the dibromide is reversible as is shown by the fact that the dibromoindene (II) is also ob-

* This work was done at the suggestion and under the direction of Professor E. P. Kohler (who died in 1938), and was accepted in partial fulfilment of the requirement for the degree of Ph.D. at Harvard University.

(1) Straus, *Ber.*, **39**, 2977 (1906); **40**, 2689 (1907); **42**, 1804 (1909).

(2) Straus, *Ann.*, **393**, 235–337 (1912).

(3) Barre and Kohler, THIS JOURNAL, **50**, 2038 (1928).

tained from α-bromo-β-phenylbenzalacetophenone by the action of hydrogen bromide. Since hydrogen bromide is also a dehydrating agent, the formation of the indene derivative (II) from the enolic form (VI) of the dibromide (V) is easily explained under the conditions of the reaction."

Inasmuch as phosphorus pentachloride is an active dehydrating agent and at the same time produces hydrogen chloride, it would be expected that the loss of hydrogen chloride to form the monochloro ketone corresponding to their compound (I) would be prevented, and that the dehydrating action would favor the formation of an indene corresponding to (II). It, therefore, seems likely that the suppositions of Barre and Kohler are equally applicable to the action of phosphorus pentachloride on β-phenylbenzalacetophenone.

Experimental

Treatment of β-Phenylbenzalacetophenone with Phosphorus Pentachloride.—In attempts to isolate products corresponding to those found by Straus, several variations in the procedure were employed. Each time a reddish oil was produced from which no crystals were obtained.

Five grams of the ketone was dissolved in 50 cc. of dry benzene, 5.5–6 g. of phosphorus pentachloride added, the mixture allowed to reflux on the steam-bath for one hour, cooled and poured over cracked ice. The ice was removed as soon as the benzene had melted and the liquids were separated. The benzene layer was washed several times with cold water, dried over sodium sulfate or calcium chloride, and concentrated at room temperature to a thick reddish oil which must have contained 1,2-dichloro-1,3-diphenylindene.

A product having the same appearance and properties was obtained when 5 g. of ketone dissolved in benzene was treated with 4.5 g. of phosphorus pentachloride and the mixture, after standing at room temperature for four days, was poured over cracked ice, washed with water, washed with sodium bicarbonate solution, dried over calcium chloride, and concentrated.

Better yields of secondary products are obtained when the ketone is treated with 2.2 mols of phosphorus pentachloride, the flask being fitted with a reflux condenser carrying a tube for the removal of hydrogen chloride fumes. The mixture is boiled for one to two hours, after which it may be concentrated by evaporation, since most of the hydrogen chloride has already escaped.

Ozonization of 1,2-Dichloro-1,3-diphenylindene.—Since products similar to those found by Straus were possible, it was considered wise to ozonize the red oil (uncrystallized product) to see what evidence could be obtained. The concentrated residue from the phosphorus pentachloride treatment was taken up in carbon tetrachloride. The solution was ozonized for four hours using a slow stream of 6–8% ozone, and the ozonide decomposed by shaking with cold sodium bisulfite solution for several hours. The carbon tetrachloride was evaporated and the resulting mixture was extracted with ether. After evaporating the ether, the residue was steam distilled, the distillate extracted with ether, and the ether solution evaporated, leaving a product which proved to be benzophenone, doubtless coming from unchanged ketone.

The residue from the steam distillation was taken up in ether, dried over calcium chloride, and allowed to crystallize. After recrystallization from methyl alcohol, this melted at 145–146.5°. A mixed melting point with an authentic sample proved this substance to be *o*-dibenzoylbenzene.

Preparation of 1-Ethoxy-2-chloro-1,3-diphenylindene.—The concentrated benzene solution from the phosphorus pentachloride treatment is dissolved in ethyl alcohol and evaporated by boiling to one-third the original volume or less and enough ethyl alcohol added to bring the solution to the original volume, which may again be evaporated by boiling. This method of heating serves not only to cause a reaction with the ethyl alcohol but also to remove the benzene, in which the indene has a high solubility. A nicely crystalline product separates, which may be recrystallized from ethyl alcohol, m. p. 135.5–136°.

Anal. Calcd. for $C_{23}H_{19}OCl$: C, 79.6; H, 5.5; Cl, 10.2; OC_2H_5, 13.0. Found: C, 80.1, 79.3, 79.6; H, 5.4 (4.3), 5.7; Cl, 10.2, 10.0; OC_2H_5, 12.1, 12.7.

Ozonization of the 1-Ethoxy-2-chloro-1,3-diphenylindene.—One gram of the 1-ethoxy-2-chloro-1,3-diphenylindene dissolved in carbon tetrachloride was ozonized for four and a half hours. The ozonide was decomposed by shaking with a cold dilute (1%) solution of hydrogen peroxide and the carbon tetrachloride removed by evaporation. The apparatus was washed with alcohol and the washings were added to the main solution. The mixture was allowed to stand on the steam-bath for about eight hours, serving to remove the alcohol and ensuring the liberation of carbon dioxide from any α-ketocarboxylic acid, to give the ketone sought. The mixture was cooled, extracted with ether, the ether solution dried over calcium chloride and on standing overnight the *o*-dibenzoylbenzene had crystallized out. The product was recrystallized from methyl alcohol and a mixed melting point proved its identity.

Summary

1,2-Dichloro-1,3-diphenylindene has been prepared by the action of phosphorus pentachloride on β-phenylbenzalacetophenone, its identity shown by ozonization, and an ethoxy derivative prepared and ozonized.

EUREKA COLLEGE
EUREKA, ILLINOIS

RECEIVED JANUARY 24, 1940

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

The Formation of Sulfonium Compounds from Benzyl Iodide and Organic Disulfides

BY OTTO HAAS AND GREGG DOUGHERTY

Steinkopf and Müller[1] found that sulfonium salts were formed when alkyl disulfides are heated with alkyl halides. Since their experiments were carried out at 100° in sealed tubes for thirty hours, it seemed possible that the products resulted from rather profound decompositions. It was of interest therefore to study this reaction under mild conditions which would favor greater stability of the primary products, and possibly lead to a surer knowledge of the mechanism by which the products were formed.

Using mercuric iodide or ferric chloride as catalysts, it has now been found that benzyl iodide reacting on organic disulfides in acetone solution, forms the sulfonium salts of the monosulfides at room temperature. The compounds are isolated in the form of the addition complex with the salt used as a catalyst. (In this way the following have been prepared: tribenzylsulfonium iodide-mercuric iodide, dibenzylethylsulfonium iodide-mercuric iodide, dibenzylbutylsulfonium iodide-mercuric iodide, tribenzylsulfonium iodide-ferric chloride.) Unlike the results obtained by Hilditch and Smiles, who worked with ethyl iodide, diethyl disulfide and mercuric iodide, no disulfide sulfonium salts could be isolated.[2]

These reactions may be explained by a mechanism similar to that proposed by Steinkopf and Müller

$$R{-}S{-}S{-}R + HgI_2 + C_6H_5{-}CH_2{-}I \longrightarrow R{-}S{-}S{-}R{\cdot}HgI_2 \quad (1)$$
$$\qquad\qquad\qquad

the solution and this corresponds to 96.6% of the iodine originally added.

Summary

The reaction of benzyl iodide with three organic disulfides, in the presence of mercuric iodide or ferric chloride, has been studied.

Four sulfonium compounds, in the form of the addition complex with the metallic halide, were prepared. Two of these are new compounds.

A mechanism for the reaction has been proposed.

PRINCETON, N. J. RECEIVED FEBRUARY 8, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ALABAMA]

Reactions of Sulfur and Vapors of Organic Compounds at Different Temperatures[1]

BY GEO. D. PALMER, S. J. LLOYD, W. P. MCLURE, NORMAN LEMAISTRE, W. S. WARING AND L. W. BACHMAN

The preparation of a new series of sulfur dyes by a vapor method using benzene and other organic compounds in contact with molten sulfur at temperatures *above* 300° has been reported.[2] With similar apparatus, we are now able to report the preparation of two new classes of sulfur organic compounds prepared at temperatures *below* 300°.

Experimental

Preparation of New Sulfur Organic Compounds.—We find that the vapors of many organic substances, including benzene, toluene, aniline, phenol, etc., when passed through molten sulfur at 240–260° form resinous sulfur dyes (A) which are in some cases rubber-like after purification, whereas at 260–300° non-resinous sulfur organic compounds (B) which are not dyes result. These are brown to black powdery solids, insoluble in sodium sulfide and carbon bisulfide. Hydrogen sulfide is a by-product, much more being evolved in preparation of A than B. The yields of A are much better than those of B and are comparable to the yields of compounds prepared above 300° (C).[2]

Purification and Analyses.—Eighteen samples were purified with carbon bisulfide, acetone, benzene, and water for 525 hours in large-scale Soxhlet extractors. Analyses for sulfur were made at intervals until the percentage of sulfur in each substance became constant.

Discussion

All sulfur dyes prepared by this vapor method and producing intense colors contain 50 to 83% sulfur. A few aliphatic substances which have yielded small amounts of low-sulfur-content dyes have produced much less intense colors on cotton and rayon.

It appears that the higher the sulfur content of the dye, the less the sodium sulfide (in aqueous solution) required to dissolve it. It also appears that the higher the sulfur content, the more resinous is the material. The resinous property of the chlorobenzene product (A) is lost when it is dissolved in aqueous sodium sulfide, but is regained by precipitation with a mineral acid.

TABLE I

COMPOSITION OF PURIFIED SULFUR ORGANIC SUBSTANCES PREPARED BELOW 300°

Compd. reacting with sulfur	Opt. temp. for prepn., °C.	S, %	N, %	Cl, %
Benzene	260–300	30.95		
Aniline	260–300	30.96	9.63	
Chlorobenzene	240–260	83.44		1.08

TABLE II

PROPERTIES OF DYES PREPARED FROM CHLOROBENZENE AND SULFUR ABOVE AND BELOW 300°

Opt. temp., for prepn., °C.	Phys. form	Color of solid	Soly. in CS_2	Soly. in aq. Na_2S	Color on cot. and rayon
360–444.6	Powd.	Red	Insol.	Sl.	Red-brown
240–260	Res. matl.	Gray-black	Sl.	Fairly	Dark-brown

TABLE III

COMPOSITION OF PURIFIED SULFUR DYES PREPARED AT 360–444.6°

Sample	Compound reacting with sulfur	C, %	H, %	S, %	N, %	O, %
1	Benzene	34.54	0.92	62.46		
2	Toluene	36.17	0.93	62.68		
3	Phenol	34.95	1.97	55.15		7.93
4	Aniline	37.88	1.23	53.38	6.56	

Empirical formulas have been calculated for dyes 1 and 2 in Table III, and a constancy of $C_3H_1S_2$ is indicated. The grouping in these high sulfur content organic substances prepared from hydrocarbons and sulfur at 360–444.6 is apparently similar to the recurrent grouping in the formula of thiokol[3] in that in each case *one* hydro-

(1) Presented at the Baltimore meeting of the American Chemical Society, April, 1939.

(2) Geo. D. Palmer and S. J. Lloyd, THIS JOURNAL, **52**, 3388 (1930).

(3) J. C. Patrick, *Modern Plastics*, [2] **14**, 46 (1936).

carbon group is attached to *four* sulfur atoms. Thus

$S_2C_2H_4S_2$ (Thiokol)
$S_2C_6H_2S_2$ (Sulfur dye from benzene)

Summary

1. By contacting vapors of organic compounds with molten sulfur *below* 300°, two new classes of sulfur organic compounds have been prepared, with hydrogen sulfide as a by-product.

2. Products prepared at 240–260° are resinous sulfur dyes, while products prepared at 260–300° are non-resinous and are not sulfur dyes.

3. High sulfur content is necessary in the sulfur dyes for the production of intense colors.

4. Additional ideas as to the structure of sulfur dyes prepared by vapor methods have been presented.

UNIVERSITY, ALABAMA RECEIVED DECEMBER 8, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF PHYSICAL CHEMISTRY, NO. 455, AND FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, NO. 217, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

The Inversion of Sucrose

BY LAWRENCE J. HEIDT AND CLIFFORD B. PURVES

Recently we published data on the rates of hydrolysis of several fructosides including sucrose at 30 to 60° and calculated energies of activation, E, assuming that E did not vary with temperature. At the same time Leininger and Kilpatrick[1] found that in more concentrated solutions of sucrose E was smaller at 30 than at 0°, but that dE/dT approached zero as T increased. In addition, their data gave smaller values of E at 5.8 than at 0.5 N hydrochloric acid. Nevertheless, the rate constants obtained by extrapolating their data to our acid concentration of 0.01 N gave, within the limits of error, the same values of E and dE/dT between 25 and 35° as our previously published[2] values of $E = 25.75$ kcal. and $dE/dT = 0$ between 30 and 60°. They followed the inversion by noting the accompanying contraction of a fixed weight of solution. We used the copper reduction technique to measure the rate of formation of reducing sugars. The divergence of dE/dT from 0 obtained by the dilatometric method at temperatures lower than 25° led us to see whether this divergence could also be observed by the copper reduction technique when working in the same range of temperature and at the same concentrations of reactants used in reference 1. We were especially interested in this problem because conclusions like those we drew by comparing activation energies for the hydrolysis of fructosides[2] would be vitiated, of course, if the values of E were determined where dE/dT was not zero.

The reagents,[2] experimental procedure[2] and apparatus[3] have been described. Reactions at 10.00° took place in a thermostat kindly lent by Professor Scatchard. Especial care was taken to transfer each sample quickly from the reaction cell to just enough caustic soda solution at 0° so that the resulting solution was neutral to phenolphthalein. These neutral solutions were kept at 0° until analyzed.[2]

Corrections for the sucrose, sodium chloride, and concentrations of the reducing sugars present in the analyses were usually negligible. For example, 5 cc. of a 5% solution of sucrose formed cuprous oxide equivalent to 8 cc. of the 0.002 M sodium thiosulfate[4] and 1 cc. of a 23% solution of sodium chloride increased by 3.5% the cuprous oxide formed by the invert sugar. To reduce titration errors, the estimations of the reducing sugar in each sample withdrawn from the reaction cell were made at several concentrations scattered over the range covered in the calibrations.

Concentrations were referred to a liter of solution at the temperature the sucrose was inverted. Acid concentrations were obtained in each case by titrating with standard base weighed aliquots whose volumes at the temperature of the hydrolysis were carefully measured. Phenolphthalein was used as the indicator. The titrations agreed in every case with calculations based on the dilution of the standardized acid used to make up the sucrose solutions, so no measurable amount of acid was produced or consumed during the inversion.[5]

(1) Leininger and Kilpatrick, THIS JOURNAL, **60**, 2891 (1938).
(2) Heidt and Purves, *ibid.*, **60**, 1206 (1938).
(3) Heidt, *ibid.*, **61**, 3455 (1939).
(4) In the earlier work[2] this hypo was denoted as 0.002 N.
(5) These titrations, however, would not reveal slight decreases in the pH like those noted in the photosensitized reaction: Heidt, THIS JOURNAL, **61**, 3223 (1939).

The fraction of sucrose inverted was the same within 1%, whether calculated by the methods described by Mathews and Jackson[6] or by Guggenheim,[7] or from the concentration of invert sugar when inversion was complete.

The invert sugar found when inversion was complete agreed within 1% with the value obtained for the equivalent quantity, (360/342) × wt. of sucrose, of equal weights of glucose and fructose. The invert sugar, therefore, was not affected measurably by the hydrochloric acid present in our experiments. This is in accord with previous work.[6]

The logarithm of the concentration of sucrose remaining in an experiment was a linear function of time within the limits of error. The fraction of sucrose inverted per minute, given as the velocity constant k in Table I, was obtained, therefore, from the slope of the straight line through these points. Each line was obtained by the method of least squares with each point given a weight about equal to the average volume of the neutralized solutions used in the analysis. Reaction rates were followed until at least 60% of the sucrose had been inverted. In the earlier work,[2] k was obtained graphically.

The data are summarized in Table I.

In Fig. 1, lines A and C show the change in log k^* with $1/T$, and the B lines the change in log k^* with the concentration of HCl. The equations for these lines were calculated by the method of least squares and the quadratic mean errors in the constants of the equations were obtained in a way outlined elsewhere.[8] The probable error equals the quadratic mean error multiplied by 0.6745. The dots in Fig. 1 represent the common logarithm (log) of our average values of k^*.

The ordinates for the B lines are on the left side of the figure. The lower of these lines represents the data obtained at −0.01° by Leininger and Kilpatrick,[1] who found (1), log k^* = $\bar{4}$·1057 + 0.2394 [HCl]. The upper of the B lines represents our data at 0.00° which gave (2), log k^* = $\bar{4}$·1189 + 0.2495 [HCl]. The difference between the slopes of these lines is greater than the reproducibility of the velocity constants in either method.

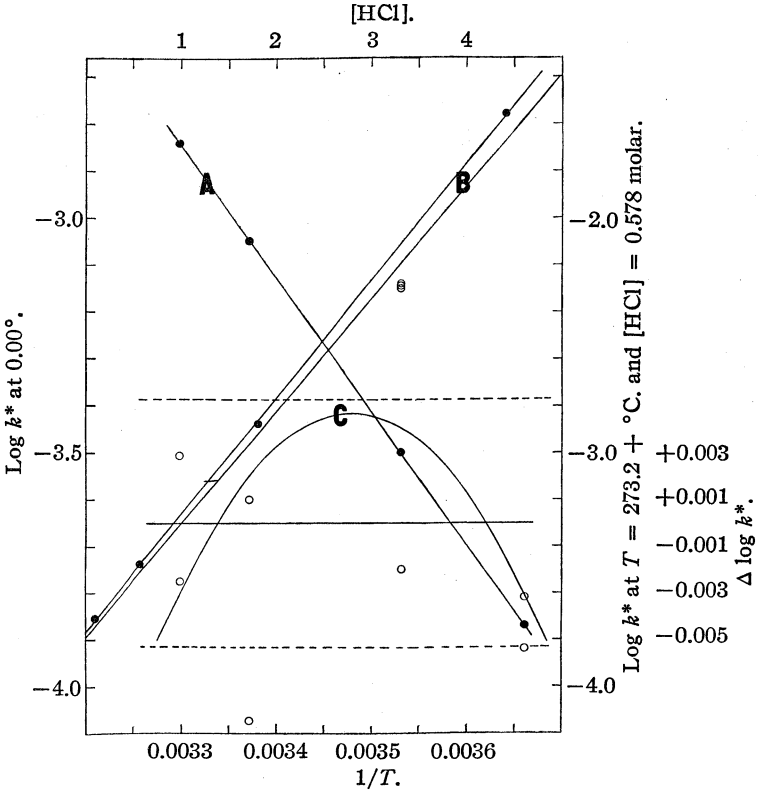


Fig. 1.

TABLE I

There was present initially about 2 g. of sucrose, weighed to 0.1 mg. per 100 cc. of solution. The fraction inverted per minute = k and k^* = k/[HCl].

Moles of HCl in a liter	10^4k	10^4k^*	°C.
4.41	74.1	16.8	0.00
4.41	73.1	16.6	.00
1.81	6.55	3.62	.00
1.81	6.63	3.67	.00
0.575	1.05	1.82	.00
.580	1.06	1.83	.00
.0965	0.136	1.40	.00
.0965	0.135	1.40	.00
.578	5.74	9.93	10.00
.578	5.92	10.3	10.00
.576	5.88	10.2	10.00
.576	5.89	10.2	10.00
.578	46.6	80.6	23.40
.578	45.6	78.9	23.40
.577	122	211	30.05
.577	120	208	30.05

(6) Mathews and Jackson, *Bur. Standards J. Research*, **11**, 619 (1933).

(7) Guggenheim, *Phil. Mag.*, **1**, 538 (1926).

(8) Whittaker and Robinson, "The Calculus of Observations," Chap. IX, D. Van Nostrand Co., New York, N. Y., 1924.

A manipulation tending to make our values of k^* high was the short time, about thirty seconds, that the solution undergoing hydrolysis was warmed slightly by the pipet, initially at 25°, while being transferred to the caustic soda solution. This produced a negligible effect upon k^* when $k < 0.0005$ at 0° so that it affected less than 1% any of the rate constants obtained at 0.58 N hydrochloric acid; however, it would account for part of the increasing divergence of the B lines as the concentration of hydrochloric acid was increased.

The possible errors in their refined dilatometric method have been discussed ably by Leininger and Kilpatrick.[1] Their data extended from 0.6 to 5.8 N hydrochloric acid where the logarithm of the activity of the acid also varies almost linearly with its concentration although deviating sharply from linearity in more dilute solutions. Nevertheless, they were careful to dot in the extension of their lines beyond their experimental values and thus correctly assumed that their linear plots could be extrapolated to give k^* down to [HCl] = 0. They thereby implied that k^* was not directly proportional to the activity of the hydrochloric acid, and their hypothesis is supported by our data at 0.1 N hydrochloric acid which, within the limits of error, falls on our linear plot instead of paralleling the activity of the hydrochloric acid.

Line A, whose ordinates are given on the right side of the figure, gives the linear dependence upon $1/T$ of our values of (3), $\log k^* = (17.0172 \pm 0.0678) - (5669 \pm 19.5)\ (1/T)$. The circles in the figure represent the deviations from line A of the individual values of $\log k^*$ included in the average values represented by the dots. The ordinates of these deviations, $\Delta \log k^*$, are on a scale obtained by magnifying one hundred times the scale of ordinates used for line A. An observation which did not deviate from line A would fall on the solid horizontal line in the figure, and one representing the probable deviation, 0.0053, would fall on either of the dotted horizontal lines. The second degree parabola representing the observed deviations is given by line C. The equation for this line plus that for line A is (4), $\log k^* = (14.1882 \pm 2.0960) - (4040 \pm 1208)\ (1/T) - (234057 \pm 173840)\ (1/T)^2$.

The quadratic mean error in the coefficient of $(1/T)^2$ in equation (4) is so large, according to the t test,[9] that the straight line given by equation (3) adequately represents our data.[10] The probable deviation in any experimental value of $\log k^*$ is 0.0053 from (3) and 0.0046 from (4) or 1.2% in k^*.

The energy of activation, in kcal., by equation (3) is 25.94. If equation (4) differed significantly from (3), E would be 26.35 at 0° and 25.55 at 30°. At the same concentrations of reactants, the average value of E from the measurements with a dilatometer[1] was 26.0 kcal. decreasing[11] from 26.6 at 0° to 25.4 at 30°.

When our concentrations are expressed as mole fractions, k^* is replaced by $k' = k^*\ (55.5062\ d - 1.0240\ N - 1.0517)$. The normality, N, of the acid is given in Table I, and d, the weight in grams of one ml. of solution at the temperature of inversion, was roughly 1.017 at 0.0°, 1.0122 at 10.0°, 1.0116 at 23.4° and 1.0085 at 30.0°. Our data now fit the equations (5), $\log k' = (18.7083 \pm 0.0626) - (5655 \pm 18)\ (1/T)$ and (6), $\log k' = (14.5375 \pm 2.0499) - (3251 \pm 1180)\ (1/T) - (346044 \pm 169935)\ (1/T)^2$. The probable deviation in any experimental value of $\log k'$ is 0.0049 from (5) and 0.0045 from (6). Also, from (6) E equals 26.5 kcal. at 0° and 25.35 at 30°, but again the quadratic mean error in the coefficient of $(1/T)^2$ is so large that the straight line adequately represents the data. Moreover, expressing concentrations as mole fractions instead of moles per liter of solution does not improve significantly the fit of our data to either a straight line or second degree parabola.

(9) R. D. Fisher, "Statistical Methods for Research Workers," Chapter V, Oliver and Boyd, London, 1936. The "Table of t" given near the end of this book lists a probability equal to 0.3 of getting by accident 234057 as the coefficient of $(1/T)^2$. This probability is much greater than the value of 0.05 given arbitrarily by this author as an upper limit for a significant result.

(10) Any systematic errors in the measurements *not* having the same percentage effect upon each value of k^* could vitiate this conclusion.

(11) The data of Leininger and Kilpatrick[1] (L. and K.) at 10, 15, 20, 25 and 30° and 1.120 to 1.124 N hydrochloric acid, and $\log k^*$ at 1.122 N acid and −0.01° calculated from their equation 4a give (7), $\log k^* = (16.9111 \pm 0.0856) - (5608 \pm 25)(1/T)$ and (8), $\log k^* = (11.7937 \pm 0.8956) - (2663 \pm 515)(1/T) - (423057 \pm 74000)(1/T)^2$. The probable deviation of $\log k^*$ is 0.0049 from (7) and 0.0017 from (8), and the probability is less than one in a hundred of obtaining accidentally the coefficient of $(1/T)^2$ given in (8) from which E equals 26.2 kcal. at 0° and 25.0 at 30°. These calculations, therefore, support the conclusion of L. and K. that their data give values of E changing with T. Moreover, when their concentrations are converted to mole fractions, values of $\log k'$ are obtained giving values of E also changing significantly with T. In addition, a comparison of the nearly equal probable deviations of the data from equations (3), (4) and (7) with that of $\log k^*$ from (8) reveals that unless $\log k^*$ can be determined to 0.4% or less over an interval of 30° changes in E with T as small as found by L. and K. are not significant. Moreover, corrections for the effect of the mutarotation of glucose upon the rates observed by L. and K. would straighten their plots of $\log k^*$ *vs.* $1/T$. It is quite possible that these and other corrections would change $\log k^*$ as much as 0.5% more at 0° than at 30° which would remove from their data any significant change in E with T for the inversion of sucrose.

Summary

Rates of inversion of sucrose measured by the reducing sugars produced were found to be slightly higher than the rates previously obtained by the dilatometric method at the same temperatures and concentrations of hydrochloric acid and sucrose.

The activation energy obtained is 25.9 kcal. and does not vary significantly with the temperature between 0 and 30°.

The logarithms of the velocity constants at 0° are a linear function of the concentration of hydrochloric acid between 0.1 and 4.4 *N*.

CAMBRIDGE, MASS. RECEIVED JANUARY 23, 1940

CONTRIBUTION FROM THE WILLIAM G. KERCKHOFF LABORATORIES OF THE BIOLOGICAL SCIENCES, CALIFORNIA INSTITUTE OF TECHNOLOGY]

Thermal Data. XII. The Heats of Combustion of Urea and Guanidine Carbonate and their Standard Free Energies of Formation

BY HUGH M. HUFFMAN

In continuation of our program,[1] involving the study of the thermal properties of organic compounds of physiological interest, we have determined the heats of combustion of urea and of guanidine carbonate. These data have been used in conjunction with other data to calculate the standard free energies of formation of these compounds.

Experimental

Calorimetric Method.—The calorimetric method has been described in previous publications.[2] Since no important changes have been made, only the essential details will be given. All of the combustions were made in a Parr bomb having a volume of 0.380 liter and with an initial oxygen pressure of 30 atmospheres and with 1 ml. of water in the bomb.

The energy equivalent of the calorimetric system was controlled throughout the investigation by frequent calibration with Bureau of Standards benzoic acid standard sample 39e, having for its isothermal heat of combustion under standard conditions[3] and at 25° the value of $-\Delta U_B/m$ = 26,419[4] N.B.S. international joules. The conditions in our bomb are not quite standard, necessitating a correction of this value to 26,418 N.B.S. international joules.

A minor change was made in the calorimeter after the combustions on guanidine carbonate and hence a recalibration was required. The energy equivalent of the calorimetric system in the guanidine carbonate series was 3157.4 cal., mean of fifteen calibration experiments, with a standard deviation of 0.0016% and in the urea series 3157.0 cal., mean of seventeen calibration experiments, with a standard deviation[5] of 0.0021%. The results of all of our combustion experiments are expressed in terms of the defined conventional calorie which is derived from the N.B.S. international joule by dividing by 4.1833. The units and corrections are the same as those given in previous papers.[6] The molecular weights are based on the 1939 table of atomic weights. All of the thermal data are given for the isothermal process at 25° and for true mass.

Purification and Heats of Combustion

Urea.—Three combustion samples a, b and c were prepared from J. T. Baker C. P. urea by one and three crystallizations from redistilled water and by two crystallizations from purified methyl alcohol, respectively.

Guanidine Carbonate.—Material from Eastman Kodak Co. was dissolved in hot water and allowed to cool, it was then precipitated by the addition of about 2.5 volumes of purified ethyl alcohol. This process was repeated to give sample (a). Material from Hoffman–LaRoche was precipitated once as above to give sample (b).

Nitrogen determinations on the urea gave the theoretical results and the ash content was negligible. Titrations of the guanidine carbonate with dilute hydrochloric acid gave 99.7 and 99.8% of the theoretical. The ash content was about 0.03%.

The results of the combustions of these compounds are given in Table I. In the case of guanidine carbonate we have arbitrarily corrected the mass by subtracting from the observed mass the mass of ash found after each combustion. The uncertainties given in the table are the mean deviations from the mean.

In addition to the experimental values we have also calculated the quantities $-\Delta U_B$, $-\Delta U_R$, $-\Delta H_R$ and $-\Delta H_f^\circ$ which we have defined previously.[2b] To obtain the values of $-\Delta H_{f298}^\circ$ we have used for the heats of formation of water and carbon dioxide at 25° the value 68,318.1[7] and 94,030[8] calories, respectively.

Discussion

Urea has been burned by several workers (Berthelot 1890, Stohmann 1893, Krummacher 1904, Emery and Benedict 1911). It is not possible to make a careful comparison of our results

(1) Huffman and Borsook, THIS JOURNAL, **54**, 4297 (1932).

(2) (a) Huffman and Ellis, *ibid.*, **57**, 41 (1935); (b) Stiehler and Huffman, *ibid.*, **57**, 1734 (1935).

(3) Washburn, *Bur. Standards J. Research*, **10**, 552 (1933).

(4) Jessup and Green, *ibid.*, **13**, 496 (1934).

(5) Rossini and Deming, *J. Wash. Acad. Sci.*, **29**, 416 (1939).

(6) Huffman, THIS JOURNAL, **60**, 1171 (1938).

(7) Rossini, *Bur. Standards J. Research*, **22**, 407 (1939).

(8) Rossini and Jessup, *ibid.*, **21**, 491 (1938).

TABLE I

THE EXPERIMENTAL DATA AT 25°

Sample	Desiccation, hours P_2O_5 Vac. 70°	Oven 100°	True mass	Total heat evolved, cal.	Cal. from HNO_3	Cal. from oil	Cal. from paper and EIt	$-\Delta U_B/m$ cd. g^{-1}	Dev.
				Urea					
(a)	2160		2.45335	6330.9	24.4	101.8	18.1	2521.7	0.1
(a)	4150		2.45231	6341.7	24.9	117.6	16.8	2521.0	.6
(a)	4100	90	2.43084	6355.1	24.2	183.8	17.4	2521.6	.0
(b)	2160		2.45441	6313.3	25.2	80.4	17.3	2522.2	.6
(c)	2160		2.45406	6335.4	24.7	104.6	17.6	2521.7	.1
(c)	4100	24	2.43823	6345.8	24.9	155.6	17.6	2521.4	.2
							Mean	2521.6	± .3
				Guanidine Carbonate					
(a)	1248		2.41774	6345.9	24.8	116.2	16.9	2559.4	0.4
(a)	1440		2.41750	6344.0	23.6	116.1	16.6	2559.5	.5
(a)	1080	168	2.41688	6337.5	23.5	111.9	17.4	2559.0	.0
(a)	408	72	2.40356	6350.6	22.2	162.5	17.6	2558.0	1.0
(a)		264	2.44756	6413.0	23.0	110.1	16.9	2558.9	0.1
(b)	1248		2.41717	6331.6	22.7	106.6	16.4	2559.1	.1
(b)	1440		2.29695	6419.2	25.0	499.5	17.9	2558.5	− .5
(b)	1248	120	2.41085	6327.0	24.0	114.9	17.9	2559.3	.3
							Mean	2559.0	± .4

with those of the earlier workers because of insufficient data. We have made a rough recalculation of the data of Emery and Benedict[9] and find that their value of $-\Delta H_R$ is about 0.2% higher than that of this investigation. So far as we are aware there are no existing data for the combustion of guanidine carbonate.

The derived data are given in Table II. The uncertainties assigned to these data are calculated

TABLE II

SUMMARY OF DERIVED DATA AT 25°

Substance	Urea	Guanidine carbonate
Formula	CH_4ON_2	$C_3H_{12}O_3N_6$
Molecular weight	60.058	180.175
Density	1.335	1.251
$-\Delta U_B$, kcal. $mole^{-1}$	151.44 ± 0.04[a]	461.07 ± 0.13[a]
$-\Delta U_R$, kcal. $mole^{-1}$	151.29 ± .04	460.67 ± .13
$-\Delta H_R$, kcal. $mole^{-1}$	151.00 ± .04	459.77 ± .13
$-\Delta H_f^\circ$, kcal. $mole^{-1}$	79.67 ± .05	232.22 ± .15
$d\Delta U_R/dT$, $mole^{-1}$ deg.$^{-1}$ cal.	−18	−59

[a] Calculated uncertainty interval.

from the standard deviations of the experimental data multiplied by two and combined with the uncertainties assigned to the various auxiliary data which were used. See reference (5) for details of these calculations. As far as we are aware there are no factors which would cause any absolute error in these determinations hence the assigned uncertainties may be taken as a measure of the absolute accuracy of these data.

(9) Emery and Benedict, *Am. J. Physiol.*, **28**, 311 (1911).

The Free Energies.—We have also calculated the free energies of these compounds using the entropy of urea as determined by Parks, Huffman and Barmore[10] and the value of Huffman, Ellis and Borsook[11] for guanidine carbonate. The values of the free energies and other necessary data are tabulated in Table III. To obtain ΔS

TABLE III

THERMAL DATA AT 298.1°K.

Substance	ΔH°, kcal.	S, cal. deg^{-1} mole^{-1}	ΔS, cal. deg^{-1} mole^{-1}	ΔF°, kcal.
Urea	− 79.67	25.2	−108.9	− 47.21 ± 0.18[a]
Guanidine carbonate	−232.22	70.6	−331.7	−144.34 ± 0.45

[a] Estimated maximum uncertainty.

we have used for the entropies of C (graph), H_2, O_2 and N_2 the values 1.36,[12] 31.23,[13] 49.03[14] and 45.79[15] cal. degree^{-1} mole^{-1}, respectively. We have assigned uncertainties to the tabulated free energies but in this case this is only an estimate since we are unable to evaluate precisely the uncertainty in the entropies of the compounds. We do feel however that this is a very conservative estimate, especially in the case of urea.

Urea was used by Parks, Huffman and Barmore[10] to test the third law of thermodynamics.

(10) Parks, Huffman and Barmore, THIS JOURNAL, **55**, 2733 (1933).
(11) Huffman, Ellis and Borsook, *ibid.*, **62**, 297 (1940).
(12) Jacobs and Parks, *ibid.*, **56**, 1513 (1934).
(13) Giauque, *ibid.*, **52**, 4816 (1930).
(14) Giauque and Johnston, *ibid.*, **51**, 2300 (1929).
(15) Giauque and Clayton, *ibid.*, **55**, 4875 (1933).

In view of our new combustion data and also of the availability of more reliable free energy data for water and carbon dioxide it is interesting to again compare the free energy of urea as calculated from equilibrium data and from third law data.

The calculation from the equilibrium data may be summed up as follows

$$CO_2(g)+2NH_3(g) = H_2O(g)+CO(NH_2)_2(s);\ \Delta F_{298}=290^{16}$$
$$H_2O(g) = H_2 + 1/2O_2;\ \Delta F = 54{,}638^{7}$$
$$C(graph) + O_2 = CO_2(g);\ \Delta F = -94{,}239^{8}$$
$$N_2 + 3H_2 = 2NH_3;\ \Delta F = 7820^{17}$$
$$C(graph) + 2H_2 + N_2 + 1/2O_2 = CO(NH_2)_2(s);\ \Delta F = -47{,}131$$

This result is only 80 calories higher than the third law value and is less than the uncertainty in the $T\Delta S$ term due to the uncertainty in the entropy of urea.

(16) Lewis and Burrows, THIS JOURNAL, **34**, 1515 (1912).

(17) Lewis and Randall, "Thermodynamics," McGraw-Hill Book Co., Inc., New York, N. Y., 1923, p. 557.

In conclusion we wish to thank Dr. E. L. Ellis for the purification of the compounds used in this investigation.

Summary

1. The isothermal heats of combustion of urea and guanidine carbonate have been determined at 25°.

2. The free energies of urea and guanidine carbonate have been calculated.

3. A comparison of the free energy of urea from equilibrium data and third law data has been made.

PASADENA, CALIF. RECEIVED DECEMBER 28, 1939

[CONTRIBUTION FROM THE RYERSON PHYSICAL LABORATORY, UNIVERSITY OF CHICAGO]

The Crystal Structure of Sodium Formate, $NaHCO_2$[1]

BY W. H. ZACHARIASEN

The present investigation was undertaken primarily to obtain accurate values for the structure of the formate group.

Crystals of sodium formate, $NaHCO_2$, are reported[2] to have monoclinic-holohedral symmetry with crystallographic elements $a_1':a_2':a_3' = 0.9196:1:1.6512$, $\alpha_2' = 93°37'$. In this article another coördinate system, a_1, a_2, a_3, will be used. The correlation between the two sets of axes is $a_1 = a_1'$, $a_2 = a_2'$, $a_3 = {}^1/_2(-a_1' + a_3')$, and one finds readily $a_1:a_2:a_3 = 0.9196:1:0.9700$, $\alpha_2 = 121°51'$.

The crystals studied were obtained by recrystallization from aqueous solutions. Most of the specimens obtained proved to be twinned with (001) as the twinning plane. The single crystals were elongated in the direction a_3 and showed the faces (010), (110) and (001). The compound is somewhat hygroscopic.

A great many oscillation photographs, using CuKα radiation, were prepared. The directions [001], [100], [101] and [010] served as rotation axes. The crystals were shaped into approximate cylinders along the various rotation axes so that corrections for absorption readily could be applied.

(1) Some of the results of this investigation were published in an abstract which appeared in *Phys. Rev.*, **53**, 917 (1938).

(2) P. Groth, "Chemische Krystallographie," Vol. III, Leipzig, 1901.

The structure determination was based upon the reflections in the equator layer lines for which the intensity was set proportional to

$$|F_H|^2 \frac{1+\cos^2 2\theta}{\sin 2\theta} A$$

where A is the absorption factor.

The dimensions of the unit cell were found to be $a_1 = 6.19 \pm 0.01$ Å., $a_2 = 6.72 \pm 0.01$ Å., $a_3 = 6.49 \pm 0.01$ Å., with $\alpha_2 = 121°42' \pm 10'$. The reported density of 1.91–1.93 gives four molecules of sodium formate in the unit cell. No reflections appear for which $H_1 + H_2$ is odd, so the translation lattice is base centered. Furthermore, reflections H_1OH_3 are absent if H_3 is odd, showing that the symmetry plane is a glide-plane rather than a reflection plane. On the assumption that the reported point group is correct, the space group becomes $C2_1/n(C_{2h}^6)$.

In order to obtain a reasonable structure for the formate group, carbon and hydrogen atoms must lie on the twofold rotation axes. A Patterson analysis of the reflections H_1OH_3 proved conclusively that the sodium atoms also occupy positions on the twofold axes while the eight oxygen atoms are in a set of general positions of the space group. The distribution of the atoms is accordingly as follows: 4 Na in $\pm$ ($^1/_4$, u_1, $^1/_4$), 4 H in

TABLE I

OBSERVED AND CALCULATED STRUCTURE FACTORS

H_1OH_3	F	|F|	H_1H_2O	F	|F|	$H_1H_2\bar{H}_1$	F	|F|	OH_2H_3	F	|F|
002	−78	45	110	− 2	9	$11\bar{1}$	33	27	020	−59	35
$20\bar{2}$	37	31	020	−59	35	020	−59	35	021	12	19
200	− 8	14	200	− 8	15	$20\bar{2}$	37	31	002	−78	45
$20\bar{4}$	−52	34	130	28	30	$22\bar{2}$	− 9	13	022	35	38
$40\bar{2}$	−25	19	220	−10	15	$13\bar{1}$	−41	21	040	−14	16
202	6	10	040	−14	16	$31\bar{3}$	6	8	023	−23	25
004	29	20	310	−33	42	040	−14	16	041	11	15
$40\bar{4}$	8	10	240	20	21	$24\bar{2}$	−18	13	042	14	16
400	41	32	330	− 9	9	$40\bar{4}$	8	8	004	29	20
$20\bar{6}$	43	23	150	−26	27	$33\bar{3}$	4	4	024	− 9	7
$40\bar{6}$	− 8	10	400	41	42	$42\bar{4}$	6	6	043	6	7
204	−15	16	420	−18	19	$15\bar{1}$	− 1	0	060	17	13
$60\bar{4}$	−41	22	060	17	14	060	17	10	061	−24	19
402	−40	25	350	18	20	$51\bar{5}$	8	8	044	−12	9
$60\bar{2}$	37	25	510	−10	11	$35\bar{3}$	−30	16	025	26	17
006	− 8	7	440	−10	8	$44\bar{4}$	−14	9	062	−12	10
$60\bar{6}$	30	15	260	1	0	$26\bar{2}$	5	3	063	11	11
600	−21	14	530	21	17	$53\bar{5}$	− 6	5	006	− 8	5
$40\bar{8}$	14	9	170	− 5	4	$17\bar{1}$	15	9	045	−17	10
$60\bar{8}$	−16	6	600	−21	12	$60\bar{6}$	30	12	026	− 1	0
			620	9	5	$62\bar{6}$	−15	6	064	4	3
			460	8	4	$46\bar{4}$	− 2	0	080	− 4	0
			370	− 6	5	$55\bar{5}$	−14	7	046	9	5
			080	− 4	0	$37\bar{3}$	28	11	081	6	4
			550	−18	8	080	− 4	0	082	1	3
			280	−20	8	$64\bar{6}$	− 6	4			
						$28\bar{2}$	11	3			
						$71\bar{7}$	11	4			

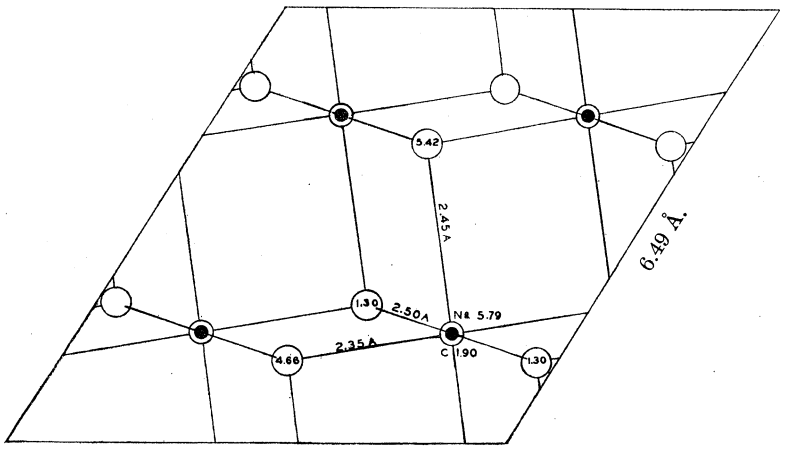
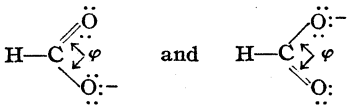


Fig. 1.—A projection of the structure on the (010) plane. Bonds between sodium and oxygen atoms are shown as connection lines. The length of the Na–O bonds and the heights of the atoms above the projection plane are indicated.

$\pm$ ($^1/_4$, u_2, $^1/_4$), 4 C in $\pm$ ($^1/_4$, u_3, $^1/_4$), 8 O in $\pm$ (x_1, x_2, x_3).

Approximate values for the parameters u_1, u_3, x_1, x_2, x_3 were found without difficulty (since the hydrogen atoms play a negligible part in the scattering, the parameter u_2 cannot be determined directly), while the accurate values were obtained from a series of Fourier projections. The results are: $u_1 = -0.139 \pm 0.001$; $u_3 = 0.283 \pm 0.002$; $x_1 = 0.043 \pm 0.002$; $x_2 = 0.194 \pm 0.002$; $x_3 = 0.185 \pm 0.002$. Setting $u_2 = 0.43$, one gets the reasonable value of 0.99 Å. for C–H separation in the formate group.

The agreement between observed and calculated structure factors is satisfactory, as shown in Table I. Figure 1 shows the projection of the crystal lattice on the (010) plane. As a consequence of the space group symmetry the two oxygen atoms are equivalent in the formate group, corresponding to complete resonance between the two structures



The bond angle φ is 124° and the C–O distance is

1.27 Å. For the dimer of formic acid the values $\varphi = 125°$ and C–O = 1.29 Å. were obtained from electron diffraction studies.[3]

Each sodium atom is linked to six oxygen atoms belonging to five different formate radicals. The sodium to oxygen distances are 2.35, 2.45 and 2.50 Å. with an average value of 2.44 Å., which is exactly equal to the distance predicted on the basis of ionic radii.[4] The atoms are arranged in layers parallel to the (001) plane as shown in Fig. 1; the separation of the layers is 2.76 Å. Four of the six oxygen atoms bonded to a given sodium atom lie in the same layer and the other two in the two adjacent layers. The bonds between different layers are thus few in number (only one bond per 10.4 sq. Å.) and excellent cleavage parallel to (001) results.

An inspection of Fig. 1 will show that there is a pseudo twofold screw axis normal to the plane (001), *i. e.*, normal to the layers. As a consequence it becomes possible to obtain satisfactory binding between two consecutive layers when one layer is turned through 180° and displaced parallel to itself. This fact is directly responsible for the formation of twinned crystals so common in this compound. Figure 2 illustrates the structure of such a twinned crystal.

The optical properties of sodium formate crystals are not known; but it becomes possible to make some predictions. The optical anisotropy must be ascribed almost entirely to the presence of the formate groups. These are all parallel in the crystal and they are highly anisotropic. Thus the crystals must exhibit strong birefringence. The normal to the plane of the formate group is the direction of smallest polarizability, while the direction of greatest polarizability is in the plane of the group parallel to the connection line between the two oxygen atoms. It may accordingly be stated that (010) is the plane of the optical axes, and that the vibration direction corresponding to the smallest refractive index makes an angle of about 13° with a_3 in the obtuse angle α_2.

(3) L. Pauling and L. O. Brockway, *Proc. Natl. Acad. Sci. U. S.*, **20**, 336 (1934).

(4) W. H. Zachariasen, *Z. Krist.*, **80**, 137 (1931).

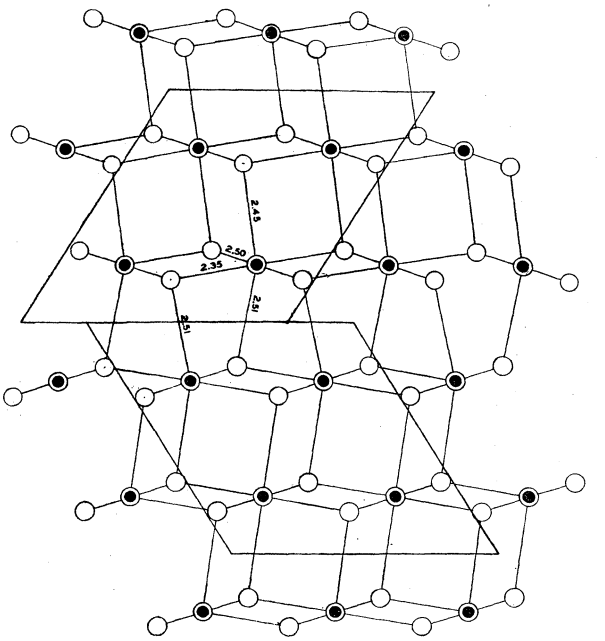


Fig. 2.—This illustrates the explanation of the observed twinning.

Summary

Crystals of sodium formate are monoclinic with four molecules of sodium formate per unit cell. The lattice dimensions are: $a_1 = 6.19 \pm 0.01$ Å., $a_2 = 6.72 \pm 0.01$ Å., $a_3 = 6.49 \pm 0.01$ Å., $\alpha_2 = 121°42' \pm 10'$. The space group is $C2/c(C_{2h}^6)$. Sodium, hydrogen and carbon atoms are on twofold rotation axes, oxygen atoms in general positions. The parameter values are:

	x_1	x_2	x_3
Na	1/4	−0.139 ± 0.001	1/4
C	1/4	.283 ± .002	1/4
H	1/4	.43	1/4
O	0.043 ± 0.002	.194 ± .002	0.185 ± 0.002

There is complete resonance between the two C–O bonds of the formate group. The C–O distance is 1.27 Å. and the bond angle is 124°. Sodium has six oxygen neighbors at an average distance of 2.44 Å.

CHICAGO, ILLINOIS RECEIVED FEBRUARY 9, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE CITY COLLEGE OF NEW YORK]

The Coprecipitation of Barium Ion with Hydrous Aluminum, Chromic and Ferric Oxides in the Presence of Ammonium Ion

BY LEO LEHRMAN, JEROME BEEN AND MILTON MANES

It is well-known that in systematic qualitative analysis considerable amounts of barium are lost before its detection.[1] This loss vitally affects a quantitative analysis of this cation and must be taken into account in such a determination. The cause has been attributed by some to the following two factors, which result in the precipitation of barium compounds: (1) oxidation of sulfide ion to sulfate ion in both the hydrogen sulfide and ammonium sulfide groups; (2) absorption of carbon dioxide by the alkaline ammonium sulfide solution.[2] However, some preliminary experiments showed that in the ammonium sulfide group in the presence of ammonium salts, which is usually the case, neither of the above effects was involved. Yet the amount of barium recovered in the filtrate was less than in the original solution. In the ammonium sulfide group there are two kinds of precipitates, hydrous oxides and sulfides. Inasmuch as they might act differently, it was decided to study them separately.[3]

When a precipitate forms, several causes, *i. e.*, occlusion, mixed crystal formation, solid solution, surface adsorption, compound formation and postprecipitation, might account for the retention (coprecipitation) of soluble material.[4] One or more of these causes might account for the coprecipitation of barium ion by the hydrous oxides. Since they are either amorphous or consist of extremely minute crystals, it is quite likely that surface adsorption takes place. This is especially probable in an alkaline solution where the precipitates would be negatively charged and therefore favor the adsorption of cations.[5] Furthermore, it has been shown that ammonium ion has an effect on the coprecipitation of other cations with hydrous oxides.[6]

The purpose of our investigation was to determine what factors cause the loss of barium ion so that they might eventually be removed.

Experimental

For the metal ions, solutions of chlorides made from reagent grade material were used. All solutions were tested for sulfate ion and found to contain a negligible amount. All experiments were run in duplicate. If the results did not agree, the experiments were repeated.

Precipitation of Barium Due to Absorption of Carbon Dioxide by an Ammonia Solution in the Presence of Ammonium Chloride.—To 5 ml. of barium chloride solution, equivalent to 40 mg. of barium, was added 1 g. of ammonium chloride, 10 ml. of concentrated ammonia solution, the volume made up to 25 ml. with water and allowed to stand in an open flask. A similar solution was prepared and put in a stoppered flask. These two experiments were duplicated, only the amount of ammonium chloride was 4 g. After three hours all the solutions were perfectly clear. In the open flasks after one day, a small amount of precipitate was present in the solution containing 1 g. of ammonium chloride, while the other had a slight but visible one. The precipitation increased very slowly the longer (in days) the flasks remained open. In the stoppered flasks no precipitation occurred even after fourteen days. It is seen that a rather long period of time is necessary before enough carbon dioxide is absorbed to cause precipitation of barium carbonate in the presence of ammonium salts. This is much longer than the usual time for filtering and washing.

The Retention of Barium by Precipitated Hydrous Aluminum, Chromic and Ferric Oxides.—To 50 mg. of aluminum ion and 100 mg. of chromic and ferric ions, separately, were added 1 g. of ammonium chloride, varying amounts of barium ion from 8–40 mg. and 5 ml. of 0.02% gelatin solution.[7] The solutions were heated to boiling, 5 ml. of concentrated ammonia added, which is an adequate excess to ensure complete precipitation, and the final volumes made up to 25 ml. The solutions were filtered and the precipitates washed with distilled water until free of barium ion. The number of washings varied from 8 to 12 of 15 ml. each. Though the hydrous ferric

(1) Curtman and Frankel, THIS JOURNAL, **33**, 724 (1911).

(2) (a) Curtman and Frankel, *ibid.*, **33**, 724 (1911); (b) Zolotukhin, *Acta Univ. Vorogiensis*, **9**, 69 (1937).

(3) The experiments with sulfides will be described in a later paper dealing with the behavior of these substances.

(4) (a) Fajans and Beer, *Ber.*, **46**, 3486 (1913); (b) Paneth, *Physik. Z.*, **15**, 924 (1914); (c) Kolthoff, *J. Phys. Chem.*, **36**, 860 (1932); (d) Kolthoff, *Chem. Rev.*, **17**, 293 (1935); (e) Kolthoff, *J. Phys. Chem.*, **40**, 1027 (1936); (f) Schneider and Rieman, THIS JOURNAL, **59**, 354 (1937); (g) Karaoglanov, *Ann. univ. Sofia II, Livre* **2**, **34**, 81 (1937–1938).

(5) (a) Dhar, Sen and Chatterji, *Kolloid Z.*, **33**, 29 (1923); (b) Weiser, "The Hydrous Oxides," McGraw-Hill Book Co., New York, N. Y., 1st ed., 1926, p. 403–406; (c) Charriou, *J. chim. phys.*, **23**, 621, 673 (1926).

(6) (a) Weiser, "The Hydrous Oxides," McGraw-Hill Book Co., New York, N. Y., 1st ed., 1926, p. 406; (b) Charriou, *J. chim. phys.*, **23**, 621, 673 (1926); (c) Kolthoff and Stenger, *J. Phys. Chem.*, **36**, 2113 (1926); (d) Kolthoff and Moskovitz, *ibid.*, **41**, 629 (1937). This article contains a condensed review of the literature on this effect. (e) Kolthoff and Overholser, *ibid.*, **43**, 767, 909 (1939).

(7) The gelatin made it possible to wash the precipitates with distilled water with very little peptizing action; Caldwell and Moyer, THIS JOURNAL, **57**, 2372 (1935).

oxide required the most and the hydrous aluminum oxide the least, the former filtered and was washed much quicker. The filtrate and washings were evaporated to about 10 ml., filtered to remove small amounts of the precipitates that might have passed through and the filter paper washed until free of barium ion. The filtrate and washings were concentrated to about 10 ml., the barium precipitated as barium sulfate in special, calibrated tubes[8] and allowed to settle overnight. The amount of barium was determined first by measuring the height of the precipitate. This was compared with an equal height of barium sulfate in a similar tube, representing a known amount of barium, precipitated under the same conditions. Before using this rapid method, its accuracy was tested gravimetrically and found to give comparable results. It was noted that the height of the precipitated barium sulfate is a linear function of the amount of barium. Table I shows the results obtained.

TABLE I

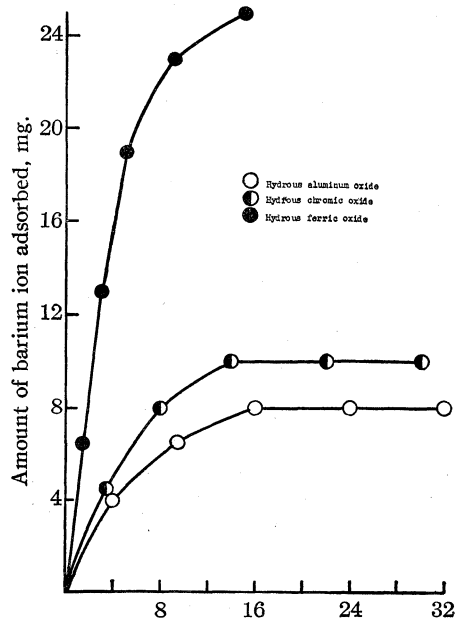
THE RETENTION OF BARIUM ION BY HYDROUS ALUMINUM, CHROMIC AND FERRIC OXIDES

Metal	Ba^{++} used, mg.	Ba^{++} in filtrate, mg.	Ba^{++} lost, mg.
Al^{+++}	40	32	8
Al^{+++}	32	24	8
Al^{+++}	24	16	8
Al^{+++}	16	9.5	6.5
Al^{+++}	8	4	4
Cr^{+++}	40	30	10
Cr^{+++}	32	22	10
Cr^{+++}	24	14	10
Cr^{+++}	16	8	8
Cr^{+++}	8	3.5	4.5
Fe^{+++}	40	15	25
Fe^{+++}	32	9	23
Fe^{+++}	24	5	19
Fe^{+++}	16	3	13
Fe^{+++}	8	1.5	6.5

Figure 1 is the graph obtained by plotting the amount of barium found in the filtrate as abscissa and the amount retained (lost) by the different hydrous oxides as ordinates. It is a typical Freundlich isotherm, probably showing adsorption, inasmuch as the precipitations take place under fairly constant conditions, thus yielding an adsorbent of constant specific surface area (*i. e.*, surface per unit mass of adsorbent).

Effect of Aging the Hydrous Oxides on the Amount of Barium Ion Retained.—For this purpose, two sets of experiments were carried out using solutions containing 500 mg. of aluminum, chromic and ferric ions separately, 40 mg. of barium ion, 10 ml. of 0.02% gelatin solution and 1 g. of ammonium chloride. In the first set the procedure was the same as above. In the second set the solutions were allowed to age in stoppered flasks for six days before filtering, washing and determining the amount of barium in the filtrates and washings. These two sets of experiments were repeated with 4 g. of ammonium chloride. To obtain additional data on the effect of ammonium

(8) Curtman, "Qualitative Chemical Analysis," revised edition; The Macmillan Co., New York, N. Y., 1938, p. 298.



Amount of barium ion in filtrate (equilibrium solution), mg.

Fig. 1.—Adsorption isotherms of barium ion with hydrous aluminum, chromic and ferric oxides in the presence of 1 g. of ammonium chloride.

chloride on the amount of barium ion lost the first set of experiments was repeated in saturated ammonium chloride solutions. The results are shown in Table II.

TABLE II

EFFECT OF AGING HYDROUS ALUMINUM, CHROMIC AND FERRIC OXIDES ON THE AMOUNT OF BARIUM ION RETAINED

Metal	NH_4Cl, g.	Days aged	Ba^{++} in filtrate, mg.	Ba^{++} lost, mg.
Al^{+++}	1	0	16	24
Al^{+++}	1	6	11	29
Al^{+++}	4	0	20	20
Al^{+++}	4	6	17	23
Al^{+++}	satd.	0	30	10
Cr^{+++}	1	0	7	33
Cr^{+++}	1	6	4	36
Cr^{+++}	4	0	10	30
Cr^{+++}	4	6	7	33
Cr^{+++}	satd.	0	29	11
Fe^{+++}	1	0	4	36
Fe^{+++}	1	6	11	29
Fe^{+++}	4	0	11	29
Fe^{+++}	4	6	18	22
Fe^{+++}	satd.	0	28	12

It is seen that aging decreases the amount of barium retained by hydrous ferric oxide while the opposite effect is shown with hydrous aluminum and chromic oxides. Increasing the amount of ammonium chloride reduces the loss of barium ion. This effect is slightly different for each hydrous oxide but practically the same whether they are aged or not.

Effect of Adding the Barium Ion, after the Formation of the Hydrous Oxides, on the Amount Lost.—Two sets of

experiments were performed. For the first set, solutions were made consisting of mixtures of equal amounts of aluminum and chromic ion, because of their similar action as shown in the previous experiments, varying from 15–250 mg. each, 40 mg. of barium ion, 10 ml. of 0.02% gelatin and 1 and 4 g. of ammonium chloride. The hydrous oxides were precipitated with ammonia as in the experiments above and the amount of barium in the filtrates and washings determined. In the second set the barium ion was added immediately after precipitation and then the amount in the filtrates and washings determined. For the purpose of noting the action of hydrous ferric oxide, the second set of experiments was repeated with 500 mg. of ferric ion. The results are shown in Table III.

TABLE III

EFFECT OF ADDING BARIUM ION, AFTER PRECIPITATION OF THE HYDROUS OXIDES, ON THE AMOUNT LOST

Mg. of metal	NH_4Cl, g.	Ba^{++}, when added	Ba^{++} in filtrate, mg.	Ba^{++} lost, mg.
500 Al^{+++} and Cr^{+++}	1	Before	19	21
500 Al^{+++} and Cr^{+++}	1	After	23	17
500 Al^{+++} and Cr^{+++}	4	Before	28	12
500 Al^{+++} and Cr^{+++}	4	After	30	10
200 Al^{+++} and Cr^{+++}	1	Before	21	19
200 Al^{+++} and Cr^{+++}	1	After	25	15
200 Al^{+++} and Cr^{+++}	4	Before	29	11
200 Al^{+++} and Cr^{+++}	4	After	30	10
50 Al^{+++} and Cr^{+++}	1	Before	35	5
50 Al^{+++} and Cr^{+++}	1	After	36	4
30 Al^{+++} and Cr^{+++}	1	Before	37	3
30 Al^{+++} and Cr^{+++}	1	After	37.5	2.5
500 Fe^{+++}	1	After	8	32
500 Fe^{+++}	4	After	14	26

In every case there is less barium ion retained (lost) if it is added after precipitation than if present in the original solution. However, it is seen that in similar experiments nearly as much barium ion is lost with 500 mg. of precipitate as with 200 mg. While adsorption is probably taking place, yet different amounts of adsorbent are being formed in the same volume (25 ml.). Thus it cannot be assumed that the conditions of the precipitation process are the same. Specific surface areas, therefore, might not be constant and the same conditions as to saturation would not result. Unfortunately the purpose of this work was to study the problem as it arises from the use of an accepted analytical method. Later, in the discussion, possible explanations will be given of these unusual results.

Combined Effect of Aging the Mixed Hydrous Aluminum and Chromic Oxides and the Addition of Barium Ion at Different Times on the Amount Retained.—Four sets of experiments were carried out. Solutions containing mixtures of 100 and 250 mg. each of aluminum and chromic ions, 10 ml. of 0.02% gelatin and 1 and 4 g. of ammonium chloride were prepared. In the first set 40 mg. of barium ion was added to the solutions, the hydrous oxides precipitated with concentrated ammonia as usual and the solutions allowed to age six days in stoppered flasks. Then the solutions were filtered, the precipitates washed free of barium ion, the filtrates and washings evaporated and the amount of barium ion determined. In the second set the procedure was repeated, only the 40 mg. of barium ion was added immediately after precipitation and then the solutions allowed to age six days in stoppered flasks. The third set duplicated the procedure except that the 40 mg. of barium ion was added after the hydrous oxides had aged for six days in stoppered flasks and then the solutions were filtered. In the last set the previous procedure was repeated with the addition of allowing the solutions to re-age two days in stoppered flasks after the 40 mg. of barium had been added. Table IV shows the results obtained.

TABLE IV

COMBINED EFFECT OF AGING THE HYDROUS OXIDES AND THE ADDITION OF BARIUM ION AT DIFFERENT TIMES ON THE AMOUNT RETAINED

Mg. of metal	Amount of NH_4Cl	When Ba^{++} was added	Ba^{++} in filtrate, mg.	Ba^{++} lost, mg.
500 Al^{+++} and Cr^{+++}	1	Before pptn., before aging	11	29
500 Al^{+++} and Cr^{+++}	1	After pptn., before aging	21	19
500 Al^{+++} and Cr^{+++}	1	After aging	26	14
500 Al^{+++} and Cr^{+++}	1	After aging, before reaging	27	13
500 Al^{+++} and Cr^{+++}	4	Before pptn., before aging	23	17
500 Al^{+++} and Cr^{+++}	4	After pptn., before aging	25	15
500 Al^{+++} and Cr^{+++}	4	After aging	28	12
500 Al^{+++} and Cr^{+++}	4	After aging, before reaging	35	5
200 Al^{+++} and Cr^{+++}	1	Before pptn., before aging	17	23
200 Al^{+++} and Cr^{+++}	1	After pptn., before aging	23	17
200 Al^{+++} and Cr^{+++}	1	After aging	28	12
200 Al^{+++} and Cr^{+++}	1	After aging, before reaging	33	7
200 Al^{+++} and Cr^{+++}	4	Before pptn., before aging	25	15
200 Al^{+++} and Cr^{+++}	4	After pptn., before aging	28	12
200 Al^{+++} and Cr^{+++}	4	After aging	33	7
200 Al^{+++} and Cr^{+++}	4	After aging, before reaging	37	3

A study of the results, especially when compared with those in previous tables, yields certain information. The same conclusion obtained from the data in Table III, *viz*,. less barium ion is lost if it is added after precipitation than if present in the original solution, also holds here. On comparing the results of this Table with similar experiments in Table III it is seen that aging the hydrous oxides in the presence of barium ion increases the amount retained (lost). Apparently, however, the loss from aging must be due to more than one factor as reaging results in a decrease of this loss. The anomalous behavior, *i. e.*, nearly the same loss of barium ion with 500 mg. of precipitate as with 200 mg., noted in connection with Table III, is also seen here.

Discussion

From the results of the first experiments it is evident that the loss of barium ion is not due to its precipitation as a carbonate, brought on by the absorption of carbon dioxide, contrary to Zolotukhin's assertion.[9] Yet, in later experiments, a definite amount of barium ion is lost where solutions containing precipitated hydrous oxides are kept in stoppered flasks. It is interesting to note in this connection that Curtman and Frankel, in determining the loss of barium ion due to the absorption of carbon dioxide by ammonia, said,

(9) Ref. 2b.

"Contrary to expectations, the loss in this operation was far greater than one might think."[10]

From the nature of the hydrous oxides and the fact that Fig. 1 is a typical Freundlich isotherm, the loss of barium ion is probably due to adsorption. In every experiment carried out, as the amount of ammonium salt present was increased, less barium was lost. Evidently ammonium ion replaces barium in the adsorption. This is in agreement with results reported by others.[6] This explains why Zolotukhin found that on washing the hydrous oxides with solutions of ammonium salts less barium ion was lost. In a saturated solution of ammonium salts some barium ion is still not recovered. This might be due to an incomplete replacement of barium by ammonium ion in the adsorption or else to occlusion of cations by the hydrous oxides as they are being formed. Increasing the amount of ammonium ion has a similar action, though different in extent, on the decrease of the loss of barium ion for each of the hydrous oxides. Yet in a saturated solution of ammonium ion, all three hydrous oxides, separately, adsorb about the same amount of barium ion. Important in analysis is the fact that while a high concentration of ammonium ion will decrease the adsorption of barium ion, it will not allow for its complete recovery. If the loss is due to surface adsorption, then it will be the same whether the barium ion is present before the hydrous oxides are precipitated or added immediately after. The results in Table III show there is a difference in the amount of barium ion lost depending on whether it is present before or after the precipitation. This indicates that besides surface adsorption some other effect must be occurring.

It already has been mentioned in connection with Tables III and IV that certain results appear to be anomalous. From Table I and Fig. 1 the surfaces of the precipitates of hydrous aluminum and chromic oxides are saturated when there is 14 mg. and 16 mg., respectively, or more barium ion in the filtrate. Besides there is a constant ratio of the amount of barium ion adsorbed to the amount of adsorbent when saturated. Therefore, in Table III, in similar experiments where 30, 50 and 200 mg. of mixed aluminum and chromic ion is precipitated in the presence of barium ion, the surfaces of the precipitates are saturated. Not only is there more than the criterion amount of barium ion in the filtrate, but there is a constant ratio of 1 mg. of barium ion retained to 10 mg. of mixed hydrous oxides. In the similar experiments where the barium ion was added after the precipitation, in order to eliminate occlusion, a slightly lower ratio, as is to be expected, of about 1:12 is obtained. But in the case of the experiments using 500 mg. of aluminum and chromic ion, the amount of barium ion retained is too low for saturation and therefore the amount in the filtrate is too high. It would seem, for some reason not apparent, that the surfaces of the precipitates in the latter are *not* saturated with barium ion. With a large amount of precipitate it might take a longer time before saturation is reached,[11] or internal surfaces do not come in contact with barium ion.[12]

If occlusion takes place while the precipitate is forming, then the amount of barium lost would be less if it is added after the hydrous oxides are formed. That this effect is present can be seen from the results in Table III. Furthermore, aging the precipitate should reduce the amount of barium occluded,[13] provided there is no post precipitation. If there is, then aging the precipitates would increase the amount of barium ion lost. Thus it is seen that while all three hydrous oxides cause loss of some barium ion by occlusion, there is postprecipitation with only hydrous aluminum and chromic oxides (see Table II). That the latter effect is appreciable is shown by the larger loss of barium ion on aging, which would tend to undo occlusion at the same time and therefore decrease the amount of barium ion lost. When hydrous aluminum and chromic oxides age, some change takes place which affects postprecipitation negatively. This is seen from the reaging experiments in Table IV where less barium ion is lost if it is added to aged hydrous oxides and then aged again. Some experiments were repeated in which the hydrous oxides were aged in the presence of barium ion for two days instead of six. The same results were obtained for the amount of barium ion lost, showing the postprecipitation was complete within two days.

Summary

1. The loss of barium ion when hydrous aluminum, chromic and ferric oxides are pre-

(10) Ref. 1, p. 728.

(11) Kolthoff and Stenger, *J. Phys. Chem.*, **36**, 2113 (1932).

(12) (a) Reference (11); (b) Kolthoff and Overholser, *ibid.*, **43**, 778 (1939).

(13) Reference 4(c), page 881.

cipitated by ammonia in the presence of ammonium salts is not due to the formation of barium carbonate by absorption of carbon dioxide.

2. The loss of barium ion when hydrous aluminum, chromic and ferric oxides are precipitated by ammonia in the presence of ammonium salts is probably due partly to surface adsorption.

3. Ammonium ion replaces barium in the adsorption, yet all the barium ion is not recovered even in a saturated solution of ammonium salts.

4. All three hydrous oxides cause the loss during precipitation of some barium ion by occlusion.

5. Hydrous aluminum and chromic oxides also cause the loss of some barium ion by postprecipitation.

6. When large amounts of hydrous oxides are precipitated, the surfaces do not become saturated with barium ion.

NEW YORK CITY, N. Y. RECEIVED SEPTEMBER 21, 1939

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, OKLAHOMA AGRICULTURAL AND MECHANICAL COLLEGE]

Equilibrium in an Esterification Reaction with Perchloric Acid as Catalyst

BY H. M. TRIMBLE AND EARL L. RICHARDSON

Many workers have found that the equilibrium concentrations in reversible homogeneous reactions change when a catalyst is introduced, and that the degree of change varies with the concentration of the catalyst. Few, however, have investigated the phenomenon with other than small concentrations of the catalyst. This paper reports the results of a study of the reaction

$$CH_3COOH + C_2H_5OH \rightleftharpoons CH_3COOC_2H_5 + H_2O$$

in the presence of perchloric acid over a wide range of concentration. The efficiency of this substance in promoting simple esterification has not been examined previously, so far as the authors have been able to determine.

Experimental

Reagent grade perchloric acid, 70%, conforming to A. C. S. specifications was redistilled. It was diluted as needed to give aqueous solutions varying from 0.37 to 71.2% perchloric acid by weight which were used in making up the different reaction mixtures. Reagent grade glacial acetic acid was redistilled, saving the middle 75%. Repeated analyses showed it to be 99.8% pure. Ethyl alcohol was freed from aldehydes by treating it with silver oxide as described by Dunlap[1] and distilling. Its density was determined at 30° several times during the course of the work and found to remain constant at 0.80056 ± 0.00004. Reference to the tables by Osborne[2] shows that it contained 93.2% C_2H_5OH. The base used in all the titrations was approximately half normal sodium hydroxide. It contained a small excess of barium chloride, and it was protected at all times with soda lime tubes to ensure the absence of carbonate. It was standardized by means of reagent grade potassium hydrogen phthalate with phenolphthalein as indicator.

(1) Dunlap, THIS JOURNAL, **28**, 397 (1906).

(2) Osborne, *Bull. Bureau Standards*, **9**, 424–425 (1913).

The experiments were run at 30.00 ± 0.05°. The reaction vessels were 100- or 250-ml. bottles with well-fitting ground-glass stoppers. In experiments 1 to 7, 10-ml. portions of perchloric acid solution and 2-ml. portions each of acetic acid and ethyl alcohol, all measured at 30° by means of precision pipets, were taken in making up the reaction mixtures; in the other experiments half these quantities were used. The stoppers were sealed externally with paraffin wax and the bottles were immersed in the bath for three days or longer to allow the reaction to proceed to equilibrium. Titrations of the total acid present at equilibrium were carried out rapidly in the reaction vessels after adding ice water. Each experiment was run in triplicate, and repeated if the results failed to check satisfactorily. Portions of the perchloric acid solution used for each experiment were weighed and titrated at the same time as the mixture itself. The quantities of the organic substances delivered were checked by weighing, and found

TABLE I

EQUILIBRIUM DATA AND RESULTS

Expt.	$HClO_4$ soln., m	$HClO_4$	H_2O	EtOAc	M Mole % $HClO_4$	K[a] apparent
1	0.038	0.00038	0.5636	0.00476	0.06	3.32
2	.066	.00066	.5634	.00492	.11	3.47
3	.097	.00096	.5612	.00498	.15	3.51
4	.144	.00142	.5608	.00513	.23	3.65
5	.342	.00335	.5561	.00530	.54	3.79
6	.733	.00707	.5482	.00576	1.15	4.19
7	.92	.00876	.5438	.00600	1.57	4.41
8	1.37	.00647	.2695	.00329	2.11	5.00
9	2.26	.01033	.2615	.00364	3.43	5.67
10	3.04	.01347	.2533	.00407	4.55	6.57
11	3.77	.01628	.2480	.00436	5.55	7.22
12	4.29	.01822	.2440	.00458	6.26	7.74
13	4.73	.01946	.2370	.00485	6.83	8.33
14	6.15	.02432	.2284	.00528	8.66	9.42
15	8.02	.02989	.2165	.00583	10.92	10.88
16	9.26	.03288	.2067	.00610	12.32	11.45
17	12.79	.04090	.1890	.00664	15.94	12.67
18	15.93	.04706	.1745	.00693	18.98	12.95
19	19.01	.05201	.1627	.00718	21.60	13.19
20	24.61	.05924	.1448	.00760	25.79	13.51

[a] $K_{apparent}$ = moles EtOAc × moles H_2O/moles AcOH × moles EtOH.

to be constant to within ±0.1%. The alcohol contained 0.00360 mole of water per ml., and the water in the acetic acid was negligible. The essential data and results of the study are given in Table I. The graph shows the relation between the apparent equilibrium constant as calculated and the mole per cent. of perchloric acid present in the equilibrium mixtures. To save space the moles of ethyl alcohol and acetic acid at equilibrium have been omitted from the table. These values may be found for each experiment by subtracting the values of column 5 from 0.03190 for alcohol and 0.03456 for acetic acid in experiments 1 to 7, and from half these numbers for the others. These were the respective quantities of these substances introduced in making up the reaction mixtures.

A search of the literature indicates that perchloric acid will not oxidize any of the constituents of these mixtures, or react with alcohol to form an ester under the conditions of these experiments. This conclusion was borne out by suitable tests which were performed.

The relation of the apparent equilibrium constant to the mole per cent. of perchloric acid present is well expressed by the equation $K = 3.45 + 0.68\,M$ up to about $M = 11$. Calculation shows that the variation of this constant with concentration of the catalyst cannot be explained as due to combination of a part of the water with it to form a definite hydrate, as has been proposed by Jones and Lapworth.[3]

(3) Jones and Lapworth, *J. Chem. Soc.*, **99**, 1427 (1911).

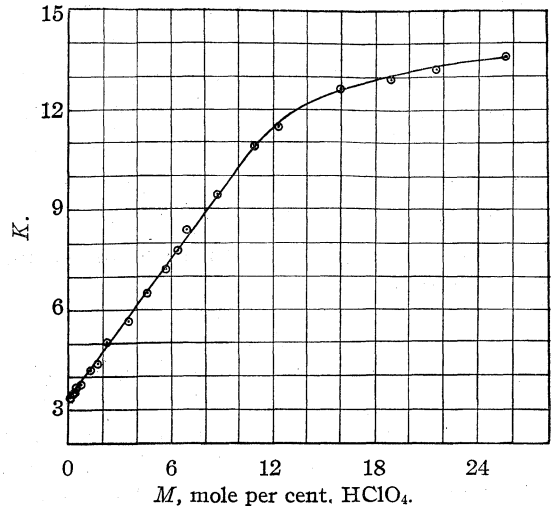


Fig. 1.—Relation of apparent equilibrium constant to mole per cent./$HClO_4$.

Summary

The results of a study of the apparent equilibrium constant for the reaction

$$CH_3COOH + C_2H_5OH \rightleftharpoons CH_3COOC_2H_5 + H_2O$$

in the presence of perchloric acid as catalyst, at concentrations up to 25.79 mole per cent., are presented.

STILLWATER, OKLAHOMA RECEIVED JANUARY 2, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF COLUMBIA UNIVERSITY]

The Kinetics of Isotopic Exchange between Carbon Dioxide, Bicarbonate Ion, Carbonate Ion and Water[1]

BY G. ALEXANDER MILLS AND HAROLD C. UREY

Introduction

The important role of carbon dioxide in nature and in industry, as well as its intrinsically interesting properties, have made it the subject of intensive study.[2] These investigations have resulted in the belief that in aqueous solution less than 1% of the carbon dioxide present exists in combination with water. The rather strong metacarbonic acid so formed is highly ionized due to its small concentration. The first dissociation constant ordinarily determined is therefore not a true dissociation constant. Usually called the apparent dissociation constant it is nevertheless a real constant.

The differentiation between free and combined carbon dioxide has been possible through the circumstance, first noticed in 1912 by McBain,[3] that carbon dioxide does not react instantaneously with water. The effect of various reagents on the rate of reaction has been studied in detail.[4] The maximum amount of alkali instantaneously neutralized by a solution of carbon dioxide corresponds to the equilibrium amount of carbonic acid, ionized and un-ionized, if dissociation of carbonic acid is assumed to be very rapid. From conductivity data the ionized portion is known. The true first dissociation constant was therefore estimated to be 4×10^{-4}. The reaction also has

(1) Dissertation submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Faculty of Pure Science of Columbia University in the City of New York.

(2) Quinn and Jones, "Carbon Dioxide," The Reinhold Publishing Corp., New York, N. Y., 1936.

(3) McBain, *J. Chem. Soc.*, **101**, 814 (1912).

(4) Vorlander and Strube, *Ber.*, **46**, 172 (1913); Thiele, *Ber.*, **46**, 867 (1913); Thiele and Strohecker, *ibid.*, **47**, 1061 (1914); Strohecker, *Z. Nahr.-Genussm.*, **31**, 121 (1916); Wilke, *Z. anorg. Chem.*, **119**, 365 (1921); Thiele, *ibid.*, **121**, 211 (1922).

been followed by studying the rate of change of conductivity.[5]

Faurholt[6] in 1924 was first to recognize that the reaction process was determined by the *p*H of the solution. When the *p*H is less than 8 only simple hydration is important

$$CO_2 + H_2O \rightleftarrows H_2CO_3$$

When the *p*H is greater than 10 a bimolecular reaction predominates

$$CO_2 + OH^- \rightleftarrows HCO_3^-$$

Between these limits both determine the rate of reaction. By an ingenious method depending on the difference in rates of reaction between carbon dioxide and bicarbonate ion with amines Faurholt established approximately forward and backward reaction velocity constants for both reactions.

Measuring the rate of absorption and evolution of carbon dioxide by a buffered solution Brinkman, Margaria and Roughton[7] obtained data consistent with those of Faurholt. The use of two phases possibly introduces some uncertainty as to the interpretation of the results. However, the manometric measurements are much more precise. Stadie and O'Brien[8] have studied the reaction in physiological media. The catalyst, carbonic anhydrase, which occurs in blood, accelerates the reaction very considerably. Measuring the rate of reaction also by a "boat and manometer" method Roughton and Booth[9] have found an increase in the reaction rate in the presence of buffer solutions usually employed over that in pure water. They have incorporated their results in the form of a catalytic function and have evaluated this for several inorganic salts.

The rate of absorption of gaseous carbon dioxide by solutions is in part determined by the rate of chemical reaction. The effect of various substances on this rate was studied by Riou *et al.*[10] More recently a great deal of industrial work has been done using packed columns.[11]

(5) Pusch, *Z. Elektrochem.*, **22**, 206 and 293 (1916); Thiele, *ibid.*, **22**, 423 (1916); Eucken and Grützner, *Z. physik. Chem.*, **125**, 363 (1927); Saal, *Rec. trav. chim.*, **47**, 264 (1928).

(6) Faurholt, *Z. anorg. Chem.*, **120**, 85 (1922); *J. Chim. Phys.*, **21**, 400 (1924). Values of rate constants given must be multiplied by 2.303.

(7) Brinkman, Margaria and Roughton, *Phil. Trans. Roy. Soc.*, **A232**, 65 (1933).

(8) Stadie and O'Brien, *J. Biol. Chem.*, **103**, 521 (1933); *ibid.*, **112**, 723 (1936).

(9) Roughton and Booth, *Chem. and Ind.*, **56**, 1053 (1937); *J. Physiol.*, **92**, 36P (1938); *Biochem. J.*, **32**, 2049 (1938).

(10) Riou *et al.*, *Compt. rend.*, **174**, 1463 (1922); *ibid.*, **186**, 1546 (1928).

(11) See, for example: Hitchcock and Cadot, *Ind. and Eng. Chem.*, **27**, 728 (1935); Comstock and Dodge, *ibid.*, **29**, 520 (1937).

The reaction between carbon dioxide and water results in an isotopic fractionation rather favorable for separation.[12] Experimental results[13] were lower than predicted, due, no doubt, to the slowness of the chemical reaction.

Method of Isotopic Exchange

The chemical identity of isotopes makes possible an investigation of reaction kinetics. The rate of establishment of isotopic equilibrium is measured in a system in a steady state except for the distribution of isotopes. This rate depends on the chemical reactions normally occurring. The chemical equilibrium ordinarily considered, which we may call *elementic* equilibrium, is concerned with the number of ions and molecules present. Isotopic equilibrium is concerned with the distribution of isotopes in the various ions and molecules. This latter equilibrium, except in the case of hydrogen and deuterium, results in a uniform distribution of isotopes in all compounds, since the constants for isotopic equilibrium are unity within a few per cent. The time necessary to reach isotopic equilibrium is greater than that necessary to reach ordinary equilibrium. This is true because in the former case each ion or molecule must come to equilibrium with all other ions and molecules. For example in the case of the oxygen exchange between carbon dioxide and water if the O^{18} content is not the same originally the hydration reaction must occur many times in order that there be isotopic equilibrium. Carbon dioxide dissolved in water will establish the half equilibrium concentration of carbonic acid in the order of one second. The half time necessary for oxygen exchange is about 1000 seconds.

A solution of carbon dioxide mixed with a solution of sodium bicarbonate will establish elementic equilibrium fairly quickly. If the C^{13} content of the carbon dioxide is not the same as that of the sodium bicarbonate there will be a comparatively slow change tending to establish a uniform distribution of the carbon isotopes. By drawing off samples of carbon dioxide from the solution at various times and making an isotopic analysis, the rate of change of C^{13} in the carbon dioxide can be measured. This can then be related to the rate of reaction of carbon dioxide with water.

Exchange occurs between the oxygen of carbon

(12) Urey and Greiff, THIS JOURNAL, **57**, 321 (1935); Weber, Wahl and Urey, *J. Chem. Phys.*, **3**, 129 (1935).

(13) Urey, Aten and Keston, *ibid.*, **4**, 622 (1936).

dioxide, bicarbonate ion, carbonate ion and water. Carbon dioxide with an atom fraction of O^{18} different from ordinary may be dissolved rapidly in water. Samples of carbon dioxide extracted from portions of this solution at various times will have different O^{18} contents. The rate of oxygen exchange in solutions of carbonates and bicarbonates can be measured by studying the rate of change of O^{18} content in the carbon dioxide liberated at various times. All these results can be interpreted in terms of the kinetics of the reactions normally occurring.

The reversible hydration of carbon dioxide takes place quite rapidly. Investigation of the slower isotopic reactions is therefore of advantage. This is particularly true in the case of oxygen exchange. The correction for the effect of the back reaction is easily and quantitatively made and the effect of changing *p*H is eliminated. By studying the reaction in the liquid phase only, uncertainties due to rates of diffusion and solution are avoided.

Experimental

Preparation of Isotopic Material.—Employing a countercurrent method the reaction between carbon dioxide and bicarbonate ion has been used to obtain some concentration of C^{13}.[13] The carbonate solution so produced was first boiled with sodium hydroxide to drive off excess amines. Sulfuric acid liberated carbon dioxide which was then sublimed at liquid nitrogen temperatures. The C^{13} atom fraction of this carbon dioxide was 0.0140, the natural abundance being taken as 0.0106.

Water having an O^{18} atom fraction of 0.00500 compared to 0.00200 for ordinary has been produced by the fractional distillation of water.[14] This water was purified by refluxing and distilling from alkaline permanganate at least twice and once from chromic acid. The first and last portions were not used. Carbon dioxide with an O^{18} value greater than ordinary was prepared by shaking pure carbon dioxide with this water for at least ten hours.[15] Heavy oxygen sodium carbonate was prepared by dissolving pure sodium bicarbonate in the heavy oxygen water and allowing the solution to stand a week or more. The water was distilled off, the residue ground fine and heated at 300° for three hours.

Exchange Reactions with C^{13}.—A solution of carbon dioxide with a C^{13} content greater than ordinary was mixed rapidly with a solution of ordinary sodium bicarbonate. The temperature was maintained at 0.00 ± 0.03°. Liquid samples were withdrawn from time to time into evacuated vessels. The carbon dioxide first to come off was collected. It was assumed that this was representative of the carbon dioxide existing as such in solution. Carbon dioxide was obtained from the solution remaining by addition of acid. A rough estimation was thereby obtained of the combined carbon dioxide. The samples were analyzed on a Bleakney type mass spectrograph.[16] The error in analysis is about 1% of the C^{13} present. Typical results are given in Table I and in Fig. 1. α and β are the atom fractions of C^{13} in the carbon dioxide and bicarbonate ion, respectively.

TABLE I

Run 9; 0.00 ± 0.03°; $k_1[H_2O] = 0.0038$ sec.$^{-1}$; $[CO_2] = 0.021$ *M*; $[NaHCO_3] = 0.021$ *M*.

Time in sec.	β	α	$\log (\alpha - \alpha_\infty)$
0	0.01060	0.01393	−2.79
35	.01175	.01341	−2.95
70	.01176	.01326	−3.02
265	.01199	.01253	−3.63
∞	.01230	.01230	

Run 9-B; 25.00 ± 0.02°; $k_1[H_2O] = 0.021$ sec.$^{-1}$; $[CO_2] = 0.021$ *M*; $[NaHCO_3] = 0.021$ *M*.

Time in sec.	α	$\log (\alpha - \alpha_\infty)$
0	0.01352	−2.73
20	.01246	−3.09
58	.01171	
95	.01164	

For the *p*H range studied only simple hydration occurs. The possible reactions may be represented as

$$C^{13}O_2 + H_2O \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} H_2C^{13}O_3 \rightleftharpoons H^+ + HC^{13}O_3^-$$

$$C^{12}O_2 + H_2O \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} H_2C^{12}O_3 \rightleftharpoons H^+ + HC^{12}O_3^-$$

It is assumed that the ionization of carbonic acid is rapid. The rate of decrease of C^{13} in carbon dioxide is given by the expression

$$-d[C^{13}O_2]/dt = k_1[H_2O][C^{13}O_2] - k_{-1}[H_2C^{13}O_3]$$
$$-[CO_2]d\alpha/dt = k_1[H_2O][CO_2]\alpha - k_{-1}[H_2CO_3]\beta$$

However, since elementic equilibrium has been established quickly

$$k_1[H_2O][CO_2] = k_{-1}[H_2CO_3]$$

and so

$$-d\alpha/dt = k_1[H_2O](\alpha - \beta)$$

The amount of C^{13} is constant. Therefore, at any time

$$([CO_2] + [H_2CO_3] + [NaHCO_3])\alpha_\infty = \alpha[CO_2] + \beta([H_2CO_3] + [NaHCO_3])$$

$$-\frac{d\alpha}{dt} = k_1[H_2O]\left\{1 + \frac{[CO_2]}{[H_2CO_3] + [HCO_3^-]}\right\}(\alpha - \alpha_\infty)$$

The exchange reaction is of the first order, as is true in general.[17] The value of $k_1[H_2O]$ was obtained from the slope of the plot of $\log (\alpha - \alpha_\infty)$ against time, Fig. 1.

The precision is low because the reaction is so fast, being substantially complete in a few min-

(14) Huffman and Urey, *Ind. Eng. Chem.*, **29**, 531 (1937).
(15) Cohn and Urey, THIS JOURNAL, **60**, 679 (1938).
(16) Bleakney, *Phys. Rev.*, **40**, 496 (1932).
(17) McKay, *Nature*, **142**, 997 (1938).

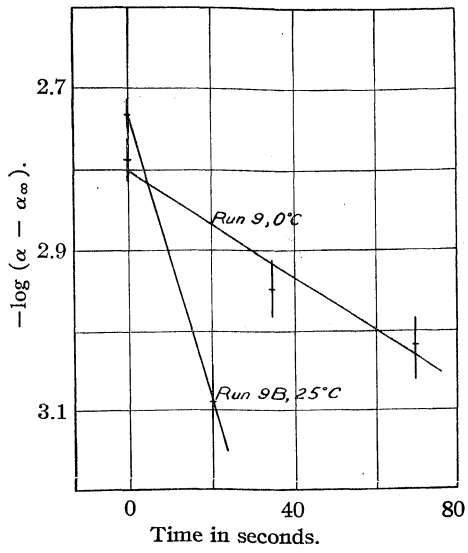


Fig. 1.

utes. Several seconds were necessary to take a sample. Also the low C^{13} atom fraction makes accurate analysis difficult. A number of experiments showed qualitatively the effect of added substances upon the reaction rate. Ethyl alcohol and basic solutions accelerated the rate while iron sol decreased it to some extent.

Exchange Reactions with O^{18}.—The rate of oxygen exchange between water and carbon dioxide depends upon the acidity of the solution.[18] The experiments made may be divided conveniently into three groups: (a) those in which the solution was acid enough so that substantially all the carbon dioxide remained in that state; (b) experiments in which the bicarbonate ion concentration was considerable; (c) reactions in basic solution where the carbonate ion was predominant. Carbon dioxide with an O^{18} content greater than ordinary was dissolved rapidly in water by shaking in a closed vessel. This solution was then placed in the reaction chamber, A, Fig. 2. From time to time a 10-cc. sample of this solution was withdrawn through the capillary manifold, B, into one of the evacuated bulbs, C. The carbon dioxide liberated was separated quickly from the water vapor by passage through an efficient trap, D, immersed in a dry-ice-bath. It was condensed in one of the sample tubes, E, by means of liquid nitrogen. The sample tube was sealed off and later analyzed for O^{18}. Frequent tests using a mass spectrograph showed that all but negligible amounts of water vapor were removed. The total time necessary to take a sample was ten seconds, though most of the carbon dioxide came off in the first part of this period. The liquid withdrawn from A was replaced with clean mercury from the reservoir, F, in order to prevent the formation of a gas phase above the liquid. Tests showed that the presence of mercury had no apparent effect on the reaction. When the time between samples was one minute or less, each sampling bulb was separately evacuated and equipped with an individual trap.

(18) Mills and Urey, THIS JOURNAL, **61**, 534 (1939).

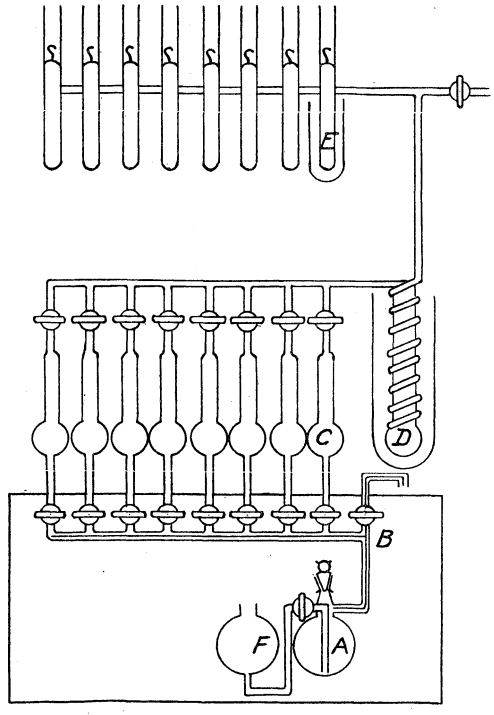


Fig. 2.

The rate of oxygen exchange between carbonate ion and water was studied. Sodium carbonate having an O^{18} content greater than ordinary was dissolved in ordinary water. Samples of this solution were withdrawn as before. In this case each sample bulb, C, contained 5 cc. of 0.3 *M* sulfuric acid. In a similar manner the oxygen exchange of various mixtures was studied. These were prepared by dissolving a known amount of heavy oxygen sodium carbonate in ordinary water and adding a known amount of standard acid, salt or phosphate buffer.

Details of typical experiments are shown in Tables II and III and in Fig. 3. α is the atom fraction of O^{18} in the liberated carbon dioxide. A summary of the results obtained in this way is given in Tables IV, V and VI.

TABLE II

Run B-15; $T = 0.00 \pm 0.03°$; $k_1[H_2O] = 0.00204$ sec.$^{-1}$; [NaCl] = 0.0452 M; [CO_2] = 0.0226 M; [HCl] = 0.0224 M.

Time in minutes	α	Log (α − 0.00210)
0	0.00498	−2.540
6	.00429	−2.660
12	.00390	−2.770
20	.00330	−2.921
25	.00308	−3.009
30	.00292	−3.086
36	.00276	−3.180
42	.00261	−3.292

TABLE III

Run B-22; $T = 0.00 \pm 0.03°$; A, observed rate, min.$^{-1}$ = 0.00969; $k_1[H_2O]$, sec.$^{-1}$ = 0.00210; Na_2CO_3 = 0.3034 g.; H_2O = 39.13 cc.; HCl = 80.87 cc., 0.05250 M.

Time in minutes	α	Log (α − 0.00210)
0	0.00483	−2.564
10	.00425	−2.668
20	.00380	−2.770
30	.00350	−2.854
40	.00317	−2.971
50	.00300	−3.046
60	.00282	−3.145
70	.00266	−3.252

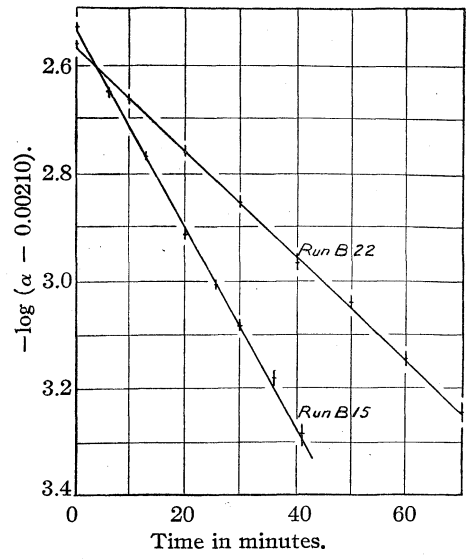


Fig. 3.

Sodium carbonate with an O^{18} atom fraction equal to 0.00500 was dissolved in ordinary water. At 25° the time of half exchange was approximately twenty-eight hours. The presence of 0.04 M sodium hydroxide so inhibited the reaction that no exchange could be detected after seventy-four hours. The results are shown in Table VII.[19]

TABLE IV

AT 0.00 ± 0.03°

Expt.	Solutions, molar concentrations: CO_2	$NaHCO_3$	NaCl	HCl	KCl	HAc	NaAc	$\frac{(NaHCO_3)}{(CO_2)}$	A, obsd. rate, min.$^{-1}$	$k_1(H_2O)$, sec.$^{-1}$
B-10	0.0131							0	0.0170	0.00195
B-15	.0226		0.0452	0.0224				0	.0177	.00204
B-19	.0242		.0485	.3010				0	.0169	.00195
B-21	.0127					0.0803	0.0237	0	.0182	.00221
B-16	.0100	0.0100	.0300					1.00	.00912	.00191
B-20	.0100	.0100	.0300		0.1100			1.00	.0101	.00212
B-22	.01153	.01232	.03538					1.07	.00969	.00210
B-23	.00633	.01899	.03165					3.00	.00419	.00181
B-14	.00460	.01840	.02756					4.00	.00318	.00173
B-29	.00232	.02600	.03064					11.2	.000684	.00093
B-27	.00013	.02650	.02676					204	.000130	.00303
B-26	.00917	.01669	.03503	$Na_2HPO_4 + KH_2PO_4$ $M/30$				1.82	.00699	.00212
B-24	.00662	.01376	.02700	$Na_2HPO_4 + KH_2PO_4$ $M/15$				2.08	.00827	.0027

TABLE V

AT 25.00 ± 0.02°

Expt.	Solutions, molar concentrations: CO_2	$NaHCO_3$	NaCl	HCl	$\frac{(NaHCO_3)}{(CO_2)}$	A, obsd. rate, min.$^{-1}$	$k(H_2O)$, sec.$^{-1}$
C-4	0.0208		0.0416	0.0086	0	0.220	0.0253
C-5	.0213		.0426	.0100	0	.256	.0294
C-1	.00636	0.01654	.02926		2.60	.0323	.0124
C-2	.00686	.01930	.03302		2.81	.0349	.0142
C-3	.00114	.01864	.02092		16.4	.0114	.0225

TABLE VI

AT 40.00 ± 0.02°

Expt.	Solutions, molar concentrations: CO_2	$NaHCO_3$	NaCl	$\frac{(NaHCO_3)}{(CO_2)}$	A, obsd. rate, min.$^{-1}$	k_1 (H_2O) sec.$^{-1}$
D-5	0.0023	0.0205	0.0251	8.91	0.130	0.128
D-3	.00058	.01742	.01858	30.0	.0417	.147
D-4	.00044	.01607	.01695	36.5	.0377	.153

(19) In one experiment heavy oxygen sodium carbonate was heated in an evacuated pyrex container to the softening point of the glass. The carbon dioxide obtained was found to have a lower O^{18} content than the original sodium carbonate. Apparently exchange occurs with glass at this temperature.

TABLE VII

OXYGEN EXCHANGE BETWEEN SODIUM CARBONATE AND WATER AT 25.00 ± 0.02°

Time in hours	O^{18} atom fraction $[Na_2CO_3] = 0.02\ M$	$[Na_2CO_3] = 0.02\ M$ $[NaOH] = 0.04\ M$
0	0.00513	
23.5	.00383	0.00465
46	.00310	.00461
73.8	.00264	.00465

Discussion of Experimental Results

For the *p*H range in which only hydration occurs the reactions possible may be represented as follows, assuming that the equilibrium between carbonic acid and its ions is rapid

$$CO^{16}O^{16} + H_2O^{16} \underset{}{\overset{k_1}{\rightleftharpoons}} H_2CO^{16}O^{16}O^{16}$$

$$CO^{16}O^{16} + H_2O^{18} \underset{}{\overset{k_{-1}}{\rightleftharpoons}} H_2CO^{16}O^{16}O^{18}$$

$$CO^{16}O^{18} + H_2O^{16} \rightleftharpoons H_2CO^{16}O^{16}O^{18}$$

$$CO^{16}O^{18} + H_2O^{18} \rightleftharpoons H_2CO^{16}O^{18}O^{18}$$

$$CO^{18}O^{18} + H_2O^{16} \rightleftharpoons H_2CO^{16}O^{18}O^{18}$$

$$CO^{18}O^{18} + H_2O^{18} \rightleftharpoons H_2CO^{18}O^{18}O^{18}$$

Then for the rate of change of O^{18} content in the carbon dioxide, carbonic acid and water

$$-\frac{dO^{18}(CO_2)}{dt} = k_1[CO^{16}O^{18}]\{[H_2O^{16}] + [H_2O^{18}]\} + 2k_1[CO^{18}O^{18}]\{[H_2O^{16}] + [H_2O^{18}]\} - {}^2/_3k_{-1}[H_2CO^{16}O^{16}O^{18}] - {}^4/_3k_{-1}[H_2CO^{16}O^{18}O^{18}] - 2k_{-1}[H_2CO^{18}O^{18}O^{18}]$$

$$-\frac{dO^{18}(H_2CO_3)}{dt} = k_{-1}[H_2CO^{16}O^{16}O^{18}] + 2k_{-1}[H_2CO^{16}O^{18}O^{18}] + 3k_{-1}[H_2CO^{18}O^{18}O^{18}] - k_1[H_2O^{16}]\{[CO^{16}O^{18}] + 2[CO^{18}O^{18}]\} - k_1[H_2O^{18}]\{[CO^{16}O^{16}] + 2[CO^{16}O^{18}] + 3[CO^{18}O^{18}]\}$$

$$-\frac{dO^{18}(H_2O)}{dt} = \frac{k_{-1}}{3}[H_2CO^{16}O^{16}O^{18}] + {}^2/_3k_{-1}[H_2CO^{16}O^{18}O^{18}] + k_{-1}[H_2CO^{18}O^{18}O^{18}] - k_1[H_2O^{18}]\{[CO^{16}O^{16}] + [CO^{16}O^{18}] + [CO^{18}O^{18}]\}$$

Let α, β and γ be the atom fractions of O^{18} in the carbon dioxide, water and carbonic acid, respectively. That is

$$\alpha = \frac{2[CO_2{}^{18}] + [CO^{16}O^{18}]}{2[CO_2]}$$

with similar expressions for β and γ. Substituting for the concentrations of the molecules present in terms of the atom fractions leads to the following equations. The same result is obtained if each molecule is assumed to be present in the proportion expected, if statistical equilibrium exists between all the isotopic varieties of each compound.

$$2[CO_2]\frac{d\alpha}{dt} = k_1[H_2O][CO_2]2(\gamma - \alpha)$$

$$3\{[H_2CO_3] + [HCO_3^-]\}\frac{d\gamma}{dt} = k_1[H_2O][CO_2](2\alpha + \beta - 3\gamma)$$

$$[H_2O]\frac{d\beta}{dt} = k_1[H_2O][CO_2][\gamma - \beta]$$

When $\{[H_2CO_3] + [HCO_3^-]\}$ is very small we may set $3\gamma = 2\alpha + \beta$. The O^{18} content of the carbonic acid is thus between that of the water and the carbon dioxide.

In solutions acid enough so that only carbon dioxide exists to any extent

$$-\frac{d\alpha}{dt} = \frac{k_1[H_2O]}{3}(\alpha - \beta)$$

The O^{18} content of the water remains effectively the same so that β may be taken as constant. The integrated expression is of the form

$$At + B + \log(\alpha - \beta) = 0$$

where $A = k_1[H_2O]\ 2.303/60$ and is the slope of the least square line determined experimentally and $k_1[H_2O]$ is in sec.$^{-1}$. The values of A and $k_1[H_2O]$ are given in Tables IV and V.

When considerable bicarbonate ion is present the rate of exchange is much slower, being proportional to the ratio $[CO_2] : \{[H_2CO_3] + [HCO_3^-]\}$. The three differential equations still represent the changes taking place. The solutions will be of the form

$$\alpha = a_1e^{-\lambda_1 t} + a_2e^{-\lambda_2 t} + a_3e^{-\lambda_3 t} \qquad (1)$$

with similar expressions for β and γ. It then turns out that

$$\lambda_1 = 0$$

$$\lambda_{2,3} = \frac{p + q \pm \sqrt{p^2 + q^2 + r^2 - 2pr - \frac{2qr}{3} + \frac{2pq}{3}}}{2}$$

where

$$p = k_1[H_2O],\ q = k_1\frac{[H_2O][CO_2]}{[H_2CO_3] + [HCO_3^-]} \text{ and } r = k_1[CO_2]$$

However, r is of the order of $^1/_{1000}$ of p or q and can be neglected. Using the boundary conditions, when

$$t = 0,\ \alpha = \beta = \alpha_0,\ \beta = \beta_0$$

and when

$$t = \infty,\quad \alpha = \beta = \gamma = \alpha_\infty$$

it turns out that the second term on the right in equation (1) for the atom fraction becomes unimportant soon after the reaction begins. During this time the O^{18} content of the carbonic acid and bicarbonate ion adjusts itself to a value less than that of the carbon dioxide. After this initial period

$$\alpha = \alpha_\infty + a_3e^{-\lambda_3 t}$$
$$\gamma = \alpha_\infty + c_3e^{-\lambda_3 t}$$

where

$$c_3\left[\frac{p}{p - \lambda_3} - \frac{p}{p - \lambda_2}\right] = (\alpha - \alpha_\infty)\left[1 - \frac{p}{p - \lambda_2}\right]$$

and

$$a_3 = \frac{p}{p - \lambda_3}c_3$$

The values of a_3 and c_3 are only a few per cent. different from unity, which they approach as the ratio $[CO_2] : [HCO_3^-]$ decreases. The value of $[H_2CO_3]$ is so small in these cases that it can be neglected.

Since the carbon dioxide liberated in the sample bulbs by sulfuric acid is representative of the carbon dioxide and sodium bicarbonate, we may represent its O^{18} fraction by

$$\delta = \frac{\alpha[CO_2] + \gamma[HCO_3^-]}{[CO_2] + [HCO_3^-]}$$

Making the proper substitutions

$$d \ln(\delta - \alpha_\infty)/dt = -\lambda_3$$

From the measured rate of the reaction obtained by evaluating A in the expression $At + B + \log(\delta - \alpha_\infty) = 0$, we obtain the value of the constant

$$p = k_1[H_2O]\text{sec.}^{-1} = A \times \frac{2.303}{60} \times \left\{ \frac{2}{1 + \frac{[CO_2]}{[HCO_3^-]} - \sqrt{1 + \frac{2}{3}\frac{[CO_2]}{[HCO_3^-]} + \left(\frac{[CO_2]}{[HCO_3^-]}\right)^2}} \right\}$$

The concentrations of $[CO_2]$ and $[HCO_3^-]$ were obtained from the weight of heavy oxygen sodium carbonate and the amounts of water and standard acid used. In an unsatisfactory attempt to determine the ratio $[CO_2] : [HCO_3^-]$ in another way the pH of the solution was determined at the reaction temperature by two opposing quinhydrone half cells. One contained the CO_2–HCO_3^- solution and the other a Sørensen phosphate buffer. The ratio $[CO_2] : [HCO_3^-]$ was calculated from the equation

$$\log \frac{[CO_2]}{[HCO_3^-]} = pK_a - p\text{H} + \log f_{HCO_3^-}$$

where $-0.5\sqrt{\mu}$ was substituted for $\log f_{HCO_3^-}$.[20] However, using standard solutions and carefully guarding against loss of carbon dioxide, e. m. f. values were obtained which yield pH values other than those calculated. A junction potential may account for this discrepancy. Keller[21] has reported a difference between the calculated pH and the observed pH for such solutions using a colorimetric method. At 40° the e. m. f. measurements were unsteady and the pH was determined using a Beaver colorimeter[22] with phenol red as indicator. The pK_a value was taken as 7.70 for these solutions whose ionic strength was about 0.05. The ratio $[CO_2] : [HCO_3^-]$ calculated from these measurements was in agreement with those obtained from weighings.

The values of A have been determined by the method of least squares from the experimental data and then $k_1[H_2O]$ evaluated. The results are given in Tables IV, V and VI.

Oxygen exchange between carbon dioxide and water takes place very slowly compared with the time necessary to establish elementic equilibrium. This is true because the carbon dioxide must come to equilibrium with all the water. When the solution was acid enough so that all the carbon dioxide remained as such in solution the values of the rate constant for the velocity of hydration have a constant value. The rate is not affected by addition of sodium chloride, sodium acetate or high concentrations of hydrochloric or acetic acid. In this range it appears that only simple hydration occurs. The results of this and other work are compared in Table VIII.

TABLE VIII

Reaction rate constants for the velocity of hydration of carbon dioxide $= k_1[H_2O]\text{sec.}^{-1}$. Those in parentheses were determined in buffer solutions. All values at 38° were obtained by extrapolation.

Reference	0°	18°	25°	38°
Faurholt, 1924, multiplied by 2.303	(0.0030)	(0.025)		(0.23)
Brinkman, Margaria and Roughton, 1933	(.0026)	(.024)		(.26)
Stadie and O'Brien, 1933	(.0027)			
Roughton and Booth, 1938	(.0027)			
	.0021			
This paper	(.0027)			
	.00205		0.0275	.10
	± .00005		± .0015	

At 0° the rate of oxygen exchange is just that found by direct kinetic measurement for the rate of hydration of carbon dioxide. This agreement indicates that there is no rapid reversible reaction of carbon dioxide with water which could result in oxygen exchange as has been sometimes supposed. At 25° the value of the rate constant is considerably lower than that previously established. The fact that at elevated temperatures the reaction is so rapid that direct kinetic measurements are less precise probably accounts for this difference. The average energy of activation between 0 and 25° is 16,800 ± 400 calories.

The velocity constant for dehydration can be determined from a knowledge of the true dissociation constant of carbonic acid. Taking this as 4×10^{-4}, then at 0°

$$k_{-1} = \frac{[CO_2]}{[HCO_3^-]} k_1[H_2O] = \frac{K(\text{true})}{K(\text{apparent})} \times 0.0020 = 4 \text{ sec.}^{-1}$$

(20) Hastings and Sendroy, *J. Biol. Chem.*, **65**, 445 (1925); Stadie and Hawes, *ibid.*, **77**, 265 (1928).

(21) Keller, *Z. anal. Chem.*, **113**, 8 (1938).

(22) Beaver, *J. Optical Soc.*, **18**, 41 (1929).

When considerable amounts of bicarbonate ion are present, the rate of oxygen exchange is much slower, being dependent on the ratio $[CO_2]:[HCO_3^-]$. As is shown in Table IV, the value of $k_1[H_2O]$ remains constant until very small values of carbon dioxide concentration are reached. Then the inaccuracy in concentration satisfactorily accounts for the deviation. Actually as shown for run B-27 the ratio has varied some 200-fold while $k_1[H_2O]$ changes by only 50%. In Table V the rate constants in run C-1 and C-2 are low. It is thought that this is due to loss of carbon dioxide, a circumstance which occurs more easily at higher temperatures and which would explain the low values. A comparison of runs B-16 and B-20 shows that increasing the salt concentration considerably does not affect the rate. Therefore it seems that under these conditions the bicarbonate ion exchanges oxygen with water only through the reversible formation of carbon dioxide by simple hydration

$$CO_2 + H_2O \rightleftarrows H_2CO_3 \rightleftarrows H^+ + HCO_3^-$$

In the presence of $M/15$ phosphate buffer an increase of about 30% in the rate is observed. This is exactly in agreement with the recent data of Roughton and Booth,[9] who have found that the presence of the phosphate buffer, usually heretofore employed, accelerates the reaction to this extent.

Sodium carbonate exchanges all its oxygen slowly with water. It is not feasible to calculate a rate constant since the purity of the sodium carbonate so affects the concentration of carbon dioxide. However, even if one-fourth the sodium carbonate were sodium bicarbonate, it can be shown that the rate of exchange is 1000 times greater than can be accounted for by simple hydration. The rapidity apparently is due to the reaction of carbon dioxide with hydroxyl ion. When the solution has been made more basic by addition of sodium hydroxide, the exchange becomes very slow due to the extremely small amount of carbon dioxide present. The slow exchange of carbonate ion[18] has been studied also by Titani and Goto.[23,24] Our more precise analytical means allow observation of smaller changes.

(23) Titani, Morita and Goto, *Bull. Chem. Soc. Japan*, **13**, 329 (1938).

(24) Titani and Goto, *ibid.*, **14**, 77 (1939).

Oxygen exchange of other inorganic ions has been studied.[24,25] It has appeared that anhydride formation would in some cases account for exchange in acid solutions. Exchange with the sulfate ion is strongly catalyzed by hydroxyl ions.[26] No such effect was observed for carbonate ion.

Summary

The rate of carbon exchange between carbon dioxide and bicarbonate ion has been studied. Approximate rate constants were determined which are consistent with those established independently for the rate of hydration of carbon dioxide.

The rate of oxygen exchange between carbon dioxide, bicarbonate ion, carbonate ion and water has been investigated. The exchange between carbon dioxide and water is due to the reversible hydration only. The addition of salts or acids did not affect this rate. The rate constant at 0° agrees with that found recently by Roughton and Booth, being one-fourth lower than the previously accepted value which was established in the presence of buffer solutions. At higher temperatures the rate found is considerably less than that previously established. The average energy of activation between 0 and 25° is 16,800 ± 400 calories.

Oxygen exchange of bicarbonate ion occurs only through the reversible formation of carbon dioxide by simple hydration when the *p*H is less than 8. The rate is not affected by the addition of sodium or potassium chloride. In the presence of phosphate buffer the reaction is accelerated.

Carbonate ion slowly exchanges its oxygen with water. The rate is faster than for simple hydration of the carbon dioxide present. This increase is presumably due to the reaction of carbon dioxide with hydroxyl ion. A high concentration of hydroxyl ion retards the exchange, since then only very small concentrations of carbon dioxide are present.

NEW YORK, N. Y. RECEIVED JANUARY 25, 1940

(25) Blumenthal and Herbert, *Trans. Faraday Soc.*, **33**, 849 (1937); Datta, Day and Ingold, *J. Chem. Soc.*, 1968 (1937); Titani and Morita, *Bull. Chem. Soc. Japan*, **13**, 667 (1938).

(26) Winter, Carlton and Briscoe, *J. Chem. Soc.*, 131 (1940), have shown that sulfate ion is not hydroxyl-catalyzed, and that at high concentration of hydroxyl ion reaction with the glass container may account for the exchange reported by Datta, Day and Ingold.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

The Strength of Carbonic Acid. The Rate of Reaction of Carbon Dioxide with Water and Hydroxyl Ion

BY A. R. OLSON AND P. V. YOULE*

A value of the order of 4×10^{-7} is accepted by most chemists as the first ionization constant of aqueous carbonic acid. If K_1 is defined as equal to

$$\frac{(H^+)(HCO_3^-)}{(\text{total } CO_2 \text{ in solution})}$$

this value is correct. For certain types of work such as those where bicarbonate ion or carbonic acid is used as a catalyst for reactions, it is necessary to distinguish between the total amount of carbon dioxide in solution and that fraction of it which is present as carbonic acid, a distinction emphasized by Brönsted.[1] In some of our unpublished work on the hydrolysis of β-butyrolactone, the catalytic character of bicarbonate ion indicated that carbonic acid was about ten times stronger than acetic acid, and so the literature was searched for information bearing on this point.

McBain[2] noted a slow neutralization of carbonic acid with phenolphthalein as indicator, an observation amplified by Vorländer and Strube[3] and by Thiel.[4] By colorimetric measurements Thiel, together with Strohecker, made a detailed study of the reactions involved, but, since much of this work was superseded in accuracy by Faurholt's, it is pertinent here to recall only one of Thiel's experiments. Thiel set the amount of carbonic acid present as equivalent to the amount of base neutralized by a given carbon dioxide solution in less than 0.4 second, which at 4° he found to be 0.67%, corresponding to a first dissociation constant of 5×10^{-4} (recalculated by Faurholt as 1.9×10^{-4}). The value 7.4×10^{-4} obtained by Lotte Pusch[5] through conductivity measurements was dismissed by Faurholt as doubtful.

Faurholt[6] determined the amount of carbonic acid present in carbon dioxide solutions by adding excess of dimethylamine to combine with the carbon dioxide in solution as carbamate so that the carbonic acid could be precipitated by barium chloride. By analyses at measured time intervals he followed the reaction of carbon dioxide with water

$$CO_2 + H_2O \xrightarrow{k_a} H_2CO_3 \qquad (1)$$

and with hydroxyl ion

$$CO_2 + OH^- \xrightarrow{k_b} HCO_3^- \qquad (2)$$

His value for k_a was checked by Stadie and O'Brien,[7] by Brinkman, Margaria and Roughton[8] using manometric and flow techniques, and by Urey and Mills[9] in a study of O^{18} exchange between carbon dioxide and water.

From Faurholt's results at 0 and 18° we calculate for reaction (1)

$$RT^2 \frac{\Delta \ln K}{\Delta t} = \Delta H = 0.7 \text{ kcal. per mole}$$

$$RT^2 \frac{\Delta \ln k_a}{\Delta t} = \Delta E = 19 \text{ kcal. per mole}$$

For the reaction with hydroxyl ion, the activation energy is from 10 to 13 kcal. per mole, according to the data used.

The velocity with which carbon dioxide adds to bases depends upon the strength of the base, as is shown by the following figures from Faurholt[10] for the reaction

$$CO_2 + R_2NH = R_2NCOOH$$

$$\frac{-d(CO_2)}{dt} = k(CO_2)(R_2NH)$$

Base	NH_3	$MeNH_2$	Me_2NH
k (18°, time in hours)	2.3×10^5	5×10^6	4×10^7

These figures also serve to justify Faurholt's method of analysis, which involved essentially a competition between two bases for the carbon dioxide.

Roughton and Booth[11] published approximate figures for the catalytic effect of bases on reaction (1). Their results conform roughly to a typical Brönsted diagram. Catalysis by bicarbonate ion corresponds to an acid strength for carbonic acid of about 5×10^{-5}, showing approximate agreement with our results.

* Commonwealth Fund Fellow, University of California.

(1) Brönsted, *Z. physik. Chem.*, **108**, 215 (1924).
(2) McBain, *J. Chem. Soc.*, **101**, 814 (1912).
(3) Vorländer and Strube, *Ber.*, **46**, 172 (1913).
(4) Thiel, *ibid.*, **46**, 241 (1913).
(5) Lotte Pusch, *Z. Elektrochem.*, **22**, 206 (1916).
(6) Faurholt, *J. chim. phys.*, **21**, 400 (1924).
(7) Stadie and O'Brien, *J. Biol. Chem.*, **203**, 521 (1933).
(8) Brinkman, Margaria and Roughton, *Phil. Trans. Roy. Soc.*, **232A**, 65 (1932).
(9) Urey and Mills, THIS JOURNAL, **61**, 534 (1939).
(10) Faurholt, *J. chim. phys.*, **22**, 1 (1925).
(11) Roughton and Booth, *Biochem. J.*, **32**, 2049 (1938).

Summary

The catalytic efficiency of HCO_3^- confirms the statements found in various published articles that the first ionization constant for carbonic acid is about 2×10^{-4}.

From the rates of the reaction $CO_2 + H_2O = H_2CO_3$ at various temperatures, the heat of activation is found to be 19 kcal./mole.

For the reaction $CO_2 + OH^- = HCO_3^-$ the heat of activation is found to be from 10 to 13 kcal./mole.

BERKELEY, CALIF. RECEIVED FEBRUARY 5, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF DUKE UNIVERSITY]

The Solubility of Cadmium and Zinc Oxalates in Salt Solutions

BY WARREN C. VOSBURGH AND J. FINK BECKMAN

In the determination of the ionization constants of cadmium and zinc oxalates by Clayton and Vosburgh[1] there were two sources of uncertainty. One was the value used for the second ionization constant of oxalic acid and the other the interpretation of the solubility data for cadmium oxalate in cadmium sulfate solutions. The redetermination of the second ionization constant of oxalic acid by Harned and Fallon[2] has made it advisable to recalculate some of the data of Clayton and Vosburgh,[1] and some new experiments have led to a better interpretation of the solubility data.

Materials.—Cadmium oxalate was prepared by precipitation as described by Clayton and Vosburgh.[1]

Potassium perchlorate was prepared from potassium hydroxide and perchloric acid. It was recrystallized three times and dried at 100°.

Cadmium perchlorate was prepared by addition of an excess of cadmium oxide to a known quantity of 60% perchloric acid solution. The solution was separated from the excess oxide and heated, whereupon some cadmium hydroxide precipitated. Filtration and dilution gave a stock solution with a *p*H of about 7 as measured by a glass electrode. The concentration determined by an electrolytic cadmium determination agreed with the concentration as calculated from the original quantity of perchloric acid. Dilution of the cadmium perchlorate solution caused a decrease in *p*H, the largest decrease observed being about one unit.

Potassium sulfate was recrystallized twice. Solutions of this and of potassium perchlorate were prepared by weight, and analysis was considered unnecessary.

Solubility Determinations.—Solutions of potassium and cadmium perchlorates and potassium sulfate were saturated with cadmium oxalate at 25 ± 0.02° (in an oil-bath) by stirring mechanically for at least two hours. Experiments showed that saturation could be attained in one hour. A large sample was drawn through a filter of Pyrex glass wool and portions of 200 ml. each were taken for analysis, without allowing the temperature to fall appreciably below 25°. The oxalate was titrated with 0.05 *N* permanganate solution by the use of a 5-ml. semi-micro buret. The permanganate solution was standardized frequently against sodium oxalate from the National Bureau of Standards under conditions similar to those used in the oxalate determinations. Experiments showed that the solvent salts did not interfere with the analyses. The results of the solubility determinations are given in Tables I–IV in the columns headed "total oxalate." It is believed that errors were within 1.5%.

The values reported for the solubility of cadmium oxalate in water by Clayton and Vosburgh[1] differ from the one in this paper by more than 1.5%, but it is believed that the latter is the more reliable and is accurate within the limit claimed.

Discussion

For the interpretation of the solubility data it is necessary to recalculate the solubility product of cadmium oxalate. Use of the value 5.18×10^{-5} for the second ionization constant of oxalic acid[2] and the experimental data of Clayton and Vosburgh[1] gives 1.44×10^{-8} for the activity solubility product.

By means of the solubility product and the activity coefficients of Kielland[3] the concentration of oxalate ion in the salt solutions was calculated. In potassium perchlorate and potassium sulfate solutions allowance was made for a small amount of autocomplex formation. For potassium perchlorate solutions the data in Table I were obtained.

TABLE I

SOLUBILITY OF CADMIUM OXALATE IN POTASSIUM PERCHLORATE SOLUTIONS

$KClO_4$ $m \times 10^3$	Total oxalate $m \times 10^3$	$\sqrt{\mu}$	$C_2O_4^-$ $m \times 10^3$	CdC_2O_4 un-ionized $m \times 10^3$
None	0.289	0.0232	0.133	0.154
5	.316	.0752	.163	.150
10	.341	.104	.179	.159
20	.365	.144	.208	.153
40	.413	.203	.247	.161
80	.475	.285	.303	.166

(1) Clayton and Vosburgh, THIS JOURNAL, **59**, 2414 (1937).

(2) Harned and Fallon, *ibid.*, **61**, 3111 (1939).

(3) Kielland, THIS JOURNAL, **59**, 1677 (1937).

The figures in the last column are the difference between the total oxalate and the concentration of oxalate ion plus twice the concentration of the complex ion $Cd(C_2O_4)_2^{=}$. The latter concentration was about 1% of the oxalate ion concentration, as will be shown later. The difference so calculated is assumed to represent undissociated cadmium oxalate and in Table I is as nearly constant as could be expected. The corresponding differences for the solutions of the other salts increased considerably with the concentration of the solvent salt. This is shown in Fig. 1, in which are represented also the data of Clayton and Vosburgh for cadmium sulfate solutions recalculated with the use of the new solubility product.

Clayton and Vosburgh assumed that the cadmium sulfate curve of Fig. 1 represented the solubility of undissociated cadmium oxalate in cadmium sulfate solutions. They also assumed that cadmium oxalate would behave similarly in other salt solutions. In view of the practically constant concentration of the undissociated oxalate in potassium perchlorate solutions, it now seems preferable to consider that small concentrations of electrolytes have no appreciable effect on the concentration of undissociated cadmium oxalate in saturated solutions.

The abnormal solubility in the cadmium perchlorate solutions cannot be ascribed to the perchlorate ion. Therefore it must be caused by the cadmium ion. The assumption of the existence of the ion $CdC_2O_4 \cdot Cd^{++}$ allows an explanation. This ion can be considered to be formed according to the equation

$$CdC_2O_4 + Cd^{++} \rightleftarrows CdC_2O_4 \cdot Cd^{++}$$

and its instability constant calculated by the equation

$$(CdC_2O_4)[Cd^{++}]/[CdC_2O_4 \cdot Cd^{++}] = K_1$$

in which parentheses indicate activity and square brackets concentration. The activity coefficients for the ions should cancel approximately.

The activity of undissociated cadmium oxalate was found by extrapolation of the curve for cadmium perchlorate in Fig. 1. This gives the value 1.44×10^{-4} m, as compared with 1.54×10^{-4} m, in Table I for the solubility in water. Since the extrapolated values for solutions of the two cadmium salts agreed well, 1.44×10^{-4} was accepted as the activity. The higher value for the potassium perchlorate and sulfate solutions involves a much larger correction for ionized cadmium oxalate, and appreciable hydrolysis may have taken place in these solutions and in water.

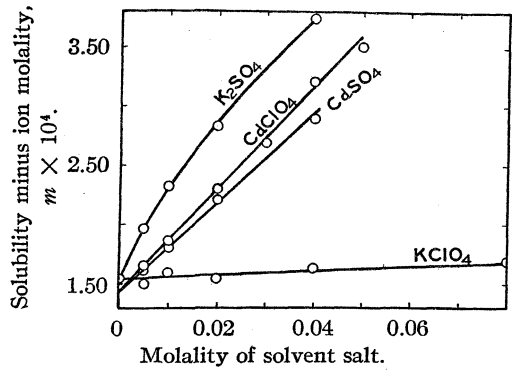


Fig. 1.—Variation of the solubility of cadmium oxalate with salt concentration. From the total solubility has been subtracted the concentration of the ionized cadmium oxalate as calculated from the solubility product.

The concentration of the ion $CdC_2O_4 \cdot Cd^{++}$ was taken as the difference between the total oxalate concentration and the sum of the oxalate ion and undissociated cadmium oxalate concentrations. The latter was assumed constant and equal to 1.44×10^{-4} m. Table II shows that K_1 is constant.

TABLE II

COMPOSITION OF CADMIUM PERCHLORATE SOLUTIONS SATURATED WITH CADMIUM OXALATE

$Cd(ClO_4)_2$ or Cd^{++} $m \times 10^3$	Total oxalate $m \times 10^3$	CdC_2O_4 $m \times 10^3$	$C_2O_4^{=}$ $m \times 10^3$	$CdC_2O_4 \cdot Cd^{++}$ $m \times 10^3$	K_1
5	0.173	0.144	0.008	0.021	0.034
10	.191	.144	.005	.042	.034
20	.234	.144	.004	.086	.034
30	.272	.144	.003	.125	.035
40	.323	.144	.003	.176	.033
50	.353	.144	.003	.206	.035

A similar calculation was made for cadmium sulfate solutions with the assumption that cadmium sulfate is only partially dissociated and the dissociation constant is 0.0050 as calculated by Davies.[4] The values for K_1 so calculated were not constant. If the concentration of the ion $CdC_2O_4 \cdot Cd^{++}$ is calculated by the use of the value 0.034 for K_1, an appreciable amount of the oxalate in the more concentrated cadmium sulfate solutions is left unaccounted for, as shown in the column headed "difference" in Table III. As a possible explanation for this difference the ion $CdC_2O_4 \cdot SO_4^{=}$ was assumed, and its equilibrium constant calculated by the expression

$$(CdC_2O_4)[SO_4^{=}]/[CdC_2O_4 \cdot SO_4^{=}] = K_2$$

(4) Davies, *J. Chem. Soc.*, 2093 (1938).

The results of this calculation, based on the experimental data of Clayton and Vosburgh, are given in Table III.

TABLE III

COMPOSITION OF CADMIUM SULFATE SOLUTIONS SATURATED WITH CADMIUM OXALATE

Total $CdSO_4$ $m \times 10^3$	Total oxalate $m \times 10^3$	Cd^{++} and $SO_4^{=}$ $m \times 10^3$	$CdC_2O_4 \cdot Cd^{++}$ $m \times 10^3$	Difference $m \times 10^3$	K_2
5	0.171	3.88	0.016	0.001	..
10	.188	7.12	.030	.006	0.17
20	.226	13.1	.056	.020	.09
40	.294	24.0	.102	.043	.08

For solutions of potassium sulfate it is necessary to assume the formation of both undissociated cadmium sulfate and the ion $CdC_2O_4 \cdot SO_4^{=}$. Because of the formation of cadmium sulfate, the oxalate ion molality is not equal to the cadmium ion molality. The values of K_2 for the ion $CdC_2O_4 \cdot SO_4^{=}$ agreed with those in Table III as well as could be expected. The data for potassium sulfate solutions are given in Table IV. The figures in the column headed "difference" were obtained by the subtraction of 1.54×10^{-4}, and the oxalate ion molality, and twice the concentration of the ion $Cd(C_2O_4)_2^{=}$ from the total oxalate molality. For the undissociated cadmium sulfate the molality 1.54×10^{-4} was used instead of 1.44×10^{-4} because the former is the extrapolated value in Fig. 1 for potassium sulfate and potassium perchlorate solutions. On account of the large activity of cadmium and oxalate ions, hydrolysis might be appreciable in these solutions and the larger figure would include a correction for this. The values for the "difference" in Table IV were taken as the molalities of the ion $CdC_2O_4 \cdot SO_4^{=}$.

TABLE IV

COMPOSITION OF POTASSIUM SULFATE SOLUTIONS SATURATED WITH CADMIUM OXALATE

K_2SO_4 $m \times 10^3$	Total oxalate $m \times 10^3$	$C_2O_4^{=}$ $m \times 10^3$	$Cd(C_2O_4)_2^{=}$ $m \times 10^3$	Difference $m \times 10^3$	K_2
5	0.390	0.230	0.002	0.002	...
10	.463	.285	.003	.018	0.079
20	.564	.368	.0035	.035	.082
40	.719	.481	.0045	.075	.076

It has been shown that the solubility of cadmium oxalate in dilute salt solutions can be explained on the assumption that the concentration of the undissociated portion is constant. This should apply to potassium oxalate solutions, and it is necessary to recalculate the data of Clayton and Vosburgh on the oxalatocadmiate ion. The results of such a recalculation are given in Table V. The concentration of the oxalatocadmiate ion, $Cd(C_2O_4)_2^{=}$, was taken as the difference between the total cadmium oxalate dissolved and the sum of the cadmium ion molality and the molality of undissociated cadmium oxalate. The instability constant was calculated by means of the equation.

$$(CdC_2O_4)[C_2O_4^{=}]/[Cd(C_2O_4)_2^{=}] = K_3$$

and the activity coefficients for the ions were assumed to cancel.

TABLE V

INSTABILITY CONSTANT OF THE OXALATOCADMIATE ION

Oxalate total $m \times 10^3$	CdC_2O_4 total $m \times 10^3$	$C_2O_4^{=}$ $m \times 10^3$	Cd^{++} $m \times 10^3$	$Cd(C_2O_4)_2^{=}$ $m \times 10^3$	K_3
5.76	0.194	5.53	0.007	0.043	0.019
9.49	.230	9.18	.005	.081	.016
24.56	.374	23.96	.004	.226	.015
27.00	.394	26.38	.003	.237	.016
28.66	.412	27.98	.003	.265	.015
48.6	.627	47.5	.003	.480	.014
97.5	1.077	95.5	.002	.931	.015

The ionization constant of cadmium oxalate at 25° can be calculated from the solubility product (1.44×10^{-8}) and the activity of the undissociated oxalate (1.44×10^{-4}), to be 1.00×10^{-4}. Money and Davies[5] found 1.3×10^{-4} at 18° by calculation from the conductivity data of Scholder.[6]

Recalculations for Zinc Oxalate.—Recalculation of the solubility product for zinc oxalate gives $K_{S.P.} = 1.28 \times 10^{-9}$. The solubility in water is 1.68×10^{-4} and if hydrolysis is neglected the concentration of undissociated oxalate is 1.29×10^{-4}. The ionization constant is 0.99×10^{-5} at 25° as compared with 1.3×10^{-5} at 18° calculated by Money and Davies.[5]

The effect of zinc sulfate on the solubility of zinc oxalate can be explained by the assumption of the ion $ZnC_2O_4 \cdot Zn^{++}$. In Table VI it is assumed that the concentration of this ion is equal to the total oxalate minus $1.29 \times 10^{-4}\ m$, with a further correction of $0.01 \times 10^{-4}\ m$ in two cases for

TABLE VI

COMPOSITION OF ZINC SULFATE SOLUTIONS SATURATED WITH ZINC OXALATE

Total $ZnSO_4$ $m \times 10^3$	Total oxalate $m \times 10^3$	Zn^{++} $m \times 10^3$	$ZnC_2O_4 \cdot Zn^{++}$ $m \times 10^3$	K_4
..	0.168	0.039	...	...
5	.167	4.0	0.037	0.014
10	.202	7.5	.072	.013
20	.269	15.4	.140	.014
40	.386	26.0	.257	.013

(5) Money and Davies, *Trans. Faraday Soc.*, **28**, 613 (1932).
(6) Scholder, *Ber.*, **60**, 1527 (1927).

oxalate ion. The K_4 in the table is the instability constant of this ion calculated from the solubility data, with the assumption that zinc sulfate is incompletely dissociated and its ionization constant[4] is 0.0054.

Recalculation of the data on the oxalatozincate ion $Zn(C_2O_4)_2^=$ in the same manner as for the oxalatocadmiate ion gives the results in Table VII. To the data of Clayton and Vosburgh have been added some experimental data of Metler and Vosburgh[7] and some of Kunschert.[8] The first three values for K_5 from the data of Metler and Vosburgh are probably too high; the analysis for zinc gave somewhat low results and the error was probably largest in the most dilute solutions. It may be concluded that in the more dilute solutions the complex ion $Zn(C_2O_4)_2^=$ is formed, but all three sets of results are in agreement in showing that at a molality of between 0.05 and 0.1 the value of K_5 begins a rapid decrease. The significance of this is discussed by Clayton and Vosburgh.

TABLE VII

INSTABILITY CONSTANT OF THE OXALATOZINCATE ION

Oxalate total $m \times 10^3$	ZnC_2O_4 total $m \times 10^3$	$C_2O_4^=$ $m \times 10^3$	$Zn(C_2O_4)_2^=$ $m \times 10^3$	K_5
	A. Clayton and Vosburgh			
10.00	0.460	9.21	0.331	0.0036
27.45	1.030	25.52	.901	.0037
48.44	1.803	44.97	1.674	.0035
111.6	6.48	98.77	6.35	.0020
	B. Metler and Vosburgh			
12.2	0.43	11.5	0.30	0.0049
12.7	.45	11.9	.32	.0048
25.9	.85	24.3	.72	.0043
52.1	1.9	48.4	1.77	.0035
51.6	1.8	48.1	1.67	.0037
108.7	5.8	98.2	5.67	.0022
224.7	19.4	186.0	19.3	.0012
262.0	25.4	211.3	25.3	.0011
	C. Kunschert (concentrations in moles per liter)			
52.2	2.2	47.9	2.1	0.0029
105.5	5.5	94.6	5.4	.0023
160.6	10.55	140	10.4	.0017
217.3	17.4	183	17.3	.0014
275.7	25.7	224	25.6	.0011

Summary

The solubility of cadmium oxalate in solutions of potassium and cadmium perchlorates and potassium sulfate has been measured.

The increase in solubility with concentration in solutions of potassium and cadmium sulfates and cadmium perchlorate, and the constancy in potassium perchlorate solutions, can be explained if the existence of the ions $CdC_2O_4 \cdot Cd^{++}$ and $CdC_2O_4 \cdot SO_4^=$ is postulated and cadmium sulfate regarded as incompletely dissociated.

The solubility of zinc oxalate in zinc sulfate solutions can be explained similarly if the ion $ZnC_2O_4 \cdot Zn^{++}$ is postulated.

The instability constants of the ions $Cd(C_2O_4)_2^=$ and $Zn(C_2O_4)_2^=$ have been recalculated.

(7) Metler and Vosburgh, THIS JOURNAL, **59**, 2421 (1937).
(8) Kunschert, *Z. anorg. Chem.*, **41**, 339 (1904).

DURHAM, NORTH CAROLINA RECEIVED JANUARY 19, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF NEW YORK UNIVERSITY]

Ternary Systems. XXV. Solid Solutions of Some Picromerites at 25°

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In continuation of the project undertaken in this Laboratory, of collecting reliable equilibrium data on the distribution of isomorphous salts between liquid and conjugate solid solutions, a series of ternary systems consisting of water and a pair of double sulfates of the picromerite series, has been investigated, at the temperature of 25°. The purpose of these measurements is ultimately to relate if possible the distribution ratio of these salts between liquid and solid phases, with certain properties of the individual salts such as their aqueous solubilities. With the necessity in mind of having as nearly as possible ideal conditions for the interpretation of solution relationships, pairs of salts were chosen for this work which because of their very close similarity in formula and in other properties would be expected to form very nearly ideal solid solutions in their mixed crystals. Reports already have been published on a number of alum pairs,[1,2] as also on some picromerite systems.[3] The present report covers

* This paper is being published, following the death of Professor Hill, by his collaborators.

** The material of this article is taken from a thesis presented by G. S. Durham for the Degree of Doctor of Philosophy at New York University, June, 1939.

(1) Hill and Kaplan, THIS JOURNAL, **60**, 550 (1938).
(2) Hill, Smith and Ricci, *ibid.*, **62**, 858 (1940).
(3) Hill and Taylor, *ibid.*, **60**, 1099 (1938).

the experimental investigation of the equilibrium relations of six pairs of picromerites studied as ternary systems with water at 25°; the picromerites, or schoenites, are a series of isomorphous monoclinic hexahydrated double sulfates of univalent and divalent bases, of which Mohr salt, $Fe(NH_4)_2(SO_4)_2 \cdot 6H_2O$, is a familiar example. In all the systems of the present study complete miscibility of the two picromerites in the solid state was found, at the temperature of the determinations.

The experimental procedure in these measurements is marked, as in the preceding papers of this series, by particular attention to the establishment of equilibrium both in respect to the solid–liquid relations and as to the equilibrium within the mixed crystals themselves, in order to leave no question as to the validity of the results for any possible theoretical interpretation. The procedure was therefore that already described, in which the solid solution equilibrium was approached, for every determination, from two opposite directions. Every complex was prepared in exact duplicate (Tubes A and B of the Tables). In Tube A one of the salts was dissolved completely in the water, and the second solid then added as the initial solid phase; this order was then reversed for Tube B of the same complex. If the two tubes give the same results for both liquid and solid compositions, equilibrium is proved. Although the attainment of this kind of solid solution equilibrium is in general very slow, it was found that by enclosing two glass marbles in each complex during the rotation, which by their motion kept the solid phase finely ground, a week was sufficient for the purpose.

The determinations involved the preparation, as described, of complexes of known composition, and analysis, at equilibrium, of both the liquid and the solid phases, the former after adequate filtration, the latter after centrifuging and air-drying; all the double salts of the systems studied are stable, as hexahydrates, exposed to ordinary air, so that this latter procedure involved no error except for the crystallization of salts from traces of residual mother liquor. In addition the algebraic extrapolation[4] of the tie-lines through the total compositions (complexes) and the compositions of the liquid solutions, was used as a check on the consistency and accuracy of the work, by comparing the extrapolated composition of the solid phase with the observed.

(4) Hill and Ricci, THIS JOURNAL, **53**, 4306 (1931).

System I. Magnesium Ammonium Sulfate–Copper Ammonium Sulfate–Water, at 25°.—Both of the double salts forming the solid components of this system are congruently soluble at room temperature. While the magnesium salt is known to remain so up to the boiling point,[5] the copper salt has not been studied at temperatures above 61°[6,7]; nevertheless it can be prepared successfully by crystallization from boiling solution of the simple sulfates of copper and ammonium, followed by prolonged cooling and stirring.[3] This method was used for both the magnesium ammonium and the copper ammonium double sulfates for the present investigation. Their composition, checked by analyses both for the metal and for the ammonium radical, was found to agree with the theoretical formulas within experimental error. The ammonium was determined by distillation into standard acid and subsequent titration, with an accuracy of 1/500. The liquids and solids of the ternary system were analyzed by determination of magnesium and of copper. Magnesium was determined following the procedure given by Kolthoff and Furman,[8] by precipitation as ortho-hydroxyquinolate and titration of the precipitated quinolate with standard potassium bromate (Berg's method[9]), the end-point being fixed by spot-tests with potassium iodide–starch paper. In the presence of copper the magnesium was precipitated after addition of excess of potassium cyanide, which avoided the necessity of previous removal of the copper. This determination likewise had an accuracy of 1/500. Copper was determined electrolytically, the analysis being exact to 1/1000.

The solubilities of the two double salts of this system, here reported, were determined with very close agreement, from both under- and super-saturation, and are based on analysis for both of the positive radicals of each salt; the values found, 16.61% for the magnesium salt and 18.60% for the copper salt, are in close agreement with recent determinations appearing in the literature.[10,11]

The results for the ternary system are given in Table I, which includes the data for the remaining systems discussed below; the table is self-explanatory. The solubilities of the pure double salts have been omitted from this table and are collected, together with density measurements, in a subsequent table (II). The usual triangular diagrams for the graphical representation of the equilibria in the ternary systems are not shown; their appearance and the general disposition of the tie-lines involved are very similar to the diagrams for the related picromerite systems reported by Hill and Taylor.[3] The composition of the solid phase was checked by algebraic extrapolation of tie-lines passing through the compositions of original complex and of liquid solution, to the straight line joining the compositions of the two picro-

(5) Benrath and Thiemann, *Z. anorg. Chem.*, **208**, 179 (1932).

(6) Schreinemakers, *Z. physik. Chem.*, **66**, 687 (1909).

(7) Caven and Mitchell, *J. Chem. Soc.*, **125**, 1428 (1924).

(8) Kolthoff and Furman, "Volumetric Analysis," Vol. II, John Wiley and Sons, Inc., New York, N. Y., 1929, p. 483.

(9) Berg, *Z. anal. Chem.*, **71**, 23 (1927).

(10) For $Mg(NH_4)_2(SO_4)_2 \cdot 6H_2O$: (a) Benrath and Thiemann, ref. 5 above, report 15.9%; (b) Porlezza, *Atti accad. Lincei*, [2] **23**, 596 (1914): 16.5%; (c) Locke, *Am. Chem. J.*, **27**, 455 (1902): 16.6%.

(11) For $Cu(NH_4)_2(SO_4)_2 \cdot 6H_2O$: (a) Hill and Taylor, ref. 3, above; (b) Caven and Mitchell, ref. 7, above.

merites, on which all the solid solutions should lie; the average absolute deviation, in per cent. of $Mg(NH_4)_2(SO_4)_2$, between the observed and the extrapolated compositions,

TABLE I

TERNARY SYSTEMS OF PICROMERITES WITH WATER AT 25°, IN WEIGHT PER CENT.

No.	Original complex % A[a]	Original complex % B[b]	Liquid phase % A	Liquid phase % B	Solid phase % A	Solid phase % B
I. Magnesium Ammonium Sulfate (A)–Copper Ammonium Sulfate (B)–Water						
1 A	15.68	4.00	13.69	3.46	55.80	14.85
B	15.68	4.00	13.76	3.46	55.84	14.90
2 A	14.55	9.00	11.20	6.42	42.67	28.49
B	14.55	9.00	11.08	6.51	42.41	28.84
3 A	13.40	14.00	9.15	8.66	33.17	38.52
B	13.40	14.00	9.17	8.64	33.14	38.54
4 A	7.00	16.74	5.77	12.43	18.28	53.91
B	7.00	16.74	5.74	12.44	18.29	53.97
5 A	2.75	17.87	2.65	15.87	6.99	65.23
B	2.75	17.87	2.61	15.88	6.63	65.27
II. Copper Potassium Sulfate (A)–Nickel Potassium Sulfate (B)–Water						
1 A	12.50	1.50	9.25	0.72	61.77	13.86
B	12.50	1.50	9.26	.69	61.76	13.85
2 A	11.00	4.00	7.84	1.505	44.92	30.50
B	11.00	4.00	7.84	1.508	44.89	30.52
3 A	9.00	6.00	6.56	2.221	33.16	42.23
B	9.00	6.00	6.55	2.218	33.06	42.30
4 A	6.50	7.50	5.07	3.084	22.23	53.24
B	6.50	7.50	5.06	3.080	22.25	53.15
5 A	3.50	8.50	2.980	4.33	10.75	64.52
B	3.50	8.50	2.981	4.34	10.86	64.46
III. Cobalt Potassium Sulfate (A)–Copper Potassium Sulfate (B)–Water						
1 A	15.00	2.00	11.74	1.312	63.17	12.19
B	15.00	2.00	11.71	1.323	63.08	12.07
2 A	13.00	5.00	9.72	2.961	48.30	27.09
B	13.00	5.00	9.71	2.965	48.61	26.83
3 A	10.50	8.50	7.63	4.60	34.40	41.08
B	10.50	8.50	7.60	4.61	34.40	40.92
4 A	7.00	11.00	5.39	6.28	21.79	53.67
B	7.00	11.00	5.37	6.30	21.90	53.62
5 A	3.50	13.00	2.918	8.20	10.04	65.45
B	3.50	13.00	2.915	8.21	10.10	65.50
IV. Zinc Potassium Sulfate (A)–Copper Potassium Sulfate (B)–Water						
1 A	15.00	2.00	10.36	1.305	66.11	9.61
B	15.00	2.00	10.38	1.302	66.23	9.60
2 A	13.00	5.00	8.54	3.012	52.96	22.66
B	13.00	5.00	8.52	3.008	52.78	22.70
3 A	10.50	8.50	6.63	4.74	39.20	36.30
B	10.50	8.50	6.65	4.74	39.24	36.29
4 A	7.00	11.00	4.74	6.41	26.16	49.43
B	7.00	11.00	4.73	6.43	26.00	49.45
5 A	3.50	13.00	2.617	8.22	12.72	62.79
B	3.50	13.00	2.616	8.22	12.64	62.83
V. Zinc Potassium Sulfate (A)–Nickel Potassium Sulfate (B)–Water						
1 A	15.50	1.50	10.64	0.457	63.81	11.75
B	15.50	1.50	10.64	.454	63.85	11.68
2 A	13.50	3.50	9.35	1.026	50.21	25.33
B	13.50	3.50	9.36	1.036	50.23	25.31
3 A	11.00	5.50	7.91	1.697	37.90	37.54
B	11.00	5.50	7.91	1.692	37.68	37.75
4 A	8.00	8.00	6.01	2.657	24.46	51.04
B	8.00	8.00	6.01	2.662	24.52	50.90
5 A	5.00	10.00	3.99	3.78	13.64	61.66
B	5.00	10.00	....	..	13.62	61.70
VI. Copper Ammonium Sulfate (A)–Copper Potassium Sulfate (B)–Water						
1 A	17.86	3.00	15.44	2.03	56.92	16.46
B	17.86	3.00	...	..	57.11	16.24
2 A	17.12	6.00	13.47	3.30	47.03	26.82
B	17.12	6.00	13.50	3.25	46.81	26.98
3 A	12.00	8.65	10.04	5.45	31.68	42.80
B	12.00	8.65	...	..	31.55	42.76
4 A	8.00	9.22	7.35	6.85	20.40	54.51
B	8.00	9.22	7.35	6.89	20.79	54.10
5 A	4.00	9.78	3.90	8.55	8.99	66.13
A	4.00	9.78	3.91	8.52	..	...
B	4.00	9.78	3.87	8.58	9.03	66.11
B	4.00	9.78	3.89	8.55	..	...

[a] A: Initial solid phase: Salt A. [b] B: Initial solid phase: Salt B.

was only 0.30%. In connection with the magnitude of this deviation, it is to be noted that since the composition of the complex is usually quite near that of the resulting liquid solution, any analytical error in the composition of either will be multiplied by a factor of from ten to twenty in the extrapolation.

System II. Copper Potassium Sulfate–Nickel Potassium Sulfate–Water, at 25°.—The nickel potassium sulfate, being congruently soluble up to the boiling point,[12] was prepared in the manner described for the salts of System I. The copper potassium double sulfate was prepared from solutions of the simple sulfates at temperatures not above 55°, to avoid precipitation of basic salt.[7,13] The purity of the double salts was checked by analysis for copper and nickel, respectively. The analytical method for this ternary system involved the consecutive electrolytic determination of these metals, the nickel after deposition and removal of the copper. The analysis is judged to be accurate to 1/1000. The solubility of the copper potassium double sulfate, 10.35% from both under- and super-saturation, is in fair agreement with published results: 10.47 (Locke[10c]), 10.46 (Caven and Mitchell[7]), and 10.02 (Trevor[14]). That of the nickel potassium double salt, 6.33%, also both from under- and from super-saturation, may be compared with Locke's value, 6.43%.[10c]

Again complete miscibility is observed between the two solid picromerites at this temperature. The average

(12) Benrath, *Z. anorg. Chem.*, **208**, 169 (1932).

(13) Mellor, "Treatise on Inorganic and Theoretical Chemistry," Vol. III, Longmans, Green and Co., London, 1923, p. 259.

(14) Trevor, *Z. physik. Chem.*, **7**, 468 (1891).

absolute deviation, in per cent. $CuK_2(SO_4)_2$, between the observed and the extrapolated compositions of the solid phase, was 0.49% for this system.

System III. Cobalt Potassium Sulfate–Copper Potassium Sulfate–Water, at 25°.—These salts were already known to form a complete series of solid solutions, the system having been studied at 0 and 7.8°, by Ploin.[15] The 25° isotherm was determined for the purpose of comparison with the other related systems. The cobalt potassium double sulfate, becoming incongruently soluble at 78° and ceasing to exist at 90°,[12] was prepared at temperatures not higher than 75°. Its purity was checked by determination of cobalt. The analytical method for the ternary system, involving the consecutive electrolytic determination of copper and cobalt, was accurate to 1/1000. The solubility here reported for the cobalt potassium double sulfate, 13.65% from both under- and supersaturation, differs widely from the older literature values, namely, 11.41% reported by Locke[10c] and 15.60% by Benrath.[12] The great difference is probably due to the difficulty of establishing true equilibrium between the various isomeric forms of hydrated cobaltic salts both in solution and in the crystalline state. The agreement between the two approaches to equilibrium both for the solubility of the cobalt potassium double sulfate itself and for the ternary complexes, does not, even in the present work, constitute absolute proof of the establishment of all the possible equilibria involved.

The average absolute deviation between extrapolated and observed percentage of $CoK_2(SO_4)_2$ in the solid phase, is very small (0.08%), indicating the high precision and the consistency, at any rate, of the various analytical steps involved.

System IV. Zinc Potassium Sulfate–Copper Potassium Sulfate–Water, at 25°.—This system also has been studied by Ploin, at 8°, showing similarly, at that temperature, complete miscibility of the two double salts.[15] The zinc potassium double sulfate was prepared at 85°, as it becomes incongruently soluble at 88° and above.[16] The purity of the salt so prepared was verified by analysis for zinc. The analytical procedure for the ternary system involved again the consecutive electrolytic deposition of copper followed by the deposition of the more active metal, in this case, zinc; the analysis was accurate to 1/1000. The solubility of the zinc potassium double sulfate, found to be 11.72% from both under- and super-saturation, was determined by direct evaporation to the anhydrous sulfates, a very accurate procedure. The result is in fair agreement with the value reported by Locke, 11.65%.[10c]

The analytical precision can be judged by the small average absolute deviation (0.08%) between extrapolated and observed compositions (as % $ZnK_2(SO_4)_2$) for the solid phase.

System V. Zinc Potassium Sulfate–Nickel Potassium Sulfate–Water, at 25°.—In this system the percentage of total solids was determined by evaporation, nickel was determined gravimetrically by precipitation with dimethylglyoxime, with an accuracy of 1/1000, and the zinc salt was then calculated by difference.

The average absolute deviation, in respect to per cent. of $ZnK_2(SO_4)_2$, between the extrapolated and observed compositions of the solid phase, was only 0.17%.

System VI. Copper Ammonium Sulfate–Copper Potassium Sulfate–Water, at 25°.—This system differs from the preceding five combinations in that here the univalent rather than the divalent cation of the picromerite is being varied. For the analysis the total copper was determined by electrolysis. The copper ammonium double salt was determined by distillation of ammonia, with an accuracy of 1/500, and the copper potassium double salt was then calculated by difference.

The deviation in this system between extrapolated and observed per cent. $Cu(NH_4)_2(SO_4)_2$ for the solid phase was 0.68%.

To permit the calculation of the molar solubilities of the various double salts involved, the densities of their pure saturated solutions at 25° were determined together with their weight per cent. solubility. These densities were determined with only moderate accuracy, by means of calibrated pipets fitted with proper filter paper to separate the liquid phase from excess of solid.

TABLE II

SOLUBILITIES OF SOME PICROMERITES AT 25°

Salt	Solubility, wt. % anhydrous salt	Density of saturated solution	Molar solubility
$Mg(NH_4)_2(SO_4)_2 \cdot 6H_2O$	16.61	1.090	0.7176
$Cu(NH_4)_2(SO_4)_2 \cdot 6H_2O$	18.60	1.160	.7399
$CuK_2(SO_4)_2 \cdot 6H_2O$	10.35	1.094	.3392
$NiK_2(SO_4)_2 \cdot 6H_2O$	6.33	1.056	.2032
$CoK_2(SO_4)_2 \cdot 6H_2O$	13.65	1.128	.4679
$ZnK_2(SO_4)_2 \cdot 6H_2O$	11.72	1.109	.3873
$Zn(NH_4)_2(SO_4)_2 \cdot 6H_2O$	12.24[3]	1.103	.4601
$Ni(NH_4)_2(SO_4)_2 \cdot 6H_2O$	7.09[3]	1.057	.2614

Distribution between Liquid Solution and Solid Solution.—The distribution of the picromerites here studied, between the equilibrium liquid and solid phases, may be considered from the point of view of Roozeboom's[17] classification of such binary solid solutions occurring in ternary systems of water and two salts. In order to interpret the above data in terms of this classification the concentrations have been recalculated into mole fractions of the two picromerites, disregarding water, in the two phases. The results, giving for each system the mole fraction of the more soluble picromerite (more soluble in molar units), are shown in Table III, and are plotted in Figs. 1 and 2, in which the curves I–VI represent, respectively, the six combinations studied; in the table and figures, the Y values represent the mole fraction of the more soluble picromerite in the liquid phase and X its mole fraction in the solid phase.

(15) Ploin, *Roczniki Chem.*, **6**, 690 (1926); *cf. C. A.*, **21**, 3503 (1927).

(16) Benrath and Cremers, *Z. anorg. Chem.*, **189**, 88 (1930).

(17) Roozeboom, *Z. physik. Chem.*, **8**, 521 (1891); **30**, 385 (1899).

TABLE III

DISTRIBUTION OF PICROMERITES BETWEEN LIQUID AND SOLID PHASES

System	Mole fraction of salt A: Y, in dissolved salts	X, in solid solution
I. A: $Mg(NH_4)_2(SO_4)_2$	0.000	0.000
B: $Cu(NH_4)_2(SO_4)_2$	.161	.108
	.349	.282
	.550	.499
	.666	.632
	.821	.813
	1.000	1.000
II. A: $CuK_2(SO_4)_2$	0.404	0.142
B: $NiK_2(SO_4)_2$	.619	.292
	.744	.436
	.837	.592
	.928	.815
III. A: $CoK_2(SO_4)_2$	.265	.136
B: $CuK_2(SO_4)_2$	.464	.292
	.628	.460
	.769	.646
	.900	.841
IV. A: $ZnK_2(SO_4)_2$	.241	.167
B: $CuK_2(SO_4)_2$	.423	.344
	.582	.518
	.738	.699
	.888	.873
V. A: $ZnK_2(SO_4)_2$	.508	.178
B: $NiK_2(SO_4)_2$	.689	.320
	.821	.496
	.899	.660
	.958	.842
VI. A: $Cu(NH_4)_2(SO_4)_2$	.342	.135
B: $CuK_2(SO_4)_2$	.550	.303
	.678	.458
	.825	.666
	.897	.800

From the tabulation and the two figures, as also from a consideration of the disposition of the tie-lines in the triangular isothermal diagrams for the systems (not shown), it appears that these systems would all fall into Type I of Roozeboom's classification, systems in which there is complete miscibility between the two solid components and in which the proportion of one of these components is higher in the liquid than in the corresponding solid phase throughout the whole series of concentrations. We again note, as has been reported in connection with recent similar studies on a series of alum systems,[2] that the component present in greater concentration in the liquid than in the solid has the higher aqueous molar solubility. It must be observed of course at this point that the data are not sufficient to rule out the possibility that the curves of Figs. 1 and

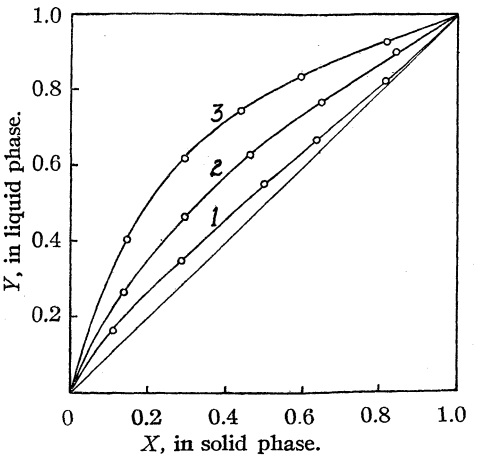


Fig. 1.—Distribution of picromerites between aqueous solution and solid solution at 25°: (1) $Mg(NH_4)_2(SO_4)_2$ in $Mg(NH_4)_2(SO_4)_2$–$Cu(NH_4)_2(SO_4)_2$; (2) $CuK_2(SO_4)_2$ in $CuK_2(SO_4)_2$–$NiK_2(SO_4)_2$; (3) $CoK_2(SO_4)_2$ in $CoK_2(SO_4)_2$–$CuK_2(SO_4)_2$.

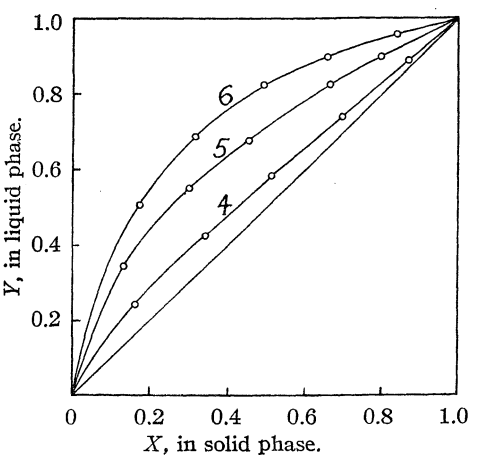


Fig. 2.—Distribution of picromerites between aqueous solution and solid solution at 25°: (4) $ZnK_2(SO_4)_2$ in $ZnK_2(SO_4)_2$–$CuK_2(SO_4)_2$; (5) $ZnK_2(SO_4)_2$ in $ZnK_2(SO_4)_2$–$NiK_2(SO_4)_2$; (6) $Cu(NH_4)_2(SO_4)_2$ in $Cu(NH_4)_2(SO_4)_2$–$CuK_2(SO_4)_2$.

2 may cross the diagonal near the extremities of the diagrams; in the case of the picromerites here reported, it appears, on the basis of further theoretical considerations not yet published, that this may actually be the case, and that these systems consequently would then fall into Type II of Roozeboom's classification, in which, starting from zero concentration of one component, the proportion of that component in the liquid phase (Y) is greater than its proportion in the solid phase (X) up to a certain point, then becoming smaller than X up to a mole fraction of one for the component. In continuation of the suggestion made in a previous article of this series, in

which the empirical equation $X = Y^m$ was advanced, these measurements, together with similar studies from this Laboratory, will be considered, in a subsequent publication, for the purpose of deriving some generalization relating the distribution ratio of these isomorphous salts between liquid and solid phases, to the molar solubilities of the individual salts in the pure solvent.

Summary

1. The following ternary systems have been studied at 25°

$Mg(NH_4)_2(SO_4)_2$–$Cu(NH_4)_2(SO_4)_2$–H_2O
$CuK_2(SO_4)_2$–$NiK_2(SO_4)_2$–H_2O
$CoK_2(SO_4)_2$–$CuK_2(SO_4)_2$–H_2O
$ZnK_2(SO_4)_2$–$CuK_2(SO_4)_2$–H_2O
$ZnK_2(SO_4)_2$–$NiK_2(SO_4)_2$–H_2O
$Cu(NH_4)_2(SO_4)_2$–$CuK_2(SO_4)_2$–H_2O

2. Continuous series of solid solutions were found in each case.

3. The results, considered from the point of view of Roozeboom's classifications of solid solutions, show all these systems to belong apparently to Type I of that classification.

NEW YORK, N. Y. RECEIVED FEBRUARY 9, 1940

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF WASHINGTON]

Freezing Point and Solubility Data for the System Chlorine Monoxide–Water

BY C. H. SECOY AND G. H. CADY

It is known that chlorine monoxide dissolves in water to give hypochlorous acid but no previous study has been made of the possible existence of hydrates of this acid nor have highly concentrated solutions of the acid been prepared and studied. In this work freezing point and solubility data have been obtained for the system chlorine monoxide–water. The only pertinent data found in the literature were the freezing point of pure chlorine monoxide, reported by Goodeve[1] to be −116°, and the freezing points of very dilute solutions of hypochlorous acid.[2]

Experimental

Preparation of Chlorine Monoxide and Hypochlorous Acid.—Chlorine monoxide was prepared by passing a stream of dry chlorine mixed with air up through a column of yellow mercuric oxide.[3] A 35-mm. glass tube, one meter long, was filled with mercuric oxide with a sufficient quantity of porcelain chips added to prevent packing. The top of this tube was sealed to 8-mm. glass tubing leading to a 24 mm. × 30 cm. test-tube fitted with a stirrer and a thermocouple well. Other workers[3] have stated that the mercuric oxide previously should be heated to 400°, for a period of an hour or longer. This treatment, however, was not used since it has been found that it is neither necessary nor helpful.[4] The spent mercuric oxide was recovered by precipitation in the cold with sodium hydroxide, washed free of sodium hydroxide, and dried at 120°.[4] The air and chlorine were dried by bubbling through sulfuric acid and passed through a T-tube into the mercuric oxide. The rate of flow of the air was about twice that of the chlorine. The air prevented any noticeable heating effect from the reaction.

The chlorine monoxide was condensed by means of a dry-ice–alcohol cooling mixture, and hypochlorous acid of the desired concentration was then obtained by adding the required amount of water and stirring until equilibrium had been reached. Chlorine monoxide and strong hypochlorous acid were found to be stable over a period of a week if kept at a temperature below −20°. However, some free chlorine invariably was formed if the solution was allowed to stand for a few hours at a higher temperature.

Temperature Measurements.—Freezing point data were obtained by thermal analysis. Temperatures were measured by a copper–constantan thermocouple calibrated at the ice-point, the dry-ice point, and the boiling point of oxygen. The conversion table reported by Giauque, Buffington, and Schulze[5] was used after applying a constant factor, characteristic of the thermocouple used, to the e. m. f. readings. The use of this factor allowed points at the calibration temperatures to fall within 0.02° of Giauque's curve. The e. m. f. was measured with a Leeds and Northrup Type K potentiometer using a voltage-sensitive galvanometer. Readings were made to the nearest tenth of a microvolt and temperatures obtained were believed to be accurate to 0.1°. The warm junction of the thermocouple was kept at the temperature of melting ice.

Method of Analysis.—The method reported by Spinks[6] was used to determine both free chlorine and available chlorine in the form of chlorine monoxide and/or hypochlorous acid. The sample, from 0.2 to 0.5 g., was transferred by means of a pipet to a weighed flask containing a

(1) Goodeve, *J. Chem. Soc.*, 2733 (1930).

(2) Jakowkin, *Z. physik. Chem.*, **29**, 613 (1899).

(3) "Gmelins Handbuch der anorganischen Chemie," 8th Ed., Vol. 6, "Chlor," Verlag Chemie, Berlin (1927), p. 228; Balard, *Ann. chim. phys.*, [2] **57**, 225 (1834); *Taylors Scientific Memoirs*, **1**, 269 (1837); Pelouze, *Ann. chim. phys.*, [3] **7**, 176 (1843).

(4) Muskat and Cady, U. S. Patent 2,155,281 (1939).

(5) Giauque, Buffington and Schulze, THIS JOURNAL, **49**, 2343 (1927).

(6) Spinks, *ibid.*, **53**, 3015 (1931).

solution of potassium iodide. The flask was then reweighed to determine the weight of the sample. The determination of the free chlorine served as a check on the possible decomposition of the hypochlorous acid, and no data were used from any sample which showed chlorine to be present.

The composition of the dihydrate, $HOCl \cdot 2H_2O$, was established by direct analysis of the crystals formed by partially freezing solutions of concentrations just above and just below 16.6 mole % chlorine monoxide. Both phases were analyzed after being separated quickly by filtration in a small centrifuge. The filter consisted of a piece of glass cloth fused to the end of a tube drawn and cut to just fit in a small test-tube which could be used in the centrifuge. After previously cooling the filter tube with dry-ice, the partly frozen slush was added to it and centrifuged for ten or fifteen seconds. The dry crystals were then transferred to a flask containing a solution of potassium iodide, weighed, and titrated. The data obtained are summarized in Tables I and II.

TABLE I

FREEZING POINTS OF WATER SOLUTIONS OF Cl_2O

Mole % Cl_2O	F., °K.	Solid phase
2.7	267.2	Ice
3.9	264.4	Ice
5.9	259.4	Ice
7.9	253.5	Ice
8.4	251.0	Ice
10.0	245.1	Ice
10.6	242.5	Ice
11.7	233.5	Eutectic
11.9	234.2	$HOCl \cdot 2H_2O$
12.0	234.5	$HOCl \cdot 2H_2O$
12.5	235.3	$HOCl \cdot 2H_2O$
13.1	235.8	$HOCl \cdot 2H_2O$
13.7	236.3	$HOCl \cdot 2H_2O$
14.4	236.6	$HOCl \cdot 2H_2O$
15.1	236.8	$HOCl \cdot 2H_2O$
15.4	236.9	$HOCl \cdot 2H_2O$
16.1	237.0	$HOCl \cdot 2H_2O$
16.6	237.1	$HOCl \cdot 2H_2O$
17.5	237.1	$HOCl \cdot 2H_2O$
18.7	237.0	$HOCl \cdot 2H_2O$
19.5	236.9	$HOCl \cdot 2H_2O$
20.7	236.8	$HOCl \cdot 2H_2O$

TABLE II

IDENTIFICATION OF THE SOLID COMPOUND

Mole % Cl_2O	
Liquid	Solid
14.6	16.3
16.4	16.8
16.9	16.7
17.3	16.3
18.0	16.5

Solubility of Chlorine Monoxide in Water.—The two liquid phases were held at the temperature desired and stirred until equilibrium was established. After allowing any suspended oily drops of chlorine monoxide to settle from the water layer, a sample of the latter was taken for analysis. Measurements were not attempted at temperatures above 264°K., because of the high vapor pressure and the tendency for decomposition to occur at higher temperatures. Results are tabulated in Table III.

TABLE III

SOLUBILITY OF Cl_2O IN H_2O

Temp., °K.	Mole % Cl_2O	Temp., °K.	Mole % Cl_2O
263.8	22.9	244.2	20.3
259.9	22.1	241.2	20.4
257.3	21.7	240.0	20.5
251.1	20.6	238.4	20.6
247.4	20.1	236.8	20.7
246.4	20.0		

Solubility of Water in Chlorine Monoxide.—A 100-cc. flask containing phosphorus pentoxide was fitted with a glass cap, designated cap A, which slid down over the neck of the flask. The cap was made tight by fitting a short piece of rubber tubing over the neck of the flask and the cap. A second similar cap, designated cap B, was connected by a side arm to a potassium iodide absorption train. A glass tube extended through the top of cap B to the surface of the phosphorus pentoxide when the flask was in place. Saturation of the chlorine monoxide was obtained by adding sufficient water to form the double layer and stirring at constant temperature until equilibrium was reached. The samples were taken by means of a dipper constructed by blowing a small bulb in the end of a piece of 6 mm. glass tubing. A side opening was then blown just above the bulb and about 2 cm. from the end of the tube. In order to remove a sample not contaminated with the water layer, a piece of 10 mm. tubing was inserted into the solution, the water layer forced outside of this tube with compressed air, and the dipper used inside the tube.

After being weighed, with cap A in place, the flask was cooled with dry-ice and a sample of the chlorine monoxide saturated with water at the desired temperature was added. The flask was then attached to the absorption train by means of cap B, and, as the temperature rose, a slow current of air dried by phosphorus pentoxide was drawn through the system until all of the chlorine monoxide had evaporated. Cap A was then replaced and the flask weighed, the increase in weight giving the weight of water in the sample. The amount of chlorine monoxide in the sample was determined by titrating the liberated iodine. Results are given in Table IV.

TABLE IV

SOLUBILITY OF H_2O IN Cl_2O

Temp., °K.	Mole % H_2O
270.0	3.4
236.8	2.9
194.6	1.8

The Freezing Point of Pure Chlorine Monoxide.—Cooling curves taken with a freshly prepared sample of chlorine monoxide, dried by passing the gas over phosphorus pentoxide, gave a freezing point of −120.6°. After adding water to the chlorine monoxide and stirring to secure saturation, the freezing point was found to be

−121.0°. Phosphorus pentoxide was then added directly to the liquid and again a freezing point of −120.6° was observed.

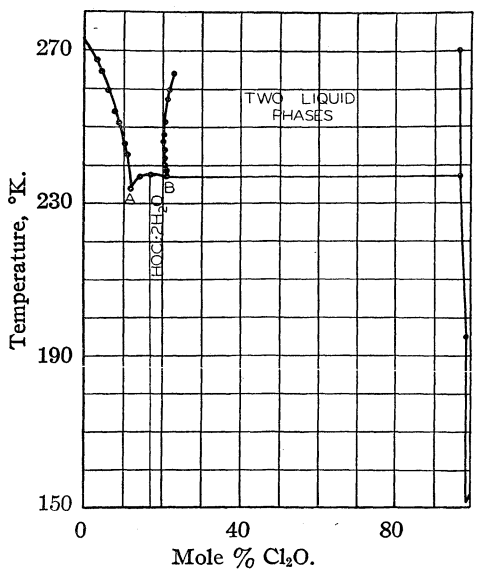


Fig. 1.—Temperature–concentration diagram for the system chlorine monoxide–water. Several experimentally determined points between A and B have been omitted on the graph (see Table I for data).

Due to the discrepancy between this result and the value of −116°, reported by Goodeve,[1] the thermocouple was recalibrated at the boiling point of oxygen. A fresh sample of chlorine monoxide, dried as before, was prepared. In order to free the chlorine monoxide from dissolved air and chlorine, approximately one-fourth of the sample was distilled off at about −75°. The freezing point then observed was −120.6°. After removing a second portion of the chlorine monoxide in the same manner, the same freezing point was obtained. Addition of water gave the same depression of 0.4°, as previously found.

The temperature–concentration diagram for the system is shown in Fig. 1. Point B, at 20.7 mole % chlorine monoxide and 236.8°K., is an invariant point representing equilibrium between two liquid phases, the solid phase and the gaseous phase. It is to be noted that solid HOCl is not obtained. A solution containing a sufficiently high concentration of chlorine monoxide to give the compound HOCl would separate into two liquid phases before freezing and give, as the solid phase, the hydrate, $HOCl \cdot 2H_2O$.

Summary

The freezing point–composition diagram for the system chlorine monoxide–water has been studied over the entire range, and solubilities of chlorine monoxide in water and of water in chlorine monoxide have been measured. Chlorine monoxide and water are a pair of partially miscible liquids. The solid phase formed from solutions of concentration greater than 11.7 mole % chlorine monoxide has the composition $HOCl \cdot 2H_2O$.

SEATTLE, WASHINGTON RECEIVED FEBRUARY 20, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

Photochemical Studies. XXX. The Fluorescence of Biacetyl. Some General Considerations Governing the Study of Fluorescence

BY F. C. HENRIQUES, JR., AND W. ALBERT NOYES, JR.

Recent studies of the fluorescence of acetone have shown that under some conditions a Stern-Volmer equation is at least approximately obeyed[1] but that if the intensity of the incident radiation is sufficiently high, noticeable increase of fluorescence with time is observed.[2] Moreover, the three intense bands of acetone fluorescence were shown to be identical with those of biacetyl. It also has been shown that the main portions of the fluorescences of acetaldehyde and of methyl ethyl ketone are identical with those of biacetyl and of acetone.[3] It seems probable, therefore, that the fluorescing molecule is the same in all of these cases and that it is probably biacetyl.

Several questions still remain unanswered concerning the so-called fluorescence of acetone, particularly those having to do with the mechanism whereby the biacetyl molecule is excited when acetone is the absorber. It has seemed advisable, therefore, to investigate the effect of certain variables on the fluorescence of biacetyl. The fluorescence of this molecule has been investigated

(1) Fisk and Noyes, *J. Chem. Phys.*, **2**, 654 (1934).

(2) Matheson and Noyes, THIS JOURNAL, **60**, 1857 (1938).

(3) Matheson and Zabor, *J. Chem. Phys.*, **7**, 536 (1939).

from several angles by Almy and his co-workers.[4,5,6,7] Their conclusions may be summarized briefly as follows: (a) the spectrum of the fluorescence is independent of the exciting wave length (3650, 4047, 4358 Å.); (b) little or no quenching by biacetyl is observed when the exciting wave length is 4358 Å., *i. e.*, as the pressure is increased, the intensity of the fluorescence is proportional to the absorbed intensity; (c) the fluorescence is quenched by oxygen and (strongly) by iodine; (d) the mean lifetime of the excited biacetyl molecules as determined by various methods is quite long, probably longer than 10^{-5} second; and (e) the quantum yield of fluorescence is quite low, being a maximum of about 0.03 fluorescence quantum per absorbed quantum at 3650 and 4358 Å.

In the present investigation a study of the effects of pressure, of temperature, of wave length, of intensity, and of added acetone on the fluorescence has been made. From this study certain seemingly valid conclusions can be drawn concerning the fate of the excited biacetyl molecules and the nature of upper electronic levels.

I. Some General Considerations Governing Fluorescence Studies

In a recent article[8] several aspects of problems relating to fluorescence have been treated. It was emphasized that with increase in pressure of the absorbing gas, there is a volume redistribution of absorbed intensity which may lead to spurious results unless the absorption coefficient is very low. That is, the measuring device will intercept a fraction of the fluorescent quanta emitted from a certain volume within the cell. If this fraction varies as the distribution of absorbed intensity throughout this volume change, no valid conclusions can be drawn concerning quenching. This problem will be examined briefly.

Referring to Fig. 1 we will assume that the fluorescence is being studied with the aid of a T-shaped cell, that the x-axis is horizontal, the y-axis vertical, and the z-axis perpendicular to the plane of the paper. For the sake of simplification a parallel beam of radiation, the intensity of which is uniform throughout a cross section perpendicular to the x-axis, is assumed. The radius of this cross section is y_1. I_0' is defined as the incident intensity at the center of the cell. It will be noted that this definition differs from that used later for I_0.

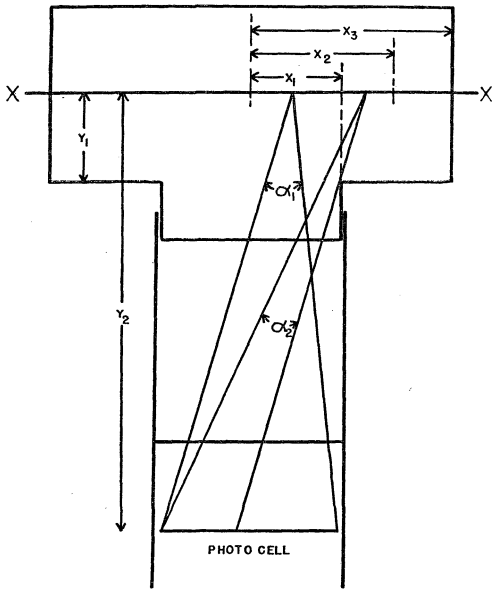


Fig. 1.

It is also evident that many complications are avoided if y_2, the distance from the axis of the main limb of the T to the light measuring device, is large compared to y_1, the radius of the tube making this limb. All radiation striking the walls is assumed to be absorbed.

Furthermore, the problem becomes very difficult to treat if the fluorescent intensity is not proportional to the absorbed intensity when all variables except the latter are kept constant. In the following paragraphs it is assumed that the intensity of the fluorescence from any volume element is proportional to the intensity absorbed when the pressure and the temperature are constant. The fluorescent radiation is assumed not to be absorbed by the gas, thus avoiding the serious complications due to radiation imprisonment.

It is obvious that the form of I_a, the intensity absorbed, must be

$$I_a = 2I_0' \frac{\int\int\int_0^{x_3} \Pi_{xyz}\, bP \cosh(bPx)\, dx\, dy\, dz}{\int\int\int_{-x_3}^{x_3} \Pi_{xyz} dx\, dy\, dz} \qquad (1)$$

where b is the absorption coefficient per unit distance along the x-axis and per unit pressure; P is the pressure. Π_{xyz} is the probability that

(4) Almy, Fuller and Kinzer, *Phys. Rev.*, **55**, 238 (1939).
(5) Almy and Fuller, *Trans. Illinois State Acad. Sci.*, **31**, 196 (1938).
(6) Fuller, Phillips and Almy, *J. Chem. Phys.*, **7**, 973 (1939).
(7) Almy, Fuller and Kinzer, *ibid.*, **8**, 37 (1940).
(8) Noyes and Henriques, *ibid.*, **7**, 767 (1939).

fluorescent light from the volume element $dx\,dy\,dz$ will reach the light measuring device.

With the assumptions made above

$$\Pi_{xyz} = \text{const. } \Pi_x \qquad (2)$$

and hence I_a may be treated to a good first approximation as a function of x alone.

For $0 \leqq x \leqq x_1$

$$\Pi_x = \alpha_1/2\pi \qquad (3)$$

where to a good approximation

$$\alpha_1 = (2x_1/y_2)\left(1 - \frac{x_1^2 + x^2}{y}\right) \qquad (4)$$

For $x_1 \leqq x \leqq x_2 = x_1(y_1 + y_2)/(y_2 - y_1)$

$$\Pi_x = \alpha_2/2\pi \qquad (5)$$

where to a first order approximation

$$\alpha_2 = \frac{x_1(y_1 + y_2) - (y_2 - y_1)x}{y_1y_2}(1 - 2x_1^2/y_2^2) \qquad (6)$$

For $x_2 \leqq x \leqq x_3$

$$\Pi_x = 0 \qquad (7)$$

By integrating equation (1) after making the proper substitutions for Π_x one obtains

$$I_a = \frac{I_0'}{2\pi\int_0^{x_3}\Pi_x dx}\left[\frac{4x_1}{y_2^3}\left(x_1^2 + \frac{1}{b^2P^2}\right)\sinh x_1bP + \frac{y_2 - y_1}{y_1y_2bP}\left(1 - \frac{2x_1^2}{y_2^2}\right)\cosh x_2bP - \left(1 + \frac{2x_1^2}{(y_2 - y_1)y_2}\right)\cosh x_1bP\right] \qquad (8)$$

Unless the absorption coefficient is extremely high, all but the first two terms in the expansion of the hyperbolic functions may be neglected. Upon integration of $\int_0^{x_3}\Pi_x dx$ and substituting, one obtains

$$I_a = I_0'bP \qquad (9)$$

Equation (9) should be valid if the assumptions made above are obeyed and if the fraction of the incident radiation absorbed between $-x_2$ and $+x_2$ is not over about 0.4. For other cases the use of equation (8) would be necessary.

II. Experimental

The biacetyl (Eastman Kodak Co.) was repeatedly fractionally distilled at low pressures. The acetone (Merck reagent) was dried with calcium chloride and distilled in the dark.

Monochromatic radiation of wave length 3650 Å. was obtained from a General Electric Vapor Lamp Co. high pressure mercury arc (Uviarc UA30A2) combined with Corning Violet Ultra Glass and a cupric ammonium sulfate filter. For 3130 Å. a silvered surface and a solution of nickel and cobalt sulfates were used. For 2537 Å. the same solutions plus a filter of gaseous chlorine were used.

A T-shaped cell of the type previously used[3] was thermostated by a water jacket so that the temperature could be kept constant to 0.5°. The fluorescent radiation was intercepted by a quartz cesium–cesium oxide photocell with plane window, the current from which was amplified by a modified Barth[9] circuit, using an FP54 tube, the batteries being continuously charged with a trickle-charger. The radiation transmitted by the cell was intercepted by a potassium hydride cell with glass envelope, the current being read directly with a sensitive galvanometer.

The pressures were measured either directly on a manometer or by means of a McLeod gage of low sensitivity. When both biacetyl and acetone were used together, they were admitted to a large mixing chamber and condensed with liquid air. After vaporization sufficient time was allowed for complete mixing, and then a portion of the mixture was expanded into the cell.

In all instances the fluorescent radiation was partially limited to certain spectral regions by the use either of a Wratten 8 or a Wratten 25 filter. The fluorescence of biacetyl consists of three bands[2,5] with maxima at 5120, 5580 and 6100 Å. These filters transmit the following percentages of incident radiation at these wave lengths, respectively: Wratten 8, 73, 86, and 89%; Wratten 25, 0, 0, and 75%. Thus the use of the Wratten 25 filter permits a study of the 6100 Å. band alone. The Wratten 8 filter served mainly to eliminate scattered light.

III. Results

No visible fluorescence could be excited in pure biacetyl by the mercury lines at either 3130 or 2537 Å.

It does not seem useful to give all of the numerical data in detail. The absorption coefficient for biacetyl, using the 3650 Å. radiation obtained as described above, was first determined. Beer's law was found to be obeyed within experimental error. At 29° the transmitted light is given by the expression

$$I_{\text{trans.}} = I_0 \exp.\ (-0.00040dP) \qquad (10)$$

where d is the thickness in centimeters and P is the pressure in millimeters. I_0 is the intensity when the biacetyl is condensed with liquid air. Almy and his co-workers give a coefficient of 0.00042 without specifying the temperature.[4] At other temperatures (from 15 to 60°), the same law seems to be obeyed quite closely providing the change in density with temperature is taken into account. Thus if the pressure is expressed in millimeters, the coefficient may be written as $0.121/T$ where T is the absolute temperature.

Table I presents examples of data obtained at 29° through a Wratten 8 filter. For the first ten points the incident intensity was practically constant and the biacetyl pressure varied. The last

(9) Penick, *Rev. Sci. Instruments*, **6**, 115 (1935).

TABLE I

FLUORESCENCE OF BIACETYL AT 29° (λ = 3650 Å.)

Pressure mm.	Transmitted intensity (arbitrary units) I_t	Intensity fluorescence + scattered light (arbitrary units) $I_f + I_s$	Fluorescent intensity (arbitrary units) I_f	Absorbed intensity (arbitrary units) I_a	$I_f/I_a \times 2.35 \times 10^{-3}$
0	49.2	1.0	0	0	....
52.0	43.2	55.9	54.9	4.49	0.0287
41.5	43.2	43.9	43.0	3.55	.0286
33.2	44.2	32.7	31.7	2.88	.0258
23.5	44.8	20.8	19.9	2.05	.0228
13.0	44.9	8.4	7.5	1.12	.0157
17.5	44.1	13.2	12.3	1.49	.0183
28.7	43.1	26.8	25.9	2.41	.0252
39.5	42.0	39.5	38.6	3.28	.0277
48.0	41.7	49.0	48.1	3.98	.0283
48.0	33.1	39.4	38.7	3.16	.0287
48.0	21.5	25.7	25.2	2.05	.0288
48.0	14.9	17.5	17.2	1.42	.0284
48.0	6.0	7.0	6.9	0.573	.0283

five points were obtained at constant pressure but with variable I_0.

The figures in the last column are based on the quantum efficiency for fluorescence of 0.029 obtained at relatively high pressures by Almy and his co-workers.[6] The factor 2.35 × 10^{-3} is empirically chosen to make the quantum efficiency have a maximum value of 0.029.

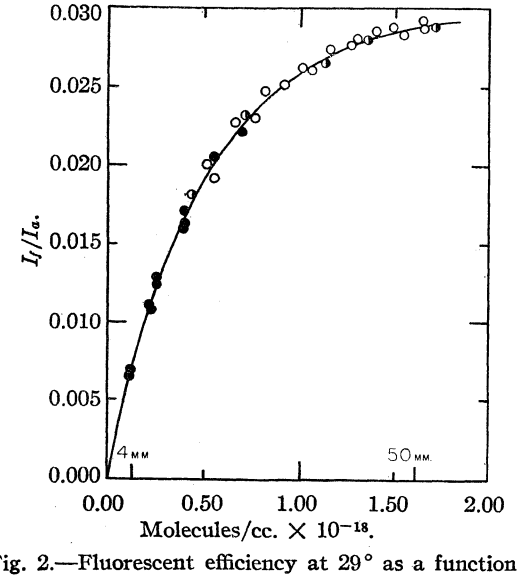


Fig. 2.—Fluorescent efficiency at 29° as a function of pressure of biacetyl: (1) ○, fluorescent radiation passed through a Wratten 8 filter. Incident light monochromated through use of Corning Violet Ultra glass and Cupric Ammonium Sulfate filter. (2) ●, fluorescence as in 1. Incident radiation monochromated by use of Violet Ultra glass alone. (3) ◑, fluorescence passed through Wratten 25 filter. Incident light as in 2. The curve is a graphical representation of equation (23).

Two conclusions relative to the data at 29° seem to be permitted from the data in Table I: (a) the fluorescence efficiency is not constant and independent of pressure but apparently decreases at low pressures; (b) at constant pressure the fluorescence efficiency is independent of the incident intensity even though the latter was varied nearly sevenfold.

The bulk of the data are summarized in Figs. 2 to 4 inclusive. In Fig. 2 it is seen that I_f/I_a increases with pressure at first rapidly and then more slowly, finally becoming practically constant. Moreover, by the use of color filters (Fig. 2) it is shown that there is no significant change of distribution of intensity among the wave lengths as a function of pressure. In Fig. 3 it is seen that I_f/I_a decreases with increase in temperature, although the general form of variation with pressure is maintained.

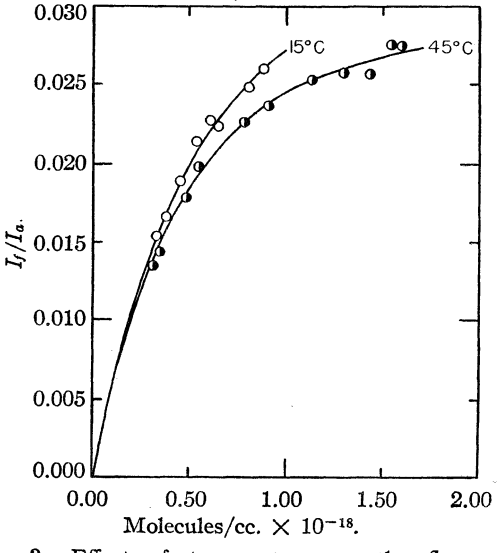


Fig. 3.—Effect of temperature on the fluorescent efficiency of biacetyl. Both curves are obtained from equation (23).

The data for Fig. 2 could not be carried to pressures higher than the vapor pressure of biacetyl. The curve might pass through a maximum if higher pressures could be attained. To afford a partial test of this point acetone was mixed with the biacetyl, the data being given in Fig. 4. Acetone was chosen because the fluorescence of this substance has been attributed to biacetyl and because resonance between the two molecules might be better than if some other foreign molecules

were used. Moreover, acetone is transparent at 3650 Å.

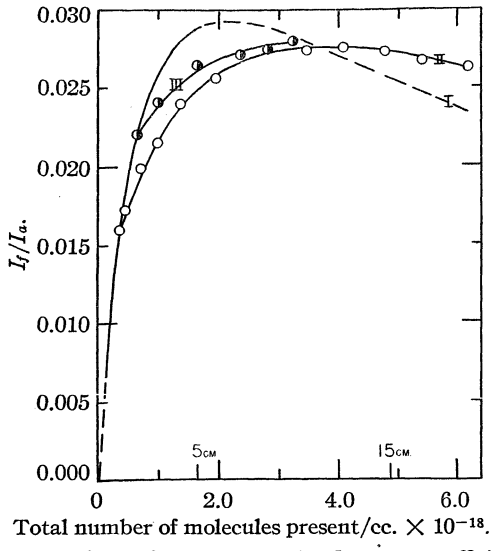


Fig. 4.—Effect of acetone on the fluorescent efficiency of biacetyl at 29°: I. No acetone was present. The broken lines are an extrapolation based on equation (24). II. Pressure of biacetyl is 11.5 mm. Pressure of acetone varies between 0 and 180 mm. III. Pressure of biacetyl is 20.0 mm. Pressure of acetone varies between 0 and 80 mm. Curves II and III are obtained from equation (22).

The addition of acetone to biacetyl increases the value of I_f/I_a but not quite to the same value that this ratio would have if the biacetyl were present alone at the same total pressure. With sufficient acetone the ratio passes through a maximum as it would probably also do if higher biacetyl pressures could have been used.

IV. Discussion

The trend of the I_f/I_a ratios with increasing pressure of biacetyl or with constant pressure of biacetyl and increasing pressure of added acetone indicates that collisions are effective, in some way, in enhancing the fluorescence. This is just the opposite of the effect one would expect from a Stern–Volmer mechanism where collisions are assumed to play only a deactivating role. This effect, whatever its cause, undoubtedly is accompanied by some collisional deactivation.

Various explanations of the data might be advanced, but most of them would rest on uncertain or completely illogical hypotheses. Thus there seems to be no *a priori* reason for believing that one vibration level of a stable upper state should have a much higher transition probability for fluorescence than other levels or at least than other adjacent levels. The spectrum of the fluorescence at various pressures and from various sources[2,3,4] indicates that transitions must occur solely or almost solely from one vibration level of the upper state, probably the lowest. Evidence presented above using color filters offers further substantiation of this point.

The most plausible explanation of the data is based on the following assumptions: (1) at 3650 Å. an upper state, B^0, is formed upon absorption which may either dissociate or undergo a transition to another state, B^1. This transition is reversible. (2) B^1 may dissociate, but the inclusion of this process is unnecessary for the explanation of the data. B^1 may, however, be transformed into a third state, B^2, by collisions. (3) B^2 may fluoresce, may be deactivated by collision, or may be converted back into B^1 by collision.

The mechanism may be stated in the equations

I_a	$B + h\nu = B^0$	(11)
$k_1(B^0)$	$B^0 =$ products	(12)
$k_2(B^0)$	$B^0 = B^1$	(13)
$k_3(B^1)$	$B^1 = B^0$	(14)
$k_4(B^1)(B)$	$B^1 + B = B^2 + B$	(15)
$k_5(B^1)(B)$	$B^1 + B = B + B$	(16)
$k_6(B^2)$	$B^2 = B + h\nu$	(17)
$k_7(B^2)(B)$	$B^2 + B = B + B$	(18)
$k_8(B^2)(B)$	$B^2 + B = B^1 + B$	(19)
$k_4'(B^1)(A)$	$B^1 + A = B^2 + A$	(20)
$k_7'(B^2)(A)$	$B^2 + A = B + A$	(21)

A represents a molecule of acetone. States B^0 and B^1 may fluoresce, but rates of fluorescent decay must be small compared to those of other reactions they undergo in this pressure range. This statement is strongly supported by the character of the spectrum. Other reactions involving acetone molecules can be shown to be unimportant. Equations (16), (18), and (21) could be replaced by other second order steps (for example, induced predissociation) which would lead to quenching.

The small amount of auto-quenching found by Almy and his co-workers[4,5,6,7] and also in this work indicates that k_5 must be small compared to k_4. The contribution of equation (19) will probably be small due to the Boltzmann factor.

With the usual assumptions regarding the steady state it is found that

$$I_a/I_f = 1/Q = \frac{k_1k_3}{k_2(k_4(B) + k_4'(A))} + \frac{(k_1 + k_2)}{k_2} + \frac{k_1k_3(k_7(B) + k_7'(A))}{k_2k_6(k_4(B) + k_4'(A))} + \frac{(k_1 + k_2)(k_7(B) + k_7'(A))}{k_2k_6} \quad (22)$$

While k_4 may vary slightly with temperature, the only constants which might be expected to vary appreciably with temperature are k_7 and k_7'.

In order to eliminate the arbitrary units used in measuring I_a and I_f, it is assumed that I_f/I_a at high pressures is 0.029 as found by Almy and co-workers.[6,7] The following empirical equation is found to fit the data between 15 and 60° for pure biacetyl

$$I_a/I_f = 15.2\cdot10^{18}/(\mathrm{B}) + 2.9 + 125\exp.(-1200/RT) + 24\cdot10^{-18}(\mathrm{B})\exp.(-1200/RT) \quad (23)$$

where (B) is in molecules per cubic centimeter. The smooth curves in Figs. 2 and 3 are obtained from equation (23) since (A) = 0.

By comparing the empirical constants of equation (23) with those in the theoretical equation (22) and converting to the more customary unit of moles per cubic centimeter we find

$$k_1/k_2 = 2 \quad (24)$$

$$k_4/k_3 = 8\cdot10^4 \text{ cc./mole} \quad (25)$$

$$k_7/k_6 = 5\cdot10^6 \exp.(-1200/RT) \text{ cc./mole} \quad (26)$$

Nothing definite can be said concerning the orders of magnitude of k_1 and k_2. Since k_1/k_2 should increase with frequency, the absence of fluorescence at 3130 and 2537 Å. is understandable. Also nothing can be said definitely concerning the magnitude of k_4 except that it might be expected to be about 10^{13}, a value found for most bimolecular reactions. If this value is assumed, k_3 is about 10^8, and the slow step in the fluorescence mechanism is equation (17). Almy and co-workers find the lifetime of the fluorescence to be about 10^{-3} second. If the responsibility for this long lifetime is placed on (17) (and this assumption cannot be further substantiated), k_6 is about 10^3. Then k_7 is found to be about $5\cdot10^9$ exp. $(-E/RT)$, leading to an effective cross section for quenching of 0.0025 Å.^{2} or to a transmission coefficient[8] of about 10^{-3}. Thus the small constant for quenching agrees with the results of Almy and co-workers at 4358 Å.

It should be pointed out that a normal rate of quenching would be obtained if k_6 were about 10^8. If the lifetime of B^2 is really as short as 10^{-8} second, the slow rate of decay of fluorescence will have to be explained by assuming that one of the states B^0 or B^1 (preferably B^1) is metastable with respect to all processes which tend to remove molecules from it.

Turning to the effect of adding acetone to the biacetyl, it is found that the results may be made to fit equation (22) if $k'_4 = 0.48\,k_4$ and $k'_7 = 0.53\,k_7$. Curves II and III in Fig. 4 are based on these values. Thus acetone is about half as effective as biacetyl either in quenching excited biacetyl to the ground state or in causing transitions from one excited state to another.

Summary

1. The proper use of the intensity of radiation absorbed for fluorescence experiments is discussed briefly.

2. Biacetyl emits no measurable fluorescence when irradiated by 3130 and 2537 Å.

3. The fluorescence of biacetyl as excited by radiation of wave length 3650 Å. has been studied as a function of pressure (4 to 50 mm.), temperature (15 to 60°), and intensity.

4. As the pressure of biacetyl increases, the quantum efficiency of fluorescence increases, indicating the apparent reverse of quenching. The fluorescence efficiency is independent of incident intensity.

5. The addition of acetone produces the same general effect of enhancing the fluorescence efficiency, although very high pressures of acetone lead to some apparent quenching.

6. The effect of temperature indicates an activation energy of about 1200 calories for the quenching process.

7. It is possible to explain the results by assuming that the state formed by absorption cannot fluoresce but is changed to other states which can fluoresce through the agency of collisions. At least three upper states seem to be involved.

ROCHESTER, NEW YORK RECEIVED JANUARY 19, 1940

[CONTRIBUTION FROM THE HAYDEN MEMORIAL LABORATORIES, NORTHEASTERN UNIVERSITY]

The Preparation of Some Branched Chain Aliphatic Sulfonic Acids

BY SAVERIO ZUFFANTI

Introduction

Most of the work that has been done on the preparation of the anhydrous aliphatic sulfonic acids deals with the straight chain acids. Vivian and Reid[1] present data on the acids containing one to six carbon atoms in the chain, while Noller and Gordon[2] have prepared those containing nine to fourteen carbon atoms in the chain.

The present paper reports data on four branched chain aliphatic sulfonic acids: isopropyl, isobutyl, *t*-butyl and isoamyl. The method used for the preparation of these acids is different from any of those used by the above authors.

TABLE I

Alkyl halide	Used, g.	Satd. soln. of Na_2SO_3, cc.	Time of reflux, days	Yield of pure Na sulfonate, g.	% Eff.
Isopropyl bromide	118.0	250	2	129.1	92.2
Isobutyl bromide	75.6	250	4	65.8	74.6
Isoamyl bromide	36.6	250	1	40.4	95.7
t-Butyl bromide	54.9	250	7	36.4	56.8

TABLE II

	Na sulfonate used, g.	Decompn. time, hr.	Acid obtained, g.	Theo. yield, g.	% Eff.
Isopropyl	29.1	10	9.8	24.6	39.8
Isobutyl	18.7	7	9.2	16.1	57.2
Isoamyl	14.0	5	11.1	12.2	91.1
t-Butyl	20.24	14	7.2	17.5	40.1

Experimental

Preparation of the Sodium Salt of Isoamyl Sulfonic Acid.—36.6 grams of isoamyl bromide was refluxed with 250 cc. of a saturated water solution of C. P. sodium sulfite until the two layers disappeared (about one day). The resulting sodium isoamyl sulfonate was obtained from the solution by evaporating to dryness and purifying by repeated fractional crystallization from a 75% alcohol solution in water, until the salt obtained was practically free from bromide; yield 40.4 g. (95.7%).

Preparation of Anhydrous Isoamyl Sulfonic Acid.—14.01 grams of the dried (110°) and pulverized sodium salt was supended in approximately 250 cc. of absolute ether (distilled over sodium) and a current of dry hydrogen chloride introduced to decompose the sodium salt. The suspended salt changes in appearance from glossy flakes to a granular residue of sodium chloride that tends to settle quickly, thus affording a means of following the decomposition which, in this case, was complete in five hours. The residue was filtered off into a weighed sintered glass crucible and the weight of the dried residue indicated a practically quantitative decomposition. The filtrate was allowed to evaporate (at room temp.) in a vacuum desiccator, leaving a dark oily residue that was soluble in water. The last traces of hydrogen chloride and ether were removed in a drying pistol (under vacuum) using carbon tetrachloride vapors as a source of heat. The material was kept in the pistol for about four hours. In this manner the anhydrous isoamyl sulfonic acid was obtained (free from ether and chloride); yield 11.1 g. (91.0%).

Preparation of *m*-Toluidine Salts.—The *m*-toluidine salts were prepared by adding *m*-toluidine to an ether solution of the sulfonic acid. The precipitated salt was filtered off and purified by recrystallization from warm ether.

Determination of Melting Points.—The melting points of the sulfonic acids were determined by first freezing the acids in a bath of acetone and dry-ice and then allowing the bath to warm up to room temperature and noting the temperature of melting.

The tables summarize the data for the four acids reported.

The physical data obtained with these acids, together with the melting points of the *m*-toluidine salts are given in Table III.

TABLE III

IDENTIFICATION OF THE SULFONIC ACIDS

	B. p. °C.	B. p. Mm.	d^{25}_4	M. p., °C.	$n^{20}D$	% Purity by titration	S, % Calcd.	S, % Found	*m*-Toluidine salts M. p., °C.
Isopropyl	159	1.4	1.1877	−37	1.4332	99.7	25.81	25.19	109
Isobutyl	171	1.2	1.1910	−61	1.4364	99.4	23.19	22.86	123
Isoamyl	177	1.5	1.1292	− 5	1.4400	99.8	21.05	20.84	115
t-Butyl	173	1.5	1.2180	−76	1.4315	99.7	23.19	22.40	131

Summary

1. Isopropyl, isobutyl, isoamyl and *t*-butyl sulfonic acids have been prepared in the anhydrous state.

2. The boiling points, melting points, densities, indices of refraction, *m*-toluidine salts and sulfur determinations have been used to characterize the above acids.

BOSTON, MASSACHUSETTS RECEIVED FEBRUARY 2, 1940

(1) Vivian and Reid, THIS JOURNAL, **57**, 2559 (1935).

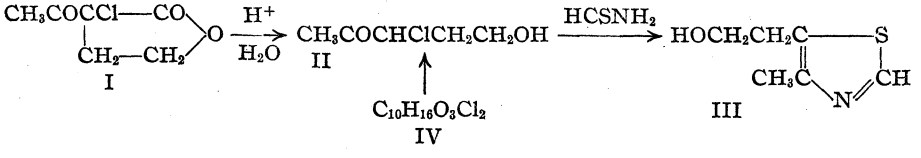
(2) Noller and Gordon, *ibid.*, **55**, 1090 (1933).

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF MERCK & CO., INC.]

Derivatives of γ-Acetopropyl Alcohol[1]

BY JOSEPH R. STEVENS AND GUSTAV A. STEIN

While attempting to prepare pure chloroacetopropyl alcohol (II), following the Buchman[2] synthesis for 4-methyl-5-(β-hydroxyethyl)-thiazole, it was found that the principal product ultimately formed by the decarboxylation of chloroacetobutyrolactone (I) is an ether, $C_{10}H_{16}O_3Cl_2$ (IV), formed from two moles of the expected alcohol by the elimination of one mole of water.



As a result, an investigation was made to determine the structure and properties of this compound, to find out whether this ether formation is possible with γ-acetopropanol and its bromo derivative, and further to prepare chloroacetopropyl alcohol (II) and study its properties.

Discussion

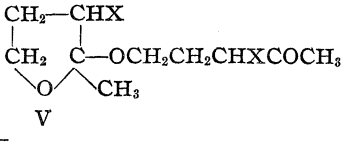
Although the ether is the principal product, chloroacetopropyl alcohol (II) is present in the reaction mixture and can be isolated from it. Chloroacetopropanol is found to be distillable at room temperature (molecular still); on mild heating, it is readily converted to its ether. By warming its *dilute* aqueous solution, the ether in turn is easily hydrolyzed to the alcohol, as demonstrated by the freezing point depression of the aqueous solution and by isolation. The ether with thioformamide hydrate yields 4-methyl-5-(β-hydroxyethyl)-thiazole (III), giving further evidence for the ease of cleavage of its ether linkage.

It is possible to distinguish between γ-chloroacetopropyl alcohol and its ether by means of their solubilities in ligroin; the former is not soluble whereas the latter is miscible. The crude reaction product (organic layer) obtained by decarboxylating chloroacetobutyrolactone (I) is miscible with ligroin, showing that the ether of chloroacetopropyl alcohol is not a secondary product formed during the purification (distillation) procedure.

Similar results are obtained in the preparation of bromoacetopropyl alcohol by bromination of γ-acetopropanol. In this case, the reaction mixture does not separate into two layers, suggesting that the product is chiefly bromoacetopropanol as it exists in the crude reaction mixture. However, when the extract is distilled at room temperature, only the ether $C_{10}H_{16}O_3Br_2$ is obtained. This ether is easily hydrolyzed to a dilute solution of bromoacetopropyl alcohol, but the extract of this solution yields only the ether. Apparently, the bromo alcohol is less stable in its free form than its chloro analog and reconverts spontaneously to its ether. From these facts one would expect the parent γ-acetopropyl alcohol to be the most stable member of this series, as was found to be the case.

γ-Acetopropyl alcohol is known in its free form and can be distilled at atmospheric pressure (b. p. 207–208°, 729 mm.). Lipp[3] observed partial dehydration of this alcohol on prolonged heating and under more severe conditions he was able to prepare an internal anhydride $(CH_3C{=}CH{-}CH_2CH_2)$ with O. In the course of this investigation, it was found that by slowly distilling γ-acetopropyl alcohol several times at 10 mm. pressure and fractionating the product, an ether between two moles of γ-acetopropanol is obtained. Small quantities of acids catalyze its formation. This substance behaves like an anhydride; it is quickly hydrolyzed with small quantities of water to γ-acetopropyl alcohol. When treated with semicarbazide in methanol, the semicarbazone of acetopropyl alcohol slowly forms.

Apparently these substances have the mixed ether structure (V) between the two recognized tautomeric forms[2] of γ-acetopropyl alcohol, the evidence for which follows

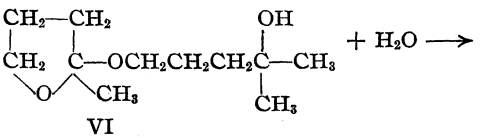


(1) This paper is No. XIX in the R. R. Williams Vitamin B1 Series (XVIII, Buchman and Richardson, THIS JOURNAL, **61**, 891–893 (1939).

(2) Buchman, *ibid.*, **58**, 1803–1805 (1936).

(3) Lipp, *Ber.*, **22**, 1196 (1889).

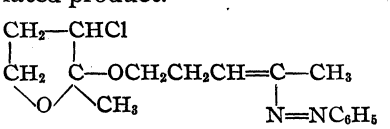
(1) The ether of acetopropyl alcohol shows no active hydrogen and one mole of Grignard reagent is consumed in a modified Zerewitinoff determination. When this reaction is carried out on a laboratory scale the reaction product is found to consist of a mixture of acetopropyl alcohol and 2-methylpentanediol-2,5, indicating the formation of an intermediate ketal (VI) which hydrolyzes



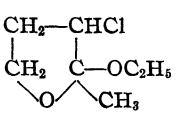
VI

$$CH_3COCH_2CH_2CH_2OH + (CH_3)_2COHCH_2CH_2CH_2OH$$

(2) The ether of chloroacetopropyl alcohol when treated with an excess of phenylhydrazine in an inert solvent gives a rapid precipitation of phenylhydrazine hydrochloride which stops when one mole has been formed, showing a marked difference between the activity of the two halogen atoms. The mother liquor yields a crystalline substance, $C_{16}H_{21}O_2N_2Cl$, corresponding to one mole each of the reactants, less a mole of water and a mole of hydrogen chloride. α-Bromoacetophenone reacts with phenylhydrazine[4] to give a similar product. By analogy chloroacetopropyl ether, if it contains a single —CO—CHCl— grouping, should yield the product (VII), which is in accordance with the composition of the isolated product.



VII



VIII

The Klingenfuss[5] ether (VIII), prepared by decarboxylating γ-chloroacetobutyrolactone in aqueous alcohol, does not react with phenylhydrazine under similar experimental conditions.

(3) Values obtained for the amount of iodine consumed in the iodoform reaction with the ether of chloroacetopropyl alcohol are about one-half as large as those for samples which have been previously heated in water in order to effect hydrolysis, indicating the presence of one free CH_3CO— group and another easily generated by hydrolysis.

The formation of the Klingenfuss ether may be considered as simple ketal formation from the cyclic tautomer of chloroacetopropanol. The presence of chloroacetopropyl alcohol during the reaction is demonstrated easily by the isolation of its ether as a principal product in the reaction mixture. In the preparation of the Klingenfuss compound (VIII), chloroacetobutyrolactone (I) may be replaced by the ether (IV).

The ether (VIII) is also easily hydrolyzed with water. When dissolved in water, in which it is soluble to a limited extent, the resulting solution gives no iodoform test. However, if the solution is brought to *p*H 3 or heated slightly and then cooled, complete hydrolysis occurs resulting in a solution which gives a strong iodoform reaction. When this solution is extracted with ether and the extract is distilled, the ether of chloroacetopropyl alcohol is obtained. From these results, it is apparent that chloroacetopropyl alcohol is the common intermediate in these reactions.

Experimental

Ether of γ-Chloro-γ-acetylpropanol.—Four hundred and ten grams of α-chloro-α-acetobutyrolactone (b. p. 74–75° at 1.5 mm.) was heated for about seven hours on the steam-bath with 410 cc. of water and 12 cc. of 38% hydrochloric acid until decarboxylation was complete.[6] On cooling, most of the ether separated as an oil, which was repeatedly extracted from the water layer with petroleum ether. After shaking the petroleum ether extracts with solid potassium carbonate, in order to render the product acid-free, the solvent was removed and the remaining oil was distilled. The cut (246 g.), b. p. 68–120° (1 mm.), on fractionation gave a product b. p. 111–112° (1 mm.); yield 200 g. (62%).

Anal. Calcd. for $C_{10}H_{16}O_3Cl_2$: C, 47.04; H, 6.32; Cl, 27.81; mol. wt., 255. Found: C, 47.13; H, 6.13; Cl, 28.07; mol. wt., 259 (dioxane).

This substance is a colorless and almost odorless liquid; it is difficultly soluble in water, easily soluble in organic solvents; d^{25} 1.2175; $n^{25}D$ 1.4748.

The ether (40 g.) when treated with thioformamide hydrate (38.5 g.) in isopropyl alcohol (17 cc.) gave 4-methyl-5-(β-hydroxyethyl)-thiazole (31.5 g.) boiling at 97.3–97.5° at 0.5 mm.; picrate m. p. (cor.) 164.5–165° (Buchnan 163°).

Anal. Calcd. for $C_{12}H_{12}O_8N_4S$: C, 38.69; H, 3.25. Found: C, 38.65; H, 3.10.

3-Chloro-3-acetylpropyl Alcohol.—When the low boiling fraction b. p. 68–75° (1 mm.) in a preparation such as that described above is collected separately and subjected to series of molecular distillations, 3×10^{-3} mm. at 20–24°, a product which is insoluble in ligroin can be isolated from the more volatile portion.

(4) Bodforss, *Ber.*, **52**, 1762, 1767 (1919); **72**, 468 (1939).

(5) Klingenfuss, U. S. Patent 2,123,653.

(6) In a private communication Dr. Buchman has suggested the use of weaker acid than that given in his original article. We have found these conditions satisfactory. Stronger acid gives more tarry products and a small amount of acetochloropropyl chloride, resulting in a contaminant in the final thiazole derivative. The principal reaction products are the same following both procedures. As judged by boiling point and chlorine analysis, Buchman apparently had fairly pure chloroacetopropyl ether which he reported as chloroacetopropyl alcohol.

Anal. Calcd. for $C_5H_9O_2Cl$: C, 43.95; H, 6.64; Cl, 25.97; mol. wt., 136.5. Found: C, 44.64; H, 6.29; Cl, 26.43; mol. wt., 146 (dioxane).

This substance is readily soluble in water. When it was redistilled at 1 mm., most of it distilled in the ether range up to 120°, with elimination of water, which was observed in a carbon dioxide trap.

Chloroacetopropyl Alcohol from its Ether by Hydrolysis.—The preparation of water solutions of this compound required warming. A minimum warming period at 60° of eighty minutes was found necessary. The solution then showed an inappreciable formation of chloride ion. The average of four determinations gave a freezing point lowering value of 1.57° per gram of added material per 10 cc. The apparent molecular weight is 119. Addition of 9 ($^1/_2$ mole of water) units to this figure, gives 128; mol. wt. chloroacetopropyl alcohol, 136.5.

Five grams of the ether was warmed at 60° for about six hours with 500 cc. of water. After allowing the mixture to stand overnight, all of the oily layer dissolved on shaking. The solution was extracted with ether, the ether solution dried and concentrated at 20°. The residual oil was distilled in a molecular still, at 27° (bath), press. 0.01 mm., d^{25} 1.210; $n^{25}D$ 1.4684.

Anal. Calcd. for $C_5H_9O_2Cl$: C, 43.95; H, 6.64. Found: C, 44.35; H, 6.48.

Ether of Bromoacetopropyl Alcohol.—Thirty-one grams of acetopropyl alcohol (b. p. 81–84° at 7 mm.) was dissolved in 150 cc. of water and 48 g. of bromine slowly added with stirring at 24–30° over a period of one and one-half hours. The aqueous layer was decanted from a small amount of oil, then treated with a little norit-charcoal. The resulting water-clear solution was extracted with ether; the ether extract after drying with sodium sulfate was concentrated at 20° under vacuum. About 55 g. of a colorless oil was obtained, part of which was distilled in a molecular still for analysis: boiling point 40° (bath) at 0.008 mm., d^{25} 1.592; $n^{25}D$ 1.4989.

Anal. Calcd. for $C_{10}H_{16}O_3Br_2$: C, 34.89; H, 4.69; mol. wt., 344. Found: C, 34.84; H, 4.56; mol. wt., 316 (dioxane).

A sample of this substance was dissolved in water and the freezing point was found to be 1.25° per g. of ether per 10 cc. of H_2O. The apparent molecular weight is 149, corrected for $^1/_2$ mole of water gives 158 as compared to 181 calculated for bromoacetopropanol. The test for Br^- ion was positive and the *p*H of the solution was 2.58. The hydrogen bromide concentration indicated by the *p*H gives rise to a 2% error in the determination.

Ether of γ-Acetopropyl Alcohol.—One hundred cc. of γ-acetopropyl alcohol, b. p. 81–84° (7 mm.), $n^{20}D$ 1.4372, containing one drop of concd. hydrochloric acid, was distilled several times. In each case the fraction of b. p. 105–115° (10 mm.) was collected. These combined cuts were fractionated and gave a product of b. p. 110–112° (10 mm.), d^{25} 0.9968; $n^{20}D$ 1.4435.

Anal. Calcd. for $C_{10}H_{18}O_3$: C, 64.59; H, 9.75; mol. wt., 186. Found: C, 64.28; H, 9.79; mol. wt., 182 (dioxane).

This substance dissolves readily in cold water; freezing point depression 1.98° per gram per 10 cc.; apparent molecular weight corrected for $^1/_2$ mole of water (+9) is 103; calculated for acetopropyl alcohol 102.

Two millimoles of semicarbazide hydrochloride was dissolved in 0.5 cc. of cold methanol, 2 millimoles of potassium acetate added and the potassium chloride centrifuged off. To the filtrate was added 1 millimole of ether of acetopropyl alcohol and the mixture allowed to stand at room temperature. The crystals that separated after a few hours had m. p. 157°. A mixed m. p. with the semicarbazone of γ-acetopropanol gave no depression.

2-Methyl-2-ethoxy-3-chlorotetrahydrofuran.—One hundred grams of chloroacetobutyrolactone, 120 g. of 80% ethyl alcohol and 36 g. of concd. sulfuric acid were stirred together and maintained at 40–50° until the evolution of carbon dioxide had ceased, which required about seven hours. After cooling, water and ether were added and the aqueous layer extracted several times with ether. The combined ether extracts were washed with a little cold water, neutralized with sodium carbonate solution and dried over calcium chloride. The ethereal solution was then distilled. The lower cuts, 50–70° at 13 mm., yielded on further fractionation about 30 g. of 2-methyl-2-ethoxy-3-chlorotetrahydrofuran (30%).

Anal. Calcd. for $C_7H_{13}O_2Cl$: C, 51.04; H, 7.97. Found: C, 51.22; H, 7.91.

The higher boiling cuts (70–120° at 1 mm.) gave about 28 g. of the pure ether of chloroacetopropyl alcohol.

Anal. Calcd. for $C_{10}H_{16}O_3Cl_2$: C, 47.04; H, 6.32. Found: C, 47.01; H, 6.12.

2-Methyl-2-ethoxy-3-chlorotetrahydrofuran from Ether of Chloroacetopropyl Alcohol.—To a cold mixture of 18 g. of sulfuric acid and 80 g. of 80% ethyl alcohol was slowly added 50 g. of chloroacetopropyl ether with cooling; the mixture was warmed at 40–50° for about seven hours and worked up as described above; yield 33 g.

Anal. Calcd. for $C_7H_{13}O_2Cl$: C, 51.04; H, 7.97. Found: C, 50.87; H, 7.77.

Ether of Chloroacetopropyl Alcohol from 2-Methyl-2-ethoxy-3-chlorotetrahydrofuran.—Twelve and one-half grams of 2-methyl-2-ethoxy-3-chlorotetrahydrofuran was shaken at room temperature with 100 cc. of water which was previously acidified with hydrochloric acid to a *p*H of 3. After a few minutes of shaking, all the oil had dissolved, and after thirty minutes the characteristic camphor-like odor of the compound had disappeared completely. At the end of one hour the solution was extracted several times with ether, etc.; the extracts yielded 5.4 g. of product, b. p. 111–112°.

Anal. Calcd. for $C_{10}H_{16}O_3Cl_2$: C, 47.04; H, 6.32. Found: C, 46.41; H, 6.36.

Reaction of Methylmagnesium Iodide on the Ether of γ-Acetopropanol.—A modified Zerewitinoff[7] analysis showed 0.24 equivalent of active hydrogen and 1.16 equivalents of reagent consumed.

Forty-three grams of the ether of γ-acetopropyl alcohol was treated with the Grignard reagent made from 66 g. of methyl iodide in the usual manner. After decomposition the aqueous layer was extracted exhaustively with ether.

(7) We are indebted to Dr. Richard Cramer of Harvard University for this determination.

The oil (39 g.) was found to be a mixture. A portion on treatment with semicarbazide gave the γ-acetopropyl alcohol semicarbazone, m. p. 157°, mixed m. p. no depression. This crude oil contained another substance in about equal amounts which was separated by extracting all of the acetopropyl alcohol with ligroin and distilling the residue; b. p. 77.5° (0.1 mm.), atmospheric pressure 218–219°. The recorded[8] boiling point of 2-methyl-2,5-dihydroxypentane is 218–219°. When heated with 10% sulfuric acid the characteristic camphor odor of 2,2-dimethyltetrahydrofuran[9] was observed.

Anal. Calcd. for $C_6H_{14}O_2$: C, 60.96; H, 11.95. Found: C, 61.07; H, 11.89.

Ether of Chloroacetopropanol and Phenylhydrazine.—A solution of 2.55 g. (0.01 mole) of the freshly distilled ether of chloroacetopropyl alcohol in about 80 cc. of absolute ethyl ether was chilled in ice; a cold solution of 2.16 g. (0.02 mole) of freshly distilled phenylhydrazine in about 20 cc. of absolute ether was added with shaking. After a few minutes the mixture became yellow and phenylhydrazine hydrochloride began to separate. After a few hours, all the phenylhydrazine hydrochloride had separated. This was filtered off, washed with ether and dried; yield 1.420 g. (0.98 mole) of phenylhydrazine hydrochloride, m. p. 240°; calcd. for 1 mole, 1.445 g. The reddish ether solution was washed with cold water until no chloride could be detected in the wash water; it was dried with calcium chloride and the ether was evaporated at room temperature, using high vacuum at the end of the concentration, in order to remove traces of ether. The remaining red viscous oil (about 3 g.) was dissolved in a minimum amount of isopropyl alcohol, and the solution chilled in a freezing mixture. The oil which separated soon crystallized. After centrifuging there remained a half oily, half crystalline mass which was recrystallized several times from warm isopropyl alcohol. The light yellow crystals thus obtained were dried in a high vacuum at room temperature; m. p. 85° (unsharp due to decomposition).

Anal. Calcd. for $C_{16}H_{21}O_2N_2Cl$: C, 62.21; H, 6.86; N, 9.07. Found: C, 62.20; H, 7.02; N, 9.19.

Titration Results with Iodine (Iodoform).—The samples for titration were dissolved in cold water (about 100 mg./100 cc.) with shaking. About 30 cc. of *N* potassium hydroxide was added, followed immediately with 70 cc. of 0.2 *N* iodine solution. The mixture was allowed to stand for fifteen minutes at room temperature. It was acidified with 40 cc. of 2.5 *N* hydrochloric acid and the free iodine titrated.

A. Ether of 3-Chloro-3-acetopropanol.—(1). Freshly prepared solution: iodine consumed 6.04 atoms; (2) after twelve hours, 7.7 atoms; (3) when the aqueous solution is heated for thirty-five minutes on a steam-bath, cooled, and treated with iodine, etc., 9.9 atoms were consumed.

The amount of iodoform which can be isolated from these mixtures is less than that calculated from the iodine consumed; apparently some of the iodination occurs on the 3 carbon atoms, complicating the reaction. The relative values are considered significant.

B. 2-Ethoxy-2-methyl-3-chlorotetrahydrofuran.—The cold aqueous solution shows no iodine consumed and no iodoform reaction. When it is heated at 100° for thirty-five minutes, cooled and assayed, 4.8 atoms of iodine are consumed. When the solution is kept at *p*H 3 for thirty minutes, neutralized and assayed, 5.3 atoms are consumed. A blank containing an equivalent of ethanol gave a negative result in this determination.

Acknowledgment.—The authors are grateful to Dr. Randolph T. Major, Dr. R. R. Williams, and Dr. E. R. Buchman for their many helpful suggestions. Mr. E. M. Chamberlin, Mr. M. Freiman and Mr. T. Perrine assisted with the experimental work. The physical measurements were made by Mr. W. A. Bastedo and the microanalyses by Mr. D. Hayman and Mr. W. Reiss.

Summary

γ-Acetopropanol is shown to be converted readily into its ether by repeated distillation. The ether readily is hydrolyzed back to the alcohol.

γ-Chloro and γ-bromoacetopropanols and their corresponding ethers are spontaneously interconvertible in water solution.

All three ethers contain one tetrahydrofuran ring, the other molecule of the propanol being in straight chain form.

2-Alkoxy-2-methyl-3-chlorotetrahydrofuran is similarly labile, being converted by mild hydrolysis to chloroacetopropanol and in turn to its ether. The reverse action proceeds in aqueous alcohol.

RAHWAY, N. J. RECEIVED NOVEMBER 4, 1939

(8) Franke and Kohn, *Monatsh.*, **28**, 1006 (1907).

(9) Henry, *Compt. rend.*, **143**, 1221 (1906); Franke and Kohn, *Monatsh.*, **28**, 1006 (1907).

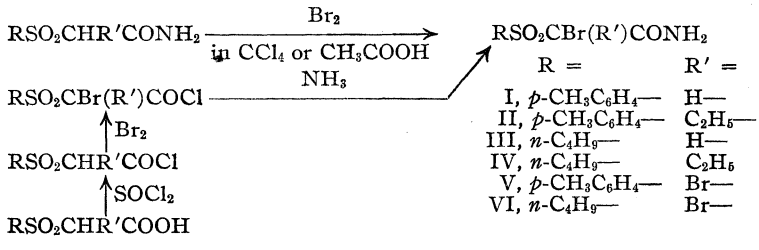
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING AT THE UNIVERSITY OF PENNSYLVANIA]

α-Bromo-α-sulfonylamides[1]

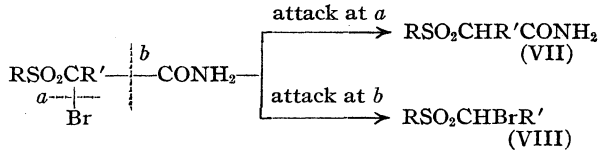
BY WILLIAM M. ZIEGLER[2] AND RALPH CONNOR

This study of α-bromo-α-sulfonylamides was undertaken for the purpose of comparing their reactions with those of the bromo derivatives of other active methylene compounds. While some reactions of the latter resemble the reactions of hypohalites ("positive halogen"[3]) rather than of halides, the ability of the sulfone group to produce this type of activation has heretofore received little attention.[4] No α-bromo-α-sulfonylamides appeared to have been prepared previously and it was first necessary to devise methods for their synthesis. Since the α-bromo-α-sulfonylamides were found to have properties identical with those of the compounds previously reported to be the isomeric N-bromoamides, the establishment of their structure constitutes a third phase of this report.

Preparation of α-Bromo-α-sulfonylamides.—Two of the α-bromo-α-sulfonylamides (I and IV) were prepared by converting α-sulfonyl acids to acid chlorides, bromination and treatment with ammonia. The method was laborious and the yields low. Much better results were obtained by treating α-sulfonylamides with bromine in moist[6] carbon tetrachloride and all of the α-sulfonylamides tested reacted readily under these conditions. Glacial acetic acid was satisfactory as a solvent for the preparation of I and III but the α-sulfonyl-*n*-butyramides were not brominated in this solvent.



Reactions of α-Bromo-α-sulfonylamides.—The reactions of these compounds were of two types. One resulted in the oxidation of the reagent and reduction of the α-bromoamide, showing the positive character of the halogen. The other type resulted in the cleavage of the —$CONH_2$ group. The predominant reaction depended both upon the reagent and upon the structure of the α-bromo-α-sulfonylamide. For example, sodium ethoxide gave the reduction product (VII) from IV but caused elimination of the —$CONH_2$ group from I to give the α-bromosulfone (VIII). Furthermore, II was not hydrolyzed under conditions which converted I to the α-bromosulfone[7] (VIII) and which resulted in attack at both the —Br and —$CONH_2$ groups of IV.



Two of the results reported in Table I are of especial importance. The liberation of two equivalents of iodine by the dibromo amides with potassium iodide in acid solution is contradictory to the report of Tröger and Hille that only one halogen atom of the dibromo amides underwent this reaction. It is also interesting to note that the time for complete reaction of the dibromo compounds with hydrazine was less than that for the corresponding monobromo compounds. It may therefore be inferred that this reaction is not stepwise and that the monobromo derivatives

(1) This communication is constructed from a thesis submitted by William M. Ziegler in partial fulfillment of the requirements for the degree of Doctor of Philosophy at the University of Pennsylvania in June, 1939.

(2) Harrison Fellow in Chemistry, 1938–1939.

(3) Waters, "Physical Aspects of Organic Chemistry," 2nd ed., George Routledge and Sons, London, 1937, p. 221.

(4) The results of Tröger and Hille[5] indicated that α-bromo-α-sulfonylamides do not contain positive halogen. Since our problem was begun, Samen [*Arkiv Kemi, Mineral. Geol.*, **12B**, No. 51 (1938); *Chem. Abs.*, **32**, 4520 (1938)] reported that triethylsulfonylmethyl bromide was reduced to triethylsulfonylmethane by treatment with hydrazine or hydriodic acid, and Mellander [*ibid.*, **12A**, No. 16, 32 (1937); *Chem. Abs.*, **31**, 5763 (1937)] found that α-bromo-α-sulfonyl acids were reduced by hydrazine.

(5) Tröger and Hille, *J. prakt. Chem.*, [2] **71**, 201 (1905).

(6) Water alone could not be used as a reaction medium, probably because of the insolubility of the α-sulfonylamides. Bromination occurred more slowly or not at all in dry carbon tetrachloride, suggesting that the reaction is similar to the basic catalysis in the bromination of ethyl acetoacetate [Pederson, *J. Phys. Chem.*, **38**, 601 (1934)]. However, aqueous sodium hypobromite was a less favorable reagent for halogenation of α-sulfonylamides than was bromine in moist carbon tetrachloride.

(7) The result of this hydrolysis was unexpected. According to Mossler [*Monatsh.*, **29**, 73 (1908)] α-bromoamides give aldehydes upon alkaline hydrolysis. A N-bromoamide would be expected to give an amine.[8]

are not intermediates in the reduction of the dibromo amides with hydrazine.

The reactions of the α-bromo-α-sulfonylamides with hydrazine, hydriodic acid, piperidine and mercaptides gave VII accompanied by nitrogen, iodine, piperidine hydrobromide and disulfide, respectively. Since similar results have been obtained with the bromo derivatives of active methylene compounds, it may be concluded that the sulfone group exerts upon halogen in the *alpha* position an effect similar to that of other labilizing groups.

Structure of the Bromoamides.—There seemed no reasonable doubt that the syntheses involving bromination of the acid chlorides would give α-bromo-α-sulfonylamides. However, I, prepared by this method, was identical with the product obtained by bromination of the α-sulfonylamide in glacial acetic acid by the procedure of Tröger and Hille[5] and reported by those workers to be a N-bromoamide (IX). Furthermore, IV prepared from the α-bromoacid chloride was identical with the products obtained by the method of Tröger and Hille and by bromination of the α-sulfonylamide in moist carbon tetrachloride. There seems to be little doubt, therefore, that the compounds assigned structures IX and X by Tröger and Hille are actually I and V.

$$p\text{-}CH_3C_6H_4SO_2CH_2CONHBr$$
IX

$$p\text{-}CH_3C_6H_4SO_2CHBrCONHBr$$
X

Attempts further to confirm the structures by synthesis of the isomeric N-bromoamides by bromination in the presence of alkali were unsuccessful because of the failure of the amides to react or the formation of dibromosulfones. The α-bromo-α-sulfonylamides did not react with nitrous acid and their conversion to α-bromo acids was therefore unsuccessful.

It should be pointed out that the arguments of Tröger and Hille for a N-bromo structure for these compounds were based largely upon the statement that the dibromoamides reacted with only one equivalent of iodide, a statement now shown to be incorrect. If further evidence for the attachment of bromine to carbon is necessary it may be gained from the following. (a) The compounds are stable toward boiling water.[8] (b) The difference in the ease of bromination of the acetamides and butyramides would not be expected to be so great if it depended upon the influence of an *alpha* ethyl group upon the reactivity of —$CONH_2$. (c) The conversion of I to an α-bromosulfone (VIII) by hydrolysis further establishes the position of the halogen.[9]

(8) Hofmann [*Ber.*, **15**, 411 (1882)] reported that N-bromoamides are decomposed by boiling water.

Experimental Part[10]

Reactions of α-Sulfonylamides[11] with Sodium Hypobromite.—To 21.4 g. of α-*p*-tolylsulfonylacetamide[12] was added 5.4 ml. (16 g.) of bromine, and the mixture shaken until about three-fourths of the amide had dissolved. The mixture was cooled in an ice-bath at −15° and a cold solution of 50% sodium hydroxide added dropwise with stirring until 10% more than the theoretical amount required to react with the bromine had been used. After standing in the ice-bath for one hour, cold water was added, the product removed by filtration and recrystallized from alcohol. The yield of *p*-tolylsulfonyldibromomethane, m. p. 116–117°,[9] was 2.9 g. (18% based on the bromine).

In another experiment 10.3 g. of α-*n*-butylsulfonyl-*n*-butyramide was mixed with 5.4 ml. (16 g.) of bromine and treated as described above. Unchanged starting material was the only product isolated.

Preparation of α-Bromoamides from Acid Chlorides

α-Bromo-α-*p*-tolylsulfonylacetamide (I).—To 21.4 g. of *p*-tolylsulfonylacetic acid[13] in 75 ml. of carbon tetrachloride, 13 g. of thionyl chloride in 25 ml. of carbon tetrachloride was added slowly. After refluxing for one hour and cooling, 6 ml. (18 g.) of bromine was added and the mixture then refluxed for ten hours, cooled, and poured into excess concentrated ammonia water at −15°. The lump that formed on stirring was removed and extracted several times with the same 200 ml. of water, cooling and removing the crystals between extractions. The crystals thus removed were recrystallized from water with the aid of charcoal. The yield was 2.40 g. (8%), m. p. 172–174°.

Anal. Calcd. for $C_9H_{10}O_3NSBr$: Br, 27.3. Found: Br, 27.2, 27.5.

α-Bromo-α-*n*-butylsulfonyl-*n*-butyramide (IV).—From 136.5 g. of ethyl α-bromo-*n*-butyrate and the mercaptide from 54.6 g. of *n*-butyl mercaptan under the conditions previously used for the preparation of the amides,[11] there was obtained 105 g. (74%) of crude ethyl α-*n*-butylthio-*n*-butyrate which was oxidized[11] in acetic acid–acetic anhydride mixture to the α-sulfonyl ester. The ester could not be crystallized and decomposed upon attempted dis-

(9) The formation of VIII might be considered possible from a N-bromoamide by hydrolysis of the latter to sodium hypobromite, followed by the action of the hypobromite upon the other hydrolysis products. This explanation of the hydrolysis result was eliminated by showing that none of the hydroylsis products were converted to VIII by sodium hypobromite.

(10) All melting points are corrected unless otherwise specified.

(11) The α-sulfonylamides were prepared by the methods described by d'Ouville and Connor, THIS JOURNAL, **60**, 33 (1938), and Pomerantz and Connor, *ibid.*, **61**, 3386 (1939).

(12) Similar results were obtained when sodium *p*-tolylsulfonylacetate was used but methyl *p*-tolyl sulfone did not react under these conditions.

(13) Gabriel, *Ber.*, **14**, 833 (1881).

tillation. The crude material was hydrolyzed with 400 ml. of 8% sodium hydroxide solution, acidified and extracted with ether. The acid obtained (93.6 g.) was converted to the acid chloride under the conditions described above, refluxed with bromine (71 g.) for twenty-five hours and treated with an excess of dry ammonia. The solvent was decanted, the residue extracted with alcohol and the alcohol solution treated with decolorizing charcoal. Removal of the solvent gave an oil which was crystallized with considerable difficulty. The solid was recrystallized several times from ether, seeding each time. The yield was 10.75 g. (6% based on the mercaptan), m. p. 56–57°. This was slightly less pure than the material obtained as described below.

Anal. Calcd. for $C_8H_{16}O_3NSBr$: Br, 27.9. Found: Br, 27.1, 27.2.

Preparation of α-Bromo-α-sulfonylamides from α-Sulfonylamides.—Five hundredths mole of the amide[11] was mixed with 100 ml. of carbon tetrachloride and 2.66 ml. (8 g.) of bromine added. With the acetamides the moisture present in unpurified carbon tetrachloride was adequate but the bromination of the butyramide was accomplished more readily by the addition of 2 ml. of water. After refluxing until the bromine color had disappeared, the solvent was removed quickly and the oil recrystallized. Slow removal of the solvent resulted in hydrolysis. A prolonged reaction period in the presence of excess water gave the dibromosulfonylmethane as shown below under the preparation of I.

α-Bromo-α-*p*-tolylsulfonylacetamide (I).—The mixture, without additional water, was refluxed for one hour and the solvent removed over a period of twenty minutes. The oil was dissolved in alcohol and allowed to crystallize. The solid was recrystallized from alcohol. From 10.7 g. of the amide there was obtained 6 g. (42%) of the product, m. p. 172–174°. The same product (51%) was obtained by the method of Tröger and Hille.[5] Neither sample lowered the melting point of the amide prepared from the α-bromo-α-sulfonyl acid chloride.

Anal. Calcd. for $C_9H_{10}O_3NSBr$: Br, 27.3; N, 4.80. Found: Br, 27.4, 27.6; N, 4.85, 4.80.

Ten and seven-tenths grams of α-*p*-tolylsulfonylacetamide in 100 ml. of carbon tetrachloride and 4 ml. of water was treated with 2.66 ml. (8 g.) of bromine and refluxed for one-half hour. The solution was then poured into a beaker and evaporated on a water-bath over a period of four hours. The sirup was dissolved in ether and filtered, the ether was then evaporated and the oil well chilled. After several hours chilling the paste that formed was mixed with enough very cold ether to dissolve the oily impurities and the material was filtered. The crystals were recrystallized from ligroin (b. p. 70–90°) and then from alcohol. The yield was 2.3 g. (28% based on the bromine) of product melting 116–117°, reported by Tröger and Hille[5] to be the melting point of *p*-tolylsulfonyldibromomethane.

α-Bromo-α-*p*-tolylsulfonyl-*n*-butyramide (II).—Two milliliters of water was added and the mixture refluxed for two and one-half hours. Half the solvent was removed and the material chilled. The product was recrystallized four times as follows: it was dissolved in a hot mixture of 75% carbon tetrachloride–25% ether, cooled and filtered. Then it was dissolved *immediately* in ether; failure to do so resulted in a product insoluble in ether. Just as solution was complete the product precipitated. It was removed by filtration and the process repeated. Twelve grams of amide gave 6.8 g. (43%) of product, m. p. 115–116°.

Anal. Calcd. for $C_{11}H_{14}O_3NSBr$: Br, 25.0; N, 4.38. Found: Br, 25.3, 25.0; N, 4.45, 4.44.

α-Bromo-α-*n*-butylsulfonylacetamide (III).—The mixture, without additional water, was heated for three-fourths hour and the solvent removed in twenty minutes. The oil was dissolved in alcohol, cooled and the product recrystallized once from benzene and twice from water. Nine grams of amide gave 5.75 g. (44%) of product, m. p. 130–131°. The procedure of Tröger and Hille[5] gave a 31% yield of the same material.

Anal. Calcd. for $C_6H_{12}O_3NSBr$: Br, 31.1; N, 5.45. Found: Br, 31.1, 31.0; N, 5.46, 5.50.

α-Bromo-α-*n*-butylsulfonyl-*n*-butyramide (IV).—The mixture with 2 ml. of water was refluxed for two hours and the solvent removed in twenty minutes. The oil was cooled and a seed crystal added. Seeding was also necessary in recrystallizing the product from ether. To obtain a seed crystal, a little of the oil was dissolved in ether and ligroin added to turbidity, then cleared with ether. The solution was allowed to stand open for three days, when the oil which first precipitated was crystallized. From 10.3 g. of the amide, 8.3 g. (58%) of product, m. p. 57–58°, was obtained. A mixed melting point with the product from the acid chloride was 56–58°.

Anal. Calcd. for $C_8H_{16}O_3NSBr$: Br, 27.9; N, 4.89. Found: Br, 27.7, 27.8; N, 4.74, 4.75.

α,α-Dibromo-α-*p*-tolylsulfonylacetamide (V).—The mixture without water but with 5.3 ml. of bromine was heated for two and one-half hours and the solvent removed in twenty minutes. The oil was taken up in alcohol and crystallized by cooling. It was then recrystallized from alcohol. The product from 10.7 g. of amide was 2.1 g. (11%), m. p. 134–135°.

Anal. Calcd. for $C_9H_9O_3NSBr_2$: Br, 43.1; N, 3.77. Found: Br, 43.3, 43.3; N, 3.65, 3.68.

α,α-Dibromo-α-*n*-butylsulfonylacetamide (VI).—This was obtained as a by-product in the preparation of III by the method of Tröger and Hille as mentioned above. The reaction mixture from 9 g. of α-*n*-butylsulfonylacetamide in 35 ml. of glacial acetic acid with 8 g. of bromine for one hour at room temperature was poured onto cracked ice and the III removed by filtration. The filtrate, after standing for three hours, gave a precipitate of VI which was recrystallized from dilute alcohol. The yield of VI was 1.8 g. (19%), m. p. 106–107°.

Anal. Calcd. for $C_6H_{11}O_3NSBr_2$: Br, 47.6; N, 4.17. Found: Br, 47.4, 47.6; N, 4.25.

Reactions of α-Bromo-α-sulfonylamides

With Sodium *n*-Butyl Mercaptide.—Four-tenths gram of sodium was dissolved in 30 ml. of absolute alcohol, and 1.7 ml. of *n*-butyl mercaptan added. This was cooled in a salt–ice-bath and a suspension prepared by dissolving 5.4 g. of II in 10 ml. of absolute alcohol and chilling, was added. The mixture was allowed to come to room temperature as the bath melted and then stand for five days.

The alcohol was evaporated to a small volume and the product poured onto chipped ice. The crystalline material was removed by filtration and recrystallized from water. The product was 2.45 g. (60%) of α-*p*-tolylsulfonyl-*n*-butyramide, m. p. 170–171°.

With Sodium *n*-Thiocresolate.—To 0.23 g. of sodium in 25 ml. of absolute alcohol was added 1.25 g. of *p*-thiocresol, then 2.85 g. (0.01 mole) of IV. The mixture was allowed to stand for five days and was then evaporated under reduced pressure until crystals separated. The residue was poured onto cracked ice, the product removed by filtration and recrystallized from alcohol. The product, 1 g. (80%), m. p. 45–46°, was ditolyldisulfide. Evaporation of the alcoholic and aqueous mother liquors gave, on recrystallization from water, 1.5 g. (73%) of α-*n*-butylsulfonyl-*n*-butyramide.[14]

This experiment was repeated using dioxane as a solvent and preparing the thiocresolate by the reaction of powdered sodium with *p*-thiocresol. There were isolated 0.75 g. (60%) of ditolyldisulfide, 0.72 g. (35%) of α-*n*-butylsulfonyl-*n*-butyramide and an oil from which nothing could be separated.

With Hydriodic Acid and with Hydrazine.—See Table I.

With Piperidine.—Six milliliters of piperidine dissolved in 10 ml. of dry dioxane was added to 6.25 g. of I dissolved in 40 ml. of dry dioxane and the mixture refluxed for seven hours. The crystalline precipitate was removed by filtration and washed with a little dioxane. The filtrate was evaporated to a smaller volume, removing both dioxane and piperidine, cooled and again filtered. The residue was washed with a little dioxane and added to the first one. The yield was 2.15 g. (60%) of piperidine hydrobromide,[15] m. p. 233–235°. Further evaporation of the filtrate resulted, on cooling and filtering, in a 2 g. (45%) yield of α-*p*-tolylsulfonylacetamide, m. p. 166–167°. Evaporation of this filtrate resulted in an oil from which nothing separated.

With Sodium Ethoxide.—To 50 ml. of absolute alcohol was added 0.23 g. of sodium. After the reaction was completed, the solution was cooled and 2.92 g. (0.01 mole) of I was added. The mixture was allowed to stand for two days at room temperature. Most of the alcohol was removed by distillation and a volume of water equal to the residue was added. On cooling and filtering 2.10 g. (84%) of *p*-tolylsulfonylmethyl bromide, m. p. 87–88°, was obtained. The identity of this compound was established by a mixed melting point with a sample prepared by a method to be described in a later paper.

To 25 ml. of absolute alcohol was added 0.23 g. of sodium. After the reaction was completed, the solution was cooled and 2.86 g. of IV was added. This was allowed to stand for four days, then most of the alcohol was evaporated, the residue poured into water and the mixture chilled. The resulting paste was recrystallized from alcohol and then water and gave 1.25 g. (61%) of α-*n*-butylsulfonyl-*n*-butyramide, m. p. 120–122°. The filtrates on evaporation gave a small quantity of oil.

(14) These reactions are comparable to the formation of di-*p*-tolyldisulfide and tribenzoylmethane from the sodium salt of *p*-thiocresol and tribenzoylmethyl chloride as reported by Kohler and Potter, THIS JOURNAL, **58**, 2168 (1936).

(15) Similar dehalogenations have been observed frequently; for example, Cope, *ibid.*, **54**, 1250 (1932).

TABLE I

REACTIONS OF α-BROMO-α-SULFONYLAMIDES

Amide	With HI,[a] % Br Calcd.	Found	With H_2NNH_2[b] N_2 (ml.) Calcd.	Found	Reaction time (hr.)	IX isolated %
I	27.4	28.2	44.8	45.0	5	82
II	25.0	24.3	39.5	39.0	4	87
III	31.1	32.2	47.5	46.5	2	80
IV	27.9	27.6	40.8	31.0	6	82
V	43.1	38.6	29.5[c]	30.0	1	83
VI	47.6	47.0	32.6[d]	33.0	1	47[d]

[a] Ten drops of 16 *N* sulfuric acid and 2 ml. of saturated potassium iodide solution were added to a solution of about 0.1 g. of the α-bromoamide in 15 ml. of glacial acetic acid. The flasks were stoppered and allowed to stand for thirty minutes with occasional shaking. The mixture was then titrated with 0.1 *N* sodium thiosulfate solution, using the disappearance of iodine color as an end-point and confirming by the addition of 0.5 ml. of 1% starch solution. Blanks were run in all experiments and, since they amounted to 10–15% of the total readings, the results reported are not considered to be quantitative. The data do show, however, that at least 90–95% of the total bromine in the compounds is able to oxidize hydriodic acid and that the observations of Tröger and Hille on the dibromo-*p*-tolylsulfonylacetamide were in error. [b] Except as otherwise indicated, about 1.00 g. of the α-sulfonyl-α-bromoamide was added to 15 ml. of water in a 50-cc. flask and a small tube containing 3.0 ml. of 10% hydrazine hydrate solution placed upright in the flask. This was then put in a water-bath at 75 ± 2°, allowed to come to this temperature, connected to a gas measuring apparatus, and the contents mixed. The mixture was kept at 75° and shaken occasionally until the evolution of nitrogen ceased. The contents of the flask were concentrated, chilled and the α-sulfonylamide removed by filtration, dried and weighed. [c] The sample weighed 0.45 g. [d] The sample weighed 0.50 g. The low recovery may be attributed to the difficulty of isolation of a rather small amount of a fairly soluble product.

With Nitrous Acid.[16]—To 5.4 g. of I dissolved in 50 ml. of alcohol–acetic acid (1:4) and kept cool, 2.6 cc. of *n*-butyl nitrite was added. The mixture was allowed to stand for twenty-four hours. Then hydrochloric acid was added and the mixture again allowed to stand for twenty-four hours; 80% of the bromoamide was recovered.

Addition of a solution of sodium nitrite to a solution of the bromoamide in acetic acid in the cold gave a 70% recovery. When the mixture was heated to 60° after one hour of standing the recovery was 85%.

Hydrolysis.—Two grams of I was sprinkled into 80 ml. of boiling 5% sodium hydroxide solution and the mixture boiled for two and one-half minutes. The material was chilled and filtered. The product was recrystallized from alcohol and yielded 0.78 g. (45%) of material melting at 89–90°. A mixed melting point with a sample of *p*-tolylsulfonylbromomethane (m. p. 90–91°) was 89–91°. This hydrolysis was carried out on the bromoamide pre-

(16) These experiments were carried out in an attempt to convert the amides to α-bromoacids as additional confirmation of their structure.

pared from the bromoacid chloride as well as that from the bromination of the amide in carbon tetrachloride. No trace of the α-sulfonyl acid was observed when the filtrate from the reaction mixture was acidified. Addition of silver nitrate solution gave silver bromide, indicating some hydrolysis of the halide.

Into 50 ml. of boiling 5% sodium hydroxide solution was sprinkled 2.86 g. of IV. The mixture was boiled about five minutes until only a faint test for ammonia was obtained. It was then chilled, acidified with nitric acid and extracted with ether. The aqueous portion gave a heavy precipitate with silver nitrate, indicating a large removal of bromine. The ether extracts were evaporated and gave a small quantity of oil that did not solidify at −15°. The amount of oil was less than 1 ml.

Two grams of II was sprinkled into 50 ml. of boiling 5% sodium hydroxide solution. The material formed opaque globules and only traces of ammonia were evolved. The mixture was refluxed for five minutes, chilled and filtered. The entire residue was unchanged amide.

Summary

Compounds reported to be N-bromo-α-sulfonylamides by Tröger and Hille have been shown to be α-bromo-α-sulfonylamides. The most satisfactory method of preparation of α-bromo-α-sulfonylamides was by direct bromination of α-sulfonylamides in moist carbon tetrachloride. Members of this series were also prepared by direct bromination of the amides in glacial acetic acid and by bromination of α-sulfonyl acid chlorides, followed by reaction with ammonia. The reactions of α-bromo-α-sulfonylamides showed that the sulfone group was similar to other labilizing groups in causing hypohalite characteristics in α-halo derivatives.

PHILADELPHIA, PENNA. RECEIVED OCTOBER 26, 1939

[CONTRIBUTION FROM THE RESEARCH DEPARTMENT, CALCO CHEMICAL DIVISION, AMERICAN CYANAMID COMPANY]

The Polyhydric Alcohol–Polybasic Acid Reaction. V. The Glyceryl Succinate and Glyceryl Maleate Polyesters

BY R. H. KIENLE AND F. E. PETKE

Although the glycol succinate reaction has been studied in some detail, no quantitative data have been published for the glyceryl succinate and the glyceryl maleate polymerization reactions. Glyceryl succinate was first prepared by Van Bemmelen.[1] It has been referred to frequently in resin literature[2] but the only published quantitative data on the polyester seem to be those of Hönel.[3] No such data appear to have been published for glyceryl maleate. In the present investigation, data are presented for the formation of these polyesters, succinic acid and succinic anhydride being used to prepare glyceryl succinate, and maleic anhydride to prepare glyceryl maleate.

The apparatus and technique used have already been fully described.[4] The purification and chemical constants of the glycerol employed similarly have been given. The maleic anhydride used was American Cyanamid Company chemically pure material, redistilled. The succinic acid and succinic anhydride were the chemically pure grade of Selden Division, American Cyanamid Company. The glycerol–succinic acid reaction was carried out at 190° in order that the data might be comparable with the recently published glyceryl phthalate (acid) investigation. The glycerol–maleic anhydride and glycerol–succinic anhydride reactions were carried out at 160°, since the reactions proceeded too rapidly at 190°.

(1) Van Bemmelen, *J. prakt. Chem.*, **69**, 84 (1856).

(2) Ellis, "The Chemistry of Synthetic Resins," Vol. I and II, Reinhold Publishing Corp., New York, N. Y.

(3) Hönel, *Paint Oil Chem. Rev.*, **91**, 19 (1931).

(4) Kienle, van der Meulen and Petke, THIS JOURNAL, **61**, 2258 (1939).

Experimental Data

The detailed data obtained for the glycerol–maleic anhydride, glycerol–succinic anhydride, and glycerol–succinic acid reactions are listed in Figs. 1, 2 and 3, respectively.

Figure 4 gives the acid value–water evolved relationship for all three reactions. When the theoretical acid value–water evolved curves are inserted in this plot, assuming only interesterification has occurred, it is found, in the case of glyceryl maleate, that the water evolved experimentally was at all times greater than theory, while in the case of both the glyceryl succinate reactions, the water evolved was at all times less than the theoretical. The equation for determining this theoretical relationship is

$$A_t = \frac{56.1(V_f - V_t)}{18(W - V_t)}$$

where A_t is the acid value at time t, V_t the water evolved at time t, V_f the total water evolved at 100% esterification, and W the total weight of reactants used. This equation is the exact form of an approximate equation used in the previous papers of this series.

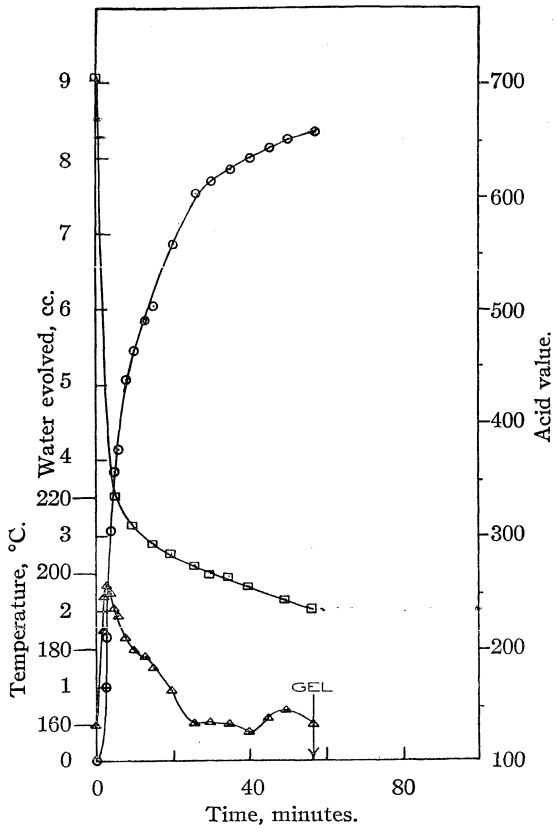


Fig. 1.—Reaction data. Glyceryl maleate: proportions, glycerol 69.0 g., maleic anhydride 110.3 g., temperature of mixing 160°, △, temperature, ⊡, acid value, ⊙, water evolved.

The log acid value–log time curves for the three reactions are shown in Fig. 5. It is interesting to note that the general shape of these curves is similar to the corresponding plots for glyceryl phthalate (anhydride) and glyceryl phthalate (acid). The changes of slope observed in the curves of the present investigation appear to occur at degrees of esterification corresponding to those previously noted for the glyceryl phthalates.

TABLE I

	Glyceryl maleate (anhydride)	Glyceryl succinate (acid)	Glyceryl succinate (anhydride)
Acid value	231	189	183.6
Saponification value	729	739.5	737.6
% Esterification	68.5	74.5	75.0
Average molecular weight	1050	1075	1085
Ultimate analysis C, %	46.9	46.7	46.7
Ultimate analysis H, %	4.6	5.2	5.4

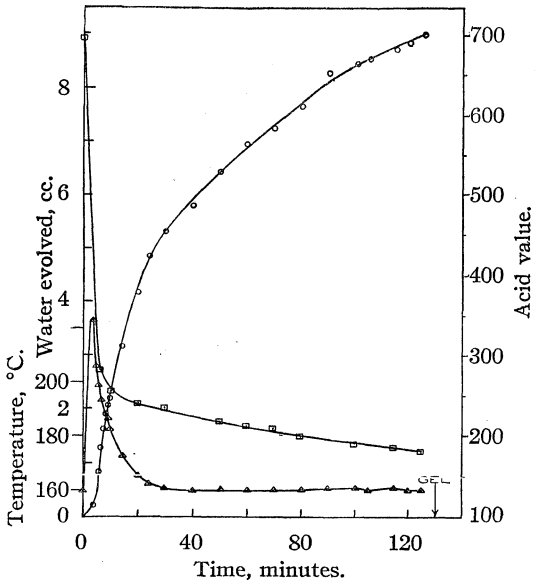


Fig. 2.—Reaction data. Glyceryl succinate (anhydride): proportions, glycerol 69.0 g., succinic anhydride 112.5 g., temperature of mixing 160°, △, temperature, ⊡, acid value, ⊙, water evolved.

Analytical Data.—Samples taken just prior to gelation in each reaction were found to be soft, rather flexible, very light amber colored resins.

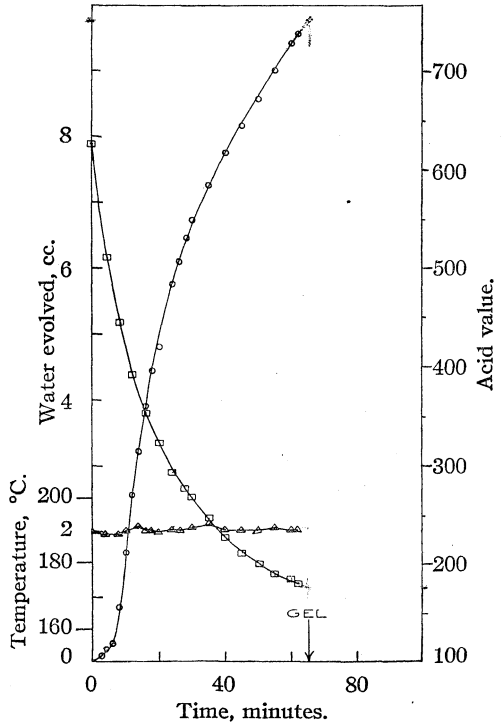


Fig. 3.—Reaction data. Glyceryl succinate (acid): proportions, glycerol 23.0 g., succinic acid 44.3 g., temperature of mixing 190°, △, temperature, ⊡, acid value, ⊙, water evolved.

The analytical data for these samples are given in Table I.

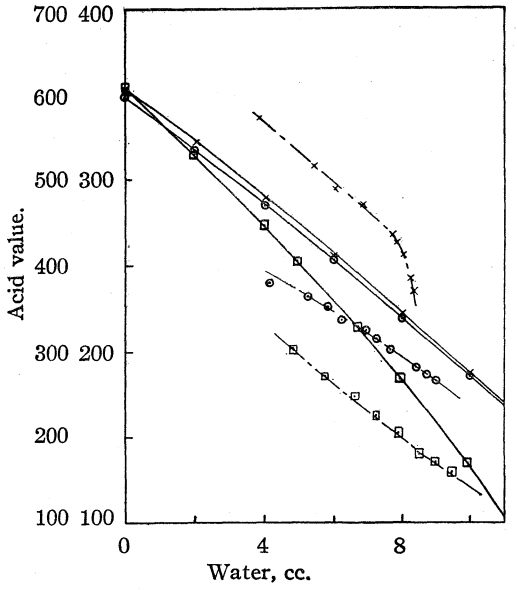


Fig. 4.—Acid value, water evolved relationship: ×, glycerol maleate, ⊙, glyceryl succinate (anhydride), ⊡, glyceryl succinate (acid), —— theory, - - - - experimental.

The infrared spectra from 1–15 μ for these resins have been measured[5] and are plotted in Fig. 6. The spectra show all the necessary linkages for polyester formation together with a suggestion of both conjugation and ring formation in the case of glyceryl maleate.

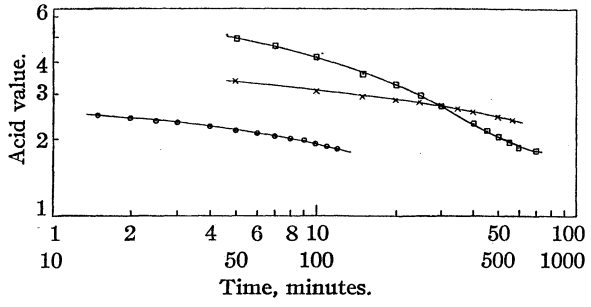


Fig. 5.—Log acid value–log time: ×, glyceryl maleate, T = 160°; glyceryl succinate anhydride, T = 160°; □, glyceryl succinate acid, T = 190°.

The spreading curves for these same polyester polymerides as monomolecular films on 0.001 N hydrochloric acid were determined and are given in Fig. 7. From these curves the areas per molecule were obtained by extrapolation and found to be 31.5 sq. Å. for glyceryl maleate and 80.5 sq. Å. for glyceryl succinate.

(5) Acknowledgment is made to Mr. R. R. Brattain for measuring these spectra.

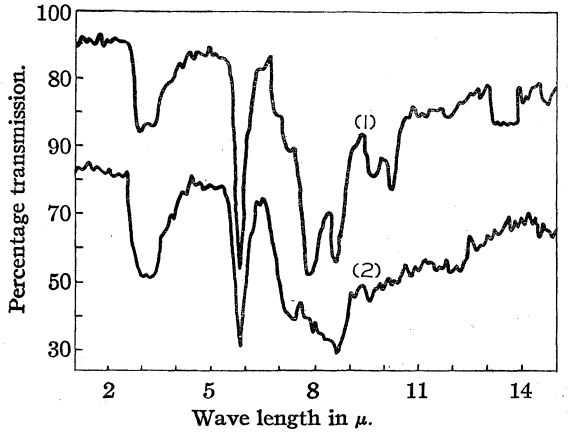


Fig. 6.—Infrared spectra: (1) glyceryl maleate, A. V. 231; (2) glyceryl succinate, A. V. 182.

In Table II there have been summarized pertinent data with respect to the sol–gel transition for the various polyester polymerides thus far reported. Also there have been included in this table the calculated acid values for the dimer and tetramer form of the several polyesters, assuming only interesterification had occurred. It is interesting to note that with the exception of glyceryl maleate, the acid value at which gelation occurs is between the two values.

TABLE II

Glyceryl polymeride	Mol. resin	React. temp., °C.	Time, to gel., min.	H_2O evolved, Va	A. V. at gelation (obsd.)	A. V. (calcd.) Dimer	Tetramer
Phthalate	1/4	160	160	7.99	120	139	117
Succinate	1/4	160	130	6.00	178	182	154
Maleate	1/4	160	57	5.44	230	187	157
Phthalate (acid)	1/3	190	164	10.80	120	139	117
Succinate (acid)	1/3	190	64	9.62	178	183	154

Discussion

In the glyceryl succinate reaction, when acid is used instead of anhydride, no initial temperature rise is observed and time is required to attain 50% esterification. From this point on to gelation, however, the reactions are fairly equivalent,

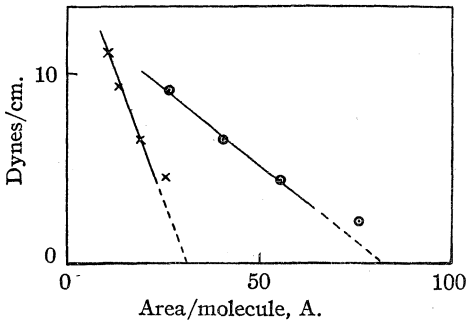


Fig. 7.—Monomolecular film data: T = 15–16°; 0.001 N HCl; ×, glyceryl maleate; ⊙, glyceryl succinate.

finally yielding polyesters with similar properties, as is evident from the analytical values shown in Table I. In the glyceryl succinate reaction, regardless of whether acid or anhydride is used, less water is evolved than is required theoretically. This seems to indicate that little more than interesterification is involved and that a portion of the water formed is retained by or dissolved in the polyesters.

The glyceryl maleate reaction is more complicated. From the beginning of the reaction to gelation more water is evolved than is predicted if only interesterification is assumed. The acid value of glyceryl maleate just prior to gelation is much higher than would be expected from the other polyesters examined. The formation of anhydrides and intraesterification, therefore, is required to explain the high acid value and the excess water evolved. Since the total evolved water in the glyceryl maleate is smaller than that resulting from the glyceryl succinate reaction, but the average molecular weights of the two resins at corresponding stages are practically equal, it would seem that addition polymerization also has occurred. The appearance of adsorption bands around 10.0 and 13.0 μ in the infrared spectrum of glyceryl maleate, common to ring compounds,[6] and the much lower spreading area of the glyceryl maleate polyester as compared with the glyceryl succinate polyester are further evidence in favor of the occurrence of addition polymerization.

In a previous paper[7] the importance of the average functionality of a highly functional polymeride with respect to when gelation will occur was discussed. In polyester polymerides, when stoichiometric proportions of reactants are used and optimum conditions of reaction are employed, it has been shown[4] that the average polymeric functionality with respect to the carboxyl groups can be calculated from the equation

$$MA_t = 56.1 \times 10^3 v$$

where v = the basicity of polyester, that is, the average polymeric functionality with respect to carboxyl groups. The calculated and observed values were found to agree very well. Gelation in all highly functional polymeric systems was shown to occur when the average polymeric functionality exceeded 3.0. In the case of glyceryl phthalate, gelation was found to result when v attained a value of 3.3 or just beyond the condition for potential gelation. At this point, not very large molecular weight polyesters are formed, but rather the mole percentage of tetramers or higher polymers has attained a low limited molar concentration sufficient to bring about a state of arrested motion. The glyceryl maleate and the glyceryl succinate data further support this concept. Thus, just before gelation, the average molecular weights are in the order of 1100–1200, while the average polymeric functionality at gelation for glyceryl maleate is approximately 4.3 and for glyceryl succinate is approximately 3.4.

Summary

1. The glyceryl succinate reaction has been investigated using both acid and anhydride. A difference was observed in the early portion of the acid reaction, but after 50% esterification had been reached, the two reactions were essentially similar. Less water was evolved than was required theoretically by interesterification. It has been suggested that part of the water formed was retained by the polyester.

2. The glyceryl maleate (anhydride) also has been studied. In this case more water was evolved than required by theory. This has been attributed to the formation of anhydrides and intraesterification along with interesterification. Data are presented indicating that addition polymerization also occurred.

3. Data for the various polymerides are summarized and gelation is explained in terms of low molecular weight polyester formation.

BOUND BROOK, N. J. RECEIVED OCTOBER 5, 1939

(6) Coblentz, "Investigation of Infra-Red Spectra," p. 136, Carnegie Institute (1905).

(7) Kienle, *J. Soc. Chem. Ind.*, **55**, 229T (1936).

[CONTRIBUTION FROM THE BASIC SCIENCE RESEARCH LABORATORY OF THE UNIVERSITY OF CINCINNATI]

Viscosities of Linear Polyesters. An Exact Relationship between Viscosity and Chain Length

BY PAUL J. FLORY

Introduction

A number of different equations have been proposed for expressing viscosity as a function of molecular constitution.[1] The fact that nearly all of these contain the molecular weight, or the chain length, explicitly indicates general recognition of the existence of a close relationship between viscosity and the size of the molecule.

One of the best known viscosity–molecular constitution relationships, proposed by Dunstan,[1a] is

$$\log \eta = aM + b$$

where η is viscosity, M is molecular weight, a is a constant the same for all homologous series, and b is a constitutive factor characteristic of a particular series. Albert[1e] has shown that the viscosities of homologous esters deviate from Dunstan's equation within the brief molecular weight range 296–352. Members of an homologous series covering a wide range of molecular weights ordinarily are not available. Consequently, it has not been possible to determine with certainty the exact nature of the dependence of viscosity on molecular weight of homologous substances.

Although it is an easy matter to prepare synthetic linear polymers having average molecular weights varying over a wide range, precise molecular weight determination is usually difficult. Correlation of viscosities of molten polymers with their molecular weights does not seem to have been attempted. In fact, very few measurements of viscosities of molten synthetic polymers have been reported,[2] although much work has been devoted to viscosities of polymers in dilute solutions.

The linear polyesters are exceptionally well suited for investigation of viscosity–molecular weight relationships. These polymers can be prepared at any desired average molecular weight over a wide range and, when the preparation is carried out under properly defined conditions, their average molecular weights may be determined accurately by titration of the unreacted carboxyl end-group.

The present investigation has disclosed that the viscosities of molten linear polyesters can be represented with astonishing accuracy by the equation

$$\log \eta = A + C'M_w^{1/2} \qquad (1)$$

where M_w is the *weight average* molecular weight (*cf. seq.*) and A and C' are constants. Or

$$\log \eta = A + CZ_w^{1/2} \qquad (2)$$

where Z_w is the *weight average* chain length (*i. e.*, number of atoms in the chain skeleton) and C is a new constant. Not only does this relationship provide a simple means for determination of average molecular weight, but it also offers a new approach to the relationship between viscosity and chemical constitution.

Experimental Methods

Materials.—Since very small amounts of impurities could affect the experimental results appreciably, the purification of the materials used in this investigation will be described in detail.

Decamethylene glycol, which had been prepared by hydrogenation of diethyl sebacate, was obtained from the University of Illinois. It was stirred vigorously for two hours with boiling 5% aqueous caustic in order to saponify any unreduced ester, then washed with water until all alkalinity had been removed. The glycol was purified further by recrystallization. One batch was recrystallized three times from ethylene dichloride, the hot solution being stirred vigorously while cooling very slowly. Because of the low solubility of decamethylene glycol in ethylene dichloride at room temperature, a second batch was recrystallized twice from an ethylene dichloride–alcohol mixture containing 10% by volume of alcohol. The yield from each recrystallization was 85 to 90%. This glycol was finally recrystallized twice from pure ethylene dichloride. Each batch was dried in air, ground in a mortar to break up aggregates, and then heated at about 65° for two hours in vacuum in order to remove traces of solvent. Both samples gave "flat" cooling curves at the freezing point, 71.9°, with less than 0.05° decrease in temperature when 80% had solidified. On the basis of a freezing point constant calculated from an estimated heat

(1) (a) A. E. Dunstan, *Z. physik. Chem.*, **56**, 370 (1906); (b) E. C. Bingham and C. E. Coombs, *Phys. Rev.*, **47**, 645 (1935); (c) S. Papkov, *Z. physik. Chem.*, **A174**, 445 (1935); (d) M. Souders, THIS JOURNAL, **60**, 154 (1938); (e) O. Albert, *Z. physik. Chem.*, **A182**, 421 (1938); (f) D. J. Lewis and A. R. Morgan, *J. Chem. Soc.*, 1341 (1939).

(2) H. I. Waterman and J. J. Leendertse, *Rec. trav. chim.*, **54**, 139 (1935), have reported the viscosities of a series of low molecular weight polymers of pentene-2 at several temperatures. E. Jenckel and K. Ueberreiter, *Z. physik. Chem.*, **A182**, 361 (1938), studied the viscosities of several polystyrenes near their softening temperatures. J. D. Ferry and G. S. Parkes, *Physics*, **6**, 356 (1935), determined the viscosity of a low molecular weight polyisobutylene at various temperatures.

of fusion (7000 cal./mole), a temperature drop of 0.05° at 80% solidification corresponds to about 0.03 mole % of impurities not soluble in the solid glycol. It must be admitted, however, that some of the most likely impurities (hydroxydecanoic acid, other glycols or possibly decyl alcohol) probably would enter the glycol crystal lattice to some extent. Experimental results obtained with the two batches of glycol are identical (*cf. seq.*).

Diethylene glycol, obtained from the Eastman Kodak Company, was fractionated carefully in a carborundum packed precision column. The boiling point, 129.5 to 130.0° at 10.5 mm., was practically constant throughout the entire distillation. A center cut was retained for use.

Adipic, sebacic, and succinic acids, obtained from the Eastman Kodak Company, were purified by recrystallizing twice from water. Each of these acids melted sharply; adipic acid at 150.6°, sebacic acid at 131.5°, and succinic acid at 187°. Their neutral equivalents were: adipic, 73.1, 73.2, 73.0, calcd. 73.06; sebacic, 101.0, 101.1, 101.3, calcd. 101.12; succinic, 59.0, 59.0, calcd. 59.04.

Viscometric Methods.—The viscometers used to measure viscosities of molten polyesters were similar in design to volumetric pipets. The capacity of the bulb and the diameter of the stem, extending about 4 cm. below the bulb, depended upon the viscosity range for which the viscometer was intended. A bulb volume of 1 cc. and an internal stem diameter of about 0.8 mm. was used for the range 0.1–3 poises. The viscometer designed for 20–300 poises had a 4-cc. bulb and 4-mm. stem.

By means of a three-way stopcock, to which the upper end of the viscometer was connected with rubber tubing, the viscometer could be connected either with nitrogen at a pressure slightly above atmospheric or with a reservoir of air at a pressure from 20 to 200 mm. less than that of the atmosphere. The difference between the atmospheric pressure and the pressure in the reservoir was registered on a mercury manometer. While the viscometer stem was immersed in the molten polymer, the surface of which was at atmospheric pressure, the stopcock was turned toward the reduced pressure reservoir. The time t required for filling the viscometer bulb was measured, after which the stopcock was immediately turned toward the nitrogen supply, causing the viscometer to empty slowly. The viscosity was calculated from

$$\eta = ctP \qquad (3)$$

where c is a constant and P is the pressure difference between the atmosphere and the reservoir, corrected for the effect of the mean difference in height between polymer in the viscometer and surrounding polymer.

The calibration constants c were determined by measuring the tP product for liquids of known viscosity. For this purpose mixtures of polymeric ethylene phthalate and *m*-cresol provided liquids having suitable viscosities. The rates of fall of accurately machined steel ball bearings ($^1/_8$" in diameter) through columns of these liquids one inch (2.5 cm.) in diameter were measured. The absolute viscosities of the liquids were then calculated from Stokes' law, supplemented with wall corrections as prescribed by Bacon.[3]

Independent standardizations using glycerol–water mixture, the viscosity of which was determined from the density using the tables published by Sheely,[4] yielded c values about 5% lower than those determined by the absolute method described above. This discrepancy is several times the experimental error, and no explanation of its source is suggested. The c's based on the absolute method have been used here. The viscosity measurements are believed to be accurate (relative to one another) within about ±2%, except at viscosities above 100 poises where the error may be about twice this. The possible 5% error in absolute values of the viscosities is of no consequence in any of the results included in this paper.

Above 10 poises it is necessary that the viscometers be allowed to empty very slowly (during five minutes or more) if an accurate subsequent measurement is to be made without cleaning the viscometer. Liquid adhering to the walls of the bulb decreases the effective volume, and hence the time t required for filling the bulb. Above 50 poises it is usually necessary to clean the viscometer between each reading if an error greater than 2% cannot be tolerated.

Several of the viscosities above 100 poises were measured using for viscometers straight glass tubes having 3 to 7 mm. inner diameters. Marks were etched at two points on the tube, usually at 2 and 12 cm., respectively, above the lower end. The time t (in sec.), required for filling the tube from the lower to the upper mark at a mean pressure difference P (in mm.), was recorded. The calibration constants c to be used in equation (3) were deduced from the mean cross sectional area of the tube with the aid of the equation (4) deduced from Poiseuille's law

$$c = 106\sigma/(h_2^2 - h_1^2) \qquad (4)$$

where σ is the cross sectional area in sq. cm., and h_1 and h_2 are the distances in cm. of the lower and upper marks, respectively, above the lower end of the tube. Comparison with results obtained with a viscometer of the type described previously confirmed the adequacy of this calibration method.

It should be pointed out that throughout the range investigated the viscous behavior of the polymers is Newtonian; that is, the rate of shear is proportional to the shearing stress. (The shearing stress is proportional to P divided by the length of the stem of the viscometer.) For example, a polymer having a viscosity of about 100 poises at 109° gave the same viscosity within ±2% over a five-fold variation of the shearing stress.

Methods of Polymerization.—Polymers were prepared by heating together precisely equivalent quantities of glycol and dibasic acid in a cylindrical Pyrex bulb sealed to the lower end of a 15-mm. vertical tube about 25 cm. long. Through a stopper in the upper end of this tube the viscometer was inserted. A gentle stream of nitrogen through the viscometer served to stir the mixture and to facilitate removal of water formed in the reaction. The effluent nitrogen and moisture passed through a 12-mm. side arm sealed to the vertical tube near its upper end. The side arm sloped upward for about 15 cm., and then led downward to a small trap for condensing moisture. Loss of a volatile reactant (glycol) was minimized by condensation in the side arm, followed by its return to the re-

(3) J. Bacon, *J. Frank. Inst.*, **221**, 251 (1936).

(4) M. L. Sheely, *Ind. Eng. Chem.*, **24**, 1060 (1932).

action mixture. Provision was made for reducing the pressure of the system by evacuation through the trap. The reaction bulb and several cm. of the vertical tube were heated by a vapor-bath (toluene, 109°; phenetole, 168°; *m*-cresol, 202°), which remained within 0.2° of constant temperature during any one experiment.

Experiments for the purpose of establishing viscosity–molecular weight relationships were carried out at 109° using as catalyst 0.10 to 0.20 equivalent % of *p*-toluenesulfonic acid (*i. e.*, from 1 to 2 mmol. of the catalyst per gram *equivalent* of dibasic acid). In order to assure rapid removal of water, the pressure was reduced to about 200 mm. After termination of an experiment conducted at this pressure and the above-mentioned temperature, the trap did not contain appreciable amounts of either glycol or acid.

At intervals during the course of the reaction the pressure was brought to atmospheric by introducing nitrogen simultaneously through the viscometer and through the trap. The viscosity was measured and a sample was removed immediately for analysis. The viscometer served as a pipet for removing samples. After having been weighed, samples having molecular weights below about 4000 were dissolved in chloroform; samples having higher molecular weights were dissolved in hot chloroform–chlorobenzene mixture. The solutions were cooled below 25° and titrated with 0.1 *N* alcoholic potassium hydroxide using phenolphthalein as indicator.[5] The end-point is very sharp in these solvents. The amounts of sample removed from the reaction bulb were sufficient to require from 4 to 10 cc. of the standard alkali. An accuracy within ±0.01 cc. was attained easily using a clean 10-cc. buret.

This polymerization method is especially well suited for the study of viscosity–molecular weight relationships. The low temperature, 109°, minimizes possible undesirable side reactions and loss of volatile reactants, which would vitiate molecular weight determination by titration (*cf. seq.*). The acid catalyst not only accelerates the reaction, but it also changes the kinetic order from third to second,[6] thus causing the molecular weight to increase approximately with the first power of the time. In the "uncatalyzed" third order reaction the molecular weight increases approximately with the square root of the time.

For studies of viscosity–temperature relationships, of viscosities of mixtures of polymers, and of density–temperature relationships, polymers containing catalyst obviously are not suitable because of the changes they will undergo during the course of the measurements. For such studies polymers were prepared by heating together equivalent amounts of glycol and dibasic acid at 202° without catalyst. Except that the pressure was not reduced during polymerization, the procedure described above was followed. Loss of glycol was considerable (about 1%) during the first few minutes, when much of the glycol had not yet reacted at either terminal OH. Molecular weights of polymers prepared by this method have been deduced from their viscosities using the viscosity–molecular weight relationship established on the basis of experiments carried out using an acid catalyst as described above. The neutral equivalent, determined by titration with alcoholic caustic, did not agree with the molecular weight calculated from the viscosity because OH and COOH groups were not present in equal number. On the basis of the discrepancy between the neutral equivalent and the molecular weight, the deficiency of glycol was calculated (see expression (11′)), and this amount was added to the polymer. After about an hour at 202°, the added glycol was completely assimilated by the polymer by means of ester interchange.

Determination of Densities.—The pycnometers used for determining densities of molten polyesters also resembled pipets. The bulb, having a capacity of about 4 cc., consisted of a section of 10-mm. glass tubing. The lower end of the bulb was sealed to a 1.5-cm. length of 5 mm. tubing which was drawn to an abrupt, thin-walled tip having an inside diameter somewhat less than 1 mm. The upper end of the bulb was sealed to a 4-cm. length of 0.5 mm. capillary tubing, which in turn was sealed to a 12-cm. length of 6-mm. tubing. A calibration mark was placed near the middle of the capillary section. The pycnometers were calibrated by weighing the water required to fill them from calibration mark to tip at 25°. The volume of the pycnometer at higher temperatures was corrected for the expansion of the Pyrex glass, using 0.96×10^{-5} per degree for its cubical expansion coefficient.[7]

After allowing sufficient time for polymer and pycnometer to reach the constant temperature of the vapor-bath, the molten polymer was drawn slowly into the pycnometer through the tip, filling it to the calibration mark. The difficulty with which viscous polymer flowed through the small capillary tubing facilitated adjustment to the mark. After permitting the pycnometer to remain briefly with its tip barely in contact with the polymer, it was removed quickly, and polymer on the outside of the tip was wiped away. Polymer in the capillary was frozen in order to prevent subsequent loss by drainage out of the tip. After careful cleaning of its exterior, the pycnometer and its contents were weighed at room temperature. The results are accurate within ±0.0001 g./cc.

Calculations.—Let a "segment" be defined as one glycol or one dibasic acid residue as contained within a polymer molecule. The extent of reaction p will represent the ratio of the number of ester groups to the number of ester plus unreacted carboxyl groups. When COOH and OH are present in equal numbers, $1 - p$ is the ratio of unreacted COOH groups (or OH groups) to the total number of segments, and the number of molecules must equal the number of unreacted carboxyls. Hence

$1 - p$ = (number of molecules)/(number of segments)

(5) Definite indication of degradation of high molecular weight polyesters containing catalyst which have been in contact with the atmosphere for a few days has been observed. Apparently, moisture absorbed from the air is capable, in the presence of catalyst, of hydrolyzing some of the ester linkages of the solid polyester. W. H. Carothers and J. A. Arvin, THIS JOURNAL, **51**, 2565 (1929), pointed out that polyesters absorb moisture readily. In the present investigation all samples were analyzed within two hours after removal, in order to avoid degradation prior to analysis.

(6) P. J. Flory, *ibid.*, **61**, 3334 (1939).

(7) This value is based on the linear expansion coefficient, 0.32×10^{-5} per degree, reported in the catalog of "Pyrex Laboratory Glassware" (1938), The Corning Glass Works, Corning, N. Y.

and the degree of polymerization DP, defined as the average number of segments per molecule, will be given by

$$DP = 1/(1 - p) \qquad (5)$$

Values of DP were calculated from titrations of samples containing p-toluenesulfonic acid as follows. Let

w = weight of sample in g.
t = titer in moles of potassium hydroxide
S = mean molecular weight of one segment
(S = half the molecular weight of —ORO—COR'CO—)
N_0 = number of moles of segments in the sample
γ = ratio of moles of p-toluenesulfonic acid monohydrate (mol. wt. = 190) to moles of segments
$w = SN_0 + (1 - p)18N_0 + 190\gamma N_0$
$t = (1 - p)N_0 + \gamma N_0$

Eliminating N_0 from these two equations and solving

$$1/(1 - p) = \frac{w - 18t}{(S + 190\gamma)t - \gamma w} \qquad (6)$$

According to (5) this expression is also equal to the degree of polymerization. The average molecular weight M_n is of course $S(DP) + 18$.

The average chain length, *i. e.*, the average number of atoms in the chain skeleton, has been taken to be

$$Z_n = zDP + 1 = z/(1 - p) + 1 \qquad (7)$$

where z is the mean number of chain atoms per segment. (For example, z for the decamethylene glycol–adipic acid polyester is 9.) The "1" has been included in (7) to represent the O atom of the terminal OH group.[8]

Discussion of Errors.—The predominant source of error in the results presented in this paper lies in the average molecular weight determination. The method given above assumes that no deleterious side reactions occur, that no appreciable quantities of impurities functionally capable of entering the reaction are present, and that the concentrations of unreacted OH and COOH groups are equal. In defense of the first of these assumptions, it can be pointed out that esterification is known to proceed without appreciable side reactions at moderate temperatures. The latter two assumptions depend upon the purity of the reactants and the quantities of reactants lost by volatilization (see above). The following discussion concerns the effects on the results of a deficiency of one reactant, and of certain impurities conceivably present.

(8) The interpretation of the results presented below would not require any modification if the "1" in (7) had been omitted. This equation must be regarded as a slightly arbitrary definition of Z_n.

Let $N_0'/2$ and $N_0''/2$ be the numbers of dibasic acid and of glycol segments, respectively, in the polymer. Let $r = N_0'/N_0''$. The extent of reaction p will be defined here as the ratio of ester groups to N_0', which equals the number of ester groups plus unreacted carboxyl groups. The total number of segments is given by

$$(N_0' + N_0'')/2 = N_0'(1 + r)/2r$$

The total number of ends of chains, *i. e.*, the total number of unreacted functional groups, is equal to

$$2N_0'(1 - p) + N_0'' - N_0' = 2N_0'(1 - p) + N_0'(1 - r)/r$$

Since each molecule has two ends

$$DP = \frac{\text{No. of segments}}{\text{(No. of ends)}/2} = \frac{1 + r}{2r(1 - p) + (1 - r)} \qquad (8)^9$$

When glycol and adipic acid segments are present in exactly equal numbers, $r = 1$, and (8) reduces to (5).

Reëxamination of the derivation of (6) shows that when r is not unity, the value of $1 - p$ derived from (6) will differ negligibly from $1 - p$ as defined here. The per cent. error in $1 - p$ calculated from (6) is approximately equal to the percentage difference between the weight of the polymer sample and the weight of another sample containing the same number of dibasic acid residues and having $r = 1$.

The error ΔDP introduced by calculation of DP from (5) when $r \neq 1$ is given by equation (5) minus equation (8).

$$\Delta DP = \frac{p(1 - r)}{(1 - p)(1 - r) + 2r(1 - p)^2} \qquad (9)$$

When p is near unity and $(1 - r)$ is small compared with $(1 - p)$, *i. e.*, when the excess of one segment is very small

$$\Delta DP \cong \frac{1 - r}{2(1 - p)^2} \cong (1 - r)(DP)^2/2 \qquad (10)$$

When glycol is present in excess $r < 1$ and ΔDP is positive; that is, the DP calculated from (5) is too large. When acid is present in excess, $r > 1$ and the calculated DP's are too small.

The approximate percentage error is

$$100(1 - r)DP/2 \qquad (11)$$

or

$$(\%\text{ excess of one segment}) \times DP/2 \qquad (11')$$

The approximate percentage errors in Z_n and in Z_w (the "weight average" chain length, *cf. seq.*),

(9) An equivalent equation has been derived by the author previously by a different method, THIS JOURNAL, **58**, 1877 (1936), equation (32). The above notation coincides with that introduced in the paper referred to.

since both are approximately proportional to DP over most of the range investigated, are also given by (11) or (11′). The approximate percentage error in $Z_w^{1/2}$, the abscissa in Figs. 2, 3, 4 and 5, is therefore

$$100(1 - r)DP/4 = 100(1 - r)Z_n/4z$$

It will be pointed out later that $Z_w \cong 2Z_n$, except at low values of Z_n. Hence, the % error in $Z_w^{1/2}$ is approximately

$$100(1 - r)Z_w/8z \qquad (12)$$

It follows that for a given value of $(1 - r)$ the *magnitude* of the abscissa error in the above-mentioned figures increases with the *cube* of the abscissa ($Z_w^{1/2}$) value. If, for example, in the polymerization of decamethylene glycol and adipic acid 0.10% excess of one reactant were present, the *magnitudes* of the errors in $Z_w^{1/2}$ at $Z_w^{1/2} = 10$, 20, 30 and 40 would be, respectively, 0.014, 0.11, 0.38 and 0.89. At $Z_w^{1/2} = 29$ the error would be about equal to the diameter of one of the experimental points in Fig. 3.

A similar analysis has been applied to the effects of a monofunctional impurity such as decyl alcohol, glycol and dibasic acid being present in equivalent amounts. The same equations, (8) to (12) inclusive, may be used if r is taken as the molar ratio of glycol to glycol plus the monofunctional reactant. Similarly, if a small amount of the glycol were replaced, mole for mole, by an hydroxy acid, these same equations could be used, taking r = (moles dibasic acid)/(moles dibasic acid plus hydroxy acid).

Results

Viscosity and Number Average Chain Length.—The present investigation was undertaken as a result of the accidental observation that the logarithm of the viscosity η of a linear polyester is approximately a linear function of the square root of the (number) average chain length. Experimental results are shown in Fig. 1 for the polyester formed from decamethylene glycol and sebacic acid. A straight line has been drawn through the points for comparison. Similar graphs of viscosities of the decamethylene glycol–adipic acid and diethylene glycol–adipic acid polyesters showed that in these cases also log η is approximately a linear function of the square root of the (number) average chain length Z_n. In all three cases, however, the experimental points seem to follow curves (concave toward the abscissa) which deviate slightly from straight lines (see Fig. 1).

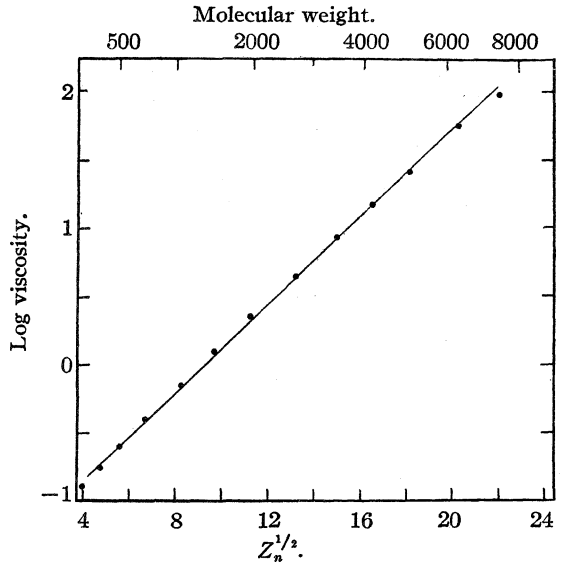


Fig. 1.—Decamethylene sebacate: log viscosity in poises at 109° *vs.* the square root of the *number average* chain length. Average molecular weights are included at the top of the figure.

Consideration of Various Averages.—When seeking a relationship between the viscosity and the average chain length of a synthetic polymer, such as a polyester, one must keep clearly in mind that these substances ordinarily are extremely inhomogeneous; some of the molecules of which they are composed are much smaller and some are much larger than the average. It would not seem improbable that the viscosity would depend upon the nature of the distribution of molecular species about the average molecular weight, as well as upon the average molecular weight itself.

Fortunately, the exact nature of the distribution of molecular species in linear polyesters is known from previous work. It has been shown[9] that the number of molecules possessing x segments is

$$N_x = N_0(1 - p)^2p^{x-1} \qquad (13)$$

where p is the extent of reaction as previously defined and N_0 is the total number of segments.[10] Let Z_x[11] refer to the chain length of the species of molecule possessing x segments. In accord with (7)

$$Z_x = zx + 1 \qquad (14)$$

or

$$Z_x \cong zx \qquad (14')$$

(10) Equation (13) rests entirely upon the postulate that reactivity of terminal functional groups does not depend on the chain length. This postulate has been confirmed by both experiment and theory.[6]

(11) Z_x must not be confused with Z_n. The latter is the number *average* chain length; the former is the chain length of an *individual* species.

The number of different average chain lengths which one could deduce for a mixture such as a polyester is unlimited. The common average molecular weight, obtained directly from end-group determinations, osmotic or cryoscopic measurements, is the *number* average.[12] The number average chain length is defined as

$$Z_n = \sum Z_x N_x / \sum N_x \qquad (15)$$

These summations, as well as those to follow, are all to be taken from $x = 1$ to ∞. Substituting (13) and (14) in this equation and evaluating the resulting summations leads to (7), which may be expressed approximately

$$Z_n \cong z/(1 - p) \qquad (7')$$

Another average, which is less familiar, is the *weight* average.[12] This is defined as

$$Z_w = \sum Z_x W_x / \sum W_x \qquad (16)$$

where W_x is the total weight of all molecules having chain length x. To a very slight approximation W_x is proportional to $Z_x N_x$. Hence

$$Z_w = \sum Z_x^2 N_x / \sum Z_x N_x$$

Substituting from (13) and (14′), we have

$$Z_w = z \sum x^2 p^{x-1} / \sum x p^{x-1} \qquad (17)$$

Upon evaluating the summations

$$Z_w = z(1 + p)/(1 - p) \qquad (18)$$

By comparison with (7′)

$$Z_n - {}^1/_2 Z_w = z/2 \qquad (19)$$

a useful formula for calculating Z_w from Z_n.

In similar fashion it can be shown that the root-mean-square chain length is

$$Z_{rms} = (1 + p)^{1/2}/(1 - p) \qquad (20)$$

i. e., it is the geometric mean of the weight and number averages.

From (7′), (18) and (20)

$$Z_n : Z_{rms} : Z_w :: 1 : (1 + p)^{1/2} : (1 + p) \qquad (21)$$

Except when the molecular weight is low, p is near unity. Hence this ratio is approximately $1 : \sqrt{2} : 2$. That is, for linear polyesters *these averages*, as well as many others which could be derived, *are approximately proportional to one another*. It follows, necessarily, that if log η is approximately linear with $Z_n^{1/2}$, it must also be approximately linear with the square root of other average chain lengths. The deviation from linearity will be slightly greater than, or for some averages perhaps less than, the deviation from linearity in the log η *vs.* $Z_n^{1/2}$ relationship (Fig. 1), since the various averages are only *approximately* proportional to one another.

Viscosity and Weight Average Chain Length.— Plots of log η *vs.* $Z_w^{1/2}$ are shown for four polymers, respectively, in Figs. 2, 3, 4 and 5. The complete set of data from one of the experiments with decamethylene adipate is presented in Table I. In all cases log η is more nearly linear with $Z_w^{1/2}$ than with $Z_n^{1/2}$. For decamethylene sebacate and decamethylene adipate there are no deviations from the straight line which are greater than the experimental error, except perhaps below $DP = 2$. In the latter case (Fig. 3) the relationship applies throughout the average molecular weight range 300–10,500, in which the viscosity increases *three thousand-fold*.

TABLE I

DECAMETHYLENE GLYCOL–ADIPIC ACID POLYESTER

Experiment II, 109°, 0.20 equivalent %, *p*-toluenesulfonic acid catalyst.

Time, minutes	$DP = 1/(1 - p)$	M_n	Z_n	Z_w	$Z_n^{1/2}$	$Z_w^{1/2}$	η in poises
25	2.98	442	27.86	46.7	5.28	6.83	0.230
45	5.21	759	47.91	86.8	6.92	9.32	0.437
67	8.49	1225	77.4	145.8	8.80	12.08	0.927
98	14.13	2027	128.2	247.4	11.32	15.73	2.30
126	18.45	2640	167.0	325.0	12.92	18.03	4.40
163	25.35	3620	229.1	449	15.13	21.19	10.00
190	29.34	4190	265.1	521	16.28	22.83	16.26
223	35.9	5120	324.4	640	18.01	25.29	28.0
265	44.3	6320	400.1	791	20.0	28.1	60.7
308	53.5	7620	482.6	956	22.0	30.9	130
363	63.6	9060	574	1139	23.9	33.7	253
415	73.7	10500	664	1320	25.8	36.3	480

The results from three different experiments on decamethylene adipate are shown as solid circles (Expt. II), open circles (Expt. IV) and squares (Expt. V), respectively, in Fig. 3. In Expt. II the glycol had been purified according to the first procedure described above; in Expts. IV and V glycol purified by the second, and more rigorous, procedure (see above) was used. The amount of catalyst was 0.20 equivalent % in Expts. II and IV, and 0.10 equivalent % in Expt. V. The coincidence of the results from these experiments with the same straight line provides some assurance that the glycol was adequately pure. It also demonstrates that the presence of very small amounts of *p*-toluenesulfonic acid did not affect the viscosities appreciably.

Deviations at moderate molecular weights in the case of decamethylene succinate (Fig. 4) may

(12) The terms "number average" and "weight average" were introduced by E. O. Kraemer and W. D. Lansing, *J. Phys. Chem.*, **39**, 153 (1935), in order to differentiate the two averages defined by equations (15) and (17), respectively. Wherever the term "average" has been used in this paper without specifying which average, it is the number average which is referred to.

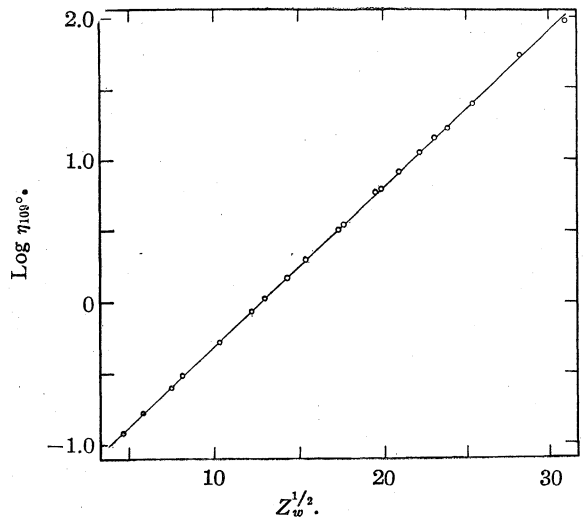


Fig. 2.—Decamethylene sebacate: log viscosity in poises at 109° *vs.* the square root of the *weight average* chain length.

be due to loss of succinic anhydride. The resulting deficiency in acid would make r (see equations (8) and (10)) become less than unity. Hence, the error in DP, and also in $Z_w^{1/2}$, would be positive, in agreement with the data. In an experiment in which the pressure was maintained somewhat lower than usual, the deviations were greater, and they became appreciable at an earlier stage of the polymerization.

In several experiments with decamethylene sebacate and with the adipate, at molecular weights of 8000 or greater, the $Z_w^{1/2}$ values suddenly

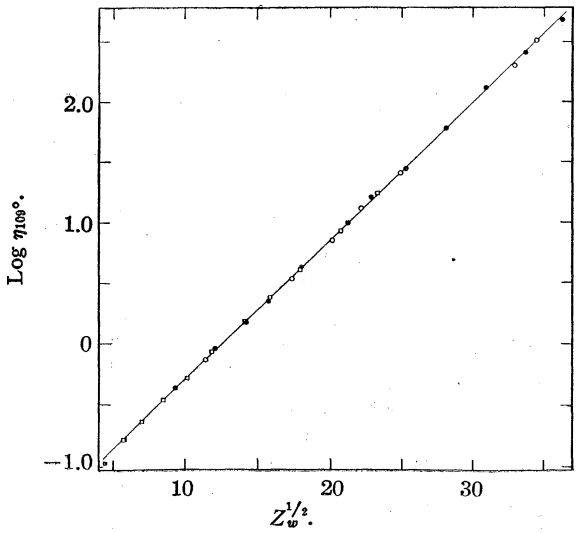


Fig. 3.—Decamethylene adipate: log viscosity in poises at 109° *vs.* the square root of the *weight average* chain length; □, 0.10 equiv. % of catalyst; ○ and ●, represent separate experiments with 0.20 equiv. % of catalyst.

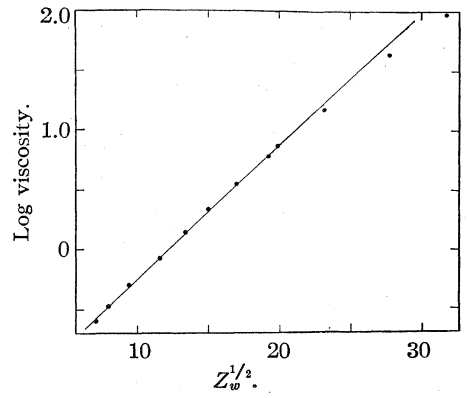


Fig. 4.—Decamethylene succinate: log viscosity in poises at 109° *vs.* the square root of the *weight average* chain length.

fell to the right of the straight lines in Figs. 2 and 3, respectively. This deviation, once it set in, always persisted at succeeding measurements, sometimes increasing in magnitude. In the experiments in which the deviation was pronounced, the pressure had been reduced below 100 mm. Perhaps these deviations are due, similarly, to volatilization of the less readily formed cyclic anhydrides of sebacic and adipic acid.

The experimental results for diethylene adipate (see Fig. 5, solid and half-filled circles) deviate considerably from the straight line at low chain lengths. In this particular case there is an appreciable change in density with chain length at low average molecular weights (*cf. seq.*). If in the low molecular weight region the viscosities

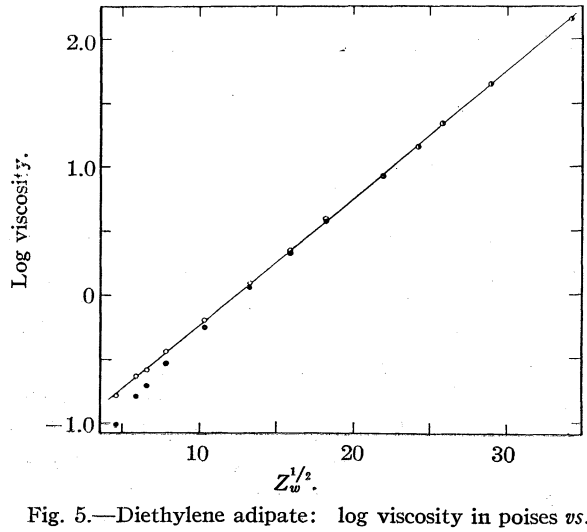


Fig. 5.—Diethylene adipate: log viscosity in poises *vs.* the square root of the *weight average* chain length; ● and ◑ represent experimental data at 109°; ○, viscosities corrected to constant density (1.1240 g./cc.); ◑, viscosities for which this correction would be negligible.

measured at constant temperature (109°) are converted to viscosities at constant *density, i. e.,* to the limiting density reached at higher chain lengths, a satisfactory linear plot (see open circles) is obtained throughout the range. The propriety of this adjustment will be discussed later.

The equations of the straight lines drawn in Figs. 2, 3, 4 and 5 are as follows

For decamethylene sebacate at 109°

$$\log_{10}\eta = -1.429 + 0.1108Z_w^{1/2} \qquad (2.2)$$

For decamethylene adipate at 109°

$$\log_{10}\eta = -1.435 + 0.1144Z_w^{1/2} \qquad (2.3)$$

For decamethylene succinate at 109°

$$\log_{10}\eta = -1.37 + 0.112Z_w^{1/2} \qquad (2.4)$$

The numerical quantities in (2.4) are less certain for reasons already discussed.

For diethylene adipate at constant density (1.1240 g./cc.)

$$\log_{10}\eta = -1.213 + 0.0992Z_w^{1/2} \qquad (2.5)$$

This equation is also satisfactory at constant temperature, 109°, at $Z_w > 100$; *i. e.,* at $M_n > 1700$.

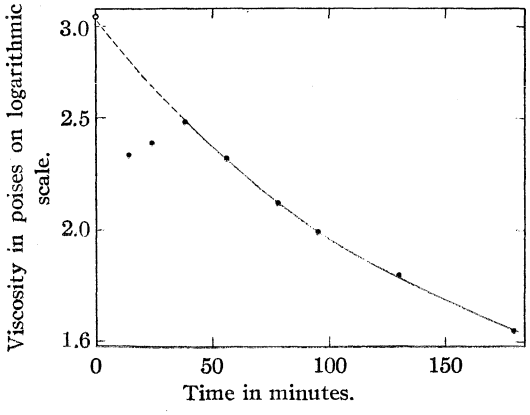


Fig. 6.—Viscosity at 109° of 19.7% mixture of series II (see Table II) as a function of time: ●, experimental points; ○, calculated initial viscosity.

The excellent linear relationships between log η and $Z_w^{1/2}$, obtained in several cases, do not prove that Z_w is necessarily the particular average to which log η should be related. Deviations when other averages are used are too small for a definite decision. Experiments with mixtures of polymers, which will be described next, have shown conclusively that the viscosity is primarily related to the *weight average* chain length.

Viscosities of Mixtures.—A low and a high molecular weight decamethylene adipate polymer were prepared at 202° without catalyst. The viscosities of various mixtures of these were measured at 109°. In spite of the stirring produced by the stream of nitrogen passing through the viscometer, dispersion of the two polymers into one another was very slow. From fifteen to thirty minutes were required before significant viscosities could be measured. Furthermore, the viscosity decreased continuously with time of heating at 109°. This decrease is believed to be due to ester interchange, which, though it does not affect Z_n, may change the distribution of various species, and in this way bring about a decrease in Z_w.[13]

The initial viscosities of the mixtures were determined by extrapolation of log η as a function of time to zero time, as shown in Fig. 6. The first two points in this figure are low due to incomplete mixing. Succeeding points fall on a smooth curve, which has been extrapolated to $t = 0$. Initial viscosities determined in this way for several mixtures of each of two pairs of decamethylene adipate polymers are given in the second column of Table II. A liberal estimate of the error involved in the extrapolation is included in parentheses.

The Z_w values for the individual polymers from which the mixtures were prepared (see 0 and 100% rows in Table II) were obtained from their viscosities by interpolation in Fig. 3. Their Z_n's were then calculated from Z_w's using equation (19). It should be noted that this method for determination of Z_n is equivalent to interpolation from the line (slightly curved) drawn through the experimental points when log η is plotted against $Z_n^{1/2}$.

TABLE II

VISCOSITIES OF MIXTURES OF DECAMETHYLENE ADIPATE POLYMERS

% by weight of higher molecular weight polymer	$\eta_{109°}$ observed	Z_n	Z_w	Calculated η's From number average	From weight average
	Series I				
(0)	0.466 (±0.002)	50.9	92.5		
16.3	1.75 (±0.15)	59.5	223.1	0.58	1.88
28.5	4.1 (±0.3)	68.0	320.6	0.72	4.15
50.4	13.5 (±0.5)	91.9	496	1.20	13.2
66.4	27.5 (±1.0)	124	624	2.18	26.9
81.8	53 (±2)	186	747	5.6	50.0
(100)	97 (±2)	451	893		
	Series II				
(0)	0.532 (±0.002)	55.7	102.2		
10.1	1.45 (±0.1)	61.2	194.4	0.61	1.45
19.7	3.03 (±0.1)	67.6	282.0	0.71	3.06
40.0	11.7 (±0.7)	86.5	467	1.07	10.9
(100)	164 (±3)	512	1014		

(13) The decrease in viscosity of a mixture with time of heating is being investigated further, and will be discussed in detail in a later paper.

Z_n's of mixtures have been obtained by number averaging the Z_n's of the components.

$$Z_n(\text{mixture}) = \frac{Z_{n,1}N_1 + Z_{n,2}N_2}{N_1 + N_2}$$

where the subscripts 1 and 2 refer to the component polymers, and N_1 and N_2 represent numbers of molecules of each polymer, respectively. Since $Z_{n,1}N_1$ and $Z_{n,2}N_2$ are proportional to the weight fractions w_1 and w_2, respectively

$$Z_n(\text{mixture}) = \frac{1}{w_1/Z_{n,1} + w_2/Z_{n,2}} \qquad (22)$$

Z_w's of the mixtures have been obtained by weight averaging Z_w's of components

$$Z_w(\text{mixture}) = w_1Z_{w,1} + w_2Z_{w,2} \qquad (23)$$

The viscosity "calculated" from the number average for a given mixture (column five) was obtained by taking the square root of Z_n for the mixture and interpolating to the corresponding η from the log η *vs.* $Z_n^{1/2}$ plot (not included here). Similarly, the viscosity "calculated" from the weight average (last column) was obtained from Z_w for the mixture using the log η *vs.* $Z_w^{1/2}$ plot (Fig. 3). The observed viscosities throughout the concentration range are in excellent agreement with those calculated on the weight average basis. The great disparity between the two calculated viscosities given in Table II is indicative of the sensitivity of the calculated viscosity to the method of averaging. Close agreement with a viscosity calculated on the basis of some other average could not be obtained, unless this average is always very nearly equal to the weight average. Not only is log η a linear function of $Z_w^{1/2}$ for a polyester having the "normal" distribution of various sized species obtained by ordinary polymerization, but log η is the *same linear function* of $Z_w^{1/2}$ for the wide variety of distributions obtained by mixing the low and high molecular weight polymers.

Viscosity–Temperature Relationships.—Viscosities of molten polyesters, prepared at 202° without catalyst, were measured at several temperatures from 202° to about 80°, which is a little above their melting points: 73° for decamethylene sebacate, 74° for decamethylene adipate, 69° for decamethylene succinate[14]; diethylene adipate polymers never could be induced to solidify even at the temperature of dry-ice. At the highest temperature, usually 202°, for which the viscosity is reported, the polymerization rate was appreciable. The first determination was therefore made at this temperature; successive viscosities were measured at intervals of several minutes, after which the polymer was cooled quickly to the next lower temperature (167°), where the rate of polymerization was much slower. The 202° viscosity was obtained by a slight extrapolation to the time when the temperature was lowered. Two viscosity determinations were carried out quickly at 167°, and the temperature was dropped to 138°. At this temperature and below, further polymerization was negligible during a reasonable length of time. After measuring the viscosity at the lowest temperature, the viscosity at 202° was determined again. After proper correction for the viscosity increase during the additional 202° heating period, the latter 202° viscosity agreed with the first.

TABLE III

VISCOSITY–TEMPERATURE DATA

Diethylene adipate polymer M_n = 900		Decamethylene adipate polymer, M_n = 4510	
Temp., °C.	Poises	Temp., °C.	Poises
167.0	0.168	201.5	3.25
137.6	.283	167.0	5.50
116.0	.454	137.9	9.98
99.2	.716	115.9	16.80
79.2	1.36	96.2	30.1
55.3	3.66	82.4	47.5
34.3	11.95		
19.2	38.3		
0.2	280		

Typical data are given in Table III; all results are included in Figs. 7, 8 and 9, where log η is plotted against the reciprocal of the absolute temperature T. The average molecular weight is included with each curve. According to the well-known equation

$$\log \eta = A' + B/T \qquad (24)$$

the points in Figs. 7, 8 and 9 should follow straight lines. This is not the case except for a range of about 50° above the melting points of the decamethylene glycol polymers. The straight lines in Figs. 7 and 8 have been drawn through the points in this region. The convex downward curvature which occurs in all cases studied is characteristic of many long chain compounds[15]; *e. g.*, *n*-paraffin hydrocarbons, long chain esters, and alkyl halides. The slopes of the diethylene adipate curves became quite large at low temperatures; *i. e.*, the temperature coefficient of viscos-

(14) These are the melting points given by C. S. Fuller and C. J. Frosch, THIS JOURNAL, 61, 2575 (1939).

(15) See M. Souders, *ibid.*, 59, 1252 (1937).

ity becomes very great. This behavior is characteristic of substances supercooled to the "glassy" region below their melting points.[16]

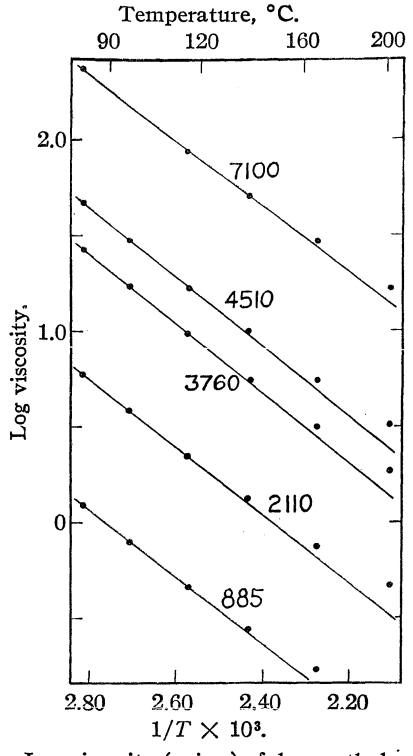


Fig. 7.—Log viscosity (poises) of decamethylene adipate polymers *vs.* reciprocal absolute temperature. Figures refer to average molecular weights of the five polymers.

The most important feature of these results is the slight dependence of the viscosity–temperature coefficient (d ln η/dT) on molecular weight. The slopes of the straight lines for decamethylene adipate (Fig. 7) are the same within 3%, which is within the experimental error. The slopes of the lines in Fig. 8 for the two decamethylene sebacate polymers are in similar agreement. The deviations from the straight lines at higher temperatures are slightly greater at low molecular weights. Careful examination shows that the curves for the three diethylene adipate polymers (Fig. 9) are parallel, except for very slight increases in slope toward higher molecular weights.

To the extent that the temperature coefficient of η is independent of molecular weight, equation (2) must be applicable at any temperature at which the polymer is molten. Furthermore, C in (2) must be independent of temperature. Within a

(16) See, for example, the results of G. S. Parks, L. E. Barton, M. E. Spaght and F. W. Richardson, *Physics*, **5**, 193 (1934), on the viscosity of supercooled glucose as a function of temperature.

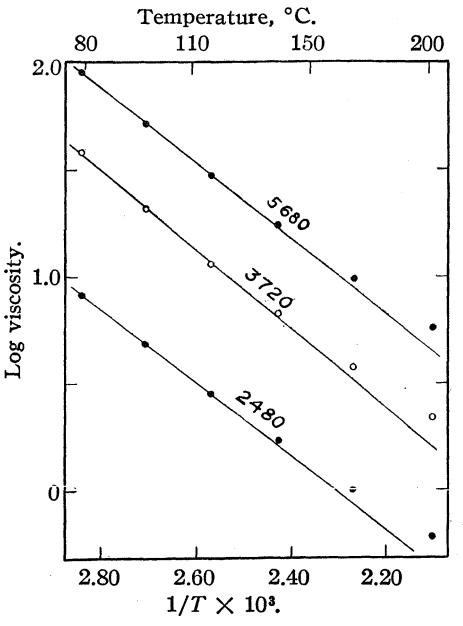


Fig. 8.—Log viscosity (poises) *vs.* reciprocal absolute temperature: ●, decamethylene sebacate; ○, decamethylene succinate; average molecular weights are included.

temperature interval in which equation (24) is applicable, (2) becomes

$$\log \eta = D + B/T + CZ_w^{1/2} \qquad (25)$$

where η is expressed as a function of chain length and temperature. (D is a new constant and B and C are the same constants used in previous equations.)

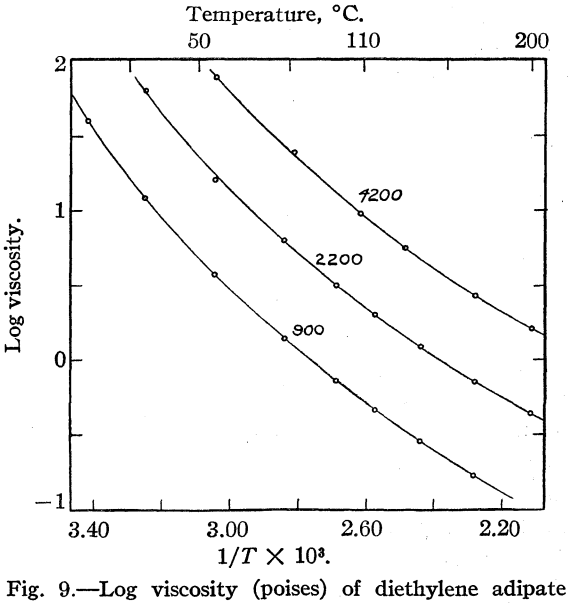


Fig. 9.—Log viscosity (poises) of diethylene adipate polymers *vs.* reciprocal absolute temperature; average molecular weights are included.

TABLE IV
MEAN SLOPES OF LOG η *vs.* $1/T$ (80 TO 120°)

Polymer	B	Activation energy for viscous flow in kcal.
Decamethylene sebacate	1760	8.05
Decamethylene adipate	1800	8.23
Decamethylene succinate	1870	8.55
Diethylene adipate	1840	8.40

Values of B for the temperature interval 80–120° are given in Table IV. Activation energies E for viscous flow, which are equal to $(2.3R)B$, are given in the third column of Table IV. This quantity has been interpreted as the energy required for the occurrence of the elementary process which is responsible for viscous flow. Eyring and Ewell[17] have pointed out the analogy of this elementary process to a chemical reaction, and have developed a theory of viscous and plastic flow on this basis. According to their concepts, E consists of two parts: the energy of formation of a hole in the liquid large enough for the entire molecule, or for that part of it which is displaced in the elementary process, to move into; and of the activation energy required for the displacement to occur when a hole is available. For simple molecules E is usually one-fourth to one-third of the heat of vaporization.[17b] Ewell[17c] has concluded, on the basis of the magnitudes of the activation energies E for viscous flow in rubber and other polymeric substances, that the hole in these cases must be only a fraction of the size of the entire molecule. Thus, the elementary process must consist either of a displacement of a small portion of the entire molecule, or of a displacement of the entire molecule through a comparatively small distance.

The activation energies for viscous flow in polyesters (Table IV) are not large; they are only two or three times those for simple esters. On the same basis as above, therefore, the elementary process in liquid polyesters must consist of a displacement which is not commensurate with the size of the molecule. Moreover, the present investigation has shown that *E does not depend upon molecular size*, since the slopes in Figs. 7, 8 and 9 are independent (or very nearly so) of average molecular weight. The conclusion that the elementary processes in low and high molecular weight polyesters are identical is virtually unavoidable.[18]

(17) (a) H. Eyring, *J. Chem. Phys.*, **4**, 283 (1936); (b) R. H. Ewell and H. Eyring, *ibid.*, **5**, 726 (1937); (c) R. H. Ewell, *J. App. Physics*, **9**, 252 (1938).

(18) Ewell and Eyring[17b] have calculated the size of the molecule (probably linear) in liquid sulfur above 190° from the viscosity–temperature coefficient, *i. e.*, from E. In view of the above results with polyesters, such a calculation is probably invalid.

Densities of Polyesters.—The importance of the free volume in relation to viscosity has been emphasized by Eyring and Ewell.[17] Van Wijk and Seeder[19] have shown that the viscosities of a number of simple non-polar molecules depend entirely upon the molar volume V throughout wide variations of both temperature and pressure. Their equation, derived from theory, is

$$\eta = \left(\frac{V}{V-b}\right)\varphi \qquad (26)$$

where b and φ are parameters dependent upon structure alone; b is the actual volume occupied by the molecules, and $V - b$ is the free volume. For other liquids they found that φ is dependent upon temperature to a small degree; in the case of configurational liquids (*e. g.*, water and alcohols) the variation of φ with temperature accounts for a considerable portion of the viscosity–temperature coefficient. In all cases, viscosity appears to vary inversely with the free volume.

These considerations provoked inquiry into the relation of the free volume to the viscosity of long chain substances. If the average actual volume of one chain atom (*i. e.*, b per chain atom) is considered to be constant, then the free volume per cc. must decrease linearly with the density when chain length or temperature is varied. Therefore, density data should offer some insight into the behavior of the free volume.

Densities of decamethylene adipate and diethylene adipate polymers were determined from time to time during polymerization at 109° in the presence of 0.1% *p*-toluenesulfonic acid catalyst. In Fig. 10 the densities are plotted as functions of the average chain lengths Z_n calculated from viscosities. The density of decamethylene adi-

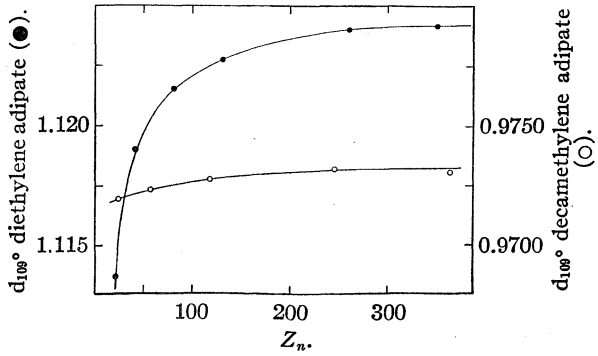


Fig. 10.—Densities (g./cc.) at 109.0° *vs. number average* chain length: ○, decamethylene adipate; ●, diethylene adipate.

(19) W. R. Van Wijk and W. A. Seeder, *Physica*, **4**, 1073 (1937); *ibid.*, **6**, 129 (1939).

pate, over the range investigated, increases by about 0.0013 density unit. This is no greater than the density change for a 2° temperature rise. Therefore, the free volume must be essentially independent of chain length, and the observed dependence of viscosity on chain length must be situated entirely in φ of (26). In other words, the observed empirical relationship (2) probably represents the direct dependence of viscosity on chain length, unobscured by effects of chain length on other properties of the liquid. If the free volume (per cc.) were not constant with increase in molecular weight, this simple relationship might not have been apparent.

The increase in density of diethylene adipate with chain length is much larger (see Fig. 10). It is tempting, because of the consequences, to attribute this change in density to a decrease in free volume. However, it should be pointed out first that the variation of d with Z_n can also be explained if it is assumed that the average molar volume V is given by

$$V = aZ_n + e \qquad (27)$$

where a is the mean volume occupied per chain atom and e is an end-group correction. For the average molecular weight, similarly

$$M_n = \alpha Z_n + \epsilon$$

where α is the mean molecular weight per chain atom of the structural unit, and ϵ is an end-group correction equal to $18 - \alpha$ (see definition of Z_n, equation (7)). Then

$$1/d = V/M_n = g + h/Z_n \qquad (28)$$

where d is density in g./cc., and

$$g = a/\alpha \qquad h = e/\alpha - \epsilon/\alpha d$$

Since the change in d is small, h as well as g may be considered constant. Then, if V is properly expressed by (27), the reciprocal of the density must be linear with $1/Z_n$ according to (28).

TABLE V

DENSITIES OF DIETHYLENE ADIPATE AT 109.0°

Z_n	d, g./cc.	$1/d$	$1/d$ calculated from (27)
21.2	1.1137	0.8979	0.8982
42.1	1.1190	.8936	.8936
81.5	1.1216	.8916	.8914
131	1.1228	.8906	.8906
261	1.1240	.8897	.8898
351	1.1241	.8896	.8896

A comparison of observed reciprocal densities with those calculated from (28), using $g = 0.8891$ and $h = 0.192$, is given in Table V. The agreement is probably within the experimental error. These values of g and h correspond to $a = 14.80$ cc. and $e = 4.43$ cc. ($\alpha = 16.63$ and $\epsilon = 1.38$ for diethylene adipate). The end-group correction, 4.43 cc., indicates that the volume occupied by the end-groups (—OH and —COOH) is greater by this amount than three times the mean volume per chain atom; *i. e.*, than $^3/_{13}$ of the volume occupied by the structural unit

$$—O—(CH_2)_2—O—(CH_2)_2—O—CO—(CH_2)_4COO—$$

Perhaps this is not unreasonable.

When the specific volumes ($1/d$) of n-paraffin hydrocarbons from C_{10} to C_{40} are plotted against $1/Z_n$, approximately a straight line is obtained, but the slope (h) leads to a volume of about 38 cc. for the two terminal H atoms. This value, which is more than twice the volume occupied by one $—CH_2—$ group, is unreasonable. The author is of the opinion that in this case the increase in density with chain length must be due, principally, to a decrease in free volume per chain atom. The agreement with (28) he regards as fortuitous.

Perhaps the density increase with chain length in the case of diethylene adipate is due likewise to a decrease in free volume, rather than to an excess volume of the end-groups. If this is true, and if (2) should be applied at constant free volume as was suggested above, then the viscosities in Fig. 5 should be corrected for the effect of the change in free volume with chain length. If it be assumed further that the effect of temperature on viscosity is entirely due to change in free volume with temperature, this correction may be introduced by converting each viscosity to the viscosity which would have been observed at the temperature at which the density equals the limiting density at large chain lengths. (Stated briefly, we assume that φ in (26) is entirely responsible for the dependence of η on chain length, and that φ is independent of temperature.)

From the viscosity–temperature coefficient (Table IV) of diethylene adipate we obtain for temperatures in the vicinity of 109°, approximately

$$\Delta \log \eta / \Delta T = 0.0125$$

From the change of density with temperature (Table VII)

$$\Delta d / \Delta T = -0.80 \times 10^{-3}$$

Combining, we obtain for the viscosity correction necessary to convert the viscosity to constant density

$$\Delta \log \eta = -15.6 \Delta d \qquad (29)$$

This simple equation is obviously valid only for small corrections.

TABLE VI

CORRECTION OF VISCOSITIES OF DIETHYLENE ADIPATE AT 109° TO VISCOSITIES AT CONSTANT DENSITY (1.1240)

Z_n	η 109° poises	$-\Delta d \times 10^4$ (from Fig. 10)	$\Delta \log \eta$ (calculated from (29))	η at d = 1.1240
14.3	0.098	150	0.223	0.164
21.1	.162	106	.165	.236
25.2	.198	80	.125	.263
33.7	.295	61	.095	.365
56.3	.563	39	.061	.647
90.6	1.16	22	.034	1.25
129	2.16	13	.020	2.26
168	3.88	8	.012	4.00

Open circles in Fig. 5 represent viscosities at the constant density, 1.1240, calculated from (29) taking $-\Delta d = 1.1240 - d$. The calculations are summarized in Table VI. The open circles fall on the same straight line with the points at higher chain lengths (half-filled circles) for which correction is negligible. Viscosities at 109° fall considerably below the straight line at small chain lengths. Thus, the interpretation presented above brings the data for low molecular weight diethylene adipate polymers into agreement with (2). The previously discussed possible explanation for the change of density with chain length of diethylene adipate cannot at present be excluded, however.

In this connection it should be mentioned that at constant temperature log η for n-paraffin hydrocarbons from C_{10} to C_{36} is definitely not linear with the square root of the number of carbon atoms ($Z_n = Z_w$ for these pure substances). With the aid of viscosity–temperature data and density–temperature data, viscosities of several n-paraffins in this range have been corrected to constant density. Log η at constant density is approximately linear with $Z^{1/2}$. The range is too brief for a definite conclusion, however. Perhaps further work will show that equation (2) is generally applicable to long chain substances at *constant free volume.*

TABLE VII

DENSITIES AND EXPANSION COEFFICIENTS OF POLYESTERS

Polyester	d at 109.0°[a] g./cc.	$-\frac{dd}{dT} \times 10^4$	Thermal expansion coeff. $= -\frac{d \ln d}{dT}$
Decamethylene sebacate	0.9378	6.6	7.0×10^{-4}
Decamethylene adipate	.9732	6.95	7.15×10^{-4}
Diethylene adipate	1.1247	8.05	7.15×10^{-4}

[a] These densities are the limiting ones for large chain lengths.

The densities of polyesters prepared without catalyst at 202° were measured at several temperatures from 80 to 167°. Within the experimental error the density is a linear function of temperature in this range. These data are listed in Table VII. The densities are a little greater and the expansion coefficients are somewhat smaller than those for analogous monomeric organic compounds.

Determination of Average Molecular Weights from Viscosities.—By means of equation (1), where $C' = C/\alpha^{1/2}$, weight average molecular weights may be calculated directly from viscosities of the polyesters. If the type of distribution is known, other averages may be computed from M_w. In particular, if the distribution is the "normal" one defined by (13) (*i. e.*, the distribution obtained by all ordinary methods of preparation), then upon taking $Z_n = M_n/\alpha$ and substituting (19) in (2)

$$M_n = (\log \eta - A)^2\alpha/2C^2 + \alpha z/2 \qquad (30)$$

by means of which the number average molecular weight can be calculated from the viscosity. Except for the small second term, log η is linear with M_n. For decamethylene adipate, for example, the viscosity being measured at 109°, equation (30) becomes

$$M_n = 603.6\ (\log \eta + 1.435)^2 + 71 \qquad (30.3)$$

Since C does not vary with temperature, molecular weights can be calculated from viscosities measured at other temperatures by converting A to the temperature of measurement, using the viscosity–temperature relationships presented above.

Equation (30) provides an unusually simple and precise method for determination of the average molecular weight of these polymers. It is true that its constants are deduced from viscosities of polymers the molecular weights of which have been determined by titration, which in itself is a simple molecular weight determination method. The titration method, however, is only applicable when purity of the reactants and precise stoichiometry of the reaction are assured, as the discussion of errors presented above makes clear. The viscosity method is not limited to such circumstances; it may be applied to polymers prepared from reactants which are not of exceptional purity, and which may not necessarily be present in exactly equivalent amounts.

It should be noted that since the molecular weight depends on the *logarithm* of η, it is not

necessary that η be determined very accurately. An error of 5% in η produces an error of only about 1.5% in M_n.

Summary

1. The viscosities (η) of molten linear polyesters having average molecular weights in the range 200 to over 10,000 have been measured. Log η has been found to be precisely a linear function of the square root of the weight average chain length throughout this range.

2. The viscosities of mixtures of two polyesters, one of them having a low and the other a high average molecular weight, agree with the same relationship, when the weight average chain length of the mixture is used therein. Thus, the relationship between viscosity and weight average chain length does not seem to depend on the type of distribution of species in the polymer.

3. The viscosity–temperature coefficient (d ln η/dT) is independent of the average molecular weight, and its magnitude is not many times greater than that found for similar monomeric substances. It has been concluded that the elementary process responsible for viscous flow must consist of displacement of only a small section of the chain, and that this elementary process is the same for polymers of all sizes.

4. The utility of the viscosity–chain length relationship as a simple and accurate means for determination of molecular weight has been discussed.

5. Densities and thermal expansion coefficients of polyesters have been measured.

6. An analysis of the errors incident to molecular weight determination by end-group titration has been presented.

CINCINNATI, OHIO RECEIVED JANUARY 12, 1940

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 728]

Esters of Alginic Acid

BY H. J. LUCAS AND W. T. STEWART[1]

Since alginic acid is a polyuronide,[2] it would be expected to form two types of esters, *viz.*, alkyl esters and acyl esters, the former because of one carboxyl group per mannuronic residue, the latter because of one or two free hydroxyl groups per mannuronic residue. Of course, the terminal residue will have one additional hydroxyl group. If all of the carboxyl groups are free or are bound as in a salt or in an ester, there would then be two free hydroxyl groups per residue (except for the terminal ones), and dialkyl esters should be possible. However, if the carboxyl groups are bound in lactone formation, then only one hydroxyl group per residue would be free. Therefore the degree of esterification which can be attained presumably would depend, at least in part, upon the extent to which the mannuronic residues of the alginic acid molecule are in the acid or in the lactone form.

Alginic acid might be expected to undergo esterification and etherification of the hydroxyl groups, much as pectin does. The latter can be formylated, acetylated and nitrated without difficulty.[3,4] Methylation of pectin fragments or of pectin which has suffered partial degradation has been accomplished by heating the silver salt with methyl iodide under pressure,[5] by dimethyl sulfate[6] and by methyl iodide and thallium ethoxide.[7] Pectin acid has been exhaustively methylated.[8] Alkylation of the carboxyl group of alginic acid has been effected by heating with methanolic hydrogen chloride.[9,10]

Acetates of alginic acid have been prepared using acetic anhydride and aqueous hydriodic acid as the acetylating agent.[11] A dimethyl ether has been obtained from alginic acid methylglycoside methyl ester (from partially degraded alginic acid and methanolic hydrogen chloride) by the use of methyl iodide and thallium ethoxide.[10]

(1) Kelco Company Fellow, 1938–39. Original manuscript received September 5, 1939.

(2) Nelson and Cretcher, THIS JOURNAL, **51**, 1914 (1929); **52**, 2130 (1930); Schoeffel and Link, *J. Biol. Chem.*, **95**, 213 (1932).

(3) Schneider and Ziervogel, *Ber.*, **69B**, 2530 (1936).

(4) Henglein and Schneider, *ibid.*, **69B**, 309 (1936).

(5) Buston and Nanji, *Biochem. J.*, **26**, 2090 (1932).

(6) F. Smith, *Chemistry and Industry*, **58**, 364 (1939).

(7) Beaven and Jones, *ibid.*, **58**, 363 (1939).

(8) Levene, Meyer and Kuna, *Science*, **89**, 370 (1939).

(9) Heen, *Tids. Kjemi Bergvesen*, **17**, 127 (1937).

(10) Hirst, Jones and Jones, *Nature*, **143**, 857 (1939); *J. Chem. Soc.*, 1880 (1939).

(11) Barry, Dillon and O'Muineachain, *Sci. Proc. Roy. Dublin Soc.*, **21**, 289 (1936).

Experimental

Alginic Acid.—This was supplied by the Kelco Company, of San Diego, who manufactured it from *Macrocystis pyrifera* by a process involving digestion of the kelp with hot aqueous sodium carbonate, precipitation of calcium alginate by the addition of aqueous calcium chloride and conversion of this to alginic acid by means of hydrochloric acid.[12] Alginic acid is a wet fibrous product of about 12% solids. The dried product leaves about 2.5% ash on ignition. For the nitration water was extracted by agitating with several portions of ethyl alcohol which were poured off. The alcohol left finally was allowed to evaporate. The alginic acid remained as a rather compact mass, water content 15%. Another portion was dissolved in aqueous sodium carbonate. The acid was precipitated from the solution by the addition of dilute hydrochloric acid. After filtration through cloth, washing twice with water and then with aqueous methanol until free of chloride, washing well with alcohol, finally with ether, and drying over sulfuric acid, the alginic acid was left as a light, fluffy mass. The ash was reduced to 2.1%. This product was used in methylation as well as in some of the nitration experiments. The presence of methanol (25%) in the water prevented peptization of alginic acid and yet allowed removal of chloride.

Nitration.—This was accomplished with a mixture of nitric acid (d. 1.47) and concentrated sulfuric acid (d. 1.84). The mixture was kept cold during the mixing of the acids and placed in a refrigerator at 3 to 5°. The product was recovered by adding ice and water and centrifuging. Mineral acid was removed by shaking the residue with ice and water and centrifuging. This was done eight times. At first, two or three preparations were worked up by filtering the nitration mixture through a sintered glass funnel, followed by washing with water. Centrifuging was found to be more satisfactory and convenient, however. Next, the nitrated product was taken up in acetone and precipitated by the addition of ether. After this was done five times, the product was placed in a vacuum desiccator over calcium chloride. The dried weight is the one recorded in Table I.

TABLE I

NITRATION OF ALGINIC ACID AT 3 TO 5°

Expt.	HNO_3, d. = 1.47, ml.	H_2SO_4, d. = 1.84, ml.	Alginic acid, g.	Moles HNO_3/moles $C_6H_8O_6$[c]	Time of standing, hr.	Product, g.	Nitrogen, %	$NO_3/C_6H_6O_6$[d]
1[a]	45	45	15	13	60	3.8	3.83	0.50[e]
2[a]	90	90	15	25	48	2.2	3.81	.49
3[b]	30	30	5	30	72	1.7	7.27	1.08
4[a]	67.5	22.5	15	19	1	12.0	5.09	0.69
5[a]	67.5	22.5	15	19	60	2.6	5.92	.83
6[a]	22.5	7.5	5	19	150	1.6	7.69	1.18
7[b]	67.5	22.5	15	23	12	9.8	5.23	0.71
8[b]	67.5	22.5	15	23	60	3.0	6.09	.85
9[a]	135	45	15	38	48	5.4	5.23	.71[f]
10[b]	45	15	5	45	48	1.8	6.94	1.01
11[b]	45	15	5	45	48	2.0	6.12	0.86

[a] Reprecipitated alginic acid, alcohol and ether washed, dried over sulfuric acid to a light, fluffy product, ash, 2.1%. [b] Alginic acid, alcohol washed, dried to a compact mass, ash, 2.5%, H_2O, 15%. [c] As free acid. [d] As lactone. [e] Ash, 0.6%. [f] Ash, 0.5%.

(12) Thornley and Walsh, U. S. Patent 1,814,981 (July 14, 1931).

For analysis all samples were dried at 60° and 30 mm. over phosphorus pentoxide. Nitrogen was determined by the micro Dumas method. The analytical results are given in Table I.

Methylation.—Several attempts were made to methylate alginic acid with dimethyl sulfate and aqueous sodium hydroxide. It was found necessary to work at a temperature of 60° and to repeat the methylation twice with fresh reagents. An opalescent solution resulted. The product was recovered by acidifying with hydrochloric acid cold, centrifuging, and washing the precipitate four times with water, centrifuging each time. The product was dried by washing with ether, in which the methylated product was insoluble. Less than one methoxyl group per mannuronic residue was introduced. The methoxyl content of these and other preparations was determined by the method of Viebock and Schwappach[13] after drying at 60° and 30 mm. over phosphorus pentoxide (Table II).

TABLE II

METHYLATION OF ALGINIC ACID

Experiment		1	2	3	4
Alginic cpd.		Acid	Acid	Acid	Ag salt
Taken, g.		17.6	1.76	56.5	1.45
Reagent	Cpd.	Me_2SO_4 + NaOH	0.2 *M* CH_2N_2 in Et_2O		MeI
	g.	[a]	35.7[b]	2485	7.25
Methylated product (A)	g.	9.8	1.6	51	0.9
	MeO, %	9.78	18.2	22.4	2.44
Ammonolyzed product (B)	MeO, %	...	5.08	7.96[c]	..
MeO per C_6 unit	A	0.58	1.13	1.40	0.14
	B	...	0.29	0.48	..

[a] Me_2SO_4, 75.6 g.; NaOH, 30%, 80 g. Three treatments at 60°. [b] For eight hours. [c] After forty-eight hours; MeO was 8.16% after twenty-four hours.

Best results were obtained with diazomethane. The alginic acid used in the methylations with diazomethane was the fluffy reprecipitated product. It was not freed of ether but was treated directly with diazomethane. Seven portions of 500 ml. (355 g.) of 0.2 *M* diazomethane in ether were added over a period of two hundred and forty hours to the acid (56.5 g. of the original dry acid). The final volume was 3.5 liters. The yellow color after addition of the first and second portions largely disappeared in a few hours, but after subsequent additions diminished but little on standing. The methylated alginic acid was recovered by drawing off most of the ether through a filter stick. The rest was removed by suction filtration under a rubber dam and by vacuum drying over concd. sulfuric acid.

Silver alginate was prepared by adding aqueous silver nitrate to aqueous ammonium alginate. The precipitate, after filtering and washing with methanol, was shaken with a solution of methyl iodide in methanol for ten hours, and the mixture allowed to stand in the dark, with occasional shaking, for two months. The product was recovered by first removing the liquid through filtration, then adding aqueous sodium cyanide to the solid and precipitating

(13) Viebock and Schwappach, *Ber.*, **63B**, 2818 (1930); *J. Assoc. Official Agr. Chem.*, **15**, 136 (1932).

TABLE III

METHYLATION OF NITRATED ALGINIC ACID AT 25°

Experiment		1	2	3
Nitrated acid	Table I	3	5	10
	N, %	7.27	5.92	6.94
	$NO_3/C_6H_8O_5$	1.08	0.83	1.01
	Grams	0.50	2.0	0.50
Reagents		2.4 g. HCl in 15 ml. MeOH	1.25 g. Me_2SO_4 0.4 g. NaOH 2 g. H_2O	9.1 g. MeI 0.13 g. Ag_2O 5 ml. Me_2CO
Time, hours		48	0.5	72
Product	Grams	0.4	1.5	0.4
	N, %	7.20	5.50	6.32
	MeO, %	10.3	3.26	6.28
Per C_6 unit	NO_3	1.18	0.78	0.97
	MeO	0.79	.21	.44

(Table IV). The materials had been dried at 60° and 30 mm. over phosphorus pentoxide for twenty-four hours. The alginic acid, the nitrated alginic acid and the material methylated by means of dimethyl sulfate and sodium hydroxide were dissolved in aqueous sodium hydroxide, using just enough base to effect solution. The product obtained by the use of diazomethane was dispersed in water. Observations were limited to very dilute solutions, 0.3%, because at higher concentrations the Tyndall effect was so pronounced that satisfactory readings could not be made.

Titration.—The neutralization equivalent of nitrated alginic acid dried at 60° and 30 mm. over concd. sulfuric acid and solid caustic was determined by titrating a solution of the sample in acetone, obtained by shaking for about two hours, with standard base to a phenolphthalein end-point. The combined neutralization–saponification equivalent was obtained by heating the sample with an excess (10%) of aqueous standard base for four hours on a steam-bath, and back titrating. The equivalent weights are shown in Table V. The calculations were made thus:

Neutralization equivalent = $158 + (NO_3/C_6 \times 45)$

Combined neutralization–saponification equivalent = neut. equiv./$(1 + NO_3/C_6)$.

TABLE IV

Material	Description Table	No.	Solvent	Concn., %	Rotation α	$[\alpha]^{25}D$	$[M]^{25}D \times 10^{-3}$
Alginic acid			Aq. NaOH	0.300	−0.41	−137°	−22
Nitrated product	I	5	Aq. NaOH	.300	.34	−113	−22
Nitrated product	I	10	Aq. NaOH	.300	.33	−110	−22
Methylated product	II	1	Aq. NaOH	.300	.29	− 97	−16
Methylated product	II	3	H_2O	.300	.35	−117	−23
Methylated product	II	3	H_2O	.300	.35	−117	−23

the sodium salt of partially methylated alginic acid by the addition of ethyl alcohol to the cyanide solution. After centrifuging and washing the resulting gelatinous precipitate with small amounts of water, dilute hydrochloric acid was added. The gelatinous material was centrifuged, washed with a small amount of water, then with ether, and dried over concd. sulfuric acid at 30 mm.

Methylation of different specimens of nitrated alginic acid was carried out in three different ways as shown in Table III. The product from methanolic hydrogen chloride was precipitated by the addition of ether, thoroughly washed with ether and dried at 30 mm. over solid sodium hydroxide and concd. sulfuric acid. The aqueous solution from dimethyl sulfate treatment was acidified and the residue remaining after centrifuging was washed with 25% ethanol–water and dried at 30 mm. over sulfuric acid. The acetone solution from the treatment with silver oxide and methyl iodide was diluted with methanol, precipitated with ether and dried as above.

Ammonolysis.—Ammonolysis of methylated alginic acid was carried out by allowing the material to stand with concd. ammonium hydroxide for twenty-four hours. The resulting viscous liquid was acidified, the precipitated acid was washed several times with 50% ethanol–water, then with ether, and dried as usual. The recovery was approximately 60%. The methoxyl content was determined as before.[13] The results are shown in Table II. That the reaction was essentially complete is shown by the small drop in methoxyl content on a second twenty-four-hour treatment (8.16 to 7.96% OCH_3).

Other Derivatives.—Attempts to prepare products soluble in acetone by the action of benzoyl chloride, benzyl chloride and phenacyl bromide on sodium alginate were not successful.

Optical Rotations.—Optical rotations were observed on alginic acid, on two different specimens of nitrated alginic acid and on two specimens of methylated alginic acid

TABLE V

TITRATION OF NITRATED ALGINIC ACID

From Table I		No. 8	No. 11
N, %		6.09	6.12
Neut. equiv.	Calcd.	197	198
	Found	198	200
Combined neut.–sapon. equiv.	Calcd.	107	107
	Found	104	109
Ash, %		0.3	0.1

Discussion

The various specimens of nitrated alginic acids are much alike in properties. They dissolve in aqueous sodium carbonate, from which they are precipitated on acidification. They are readily soluble in acetone, methanol and ethanol, less readily in 1-propanol, dioxane and methyl iodide, and but slightly soluble in acetic anhydride and glacial acetic acid. They are insoluble in ethyl ether, isopropyl ether and chloroform. These last serve to precipitate the nitrated alginic acids from their solutions in other solvents.

The extent to which nitration took place varied from 0.49 to 1.18 nitrate groups per mannuronic unit, calculated as the lactone (Table I). Addi-

tional purification by dissolving once more in acetone and precipitating with ether left the material essentially unchanged, as shown in experiments 3 and 10, for the nitrogen content in the first case changed from 7.27 to 7.02 and in the second case from 6.94 to 7.21%. The best yield was obtained in experiment 4, where the time was shortened to one hour. The extent of nitration, however, was low. When the time was lengthened the yield was less, and in a general way was lower the longer the period of standing. On the other hand, the degree of nitration usually increased as the time was lengthened.

The recovery of a small amount (2%) of material from the first acetone–ether liquor (Expt. 8, Table I) indicates that precipitation of a nitrated alginic acid from its acetone solution by the addition of ether is essentially quantitative. The recovered material analyzed 8.05% N (1.26 NO_3 per C_6 unit).

Since the maximum number of nitrate groups in the main products was essentially 1 per C_6 residue, the assumption is justified that the alginic acid while undergoing nitration was essentially in the lactone form unless the second free hydroxyl group would not nitrate under these conditions, even in the presence of a good excess of the nitrating mixture. This must be regarded as a possibility in view of the fact that with diazomethane less than one hydroxyl group was methylated (Table II). However, lactonization of alginic acid presumably would be as likely as that of nitrated alginic acid which was shown by titration to be lactonized when dried. Alginic acid being nitrated may have been lactonized during drying, or when put into the nitrating mixture.

The recovery of a small amount of higher nitrated product from the acetone–ether mother liquor (Expt. 8) would seem to indicate that higher nitration products are formed to some extent.

The various specimens of methylated alginic acid are alike in that they peptize in water but in solutions containing 25% methanol or ethanol they do not peptize. They are alike also in that they are slightly soluble in methanol and in acetone, insoluble in ethyl ether and in chloroform. They differ in that the diazomethane preparations are less soluble and do not reduce Fehling solution. The product obtained by the action of methyl sulfate and hot sodium hydroxide reduced Fehling solution. Thus the drastic conditions involved in methylating with dimethyl sulfate bring about degradation of the alginic acid molecule whereas this is not the case with diazomethane.

Ammonolysis of alginic acid methylated by diazomethane showed that in the two cases approximately 74 and 66%, respectively, of the total methylation had taken place on carboxyl groups, and 26 and 34%, respectively, on alcoholic hydroxyl groups (Table II). It showed also that in the first case 84% and in the second case 92% of the carboxyl groups had been methylated. These results are based on the assumption that only the carbomethoxy groups react with ammonia.

Methylation of specimens of nitrated alginic acid did not change the ratio of nitrate groups per C_6 unit. There is thus no replacement of these groups by methoxyl under the conditions employed (Table III). The calculation of nitrate and methoxyl content in the methylated product is made on the basis that the extent of lactone ring opening is equivalent to the degree of methylation.

From the optical data equivalent rotations $[M]^{25}D$ were calculated on the assumption that the dried samples of alginic acid, of nitrated alginic acid and of the alginic acid methylated by means of dimethyl sulfate were lactonized. However, in the solutions of these as examined the materials were lactone free since they were in the form of salts. The equivalent rotation of the product methylated with diazomethane agrees well with the rotations of the sodium salts of alginic acid and of nitrated alginic acid. Thus in the substances which essentially were lactone free (the data of Table II indicate that 92% of the carboxyl groups were methylated) and which had not suffered degradation, the equivalent rotations were in agreement.

The low equivalent rotation for the methylated product resulting from dimethyl sulfate treatment can be ascribed to degradation, for this was the only material which reduced Fehling solution. The drop in rotation may be the result of isomeric changes in the terminal mannuronic residues of the smaller degraded molecules. At one end the configuration about C-1 might change and at the other end a furanose structure might change over to a pyranose structure.[14]

From the data in Table V it is evident that when thoroughly dried, specimens of nitrated alginic acid go over to the lactone form.

(14) Levene, Meyer and Kuna[8] believe that in pectic acid some of the galacturonic units have the furanose structure.

This research was made possible by a grant from the Kelco Company of San Diego, California.

Summary

Alginic acid is converted into a nitrated alginic acid when in contact with nitric–sulfuric acid mixture. The ratio of nitrate groups per mannuronic unit, which varies from 0.49 to 1.2, largely depends upon the excess of nitric acid taken and upon the time of standing.

The failure to obtain higher nitration products is believed to be due to lactonization of the mannuronic units as the result either of drying the acid or of its coming in contact with concd. sulfuric acid.

When nitrated alginic acid is thoroughly dried lactonization of the carboxyl groups takes place.

Methylation of alginic acid by means of dimethyl sulfate and aqueous sodium hydroxide at 60° is not satisfactory since less than one methyl group per mannuronic unit is introduced, and degradation takes place.

Diazomethane is satisfactory as a methylating agent in that little or no degradation takes place. While the carboxyl group is undergoing methylation some methylation takes place on the hydroxyl group.

Nitrated alginic acid can be partially methylated but there is no replacement of nitrate by methoxyl groups.

PASADENA, CALIFORNIA RECEIVED FEBRUARY 6, 1940

[CONTRIBUTION FROM THE AVERY LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF NEBRASKA]

Some Fully Acetylated Sugar Acids and their Derivatives

BY GORDON B. ROBBINS AND F. W. UPSON

Interest in the fully acetylated aldonic acids has been stimulated by Major and Cook[1,2,3] through the preparation and application to synthesis of acid chlorides of these acids. A general method of preparing fully acetylated sugar acids has been reported by Hurd and Sowden,[4] who prepared fully acetylated *d*-gluconic, *d*-galactonic and *l*-arabonic acids by treating an acetic acid solution of the acetylated acid amide with nitrous anhydride. Direct acetylation of aldonic acid amides has been shown to be a simple and general method for preparing the fully acetylated amides.[5] Various acetylated amides which had been prepared by this method have been treated according to the method of Hurd and Sowden[4] to give new fully acetylated aldonic acids.

Direct acetylation of gluconic acid has been reported to be unsuccessful by Major and Cook.[3] We have found, however, that some aldonic acids can be acetylated directly. Several of these are described in the following investigation. In addition some other fully acetylated acids hitherto unknown were prepared by the method of Hurd and Sowden. Thus tetraacetyl-*d*-arabonic, pentaacetyl-*d*-gulonic, and hexaacetyl-*d*-α-glucoheptonic acids were prepared by this procedure. A modification of the method was employed in the preparation of pentaacetyl-*d*-talonic acid and pentaacetyl-*d*-mannonic acid monohydrate. These acids were prepared by treating the reaction mixture from the acetylation of the corresponding aldonic amide with nitrous anhydride.

It was impossible to prepare hexaacetyl-*d*-α-galaheptonic acid from the corresponding amide by this method. The acetylated amide proved too insoluble in any solvents at suitable temperatures.

The unusual stability of *d*-α-galaheptonic acid suggested the possibility of direct acetylation to give the fully acetylated acid. Direct acetylation yielded hexaacetyl-*d*-α-galaheptonic acid as was indicated by comparison of the product with the acetylated lactone, analysis of the product, and its conversion into the methyl ester. Direct acetylation of *d*-arabonic, *d*-galactonic, and *d*-talonic acids likewise yielded the corresponding fully acetylated acids which were identified by comparison with the product obtained from the acetylated amide. The yields were too low to be satisfactory for the preparation of the fully acetylated *d*-galactonic and *d*-talonic acids, but proved to be the most successful method for obtaining tetraacetyl-*d*-arabonic acid.

Attempts were made to prepare fully acetylated *d*-mannonic, *d*-gulonic and *d*-α-glucoheptonic acids

(1) Major and Cook, THIS JOURNAL, **58**, 2477 (1936).
(2) Cook and Major, *ibid.*, **58**, 2410 (1936).
(3) Major and Cook, *ibid.*, **58**, 2474 (1936).
(4) Hurd and Sowden, *ibid.*, **60**, 235 (1938).
(5) Robbins and Upson, *ibid.*, **60**, 1788 (1938).

by treating the sodium salts of these acids with acetic acid–acetic anhydride mixtures, but the acetylated lactone was produced in each case.

Phenylhydrazides of the fully acetylated sugar acids were prepared by acetylation of the aldonic phenylhydrazide as Major and Cook[3] have done in preparing pentaacetyl-*d*-gluconic phenylhydrazide. Methyl esters were prepared by treating the fully acetylated acid with diazomethane.

d-Arabonamide and *d*-arabonic acid have been prepared in the course of this study and are reported for the first time. The acetylated *d*-arabonic and *d*-α-galaheptonic lactones are also reported.

Experimental

***d*-Arabonamide.**—*d*-Arabonic lactone was prepared by treating glucose with oxygen in 2 *N* potassium hydroxide according to the method of Spengler and Pfannenstiel.[6] The potassium salt was transformed to the calcium salt which was decomposed with oxalic acid to yield the lactone. The lactone was dissolved in liquid ammonia. The ammonia was allowed to evaporate, and the amide was heated at 60° *in vacuo* to remove the last of the ammonia. The amide was recrystallized several times from ethanol.

Fully Acetylated Aldonic Amides (Compounds 2–4).[7]—The aldonamide (7.5 g.) was acetylated with a solution of zinc chloride (4 g.) in 50 cc. of acetic anhydride at 0°. After the amide had dissolved, the mixture was stirred with ice water and neutralized with sodium bicarbonate. The product was obtained by extraction with chloroform and evaporation of the extract.

Compound 2 was recrystallized from absolute ethanol.

Compound 3 was prepared from *d*-talonamide.[8] It did not crystallize until the extract had stood *in vacuo* for a time. It was recrystallized twice from the butyl ethyl ether of ethylene glycol.

Compound 4 was prepared from *d*-α-galaheptonamide.[9] The product separated upon stirring with water. Filtration was substituted for chloroform extraction. The product was recrystallized twice from glacial acetic acid.

***d*-Arabonic Acid.**—The calcium salt was prepared by the method described in the preparation of *d*-arabonamide. It was converted to the sodium salt by treating the calcium salt with equivalent amounts of oxalic acid and sodium bicarbonate. The solution of sodium salt was concentrated to a sirup and treated with acetic acid according to the method of Brackenbury and Upson[10] for the preparation of *l*-arabonic acid. The acid was purified in the same manner as the *l*-form.

Fully Acetylated Aldonic Acids (Compounds 7–10).—The aldonamide was acetylated under the conditions described above. After acetylation was complete, the mixture was treated with nitrous anhydride at 8–10° until it remained yellowish-green. It was allowed to stand for four hours at room temperature. The mixture was diluted with 100 cc. of water, made alkaline with sodium bicarbonate, acidified with dilute hydrochloric acid, and warmed to 40°. The mixture was cooled and extracted with chloroform. The extract was evaporated to a sirup and crystallized from water. It was recrystallized twice from water.

Compounds 7 and 8 were best prepared by the above procedure.

Compounds 6–10 were prepared by a modification of the above procedure using a solution of the pure acetylated aldonamide in glacial acetic acid. This procedure was found to be the most satisfactory for compounds 9 and 10.

Compound 9 could not be crystallized. The sirupy extract was dissolved in ether and filtered from any unreacted amide. The ethereal filtrate was evaporated to a gum and dried in an Abderhalden drier for analysis and specific rotation.

Direct Acetylation of Aldonic Acids (Compounds 6 and 11).—The aldonic acid (10 g.) was treated with a solution of zinc chloride (4 g.) in 50 cc. of acetic anhydride at 0° for two or three days. The reaction mixture was stirred with ice water and extracted with chloroform. The extract was evaporated to a gum which crystallized.

In the preparation of compound 6, the product partially separated from the acetylation mixture and was filtered off before treatment with ice water. The product was recrystallized from toluene.

Compound 11 was recrystallized from water.

Acetylated Aldonic Lactones (Compounds 12 and 13).—The aldonic lactone (5 g.) was treated with 25 cc. of acetic anhydride at 0° and allowed to stand for a day. The mixture was stirred with ice water and extracted with chloroform. The extract was evaporated to a gum which crystallized on standing. The product was recrystallized from ethanol.

In the preparation of compound 12, zinc chloride (2 g.) was used as catalyst. The lactone was prepared as described under the preparation of the amide.

Compound 13 was prepared using concentrated sulfuric acid (1 cc.) as catalyst.

Fully Acetylated Aldonic Phenylhydrazides (Compounds 14–20).—The aldonic phenylhydrazide (7.5 g.) was treated with a solution of zinc chloride (4 g.) in 50 cc. of acetic anhydride at 0°. The mixture stood for a day at room temperature. It was stirred with ice water and extracted with chloroform.

Compounds 14, 15, 16, 17, 19 and 20 were obtained in crystalline form upon evaporation of the extract. The products were recrystallized by solution in ethanol and addition of ether.

Compound 18 failed to crystallize upon evaporation of the chloroform. The gum was dried in an Abderhalden drier for analysis and specific rotation.

Methyl Esters of Fully Acetylated Aldonic Acids (Compounds 21–27).—The fully acetylated aldonic acid was dissolved in a small amount of ethanol, cooled, and treated with the amount of an ethereal solution of diazomethane[11] which was necessary to produce a persistent yellow color. The solution was filtered and evaporated. The product

(6) Spengler and Pfannenstiel, German Patent 618,164.

(7) Numbers refer to those in the tabulation of compounds and constants.

(8) Renfrew and Cretcher, THIS JOURNAL, **54**, 4402 (1932).

(9) Hann, Merrill and Hudson, *ibid.*, **57**, 2100 (1935).

(10) Brackenbury and Upson, *ibid.*, **55**, 2512 (1933).

(11) "Organic Syntheses," Vol. 15, 1935, pp. 48, 3.

TABLE I

No.	Compound	M. p., °C.	$[\alpha]^{25}D$ [a]	Formula	Analyses, % Calcd. C	Calcd. H	Found C	Found H
1	*d*-Arabonamide	138–139	+38.6° [b]	$C_5H_{11}O_5N$	36.34	6.72	36.37	6.73
2	Tetraacetyl-*d*-arabonamide	123	+24.3°	$C_{13}H_{19}O_9N$	46.83	5.75	46.76	5.82
3	Pentaacetyl-*d*-talonamide	104–106	+85.4°	$C_{16}H_{22}O_{11}N$	47.38	5.73	47.26	5.78
4	Hexaacetyl-*d*-α-galaheptonamide	185–187	+ 2.1°	$C_{19}H_{27}O_{13}N$	47.78	5.74	47.67	5.63
5	*d*-Arabonic acid	114–116	+10.5° [b]	$C_5H_{10}O_6$	36.13	6.07	36.12	6.00
6	Tetraacetyl-*d*-arabonic acid	135–136	+32.5°	$C_{13}H_{18}O_{10}$	46.69	5.43	46.69	5.42
7	Pentaacetyl-*d*-mannonic acid monohydrate	75–76	+24.8°	$C_{16}H_{22}O_{12}\cdot H_2O$	45.26	5.69	45.28	5.61 [c]
8	Pentaacetyl-*d*-talonic acid	142–144	+78.3°	$C_{16}H_{22}O_{12}$	47.27	5.46	47.03	5.45
9	Pentaacetyl-*d*-gulonic acid	Sirup	+ 1.8°	$C_{16}H_{22}O_{12}$	47.27	5.46	47.07	5.50
10	Hexaacetyl-*d*-α-glucoheptonic acid hemihydrate	94	+10.7°	$C_{19}H_{26}O_{14}\cdot{}^1/_2H_2O$	46.80	5.59	46.73	5.64 [d]
11	Hexaacetyl-*d*-α-galaheptonic acid	176–177	+15.3°	$C_{19}H_{26}O_{14}$	47.68	5.48	47.50	5.52
12	Triacetyl-*d*-arabonic lactone	68–69	+52.3°	$C_{11}H_{14}O_8$	48.16	5.15	48.18	5.15
13	Pentaacetyl-*d*-α-galaheptonic lactone	123–124	−16.9°	$C_{17}H_{22}O_{12}$	48.78	5.30	48.69	5.29
14	Tetraacetyl-*d*-arabonic phenylhydrazide	140–141	+ 8.4°	$C_{19}H_{24}O_9N_2$	53.76	5.71	54.04	5.74
15	Pentaacetyl-*d*-galactonic phenylhydrazide	220	+23.6°	$C_{22}H_{28}O_{11}N_2$	53.20	5.69	53.36	5.73
16	Pentaacetyl-*d*-mannonic phenylhydrazide	173	+13.0°	$C_{22}H_{28}O_{11}N_2$	53.20	5.69	53.37	5.67
17	Pentaacetyl-*d*-talonic phenylhydrazide	162–163	+35.0°	$C_{22}H_{28}O_{11}N_2$	53.20	5.69	53.52	5.75
18	Pentaacetyl-*d*-gulonic phenylhydrazide	Sirup	+37.7°	$C_{22}H_{28}O_{11}N_2$	53.20	5.69	53.13	5.63
19	Hexaacetyl-*d*-α-glucoheptonic phenylhydrazide	154	+27.4°	$C_{25}H_{32}O_{13}N_2$	52.80	5.68	52.82	5.68
20	Hexaacetyl-*d*-α-galaheptonic phenylhydrazide	112–114	+25.9°	$C_{25}H_{32}O_{13}N_2$	52.80	5.68	52.63	5.73
21	Methyl tetraacetyl-*d*-arabonate	136	+42.3°	$C_{14}H_{20}O_{10}$	48.25	5.79	48.20	5.73
22	Methyl pentaacetyl-*d*-gluconate	124	+ 9.2°	$C_{17}H_{24}O_{12}$	48.55	5.75	48.41	5.69
23	Methyl pentaacetyl-*d*-galactonate	126–127	+ 2.5°	$C_{17}H_{24}O_{12}$	48.55	5.75	48.42	5.64
24	Methyl pentaacetyl-*d*-talonate	78–79	+70.1°	$C_{17}H_{24}O_{12}$	48.55	5.75	48.41	5.70
25	Methyl pentaacetyl-*d*-gulonate	Sirup	+ 4.4°	$C_{17}H_{24}O_{12}$	48.55	5.75	48.64	5.82
26	Methyl hexaacetyl-*d*-α-glucoheptonate	93	+14.1°	$C_{20}H_{28}O_{14}$	48.76	5.73	48.47	5.70
27	Methyl hexaacetyl-*d*-α-galaheptonate	96–97	+18.8°	$C_{20}H_{28}O_{14}$	48.76	5.73	48.70	5.69

[a] Rotations taken in two-decimeter tube; concentration, 1.5–2.5 g./100 cc. Solvent is chloroform except as noted. [b] Solvent is water, concentration 6 g./100 cc. [c] Water of hydration: calcd., 4.25%; found, 4.24%. [d] Water of hydration: calcd., 1.88%; found, 1.84%.

crystallized during evaporation, and was recrystallized from ethanol with the addition of a small amount of petroleum ether.

Compounds 21, 22, 23, 24, 26 and 27 were prepared by the above directions, while compound 25, which failed to crystallize, was obtained by drying the gum in an Abderhalden drier for analysis and specific rotation.

Summary

1. The amides and phenylhydrazides of several fully acetylated aldonic acids have been prepared by direct acetylation of the aldonic acid derivative.

2. Pentaacetyl-*d*-mannonic acid monohydrate, pentaacetyl-*d*-talonic acid, pentaacetyl-*d*-gulonic acid and hexaacetyl-*d*-α-glucoheptonic acid hemihydrate have been prepared by treating the corresponding acetylated amide with nitrous anhydride.

3. Direct acetylation of aldonic acids to the fully acetylated acids has been reported for the first time. Tetraacetyl-*d*-arabonic and hexaacetyl-*d*-α-galaheptonic acids have been prepared in good yield by this method.

4. Methyl esters of several fully acetylated aldonic acids have been prepared by treating a solution of the acid with a solution of diazomethane.

5. *d*-Arabonamide, *d*-arabonic acid, triacetyl-*d*-arabonic lactone, and pentaacetyl-*d*-α-galaheptonic lactone have been prepared.

LINCOLN, NEBRASKA RECEIVED JANUARY 29, 1940

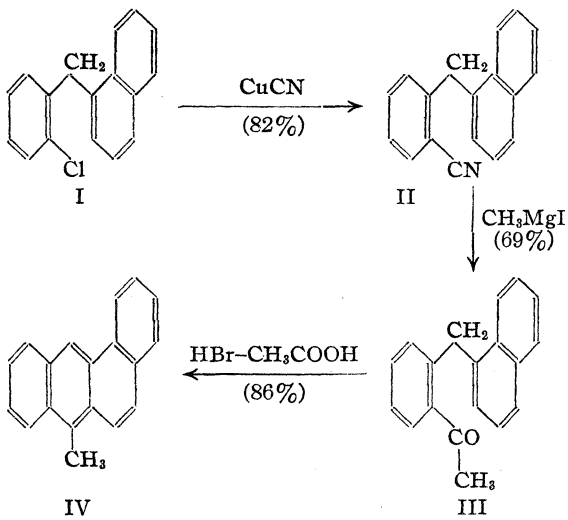
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF DUKE UNIVERSITY]

9-Methyl- and 10-Methyl-1,2-benzanthracene

BY CHARLES K. BRADSHER

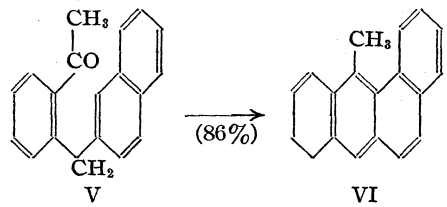
Recently[1] we have shown that *o*-benzylphenyl ketones may be cyclized to form 9-alkyl- and 9-arylanthracene hydrocarbons. The demonstrated[2] importance of *meso* substitution as a source of carcinogenic activity in derivatives of 1,2-benzanthracene made it of interest to attempt the application of the new reaction to this series.

Two carcinogenic hydrocarbons, 9-methyl- and 10-methyl-1,2-benzanthracene have now been prepared in this manner.



In the synthesis of the 10-methylbenzanthracene (IV), the crude carbinol produced by the action of α-naphthylmagnesium bromide on *o*-chlorobenzaldehyde was reduced with red phosphorus and iodine to give 1-(*o*-chlorobenzyl)-naphthalene (I). By action of cuprous cyanide, this was converted to a nitrile (II) which upon treatment with methylmagnesium iodide afforded *o*-(1-naphthylmethyl)-acetophenone (III). Cyclization to the hydrocarbon (IV) was effected in good yield by refluxing the ketone (III) for three days in a mixture of acetic and hydrobromic acids. The over-all yield of the pure hydrocarbon was 29%, calculated from the *o*-chlorobenzaldehyde taken.

The synthesis of 9-methyl-1,2-benzanthracene (VI) was accomplished similarly, starting from β-naphthylmagnesium bromide or iodide and *o*-chlorobenzaldehyde. Reduction of the carbinol, conversion to the nitrile and treatment with methylmagnesium iodide gave *o*-(2-naphthylmethyl)-acetophenone (V), which was cyclized easily to the expected hydrocarbon (VI).



Although the yield in the ring closure was exactly the same, the over-all yield was somewhat less than in the preparation of the isomer. It is interesting to note that only twenty-four hours were required for cyclization, undoubtedly due to the great reactivity of the *alpha* position in the naphthalene nucleus.[3] A parallel observation has been made in the case of the Elbs reaction.[4]

We feel that the new synthesis not only affords an eminently satisfactory route to 10-methyl-1,2-benzanthracene, but gives promise of providing a useful tool for the synthesis of new carcinogenic and antigenic compounds.

The author is indebted to Professor Louis F. Fieser, who has established the identity of the hydrocarbons prepared by comparing them with authentic specimens.

Experimental

1-(*o*-Chlorobenzyl)-naphthalene (I).—A Grignard reagent was prepared in dry ether from 45.5 g. of α-naphthyl bromide and 5.4 g. of magnesium. To this was added an ethereal solution containing 28.1 g. of *o*-chlorobenzaldehyde and the mixture allowed to stand overnight. The mixture was then decomposed with a 20% solution of ammonium chloride and the ethereal layer separated and concentrated on the steam-bath. The residue was dissolved in 500 cc. of acetic acid, and 10 g. of iodine, 10 g. of red phosphorus and 50 cc. of water added. This mixture was refluxed for twenty-seven hours and then the excess phosphorus was filtered off by suction. A quantity of ice was added to the filtrate and the mixture extracted with ether. The ethereal extract was freed of acetic acid and iodine by extraction with iced 10% sodium hy-

(1) THIS JOURNAL, **62**, 486 (1940).

(2) *E. g.*, Fieser and Newman, *ibid.*, **58**, 2376 (1936); Fieser and Hershberg, *ibid.*, **59**, 1028 (1937); Newman, *ibid.*, **59**, 1003 (1937); Bachmann, Kennaway and Kennaway, *Yale J. Biol. Med.*, **11**, 97 (1938).

(3) The cyclization of *o*-benzylacetophenone (ref. 1) requires four days.

(4) Clar, *Ber.*, **62**, 350, 1387 (1929); Fieser and Dietz, *ibid.*, **62**, 1827 (1929).

droxide solution, dried, concentrated and the residue distilled under reduced pressure. The product was a water-white liquid, b. p. 189–192° (2 mm.); yield 30.5 g. (60%).

Anal.[5] Calcd. for $C_{17}H_{13}Cl$: C, 80.76; H, 5.19. Found: C, 80.88; H, 5.12.

o-(1-Naphthylmethyl)-benzonitrile (II).—A mixture of 25.3 g. of the chloro compound (I) obtained above with 10.8 g. of cuprous cyanide and 10 cc. of pyridine was heated under an air condenser for thirty hours at 250–260°. It was then poured on a mixture of ice and sodium hydroxide and the mixture extracted with benzene. The benzene layer was filtered and then washed with dilute hydrochloric acid, water, and finally saturated sodium chloride solution. The benzene was then evaporated and the residue distilled under reduced pressure. The product was a viscous amber-colored oil, b. p. 216–217° (3 mm.), which solidified upon seeding. This material was pure enough for further reactions. A sample crystallized from ether–petroleum ether was obtained as stout prisms, m. p. 59–60°.

Anal. Calcd. for $C_{18}H_{13}N$: C, 88.85; H, 5.39. Found: C, 88.90; H, 5.46.

o-(1-Naphthylmethyl)-acetophenone (III).—A Grignard reagent was prepared from 28.4 g. of methyl iodide and 4.9 g. of magnesium. Most of the ether was distilled off and 12.2 g. of the nitrile (II) obtained above added in 150 cc. of dry benzene and the mixture refluxed overnight. After decomposition of the reaction mixture with ammonium chloride solution, the imine was extracted from the benzene layer with 2 *N* hydrochloric acid. To this acid extract, 50 cc. of concentrated hydrochloric acid was added and the mixture refluxed for one hour. The ketone thus liberated was taken up in ether. The ethereal extract was washed, dried and concentrated. The residue, distilled under reduced pressure, gave 8.9 g. (69%) of a viscous, nearly colorless liquid, b. p. 216–217° (3 mm.). This liquid was used for the cyclization experiments, but the ketone could be crystallized from ether–petroleum ether as colorless blades, m. p. 39–40°.

Anal. Calcd. for $C_{19}H_{16}O$: C, 87.66; H, 6.19. Found: C, 87.53; H, 6.29.

10-Methyl-1,2-benzanthracene (IV).—Two grams of the ketone (III) was refluxed for three days in a mixture containing 20 cc. of acetic acid and 20 cc. of 34% hydrobromic acid. At the end of this period, the hydrocarbon had crystallized from the boiling liquid. The mixture was cooled and the methylbenzanthracene collected. Once recrystallized from ethanol, it was obtained as yellow needles, m. p. 139–140° (cor.), and gave no depression of melting point when mixed with an authentic sample of 10-methyl-1,2-benzanthracene. The yield was 1.6 g. (86%), but a further quantity (0.19 g., m. p. 138–139°) could be obtained by concentration of the mother liquor.

Anal. Calcd. for $C_{19}H_{14}$: C, 94.18; H, 5.82. Found: C, 94.22; H, 5.96.

2-(o-Chlorobenzyl)-naphthalene.—A Grignard reagent was prepared in ether from 28.0 g. of β-iodonaphthalene and 2.7 g. of magnesium. An ether solution containing 14.4 g. of *o*-chlorobenzaldehyde was added and the mixture worked up as in the case of the isomer (I). The crude carbinol was reduced with red phosphorus and iodine, and the product distilled under reduced pressure. It was obtained as a nearly colorless oil, b. p. 203–204° (3 mm.); yield 7.9 g. (31%). This material was pure enough for further reaction, but could be separated from a small amount of high melting material (β,β'-dinaphthyl?) by addition of petroleum ether followed by cooling at 0° for twenty-four hours. The impurity crystallized and could be removed by filtration. Concentration of the filtrate followed by redistillation gave material of analytical purity.

Anal. Calcd. for $C_{17}H_{13}Cl$: C, 80.76; H, 5.19. Found: C, 80.89; H, 5.10.

In a single small scale experiment, starting from 9.1 g. of β-bromonaphthalene, the 2-naphthyl-(*o*-chlorophenyl)-methane was obtained in a yield of 3.5 g. (35%).

o-(2-Naphthylmethyl)-benzonitrile.—A mixture of 20.2 g. of 2-(*o*-chlorobenzyl)-naphthalene, 9.0 g. of cuprous cyanide and 10 cc. of pyridine was heated for thirty hours at 250–260° and then worked up as in the case of the isomer (II). The product, b. p. 223–226° (3 mm.), solidified immediately on cooling; yield 11.1 g. (57%). This material was used without further purification in the following reaction, but could be crystallized from methanol as colorless prisms, m. p. 84.5–85.5°.

Anal. Calcd. for $C_{18}H_{13}N$: C, 88.85; H, 5.39. Found: C, 88.87; H, 5.01.

o-(2-Naphthylmethyl)-acetophenone (V) was prepared from 9.75 g. of *o*-(2-naphthyl)-benzonitrile by the Grignard reaction in the same manner as that employed in the preparation of the isomer (III). Distilled under reduced pressure, it was obtained as a yellow, slightly fluorescent oil, b. p. 221° (3 mm.); yield 5.5 g. (52%).

Anal. Calcd. for $C_{19}H_{16}O$: C, 87.66; H, 6.19. Found: C, 87.82; H, 5.99.

9-Methyl-1,2-benzanthracene (VI).—Two grams of the ketone (V) obtained above was refluxed in a mixture of 20 cc. of acetic acid and 20 cc. of 34% hydrobromic acid. At the end of seventeen hours, the hydrocarbon solidified and after a total of twenty-four hours, refluxing was discontinued. Recrystallization of the material from methanol gave 1.6 g. (86%) of irregular, lemon-colored plates, m. p. 137.5–138.5° (cor.). This material gave no depression of melting point when mixed with an authentic specimen of 9-methyl-1,2-benzanthracene.

Anal. Calcd. for $C_{19}H_{14}$: C, 94.18; H, 5.82. Found: C, 94.00; H, 6.00.

Summary

Using a previously described method for the synthesis of *meso* substituted anthracene hydrocarbons, two carcinogenic compounds, 9-methyl- and 10-methyl-1,2-benzanthracene have been prepared.

(5) All analyses by the Arlington Laboratories.

DURHAM, N. C. RECEIVED FEBRUARY 26, 1940

[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

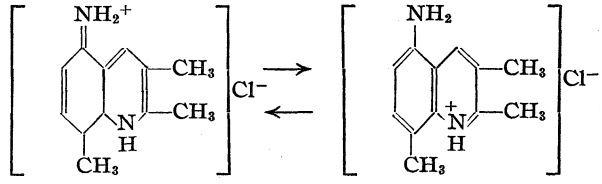
Petroleum Bases. I. Reactions of 2,3,8-Trimethylquinoline

BY ALFRED BURGER AND LUTHER R. MODLIN, JR.

Several polyalkyl pyridine and quinoline derivatives which are not easily accessible by synthetic approaches have become available recently by the separation of basic straight run and cracked petroleum fractions. Bailey and his co-workers[1] have published a long series of interesting articles dealing with the separation and the structure of individual nitrogen-containing constituents of these fractions. It seemed worth while to investigate whether some of the bases from kerosene containing the quinoline nucleus would lend themselves to the preparation of substances of pharmacological interest, since quinoline is the classical heterocyclic system encountered in a wide variety of medicinally important products.[2] One of the most readily available kerosene bases, 2,3,8-trimethylquinoline,[3] was chosen therefore as the starting material for our studies. This communication describes several reactions of this base leading to derivatives needed in the preparation of such substances which will be the subject of forthcoming publications from this Laboratory.

Nitration of 2,3,8-trimethylquinoline (I) with fuming nitric acid furnished 5-nitro-2,3,8-trimethylquinoline (II) in almost quantitative yield. Reduction of this nitro compound with stannous chloride led to the corresponding amine (III), while hydrogenation in neutral solvents in the presence of a platinum oxide catalyst not only reduced the nitro group, but also attacked the pyridine nucleus. When the reaction was interrupted after absorption of only three moles of hydrogen, the amino compound III could be isolated in yields of around 60%. Hydrogenation in the presence of Raney nickel recently recommended by Winterbottom[4] was abandoned when more than three moles of hydrogen was absorbed, and the unhydrogenated amine III could not be isolated from the reaction mixture.

The mono-hydrochloride of 2,3,8-trimethyl-5-aminoquinoline exhibits a deep brick-red color. When hydrochloric acid is added to the colored aqueous solution of this salt, the color disappears almost completely; when a sodium carbonate solution is added carefully to the resulting colorless acidic solution, the deep red color reappears, and vanishes only when the solution turns alkaline, and the base precipitates. The deep red color of the mono-hydrochloride may be explained by oscillation of the anion between the two nitrogen atoms; the salt may thus exist in resonating forms



A survey of some known 5- and 8-aminoquinoline derivatives revealed that a deepening of the color from diacidic toward monoacidic salts has been observed in several instances.[5] However, a similar change in color has been reported in the case of the salts of 6-aminolepidine.[6] In this case, a resonating system which would disappear upon addition of a second molecule of the acid cannot be held responsible for the deeper color of the monoacidic salts, because position-2 in the pyridine nucleus would be unable to hold a second hydrogen atom if the cyclic nitrogen atom assumed a positive charge.

5-Hydroxy-2,3,8-trimethylquinoline (IV), prepared from the amine III by diazotization, was converted into the methyl ether (V) by the action of diazomethane. The structure of 5-methoxy-2,3,8-trimethylquinoline was established by synthesis from 4-methoxy-2-aminotoluene and tiglic aldehyde.[7] The base obtained in this condensation, and its picrate, proved to be identical with V, and its picrate, respectively. This also establishes the position of the functional substituents in the related nitro (II), amino (III), and hydroxy (IV) derivatives. Attempts to prepare 5-nitro-2,3,8-trimethylquinoline (II) by condensation of 2-amino-4-nitrotoluene with tiglic aldehyde failed

(1) Schenck and Bailey, THIS JOURNAL, **61**, 2613 (1939), and many preceding papers.

(2) *Cf.* von Oettingen, "Therapeutic Agents of the Quinoline Group," The Chemical Catalog Company, New York, 1933; Jensch, *Z. angew. Chem.*, **50**, 891 (1937); Houben, "Fortschritte in der Heilstoffchemie," Part 2, Vol. III, Verlag Walter de Gruyter & Co., Berlin, 1939.

(3) Bailey and co-workers, THIS JOURNAL, **52**, 1239 (1930).

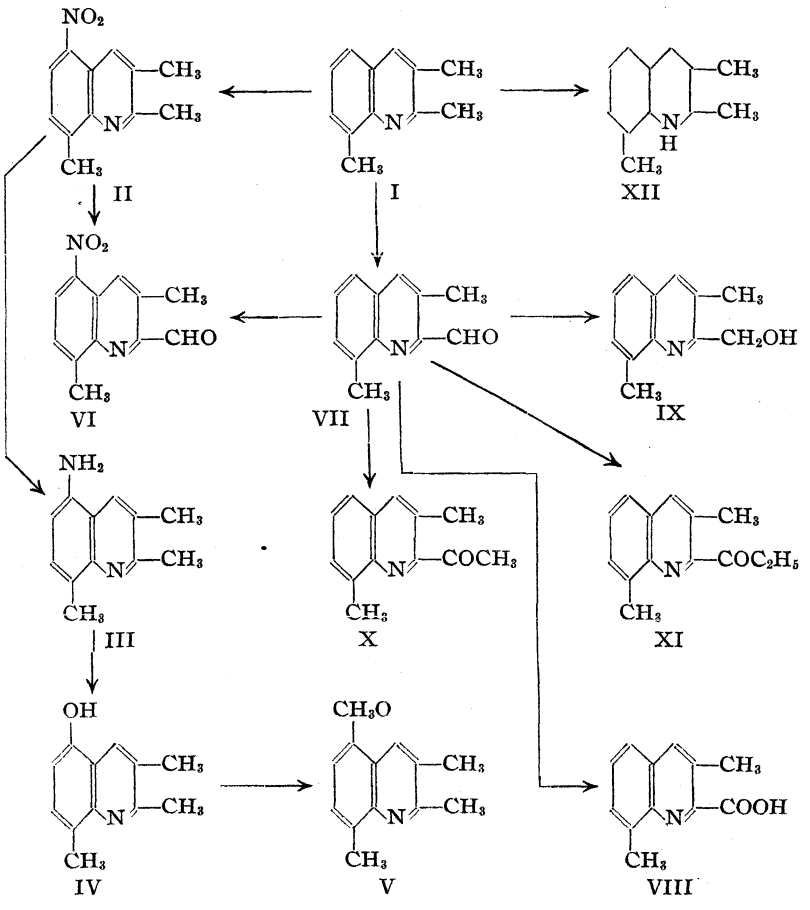
(4) Winterbottom, *ibid.*, **62**, 160 (1940).

(5) Noelting and Trautmann, *Ber.*, **23**, 3674 (1890); *cf.* Doebner and v. Miller, *ibid.*, **17**, 1703 (1884); Seka, *Monatsh.*, **45**, 287 (1927).

(6) Koenigs, *Ber.*, **23**, 2671 (1890); Busch and Koenigs, *ibid.*, **23**, 2685 (1890).

(7) *Cf.* Rohde, *ibid.*, **20**, 1911 (1887).

to yield well-defined products, probably because the nitro group of the starting material is reduced during the dehydrogenation of the intermediate dihydroquinoline derivative. Addition of arsenic acid[8] during the condensation caused extensive formation of resins and failed to improve the yield.



2,3,8-Trimethylquinoline exhibits the normal reactivity of quinaldine derivatives: for example, the 2-methyl group may be condensed with carbonyl compounds.[3] This methyl group is also the only one which is attacked by selenium dioxide. Oxidation of the base with this reagent, previously employed in similar cases,[9] proceeded very smoothly and furnished 3,8-dimethylquinoline-2-aldehyde (VII) in good yield. The position of the aldehyde group was confirmed by oxidizing the compound with silver oxide[10] to 3,8-dimethylquinoline-2-carboxylic acid (VIII).[3] Concentrated nitric acid did not oxidize the aldehyde group but caused quantitative mono-nitration of the compound. The nitro derivative thus obtained proved to be identical with 5-nitro-3,8-dimethylquinoline-2-aldehyde (VI) which had been prepared by oxidation of 5-nitro-2,3,8-trimethylquinoline (II) with selenium dioxide. Thus, the para-orienting influence of the 8-methyl group, and the ortho–para-orienting effect of the heterocyclic nucleus combine to determine the position of the entering nitro group, regardless of the type of substituent in position-2.

Catalytic reduction of 3,8-dimethylquinoline-2-aldehyde (VII) yielded 3,8-dimethylquinoline-2-methanol (IX) which contains a β-amino alcohol arrangement, —N=C—CH_2OH, and may be expected to exert some influence on blood pressure and peristalsis. We attempted to prepare the 5-amino derivative of the alcohol IX by catalytic reduction of the nitro aldehyde VI, but although the calculated amount of hydrogen was absorbed, no crystalline reaction product could be isolated. Reduction of VI to the corresponding amino aldehyde by various methods did not furnish well-defined products either.

3,8-Dimethylquinoline-2-aldehyde (VII) served as a convenient starting material in the preparation of α-quinolyl ketones. This class of compounds is not very easily accessible, and the reaction described here, namely, the action of diazoalkanes on a quinoline-2-aldehyde, may facilitate the approach to such substances. Diazomethane furnished a complex mixture containing moderate amounts of 3,8-dimethyl-2-quinolyl methyl ketone (X), while the main fraction consisted of high-boiling oils, perhaps polymers of the primary reaction products, namely, compounds of ethylene oxide character. Diazoethane gave a satisfactory yield of 3,8-dimethyl-2-quinolyl ethyl ketone (XI); both ketones were characterized by their oximes. The reaction of 3,8-dimethylquinoline-2-aldehyde with

(8) Knueppel, *Ber.*, **29**, 703 (1896); see also I. G. Farbenindustrie A.-G., French Patent 739,880 (1932) (*C. A.*, **27**, 2164).

(9) Monti, *Atti accad. Lincei*, **18**, 505 (1933); Henze, *Ber.*, **67**, 750 (1934); Kwartler and Lindwall, THIS JOURNAL, **59**, 524 (1937).

(10) Besthorn and Geisselbrecht, *Ber.*, **53**, 1017 (1920).

diazoalkanes compares with that of some aromatic aldehydes, for example, piperonal,[11] which also reacts with diazomethane to yield ethylene oxide derivatives chiefly, while the corresponding aryl ethyl ketone is the main product of the reaction with diazoethane.

Taylor, Winckles and Marks[12] found that quinoline-2-aldoxime can form chelated metal compounds, and concluded that it must have the *cis* configuration. 3,8-Dimethylquinoline-2-aldoxime and its 5-nitro derivative also give color reactions and precipitates with a number of metallic ions. This would indicate that our aldoximes also are *syn*-oximes. The oximes of 3,8-dimethyl-2-acetylquinoline (X) and 3,8-dimethyl-2-propionylquinoline (XI), on the other hand, did not exhibit any reactions with metallic ions.

Hydrogenation of 2,3,8-trimethylquinoline in glacial acetic acid solution under ordinary pressure in the presence of a platinum oxide catalyst furnished 2,3,8-trimethyldecahydroquinoline (XII) in good yield. This compound may exist in a *cis*- and a *trans*-form. While the melting points of various fractions of the hydrochloride seem to indicate differences which may be attributed to a partial separation of the stereoisomers by fractional crystallization, a final evaluation of this separation must await future experimental results.

Acknowledgment.—The authors wish to thank Professor J. R. Bailey of the University of Texas, and the Union Oil Company of California for supplying the kerosene base used in this investigation.

Experimental

3,8-Dimethylquinoline-2-aldehyde (VII).—A solution of 5 g. of 2,3,8-trimethylquinoline and 3.5 g. of selenium dioxide in 40 ml. of ethanol was boiled under reflux for six hours, and the precipitated selenium was filtered from the hot solution. The filtrate was concentrated and 3.3 g. of the aldehyde was collected as straw-colored needles. The mother liquor was precipitated with water, the reddish solid was filtered, dissolved in 10 ml. of benzene, and the solution shaken with 30 ml. of a saturated solution of sodium bisulfite for one hour. The crystalline addition product was filtered, washed with ether, and decomposed with a dilute sodium carbonate solution. Another 1.2 g. of the aldehyde was obtained in this manner, the yield totalling 82%. The aldehyde was purified by distillation under 1 mm. pressure, and recrystallization from ethanol. It appeared as long colorless needles, m. p. 107–108°.

Anal.[13] Calcd. for $C_{12}H_{11}NO$: C, 77.80; H, 5.99. Found: C, 77.85; H, 6.18.

The oxime was prepared by the method of Bachmann and Boatner.[14] It crystallized from ethanol as almost colorless needles, m. p. 172–174°.

Anal. Calcd. for $C_{12}H_{12}N_2O$: C, 71.96; H, 6.04. Found: C, 71.87; H, 5.99.

The **semicarbazone** was prepared by heating equimolecular amounts of the aldehyde and semicarbazide hydrochloride in dilute ethanol solution for five minutes The alcohol was boiled off, the solution neutralized with sodium bicarbonate and allowed to cool. The semicarbazone crystallized in little colorless needles which, after recrystallization from dilute ethanol, sintered at 185°, m. p. 190–192° (dec.).

Anal. Calcd. for $C_{13}H_{14}N_4O$: N, 23.14. Found: N, 23.82.

3,8-Dimethylquinoline-2-methanol (IX).—A solution of 5.0 g. of 3,8-dimethylquinoline-2-aldehyde in 150 ml. of ethanol was hydrogenated in the presence of 0.2 g. of a platinum oxide catalyst. Absorption of one mole of hydrogen was completed in ten minutes. After filtration from the catalyst, the solvent was evaporated under reduced pressure at 40°, and the crystalline residue was dissolved in low-boiling petroleum ether. A small amount of a white insoluble material was removed by filtration, the solution was concentrated, and the carbinol crystallized as colorless prisms, m. p. 68–69°. The yield was 90%.

Anal. Calcd. for $C_{12}H_{13}NO$: C, 76.96; H, 7.00. Found: C, 76.95; H, 7.34.

The **hydrochloride** was prepared by the action of ethanolic hydrogen chloride on the base and recrystallized from ethanol. It consisted of colorless water soluble crystals which sintered at 160°, m. p. 176–185° (dec.). The aqueous solution turned yellow on standing, but the color could be removed by extraction into ether.

Anal. Calcd. for $C_{12}H_{14}ClNO$: N, 6.27. Found: N, 6.57.

The **acetyl derivative** was obtained by allowing the carbinol to stand with an excess of acetic anhydride in pyridine solution overnight, and working up the mixture in the usual manner. It was recrystallized from dilute ethanol and appeared as colorless needles, m. p. 62–63°.

Anal. Calcd. for $C_{14}H_{15}NO_2$: C, 73.32; H, 6.60. Found: C, 73.46; H, 6.36.

Oxidation of 3,8-Dimethylquinoline-2-aldehyde.—Two-tenths gram of the aldehyde and 0.08 g. of freshly prepared silver oxide in 10 ml. of ethanol was heated under reflux for three hours. Alkaline water was added, the coagulated silver precipitate was filtered, and the filtrate was concentrated to 10 ml. Acidification with acetic acid and scratching caused 3,8-dimethylquinoline-2-carboxylic acid (VIII) to crystallize in good yield. Crystallization from a few milliliters of water yielded colorless needles, m. p. 154–155°. The melting point reported by Bailey[3] is 157°.

3,8-Dimethyl-2-quinolyl Methyl Ketone (X).—A solution of 1 g. of 3,8-dimethylquinoline-2-aldehyde in 20 ml. of

(11) Mosettig, *Ber.*, **61**, 1391 (1928); **62**, 1271 (1929); Mosettig and Czadek, *Monatsh.*, **57**, 291 (1931).

(12) Taylor, Winckles and Marks, *J. Chem. Soc.*, 2778 (1931).

(13) C and H micro determinations by Mrs. Elizabeth Johnson Mathers.

(14) Bachmann and Boatner, THIS JOURNAL, **58**, 2097 (1936).

ether and 4 ml. of methanol was treated with an ethereal solution of about 0.6 g. of diazomethane. Nitrogen began to evolve soon, and the solvent was evaporated after sixteen hours. The semi-oily residue was fractionated under 1 mm. pressure. A mostly crystalline fraction distilled first; the major fraction consisted of a brown oil of high boiling range. The crystalline fraction was recrystallized from dilute methanol and yielded 0.2 g. of yellowish needles, m. p. 90°.

Anal. Calcd. for $C_{13}H_{13}NO$: C, 78.35; H, 6.58. Found: C, 78.58; H, 6.66.

The **oxime,** prepared in ethanol–pyridine solution,[13] was crystallized from dilute methanol; colorless, m. p. 153–154°.

Anal. Calcd. for $C_{13}H_{14}N_2O$: C, 72.85; H, 6.59. Found: C, 72.80; H, 6.59.

3,8-Dimethyl-2-quinolyl Ethyl Ketone (XI).—Five-tenths gram of 3,8-dimethyiquinoline-2-aldehyde was dissolved in a solution of diazoethane (from 2 ml. of nitrosoethylurethan) in 30 ml. of ether. A vigorous reaction started soon and was completed by addition of 2 ml. of methanol. After standing overnight, the decolorized solution was evaporated, and the crystalline residue was recrystallized from slightly dilute methanol. The ketone appeared as colorless prisms, m. p. 80°. The yield was 52%.

Anal. Calcd. for $C_{14}H_{15}NO$: C, 78.83; H, 7.09. Found: C, 79.01; H, 7.10.

The **oxime** was obtained from dilute methanol as colorless crystals, m. p. 146–148°.

Anal. Calcd. for $C_{14}H_{16}N_2O$: C, 73.64; H, 7.07. Found: C, 73.49; H, 6.96.

5-Nitro-2,3,8-trimethylquinoline (II).—Twenty grams of 2,3,8-trimethylquinoline was added gradually to 200 ml. of fuming nitric acid (*d* 1.49). The solution became hot and was heated on a steam-bath for five hours. It was poured into 200 ml. of water, and the mixture was made alkaline with sodium hydroxide solution. Recrystallization from dilute ethanol rendered pale yellow needles, m. p. 124°, in a yield of 98%.

Anal. Calcd. for $C_{12}H_{12}N_2O_2$: C, 66.63; H, 5.60; N, 12.96. Found: C, 66.69; H, 5.60; N, 12.91.

5-Nitro-3,8-dimethylquinoline-2-aldehyde (VI).—(a) Thirteen and two-tenths grams of 3,8-dimethylquinoline-2-aldehyde was boiled under reflux with 132 ml. of fuming nitric acid (d. 1.49) for five hours, and the solution was poured into ammoniacal water. The nitro-aldehyde was crystallized from dilute ethanol and appeared as almost colorless felted needles, m. p. 165°. The compound contained one molecule of ethanol of crystallization. The yield was 85%.

Anal. Calcd. for $C_{12}H_{10}N_2O_3 \cdot C_2H_6O$: C, 60.84; H, 5.84. Found: C, 60.71; H, 5.63.

Ethanol of crystallization was lost when the compound was heated at 100° under 1 mm. pressure for one hour. The substance melted at 167°.

Anal. Calcd. for $C_{12}H_{10}N_2O_3$: C, 62.58; H, 4.38. Found: C, 62.39; H, 4.05.

(b) One half gram of 2,3,8-trimethyl-5-nitroquinoline was heated with 0.3 g. of selenium dioxide in 20 ml. of ethanol for fifty hours. After filtration from selenium, the solution was concentrated, and a brown oil precipitated which solidified on standing. After several crystallizations from ethanol–water the nitro-aldehyde was obtained in a yield of 38%; m. p. 164–165°. A mixture melting point with the substance obtained by procedure (a) showed no depression.

The **oxime** crystallized from dilute ethanol as a slightly yellow powder, m. p. 180–181°.

Anal. Calcd. for $C_{12}H_{11}N_3O_3$: C, 58.75; H, 4.52. Found: C, 58.64; H, 4.64.

The oximes of the aldehydes VI and VII undergo a number of reactions with metallic ions which are listed in Table I furnished by Dr. Lyle G. Overholser.

2,3,8-Trimethyl-5-aminoquinoline (III).—Two grams of 2,3,8-trimethyl-5-nitroquinoline was added to a solution of 8,5 g. of stannous chloride in 16 ml. of 17% hydrochloric acid, and the solution was heated on a steam-bath for three hours. A small amount of an orange-colored double salt separated out and was brought into solution by dilution with 25 ml. of water. The amino compound was precipitated by the addition of strong sodium hydroxide solution and was purified by sublimation at 100° under 0.1 mm. pressure. The yield was 97%. Recrystallization from dilute ethanol furnished yellow needles, m. p. 110–111°.

TABLE I

Metallic ion	3,8-Dimethylquinoline-2-aldoxime	3,8-Dimethyl-5-nitroquinoline-2-aldoxime
Ag^{+1}	Slight reduction on prolonged standing	Pale yellow color; pale yellow-greenish color in NH_4OH
Au^{+3}	Yellow color within one minute, yellow precipitate on standing	Pale yellow precipitate
Ce^{+4}	Yellow color, fades soon	
$Cu^{-}(NH_3)$	Green precipitate, soluble in strong NH_4OH	Slight precipitate in weak NH_4OH, no reaction in 1 *M* NH_4OH
Hg^{+2}		Slightly yellow precipitate
Ni	Pale green color in neutral solution, slight yellow-green precipitate in NH_4OH solution	Same reaction as with $Cu^{-}(NH_3)$
$OsCl_6^{-}$	Green color in HCl solution	Pale yellow precipitate in HCl, pale yellow color in KOH solution
Pd^{+2}	Stable green color	
Pt^{+4}	Pale yellow-green color in HCl solution	
S^{-}		Pale yellow color
Sn^{+2}		Orange-pink color in HCl solution

Anal. Calcd. for $C_{12}H_{14}N_2$: C, 77.36; H, 7.58. Found: C, 77.56; H, 7.45.

The **mono-hydrochloride,** prepared in ethereal solution, and recrystallized from ethanol, appeared as brick-red needles which sublimed at high temperatures without melting.

Anal. Calcd. for $C_{12}H_{15}ClN_2$: N, 12.59. Found: N, 12.13.

The **di-hydrochloride** was obtained as pale yellow crystals by treating the mono-hydrochloride with an excess of ethanolic hydrogen chloride. It loses hydrogen chloride slowly in the dry state, more rapidly in alcoholic solution, turning deep red.

Acetylation of the amine with acetic anhydride in pyridine solution yielded **2,3,8-trimethyl-5-acetaminoquinoline,** light colorless needles, m. p. 234–235°.

Anal. Calcd. for $C_{14}H_{16}N_2O$: C, 73.64; H, 7.07. Found: C, 73.73; H, 6.97.

2,3,8-Trimethyl-5-hydroxyquinoline (IV).—Five-tenths gram of 2,3,8-trimethyl-5-aminoquinoline, dissolved in 50 ml. of 5 *N* hydrochloric acid, was diazotized at 0° with a solution of 0.25 g. of sodium nitrite in 40 ml. of water. A small amount of urea was added, the solution heated to boiling, cooled, neutralized with sodium bicarbonate, and the phenolic base filtered. The yield was 76%. Sublimation at 125° and 0.1 mm. pressure yielded colorless rods, m. p. 219–219.5°.

Anal. Calcd. for $C_{12}H_{13}NO$: C, 76.96; H, 7.00. Found: C, 76.77; H, 6.81.

2,3,8-Trimethyl-5-methoxyquinoline (V).—(a) Methylation of the phenolic base IV with diazomethane in methanol–ether solution yielded the methoxy compound as colorless prisms, which were purified by sublimation at 75° and 0.01 mm. pressure, and recrystallization from dilute methanol; m. p. 80°.

Anal. Calcd. for $C_{13}H_{15}NO$: C, 77.56; H, 7.52. Found: C, 77.53; H, 7.31.

The **picrate** crystallized from methanol as short yellow prisms, m. p. 198–199°.

Anal. Calcd. for $C_{19}H_{18}N_4O_8$: C, 53.02; H, 4.22. Found: C, 53.19; H, 4.53.

(b) 2-Amino-4-methoxytoluene[15] was prepared by reduction of 2-nitro-4-methoxytoluene[16] with hydrogen in the presence of a platinum oxide catalyst in ethanol solution; the yield was 95%, m. p. 45°.

A solution of 4.2 g. (0.031 mole) of 2-amino-4-methoxytoluene and 3.5 ml. (0.031 mole) of tiglic aldehyde in 65 ml. of concentrated hydrochloric acid was heated on a steam-bath for two hours. The dark solution was diluted with water, and some unchanged methoxytoluidine was removed by diazotization and extraction of the resulting 2-hydroxy-4-methoxytoluene into ether. The solution was then made alkaline and 5-methoxy-2,3,8-trimethylquinoline was extracted into ether. It was purified by sublimation and crystallization and melted at 80°. The yield was 8%.

Anal. Calcd. for $C_{13}H_{15}NO$: C, 77.56; H, 7.52. Found: C, 77.64; H, 7.42.

The **picrate** melted at 197–199°.

Anal. Calcd. for $C_{19}H_{18}N_4O_8$: C, 53.02; H, 4.22. Found: C, 53.47; H, 4.34.

The mixture melting point of the 5-methoxytrimethylquinoline derivatives obtained (a) by degradation and (b) by synthesis, and that of their respective picrates, showed no depression.

2,3,8-Trimethyldecahydroquinoline (XII).—Five grams of 2,3,8-trimethylquinoline in 30 ml. of purified glacial acetic acid was hydrogenated in the presence of 0.4 g. of a platinum oxide catalyst. Another 0.3 g. of the catalyst had to be added to carry hydrogen absorption to completion. Five moles of hydrogen was absorbed in twenty-four hours. The catalyst was filtered, the solution was made alkaline, and the decahydro base was extracted into ether. It was fractionated under 10 mm. pressure, and the main fraction, a colorless oil of b. p. (10 mm.) 89–91°, was collected.

Anal. Calcd. for $C_{12}H_{23}N$: C, 79.48; H, 12.79. Found: C, 79.35; H, 12.39.

The **hydrochloride** was prepared in acetone–ether solution. It appeared as colorless crystals, m. p. 251–275° (dec.).

Anal. Calcd. for $C_{12}H_{24}ClN$: N, 6.44. Found: N, 6.53.

(15) Knecht, *Ann.*, **215**, 83 (1882).

(16) Ullmann and Dootson, *Ber.*, **51**, 19 (1918).

Summary

A number of reactions of the kerosene base, 2,3,8-trimethylquinoline, involving mainly positions 2 and 5 of the quinoline system, have been studied. The derivatives obtained in these reactions will serve as starting materials in the syntheses of compounds containing pharmacologically interesting groups.

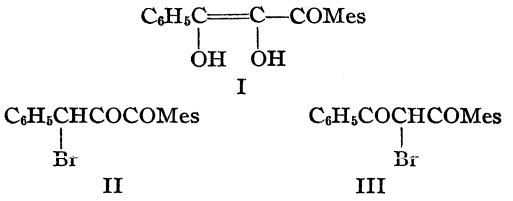
UNIVERSITY, VIRGINIA RECEIVED FEBRUARY 13, 1940

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, HOWARD UNIVERSITY]

The Properties of Benzoylmesitoylmethane

BY R. P. BARNES, CHARLES I. PIERCE[1] AND CHAPPELLE C. COCHRANE[1]

In a previous paper[2] we reported the preparation and properties of an ene-diol (I), obtained from alpha-bromo benzylmesityl diketone (II). In this paper we are reporting the results of a similar investigation of the reactions of the isomeric bromobenzoylmesitoylmethane (III).

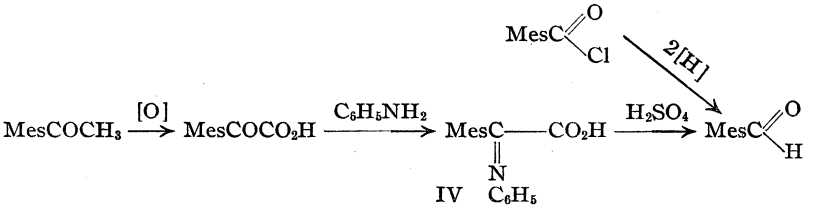


Benzoylmesitoylmethane is described by Kohler and co-workers as resulting from two series of reactions.[3,4] This substance is listed as a solid, melting at 79°, and being 100% enolic in alcoholic solution as indicated by Kurt Meyer titrations. Fuson and co-workers[5] describe mesitoylbenzoylmethane as a solid, melting at 74–77°.

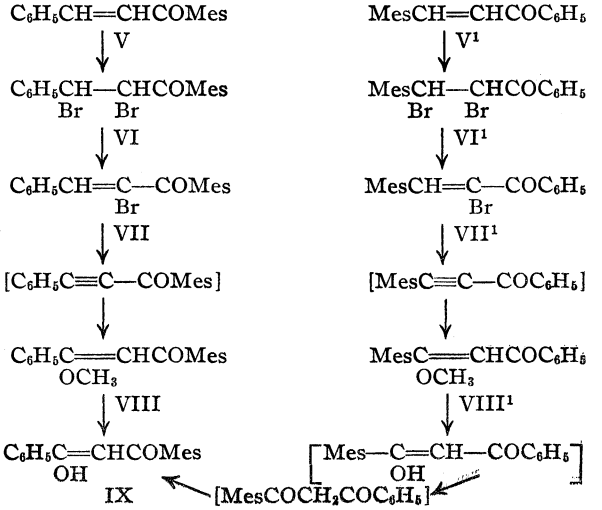
In the light of the mechanism given for the formation of the enolic modification of *beta*-diketones,[6] it seemed likely that the two series of reactions as given by Kohler and his collaborators might lead to isomeric enols of benzoylmesitoylmethane. We have carried out these two series of reactions with slight modifications, exercising care to isolate the intermediates, and have found that there is only one stable enolic modification of benzoylmesitoylmethane, which is evidence that the mesityl group acts against enolization toward itself, which is in a sense hindrance to the existence of the 1,2-addition product resulting from the shift of hydrogen to the adjacent carbonyl.

Mesitylaldehyde (IV) was prepared by two methods: (1) the catalytic reduction[7] of mesitoyl chloride; and (2) the hydrolysis of the anil of mesitylglyoxylic acid obtained from the potassium permanganate oxidation of acetyl mesitylene.[8]

The preparation of the alpha-beta-unsaturated ketones (V) and (V[1]) and their corresponding dibromides (VI) and (VI[1]) was according to the methods of Kohler.[3,4] The dibromide (VI) was converted to the alpha-bromobenzalacetomesitylene (VII), by treatment with fused potassium acetate in glacial acetic acid solution. This compound was converted into the methyl ether of 1-phenyl-3-mesitylpropene-one-3-ol-1 (VIII), from which the enol, 1-phenyl-3-mesitylpropene-one-3-ol-1 (IX) was obtained by acid hydrolysis. The monobromo unsaturated compound (VII[1])



was obtained in poor yield by the potassium acetate–glacial acetic acid treatment of the parent dibromide (VI[1]). Both the mono-bromide (VII[1]) and the dibromide (VI[1]) were converted quantitatively into the methyl ether (VIII[1]) of 1-mesityl-3-phenyl-propene-one-3-ol-1 by treatment with sodium methylate. Acid hydrolysis of this methyl ether resulted in the enol (IX), 1-phenyl-3-mesitylpropene-one-3-ol-1.



(1) In partial fulfillment of the requirements for the Master's degree.

(2) R. P. Barnes and Leila S. Green, THIS JOURNAL, **60**, 1549 (1938).

(3) E. P. Kohler and Carl E. Barnes, *ibid.*, **55**, 690 (1933).

(4) E. P. Kohler and L. W. Blanchard, Jr., *ibid.*, **57**, 367 (1935).

(5) Reynold C. Fuson, G. E. Ullyot and J. L. Hickson, *ibid.*, **61**, 410 (1939).

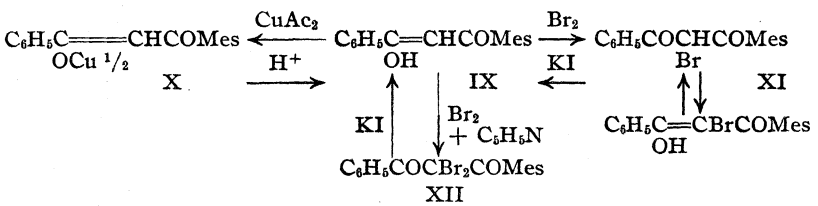
(6) E. P. Kohler and R. Johnstin, *Am. Chem. J.*, **33**, 35 (1905).

(7) Karl W. Rosenmund and F. Zetzsch, *Ber.*, **51**, 585 (1918); **54**, 425 (1921).

(8) Bouveault, *Compt. rend.*, **124**, 157 (1897).

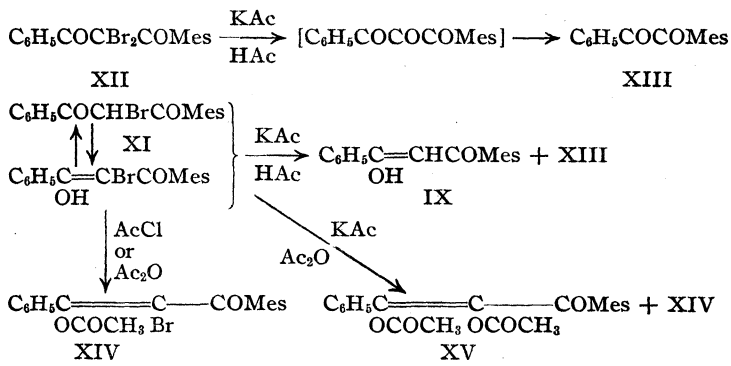
Enol (IX) gives a copper derivative (X) with copper acetate, from which the parent enol is regenerated.

This enol cannot be brominated completely to the monobromo compound by the direct addition of bromine to solutions of the enol, because the bromo compound is easily reduced by the hydrogen bromide formed. In solution in chloroform in the presence of a suspension of calcium carbonate, however, the enol is brominated quantitatively to the monobromo compound (XI), which is a colorless solid, enolic[9] to the extent of 24% in alcoholic solution. In acetic acid solution in the presence of pyridine, enol (IX) is brominated to the dibromo compound (XII).



The dibromo compound (XII) is converted to the diketone (XIII) on treatment with potassium acetate in glacial acetic acid. When the monobromo compound is treated similarly there results a mixture of the parent enol and the diketone (XIII). This is explained in terms of the equilibrium (KBr + HAc $\rightleftarrows$ KAc + HBr), the hydrogen bromide reducing the monobromo compound, and hydrolyzing any diacetate that might be formed, it being subsequently oxidized to the diketone.

The monobromo compound (XI) is acetylated[10] by both acetyl chloride and acetic anhydride to the acetate (XIV), which is not reduced by potassium iodide.



Since we could not obtain the carbinol acetate of benzoylmesitoylmethane by acetylation of the monobromo compound with potassium acetate and glacial acetic acid, we sought a solvent which would not furnish an active hydrogen. Thus the choice of acetic anhydride[10] which, in the presence of freshly fused potassium acetate, yields a mixture of the monobromo acetate (XIV) and the diacetate (XV) of mesitoylphenylacetyleneglycol.[2] The monobromo acetate (XIV), does not suffer further acetylation, since this reaction would necessarily involve a metathesis, and halogen atoms in the system, $\rangle C{=}C\overset{\diagup}{Br}$, which cannot relieve itself by rearrangement, do not take part in double decomposition reactions. Thus the acetylation process must involve two competitive reactions: first, direct esterification of the alpha-bromo ketone itself by splitting out potassium bromide resulting in the carbinol acetate which is subsequently esterified to the diacetate[10]; second, acetylation of the enolic modification of the alpha-bromo ketone, which is not further acetylated.

Further work is now in progress with 2,4,6-trimethylbenzyl phenyl diketone, the alpha diketone isomeric with mesitylbenzylglyoxal,[11] and with 2,4,6-trimethylbenzyl mesityl glyoxal.

Experimental

Preparation of Mesitylaldehyde.—(I) A solution of 90 g. of mesitoyl chloride in 270 g. of faultlessly dry xylene together with 20 g. of palladized barium sulfate was refluxed gently while a stream of dry oxygen-free hydrogen was passed through the solution. The process was continued until hydrogen chloride ceased to be evolved, about eighteen hours. The catalyst was filtered off and the filtrate distilled. The mesitylaldehyde came over at 96–98° (6 mm.). The yield was 60 g., which was 80%.

(II) A chilled mixture of 50 g. of acetylmesitylene and 200 cc. of water was treated dropwise with rapid stirring with a solution of 100 g. of potassium permanganate and 32 g. of potassium hydroxide in 3000 cc. of water. The manganese dioxide was filtered off and washed with water and the pale green solution was made strongly acid with concd. sulfuric acid and allowed to stand in the ice box overnight. A yellow oil consisting of a mixture of trimethylbenzoic, trimethylmandelic and mesitylglyoxylic acids separated out and crystallized. The mixed acids were filtered off and dried, weighing 31 g. The filtrate was extracted with ether, dried over anhydrous sodium sulfate and evaporated, yielding 19–20 g. Assuming the

(9) All titrations were done as by S. R. Cooper and R. P. Barnes, *Ind. Eng. Chem., Anal. Ed.*, **10**, 379 (1938).

(10) THIS JOURNAL, **62**, 894 (1940).

(11) R. P. Barnes, *ibid.*, **57**, 937 (1935).

total mixed acids to be mesitylglyoxylic acid, it was heated to boiling for thirty minutes with the calculated amount of aniline. The yellow solution was cooled, taken up in ether, and washed with dilute hydrochloric acid to remove the excess aniline. The ether was evaporated and the residual yellow oil warmed with 25 g. of concd. sulfuric acid. The dark red solution was allowed to cool and was taken up in the ether and washed with water to remove the excess sulfuric acid and aniline sulfate. Finally the trimethylbenzoic and trimethylmandelic acids were washed out with bicarbonate solution. The ethereal solution was dried over anhydrous sodium sulfate and distilled. The yield was 22.5–23.5 g. of mesitylaldehyde, boiling at 96–98° (6 mm.). This was 50% of the theoretical.

alpha-Bromobenzalacetomesitylene (VII).—To a solution of 234 g. of freshly fused potassium acetate in 500 cc. of hot glacial acetic acid was added 117 g. of dibromobenzalacetomesitylene. The mixture was refluxed for thirty minutes. The solution turned yellow and potassium bromide separated out. When cold the contents of the flask were poured into a large volume of water. A light brown oil separated out which upon stirring and cooling soon crystallized. The yield was 85–86 g. of crude material which was 91–92% of the theoretical. This solid was crystallized from the least amount of hot methyl alcohol, yielding 80–81 g. of lemon yellow solid, melting at 86°.

Anal. Calcd. for $C_{18}H_{17}OBr$: C, 65.6; H, 5.2. Found: C, 65.3; H, 5.1.

This monobromo compound reduces permanganate and decolorizes chloroform solutions of bromine. Phenylmagnesium bromide converts it into alpha-bromo-beta-phenylbenzylacetomesitylene.[12]

alpha-Bromo 2,4,6-Trimethylbenzalacetophenone (VII[1]).—A solution of 100 g. of fused potassium acetate and 50 g. of the dibromide in 250 cc. of glacial acetic acid was treated as indicated in the preparation of alpha-bromobenzalacetomesitylene. A yellow oil resulted from the water treatment. Extraction with ether, washing, drying and concentrating yielded 3.1 g. of pale yellow solid melting at 98° and mix-melting with the parent alpha-beta-unsaturated ketone at 98°. Further concentration produced a crystalline solid which when recrystallized from methyl alcohol amounted to 7.1 g., melted sharply at 95°, and mix-melted with the parent alpha-beta-unsaturated ketone at 73–85°.

Anal. Calcd. for $C_{18}H_{17}OBr$: C, 65.6; H, 5.2. Found: C, 65.7; H, 5.5.

It decolorizes permanganate and bromine solutions.

The Methyl Ether of 1-Mesityl-3-phenyl-propene-one-3-ol-1 (VIII[1]).—A solution of 1 g. of the monobromo unsaturated ketone in sodium methylate made from 0.1 g. of sodium in 1 g. of methyl alcohol was refluxed for one hour. On cooling, pale yellow needles separated. The mixture was poured into three times its volume of water. There was obtained 0.8 g. of material melting at 106–113°, which when recrystallized from methyl alcohol melted and mix-melted at 113° with a sample obtained by the treatment of the dibromo compound with sodium methylate.[4]

(12) E. P. Kohler, *Am. Chem. J.*, **38**, 555 (1907).

1-Phenyl-3-mesityl-propene-one-3-ol-1 (IX).—To the solution of 80.3 g. of alpha-bromobenzalacetomesitylene in the least amount of hot methyl alcohol was added slowly and carefully with shaking, a solution of 34 g. of potassium hydroxide in the least amount of hot methyl alcohol. The solution turned red and potassium bromide separated out. When cold it was poured into 300 cc. of cold water and acidified with dilute hydrochloric acid. The milky solution thus produced was extracted with ether, the ethereal extract washed with water and the ether distilled. The oily residue was dissolved in hot methyl alcohol from which, on cooling, a cream-colored solid separated. The yield was 53–55 g. of enol, melting at 76–77°. This crude yield was 79–81% of the theoretical. On recrystallizing from methyl alcohol, it melts sharply at 79°.

To a solution of 29.2 g. of the methyl ether of 1-mesityl-3-phenylpropene-one-3-ol-1 in 160 cc. of methyl alcohol was added 30 cc. of concd. hydrochloric acid, and the mixture refluxed for three hours. On cooling overnight, colorless plates separated out. This yield was 20.7 g. of crude product melting at 78°. Recrystallization from methyl alcohol gave beautiful plates, melting sharply at 79°, with no depression on mix-melting with the 79°-melting enol.

It is 100% enolic in methyl alcohol and less then 1% enolic in carbon tetrachloride.

Preparation of the Copper Derivative (X).—A saturated ether solution of 1 g. of the enol was shaken for several hours with an excess of saturated copper acetate solution. The resulting greenish-tan crystalline solid was filtered, washed and dried, and weighed 0.9 g. It melts with decomposition at 221°.

Anal. Calcd. for $C_{36}H_{34}O_4Cu$: Cu, 10.71. Found: Cu, 10.69.

When the copper derivative is shaken in chloroform solution with hydrochloric acid, the enol is regenerated.

Preparation of Bromo Benzoylmesitoylmethane (XI).—Fourteen grams of calcium carbonate was suspended in a solution of 10 g. of the enol in 30 cc. of chloroform. A solution of 6.1 g. of bromine in 10 cc. of chloroform was added slowly with rapid stirring. The bromine was absorbed rapidly without any evolution of hydrogen bromide. The mixture of calcium carbonate and calcium bromide was filtered off and the chloroform pumped off. A pale yellow viscous mass was left which crystallized upon standing in an evacuated desiccator over potassium hydroxide. Recrystallization from low-boiling petroleum ether yielded 6.2 g. of colorless prisms, melting at 64–66°.

Anal. Calcd. for $C_{18}H_{17}O_2Br$: C, 62.6; H, 4.9. Found: C, 62.9; H, 5.2.

Differential Kurt Meyer titrations show that this substance is 24% enolic. It gives a characteristic red color with alcoholic ferric chloride and is reduced to the parent enol by potassium iodide.

Five grams of the monobromo compound was dissolved in 25 cc. of glacial acetic acid and refluxed for one hour with 5 g. of freshly fused potassium acetate. It was poured into a large volume of cold water to distribute the acetic acid, whereupon a yellow oil separated out. This oil was crystallized from methyl alcohol, yielding 3 g. of the parent enol, and 0.5 g. of mesityl phenyl diketone, each identified by its melting point and mix-melting point.

Dibromo Benzoylmesitoylmethane (XII).—A solution of 20 g. of concd. sulfuric in 40 cc. of glacial acetic acid was added with cooling to a solution of 16 g. of pyridine in 40 cc. glacial acetic acid. To this mixture was added 26.8 g. of enol (IX) dissolved in 170 cc. of glacial acetic acid. Finally with cooling and vigorous shaking, 32 g. of bromine in 400 cc. of acetic acid was added. The bromine was taken up rapidly. The acetic acid was distilled under diminished pressure; the residual oil was poured into water and extracted with ether. The ethereal solution was washed with sodium bicarbonate solution and with water. The ether was evaporated and the resulting pale yellow oil crystallized from methyl alcohol yielding pale yellow crystals, melting at 101–106°. Recrystallization from low-boiling petroleum gave 16 g. of pale yellow crystals melting at 107–108°.

Anal. Calcd. for $C_{18}H_{16}O_2Br_2$: C, 50.9; H, 3.8; Br, 37.7. Found: C, 51.0; H, 3.9; Br, 37.8.

This dibromide upon treatment with glacial acetic acid and potassium acetate is converted into mesityl phenyl diketone, identified by comparison with an authentic sample.

The Acetate (XIV).—Five grams of the bromobenzoylmesitoylmethane was refluxed for one hour with an excess of acetyl chloride. The acetyl chloride was pumped off and the residue crystallized from methyl alcohol. A practically quantitative yield of colorless crystalline solid, melting at 96°, was obtained.

Anal. Calcd. for $C_{20}H_{19}O_3Br$: C, 62.0; H, 4.9. Found: C, 62.0; H, 5.2.

This substance is non-enolic and is hydrolyzed by acids to the parent bromo compound. It is not acetylated further by potassium acetate in acetic anhydride, nor is it reduced by potassium iodide in acid solution. The same compound is obtained when the bromobenzoylmesitoylmethane is treated with acetic anhydride.

The Action of Acetic Anhydride–Potassium Acetate on Bromobenzoylmesitoylmethane (XIV) and (XV).—To a hot mixture of 10 g. of freshly fused potassium acetate and 50 cc. of acetic anhydride were added 10 g. of the monobromo compound. This mixture was refluxed gently for forty-five minutes. The solution turned dark brown and potassium bromide separated out. When cold it was poured into a large volume of cold water and stirred vigorously until the acetic anhydride was decomposed. It was then taken up in ether, washed with sodium bicarbonate solution, and finally with water, dried and evaporated. The residue was dissolved in methyl alcohol, from which by fractional crystallization 5 g. of the bromo acetate, melting at 96°, and 1.0 g. of the diacetate, melting at 131°, were obtained. Both products were identified by their mixed-melting points with known samples.

Summary

In this paper we have reported the properties of the enolic modification of benzoylmesitoylmethane, which properties are influenced considerably by the presence of the mesityl nucleus, which seems not only to activate the *alpha* substituents but also to have a directing influence upon enolization.

WASHINGTON, D. C. RECEIVED FEBRUARY 12, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF MOUNT HOLYOKE COLLEGE]

Ring Closure of Acylic Ureides Resulting from the Elimination of Alcohol: A Study of the Esters of beta-Phenylalanine-N-acetic Acid and Related Compounds[1]

BY DOROTHY A. HAHN, MARGARET J. MCLEAN AND MARGARET M. ENDICOTT

Further study of the derivatives of β-phenylalanine-N-acetic acid has resulted in the synthesis of the isomer of C-5-benzylhydantoin-N-1-acetate, to which reference was made in an earlier report.[1a] It was then stated that although the formation of two isomeric hydantoin-acids was theoretically possible following the hydrolysis of the ureidic salt

(I) $H_2NCON\begin{matrix}CH_2COOK\\CH(CH_2C_6H_5)COOK\end{matrix}$

under the action of hydrochloric acid, ring closure actually had been observed to take place in one sense only.[2] Moreover, since the product[3]

(II) $HOOCCH_2\overline{NCONHCOCHCH_2C_6H_5}$

was precipitated instantly in yields averaging more than 90% of the theoretical, it seemed reasonable to conclude that the rates at which the two carboxyl groups were capable of reacting respectively with the hydrogen of the amide group in the ureide must differ greatly in magnitude. It appeared probable therefore that the formation of the isomer

(III) $HOOC(CH_2C_6H_5)CH\overline{NCONHCOCH_2}$

could not be expected under ordinary conditions. However, it was still possible that in the case of a compound having the configuration

(1) Original manuscript received November 7, 1939.

(1a) Hahn and Endicott, THIS JOURNAL, **60**, 1045 (1938).

(2) A similar observation has been reported by E. Ware, *ibid.*, **60**, 2653 (1938), who found that although two isomeric hydantoins were theoretically possible as a result of the cyclization of a hydantoic derivative of tyrosine-N-acetic acid, only one product could be isolated and identified, namely, $HOOCCH_2\overline{NCON(C_6H_5)COCHCH_2}$-$C_6H_4OH$.

(3) The configuration of this compound has been definitely established, Hahn and Endicott, *loc. cit.*, p. 1042.

(IV) $H_2NCON\langle^{CH_2COOR^4}_{CH(CH_2C_6H_5)COOK}$

ring closure, taking place in an alkaline medium and accompanied by the elimination of alcohol, might occur. This possibility has been realized and it can now be stated that cyclization of this type has been effected following the synthesis of certain derivatives of β-phenylalanine-N-acetic acid, a brief discussion of which follows.

The mono-alkyl esters of this unsymmetrical acid, together with the corresponding hydrochlorides, may be assumed to be capable of existing in two isomeric modifications, such as, for example

(a) $HCl\cdot NH\langle^{CH_2COOR}_{CH(CH_2C_6H_5)COOH}$ and

(b) $HCl\cdot NH\langle^{CH_2COOH}_{CH(CH_2C_6H_5)COOR}$

It has been found, however, that only *one* salt of this type can be isolated as a result of dissolving the imino acid in a hydrogen chloride solution of either methyl or ethyl alcohol. For reasons to be discussed later these products, which under very specific conditions were precipitated in almost pure condition and in yields averaging 70% of the theoretical, were assumed to possess the configurations

(V) $HCl\cdot NH\langle^{CH_2COOCH_3}_{CH(CH_2C_6H_5)COOH}$ and

(VI) $HCl\cdot NH\langle^{CH_2COOC_2H_5}_{CH(CH_2C_6H_5)COOH}$

The filtrate contained a mixture of the hydrochlorides of the free acid, its mono- and di-alkyl esters.[5]

Following their final purification, both salts were transformed (under loss of hydrogen chloride) into the corresponding free esters:

(VII) $^+NH_2\langle^{CH_2COOCH_3}_{CH(CH_2C_6H_5)COO^-}$ and

(VIII)[6] $^+NH_2\langle^{CH_2COOC_2H_5}_{CH(CH_2C_6H_5)COO^-}$

These compounds are almost insoluble in water, alcohol and other organic solvents but both dissolve readily in ammoniacal solutions of alcohol to form one and the same monamide

(IX) $^+NH_2\langle^{CH_2CONH_2}_{CH(CH_2C_6H_5)COO^-}$

From this it follows that both esters possess the same configuration.[7]

The formulas that have been assigned to the compounds V, VI, VII and VIII, irrespective of their close chemical interrelationships, depend upon the fact that under the action of aqueous potassium cyanate *all four* were transformed into acyclic ureides which in weakly alkaline media underwent ring closure to give one and the same final product, XI. In the case of the compound VII, for example, the course of this reaction may be indicated most simply as

(VII) $^+NH_2\langle^{CHCOOCH_3}_{CH(CH_2C_6H_5)COO^-} \longrightarrow$

(X) $H_2NCON\langle^{CH_2COOCH_3}_{CH(CH_2C_6H_5)COOK} \longrightarrow$

$KOOC(CH_2C_6H_5)CH\overline{NCONHCOCH_2}$ + CH_3OH[8]

(XI)

The presence in the reaction mixture of a compound having the configuration XI was assumed from the fact that addition of hydrochloric acid resulted in the formation of an hydantoin acid, which on analysis was found to be isomeric with II.[3] While the formula which has been assigned to this new compound III has not as yet been confirmed as the result of a second synthesis, it is supported by a consideration of the following facts. The acids II and III show a striking similarity in their physical and chemical properties. For example, a comparison of their absorption curves reveals a very close relationship, since both show selective absorption that is identical

(4) Whenever used, R may be understood to denote either a methyl or an ethyl group.

(5) That this filtrate contained no decomposition products was shown by the fact that when evaporated to dryness and the residue treated as described by Hahn and Endicott (*loc. cit.*, p. 1041, footnote 4), the free imino-acid was regenerated in amounts corresponding very closely to the theoretical. Reference will be made frequently to this as a general procedure for recovering the free imino-acid.

(6) It may be noted that in the case of imino-diacetic acid only a single compound of this type was isolated. This was referred to by Jongkees [*Rec. trav. chim.*, **27**, 297 (1908)] as an "ether-salt," $NH(CH_2COOC_2H_5)CH_2COOH$, in which the function of the acid neutralizes that of the secondary amine since the compound is almost neutral to turmeric. It seems curious that the corresponding methyl ester was never separated, but this may be due to the fact that, as in the case of the corresponding derivatives of beta-phenylalanine-N-acetic acid, it was more difficult to prepare. For example, while the hydrochloride V is extremely stable in aqueous solution, VI is partially hydrolyzed even at ordinary temperatures and when the dry salt was treated with boiling water, its solution was followed almost instantly by the precipitation of VIII.

(7) A comparison of the electrolytic dissociation constants of VII, VIII and IX has revealed, moreover, that all three behave like weak monobasic acids. These constants agree very closely and are of the order of 10^{-7} (McLean, unpublished work).

(8) Ring closures accompanied by the elimination of alcohol which resulted in the formation of both hydantoin and hydantoin-N-1-acetic acid, have been reported by J. R. Bailey, *Am. Chem. J.*, **28**, 393 (1902), and by Bailey and Snyder, THIS JOURNAL, **37**, 945 (1915).

up to 37000 cm.$^{-1}$. Differences are to be found only in the intensities of absorption characteristic of the phenyl group and these may be accounted for as due to differences in the relative positions of this group in the two molecules.[9] Both acids have been shown to be dibasic as a result of electrometric titrations,[10] although due to a weakly acidic hydrogen atom in the N-3-position, each yields respectively only a single stable mono-sodium salt. The corresponding methyl esters also have been prepared and found to be isomeric and not identical. It may be added that the acid III has been obtained in yields of 70% from each of the compounds designated as V, VI, VII and VIII and that the course of the reaction in the case of VII has been demonstrated by the fact that methyl C-5-benzylhydantoin-N-1-acetate,[11] which could be formed only as a result of ring closure of X under the action of hydrochloric acid, was actually isolated from the reaction mixture.

In conclusion it may be stated that only one dialkyl ester of β-phenylalanine-N-acetic acid has as yet been prepared and that this was separated in pure condition only in the form of its hydrochloride

(XII)[12] $HCl\cdot NH\begin{cases}CH_2COOCH_3\\CH(CH_2C_6H_5)COOCH_3\end{cases}$

It is interesting to note that when this salt was treated with potassium cyanate and the reaction product subsequently hydrolyzed, both of the hydantoin-acids II and III were again isolated.

Experimental

The β-phenylalanine-N-acetic acid used in these experiments was prepared by alkaline hydrolysis of ethyl N-3-methyl-C-5-benzylhydantoin-N-1-acetate[13] and was purified by recrystallization from boiling water.

The hydrochloride of the mono-methyl ester, V, $HCl\cdot NH(CH_2COOCH_3)CH(CH_2C_6H_5)COOH$, m. p. 185–186° (dec.), was obtained in yields averaging 70 to 75% by dissolving the free acid in methyl alcohol under the action of hydrogen chloride. For example, to a clear solution of 5 g. of the free acid in 15 cc. of absolute methyl alcohol one-third saturated with dry hydrogen chloride,[14] after standing thirty minutes at 0° and then forty-eight hours at room temperature, 50 cc. of absolute ether was added.[15] After two hours the resulting white crystals were washed with a mixture of alcohol and ether (1:10)[16] and dried; weight 4.43 g.; m. p. 183–186°. On recrystallization from boiling acetone they decomposed sharply at 185–186°.

Anal. Calcd. for $C_{12}H_{15}O_4N\cdot HCl$: C, 52.65; H, 5.87; N, 5.12; Cl, 12.96. Found: C, 52.90; H, 5.85; N, 5.09; Cl, 12.79.

The salt is soluble in cold absolute methyl alcohol (1 g. in less than 3 cc.) and in acetone (1 g. in 500 cc. boiling and in 1250 cc. at 20°) but insoluble in ether. It loses hydrochloric acid readily to form the free ester VII when treated with the calculated quantity of dilute alkali but is stable in aqueous[17] and alcohol solutions. It yields the corresponding salt of the imino acid when warmed with concentrated hydrochloric acid,[18] and sodium and potassium salts on alkaline hydrolysis.[18]

The hydrochloride of dimethyl-β-phenylalanine-N-acetate, XII, $HCl\cdot NH(CH_2COOCH_3)CH(CH_2C_6H_5)COOCH_3$, m. p. 144–145° (dec.), was obtained in 70% yields from the hydrochloride of the imino acid after five days[19] of alternate saturation of a concentrated absolute methyl alcohol solution (8.5 g. in 25 cc.) with dry hydrogen chloride at 0°, and refluxing over a steam-bath. The clear solution evaporated to dryness under air blast gave a red gum which when dissolved in boiling acetone deposited white crystals; weight 6.8 g.; m. p. 138–142°. Recrystallized from acetone they decomposed sharply at 144–145°.[20]

Anal. Calcd. for $C_{13}H_{17}O_4N\cdot HCl$: C, 54.26; H, 6.30; N, 4.87; Cl, 12.32. Found: C, 54.20; H, 6.23; N, 4.70; Cl, 12.33.

The salt is very soluble in cold absolute methyl alcohol and moderately in acetone (1 g. in 75 cc. boiling and in 190 cc. at 20°)[21] but insoluble in ether. It separates from alcohol solutions on addition of ether in long, silk-like,

(9) McLean, unpublished work.

(10) Their respective pK_1 and pK_2 dissociations are II, 2.81 and 8.96; III, 2.91 and 9.20. Compare Pickett and McLean, THIS JOURNAL, **61**, 423 (1939).

(11) The identity of this ester was confirmed by a mixed melting point with an analyzed specimen previously synthesized. Compare Hahn and Endicott, *loc. cit.*, p. 1044.

(12) The hydrochloride of the corresponding diethyl ester and the corresponding derivative of iminodiacetic acid could not be isolated, although Jongkees (*loc. cit.*, p. 296) finally obtained a small quantity of a crystalline compound to which he assigned the formula $HCl\cdot NH(CH_2COOC_2H_5)_2\cdot H_2O$.

(13) Hahn and Endicott, *loc. cit.*, 1042; also compare Hahn and Litzinger, *ibid.*, **54**, 4663 (1932), and Litzinger, *ibid.*, **56**, 676 (1934).

(14) Yields were lower and extremely variable when hydrogen chloride was passed directly into a suspension of the free acid in alcohol.

(15) Excess ether caused the precipitation of an oil.

(16) The filtrate on evaporation under air blast gave a gum from which hydrochlorides of the imino acid and of its mono- and dimethyl esters were separated, but which when warmed with dilute hydrochloric acid was completely transformed into the free imino acid.[5] A similar gum was obtained when an alcohol solution of the hydrochloride of the imino acid was evaporated to dryness.

(17) The salt is very soluble in cold water, from which it separates undecomposed but dilute solutions (10 g. in 100 cc.) after prolonged boiling (twelve hours) deposit a gum (0.3 g.) on cooling. This consists of a mixture of the free ester and its hydrochloride.

(18) Identification effected by comparison with analyzed specimens, Hahn and Endicott, *loc. cit.*, p. 1043.

(19) When action was stopped after four or five hours, a mixture was obtained from which less than 40% of the above salt could be separated. Compare Jongkees, *loc. cit.*, pp. 295–296.

(20) The same salt was obtained from oils or gums similar to those described in footnote 16. Separation was effected by dissolving the gum in water, and extracting with ether following additions of sodium bicarbonate. The ether solution when *perfectly dry* and saturated with hydrogen chloride, deposited the salt in form of a gum which on stirring changed into white crystals, m. p. 144–145°.

(21) Due to marked differences in their solubilities in acetone, mixtures consisting *exclusively* of the hydrochlorides of the mono- and di-methyl esters may be separated readily.

glistening white needles that form in rosettes. Warmed with dilute hydrochloric acid it gave the free acid.[5]

The hydrochloride of the mono-ethyl ester of β-phenylalanine-N-acetic acid, VI, $HCl\cdot NH(CH_2COOC_2H_5)CH(CH_2C_6H_5)COOH$, m. p. 170–172° (dec.), was obtained from the free acid in yields of 70–75%, when absolute ethyl alcohol was substituted for methyl in the corresponding experiment, V. The product, consisting of hard white crystals,[22] was recrystallized from boiling acetone.

Anal. Calcd. for $C_{13}H_{17}O_4N\cdot HCl$: C, 54.26; H, 6.30; N, 4.87; Cl, 12.32. Found: C, 54.50; H, 6.34; N, 4.84; Cl, 12.25.

The salt is very soluble in cold absolute ethyl alcohol but only slightly in acetone (1 g. in 300 cc. boiling and in 750 cc. at 20°) and insoluble in ether. It differs in its reactions from the corresponding methyl derivative only in that it loses its hydrochloric acid when dissolved in water.[23]

The free mono-methyl ester of β-phenylalanine-N-acetic acid, VII, $^+NH_2(CH_2COOCH_3)CH(CH_2C_6H_5)COO^-$, m. p. 208–210° (dec.), was obtained from the corresponding hydrochloride by adding at 0° an equivalent of (a) sodium methoxide to its methyl alcohol solution, or (b) potassium bicarbonate to an aqueous solution. The gelatinous precipitate, consisting of salt mixed with free ester which formed in both cases, was resolved into fine white crystals on stirring or warming. Thus when 0.34 g. of sodium in 25 cc. of absolute methyl alcohol was added to 4 g. of salt in 10 cc., crystals m. p. 201–203° and weight 3.1 g. were obtained. After extraction with cold water and recrystallization from methyl alcohol, these were dried in a high vacuum at 20°.

Anal. Calcd. for $C_{12}H_{15}O_4N$: C, 60.75; H, 6.36; N, 5.91. Found: C, 60.51; H, 6.61; N, 6.18.

This "ester-salt" is only slightly soluble in absolute methyl alcohol (1 g. in 180 cc. boiling and in 250 cc. at 20°) and water (1 g. in 70 cc. boiling and in 200 cc. at 20°) but dissolves freely in aqueous alkali or acid. When warmed with dilute hydrochloric acid it passed quantitatively into the free imino acid.[5]

The free mono-ethyl ester, VIII, $^+NH_2(CH_2COOC_2H_5)CH(CH_2C_6H_5)COO^-$, m. p. 206–208° (dec.), was obtained when the corresponding dry salt VI was treated with boiling water. A clear colorless solution was first formed, then a gelatinous precipitate which dissolved on heating and finally a white crystalline compound. The latter was pure and the change quantitative in cases where the heating was prolonged for an hour. After recrystallization from boiling water, it was dried in a high vacuum at 20°.

Anal. Calcd. for $C_{13}H_{17}O_4N$: C, 62.14; H, 6.82; N, 5.58. Found: C, 62.30; H, 6.93; N, 5.75.

The "ester-salt" is even less soluble than the corresponding methyl derivative in alcohol (1 g. in 650 cc. boiling) and water but dissolves freely in aqueous alkali and acid. Warmed with dilute hydrochloric acid it passed quantitatively into the free imino acid.[5]

The monamide, IX, $^+NH_2(CH_2CONH_2)CH(CH_2C_6H_5)COO^-$, m. p. 196–197° (dec.), was obtained by passing dry ammonia into an absolute alcohol suspension of either VII or VIII at 20° and concentrating the resulting clear solution. The product was mixed with considerable quantities of the original ester but could be separated by extraction with small quantities of cold water made faintly alkaline with ammonia. Recrystallized from the same solvent, it separated in long, white, silk-like needles which completely filled the space occupied by the solution.

Anal. Calcd. for $C_{11}H_{14}O_3N_2$: C, 59.44; H, 6.35; N, 12.61. Found: C, 59.28; H, 6.66; N, 12.71.

The amide is only slightly soluble in alcohol (1 g. in 200 cc. boiling and in 400 cc. at 20°), but is very soluble in cold water. For example 2 g. in 20 cc., concentrated to 10 cc. under air blast, gives a precipitate of only 1 g., partial hydrolysis being avoided only by the presence of a trace of ammonia. Warmed with dilute hydrochloric acid, the amide passed quantitatively into the imino acid.[5]

Hydantoin-N-1-benzylacetic acid, III, $HOOC(CH_2C_6H_5)CH\overset{\frown}{NCONHCOCH_2}$, m. p. 157–158°, was obtained from four compounds (the hydrochlorides V and VI and the esters, VII and VIII) by treating an aqueous alcohol solution or suspension of each with aqueous potassium cyanate slightly in excess of the amount equivalent to the dissociable hydrogen present.

In previewing the course of these reactions it was assumed that if, for example, the compound VII were used as the starting point, primary ionic exchanges (a) would result in the formation of the cyanate, $HOCN\cdot NH(CH_2COOCH_3)CH(CH_2C_6H_5)COOK$. The latter might then be expected to rearrange (b) into the acyclic ureide, $NH_2CON(CH_2COOCH_3)CH(CH_2C_6H_5)COOK$, X; after which ring closure (c) accompanied by the elimination of methyl alcohol and the formation of the hydantoin salt, $KOOC(CH_2C_6H_5)CH\overset{\frown}{NCONHCOCH_2}$, XI, might or might not occur. It appeared probable, moreover, that the progress made in each of these transformations could be ascertained by stopping the reaction at the end of different time intervals as a result of adding hydrochloric acid in amounts exactly equivalent to the potassium in the cyanate that had been used in the experiment. Under these conditions, for example, the compound VII would be completely regenerated if no change other than that indicated by (a) had taken place.[24] If, however, even partial rearrangement (b) had occurred, the liberation of the corresponding hydantoic acid almost certainly would be followed by ring closure accompanied by the elimination of water. In this case the product, methyl C-5-benzylhydantoin-N-1-acetate, could also be readily separated and identified.[11] Finally if the transformation indicated by (c) had taken place, a new hydantoin acid, III, isomeric with II, would be formed. Complications arising from alkaline hydrolysis having taken place during the time allowed for the transformations (a), (b) and (c) also were considered. In that event dipotassium derivatives of both the cyanate, and the corresponding ureide X would be formed, *i. e.* $HOCN\cdot NH(CH_2COOK)CH(CH_2C_6H_5)COOK$, and NH_2-

(22) The filtrate from these crystals gave a gum which was exactly analogous to that described under footnote 16.

(23) The ease with which the mineral acid may be lost has been noted in the case of the salt of the imino acid itself.[5] For other examples compare Stadnikoff, *Ber.*, **41**, 4365 (1908), and **44**, 41 (1911); also Hahn and White, THIS JOURNAL, **54**, 2054 (1932).

(24) This was found actually to be the case when the reaction was stopped at the end of fifteen minutes.

$CON(CH_2COOK)CH(CH_2C_6H_5)COOK$ (I).[1] Introduction of mineral acid would then result in the precipitation of two additional compounds, namely, the free imino acid and the hydantoin-acid II.

In practice the final product was a mixture of all five compounds. For example 4.0 g. of the salt V dissolved in 90 cc. of 80% methyl alcohol was treated with 1.37 g. of solid potassium cyanate and then warmed gently in order to dissolve the resulting precipitate (VII). After cooling to 0° the clear solution was stirred mechanically for one hour, left at room temperature for forty-five hours, concentrated to 20 cc. under air blast and finally treated with 15.7 cc. of 1.018 *N* hydrochloric acid. Extraction with chloroform and then with alcohol-free ether yielded 0.42 and 2.0 g., respectively, of the hydantoin acids II and III and 0.36 g. of the methyl ester of the former, leaving a residue of 0.13 g. of the free imino acid and 0.30 g. of its mono methyl ester. Table I shows the relative percentages of hydantoin derivatives obtained under other conditions.[25]

TABLE I

% Aq. CH_3OH	Reaction period preceding addition of HCl, hr.	% of various products resulting from ring closures III	II	Ester of II
80	1.5	33	Trace only	13.0
80	24	72	Trace only	12.0
65	1.5	40	3.4	11.1
50	1.5	26	26	6.0

In later experiments 80% alcohol was used and excess hydrochloric acid added at the end of twenty-four to forty-eight hours, when the mixture was heated to ensure the hydrolysis of any esters before extracting the acids II and III with chloroform. After evaporation of the chloroform, the mixture was separated by fractional recrystallization from boiling water when III, m. p. 157–158°, was obtained in yields of 70 to 75%.

Anal. Calcd. for $C_{12}H_{12}O_4N_2$: C, 58.06; H, 4.87; N, 11.29. Found: C, 58.02; H, 5.08; N, 11.36.

The hydantoin acid III is not only more soluble than its isomer in water (1 g. in 3 cc. boiling and in 70 cc. at 20°) but when recrystallized from dilute solutions, separates in characteristic rosettes of 30 or more thin, flat hexagonal prisms 2 × 5 mm. at the base but tapering to a sharp point, with a length of 10 to 15 mm.,[26] that can be separated mechanically. Both acids separate as oils from concentrated aqueous solutions, and are very soluble in chloroform but only slightly soluble in ether.

Sodium hydantoin-N-1-benzylacetate was obtained in two different modifications, (a) anhydrous, which began to decompose at 188° and was completely carbonized at 300°, and (b) an alcoholate, which first melted between 60° and 70° with loss of alcohol and then solidified again at 91°. When heated higher this white solid began to decompose at 188° and was completely carbonized at 300°. In both cases the hydantoin-acid III, dissolved in alcohol (3.0 g. in 30 cc.), was treated with aqueous sodium hydroxide (0.4 g. in 5 cc.) and in both cases the product separated in fine white crystals.

Anal. (a) Calcd. for $C_{12}H_{11}O_4N_2Na$: Na, 8.51. Found: Na, 8.71. (b) Calcd. for $C_{12}H_{11}O_4N_2Na \cdot C_2H_5OH$: Na, 7.27; C_2H_5OH, 14.50. Found: Na, 7.39; C_2H_5OH, 13.85.

Both modifications are very soluble in water, only slightly soluble in boiling ethyl alcohol (1.0 g. in 250 cc.) and insoluble in ether. That neither is identical with sodium C-5-benzylhydantoin-N-1-acetate[26] was demonstrated by mixed melting points. Aqueous solutions treated with hydrochloric acid passed quantitatively into the corresponding hydantoin-acid III.

Methyl hydantoin-N-1-benzylacetate, m. p. 105–106.5°, was obtained in 85% yields by passing dry hydrogen chloride into a solution of III in absolute methyl alcohol. The product was separated from traces of III in the usual manner and then recrystallized from boiling 50% alcohol, from which it separated in small, colorless, transparent cubes.

Anal. Calcd. for $C_{13}H_{14}O_4N_2$: C, 59.51; H, 5.30. Found: C, 59.61; H, 5.38.

The ester is extremely soluble in cold methyl alcohol and slightly soluble in boiling water. That it is isomeric and not identical with methyl C-5-benzylhydantoin-N-1-acetate[11] was demonstrated by means of a mixed melting point determination.

Summary

Another example of ring closure accompanied by the elimination of alcohol and the formation of an hydantoin is described, together with the preparation of several new derivatives of β-phenylalanine-N-acetic acid.

SOUTH HADLEY, MASS. RECEIVED MARCH 1, 1940

(25) The concentration of V was the same in all experiments, but the heat required for the solution of the ester VII was never satisfactorily controlled and this undoubtedly led to variations in percentage yields not otherwise explained. It may be added that while no appreciable differences were observed when V and VII were used as starting points, the substitution of VI and VIII appeared to result in a definite increase in the speed with which the reaction mixture approached a condition of equilibrium. However, the maximum yields of III from all four compounds were approximately 70% of the theoretical.

(26) Compare Hahn and Endicott, *loc. cit.*, p. 1044.

[CONTRIBUTION FROM THE CHEMICAL RESEARCH LABORATORY OF BAKER & CO., INC.]

Hydrogenation of Quinone with Palladium and Platinum Catalysts

BY EDGAR F. ROSENBLATT

The hydrogenation of quinone has recently been studied by Otto Neunhoeffer and Willibald Pelz,[1] with the interesting result that hydrogenations with palladium catalysts are feasible also in a carbon monoxide atmosphere instead of the commonly used hydrogen. To compare it with hydrogen hydrogenations, they also studied[1] the hydrogenation of different quinones in a hydrogen atmosphere and found to their surprise that, in contrast to the results with carbon monoxide, palladium could not catalyze the reduction of quinone in a hydrogen atmosphere; from this experimental result they draw the conclusion that reversible systems cannot be hydrogenated with palladium and hydrogen. Such a conclusion conflicts with a publication by Donald T. Bonney and Wilbert J. Huff,[2] recommending the use of a solution of anthraquinone disulfonates and colloidal palladium for the absorption of hydrogen in gas analysis.

A clarification of this discrepancy seemed desirable, so the experiments described herein were undertaken. We may say at once that we have confirmed the experimental results of Neunhoeffer and Pelz, but only under their very special conditions, *i. e.*, in an aqueous hydrochloric acid solution. However, the general deduction that palladium is not a catalyst for reversible systems in a hydrogen atmosphere, is erroneous, as in aqueous as well as alcoholic solution the hydrogenation of quinone to hydroquinone proceeds with remarkable speed, *as long as no mineral acid is present.*

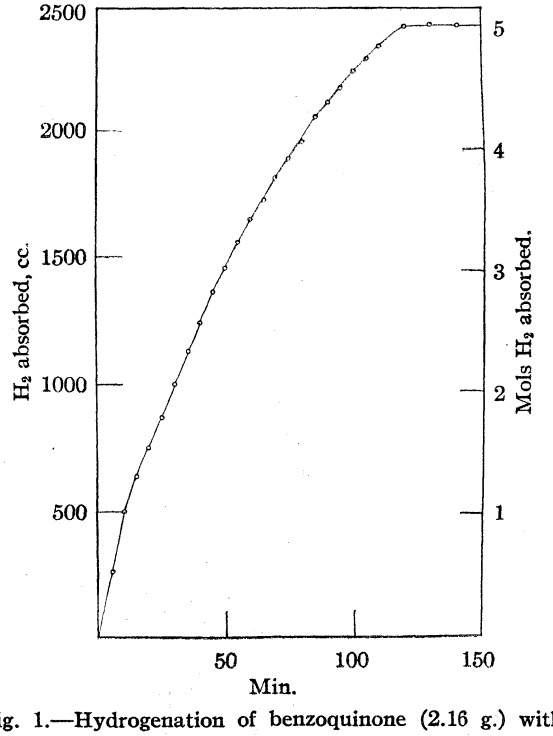


Fig. 1.—Hydrogenation of benzoquinone (2.16 g.) with platinum in HCl.

Our experiments are instructive also in another respect: though the platinum metals are quite generally recognized as excellent catalysts, due to their activity at low temperature and low pressure, there is considerable uncertainty regarding their relative activity, for instance that of palladium compared with platinum. From the following experiments, it can be seen that platinum, but not palladium, can catalyze the hydrogenation of quinone in a hydrochloric acid solution to cyclohexanol (as also found by Neunhoeffer and Pelz). However, in aqueous or alcoholic solution, the hydrogenation of quinone to hydroquinone takes place with either catalyst, and under these conditions the reaction with palladium charcoal is many times faster even than with platinum charcoal (see Fig. 3). Though it is not advisable to jump to hasty conclusions in such a complicated field as catalytic hydrogenation, it is suggestive that a similar result is obtained in many other instances, tending to show that palladium is a mild but extremely fast catalyst, while platinum is more powerful but slower.

Figure 1 shows the hydrogenation of 2.16 g. (0.02 mole) of quinone in 5% hydrochloric solution with the commercial platinum charcoal catalyst of Baker & Co., Inc. (1 g. charcoal was used containing 50 mg. Pt). The change of speed after the absorption of 1 mol of hydrogen is perceptible, especially if compared with normal hydrogenations, which run with undiminished speed almost to the reaction end. In one experiment, the hydrogenation was interrupted after the absorption of 1 mol of hydrogen, the catalyst filtered

(1) Neunhoeffer and Pelz, *Ber.*, **72**, 433 (1939).
(2) Bonney and Huff, *Ind. Eng. Chem., Anal. Ed.*, **9**, 157 (1937).

off and the filtrate evaporated; the residue was found to be hydroquinone, which therefore represents the first stage of the complete reaction leading to cyclohexanol.

Figure 2 shows how, in the absence of mineral acids, the hydrogenation of benzoquinone comes to a sudden stop after the hydroquinone stage has been reached. Curve 1 represents the hydrogenation of 2.16 g. of benzoquinone, with the same platinum catalyst as before, in acetic acid solution, curve 2 in ethyl alcohol. Curve 3 represents the hydrogenation in ethyl alcohol with the commercial palladium charcoal catalyst of Baker & Co., Inc. (1 g. charcoal containing 50 mg. Pd). Benzoquinone also can be hydrogenated with palladium in water, in which the quinone is not very soluble. This reduces the reaction speed considerably so that this hydrogenation curve lies between curves 1 and 2. The curve is not drawn as the reaction is not strictly comparable with the others.

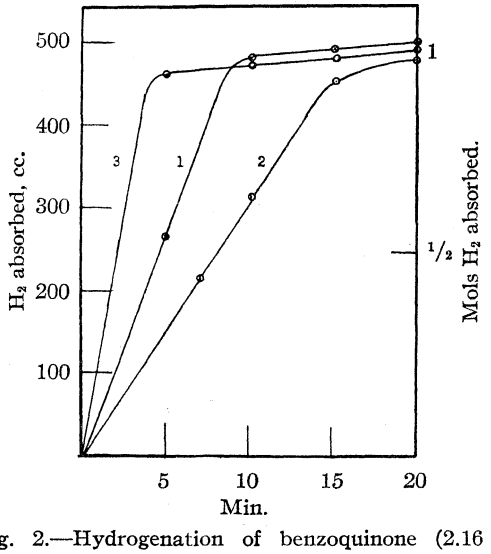


Fig. 2.—Hydrogenation of benzoquinone (2.16 g.): 1, Pt in acetic acid; 2, Pt in ethyl alcohol; 3, Pd in ethyl alcohol.

Figure 3 shows the greater speed of the reaction with a palladium catalyst; furthermore, it clearly indicates that there is no slowing down after the absorption of the 0.5 mol of hydrogen, *i. e.*, at the meriquinoid stage. In both cases 4 g. of benzoquinone was used, but in the case of platinum only a small part of the benzoquinone was hydrogenated when the experiment was interrupted.

A few experiments were made relating to the hydrogenation of other quinones, *i. e.*, *p*-toluquinone and anthraquinone in alcoholic solutions. The hydrogenation of *p*-toluquinone proceeds with practically the same speed as benzoquinone. The hydrogenation of anthraquinone is much slower due to the restricted solubility in ethyl alcohol. The reverse reaction, the dehydrogenation of hydroquinone to quinone, could be observed only in the case of anthrahydroquinone, which partially reoxidized before the palladium catalyst could be filtered off.

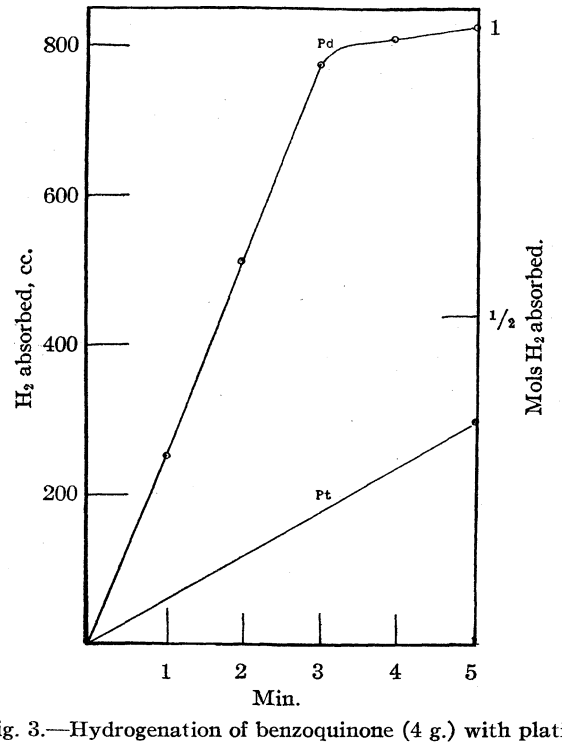


Fig. 3.—Hydrogenation of benzoquinone (4 g.) with platinum or palladium in methyl alcohol.

Experimental

All hydrogenations were done at room temperature and at atmospheric pressure. The reaction vessel was a thick-walled Pyrex Erlenmeyer flask of 1000-cc. content, which was placed in a shaking machine (275 oscillations per minute, the lateral stroke $1^1/_2$″ (3.7 cm.) long). The progress of the reaction could be followed by measuring the decrease in volume, due to the absorption of hydrogen. The results have not been corrected for barometer readings, temperature or humidity; since the last named factor is of the greatest relative importance, and is so difficult to evaluate accurately in the presence of different organic solvents, it seemed unnecessary to correct for pressure and temperature. Under our conditions the hydrogen absorption was around 24 liters per mole of hydrogen, instead of 22.4 liters. One hundred cc. of solvent was used in each experiment.

The catalyst was the commercial 5% platinum charcoal and 5% palladium charcoal (Baker & Co., Inc.), 1 g. of charcoal containing 50 mg. of platinum or palladium, re-

spectively, being used. The same catalyst was used throughout, as it could be filtered and dried at 100° after each experiment without impairing its activity.

Summary

The hydrogenation of various quinones in a hydrogen atmosphere in the presence of palladium catalysts produces hydroquinone with great speed, provided mineral acids are absent. The same reaction takes place with platinum charcoal, but more slowly. Platinum charcoal is active even in the presence of mineral acid, hydroquinone being only the first stage of the reaction which has cyclohexanol as the final product.

NEWARK, N. J. RECEIVED FEBRUARY 12, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING OF THE UNIVERSITY OF PENNSYLVANIA]

The Kinetics of Neutralization

BY MARTIN KILPATRICK

In a recent paper Lewis and Seaborg[1] have reported the study of the rate of fading of the blue trinitrotriphenylmethide ion in acid solutions. They interpret their results in terms of their classification of acids and bases as primary and secondary.[2,3]

Another kinetic interpretation of their results merits consideration. Considering the reaction to be catalyzed by acids we may write

$$B_S^- \underset{k_{-1}A^-}{\overset{k_1\,HA}{\rightleftharpoons}} B_P^- \qquad (1)$$

where B_S^- represents the blue ion, called the secondary base by Lewis, B_P^- the form called the primary base, HA any acid, and A^- its conjugate base. This reaction is followed by the reaction

$$B_P^- + HA \overset{k_2}{\rightleftharpoons} HB + A^- \qquad (2)$$

In other words, equation (1) is step (a) in the paper of Lewis and Seaborg (who do not, however, consider the acid–base catalytic nature of the reaction) and equation (2) represents the second step. In equation (1) B_S^- is transformed to B_P^- by the catalyst HA, the reverse process being catalyzed by the base A^-. Now if the reaction $B_P^- + HA$ is much faster than the reaction $B_S^- \rightarrow B_P^-$, and if $k_2C_{HA} \gg k_{-1}C_{A^-}$, the rate equation would be

$$-\frac{dC_{B_S^-}}{dt} = k_1C_{B_S^-}C_{HA} \qquad (3)$$

and the reaction would be of the second order in agreement with the experimental findings of Lewis and Seaborg. Lewis and Seaborg consider that a small concentration of B_P^- is maintained in equilibrium with B_S^- and that the rate-determining step is the reaction of the primary base B_P^- with the acid HA. They conclude that ". . . the measured heat of activation should be the same for the several acids and equal to the difference in energy between the primary and secondary forms of the base." In the present paper it is assumed that the change from B_S^- to B_P^- requires an acid catalyst and that B_P^- reacts rapidly with the acid if it is sufficiently strong.

The measured energies of activation for the stronger acids are found to average 9.1 kcal., and the energy of activation is calculated to be 8.9 for alcohol. The constancy of this value is not in contradiction to a catalytic mechanism. For example, in the mutarotation of glucose the measured energies of activation for such different catalysts as water, pyridine, acetate ion, and hydrogen ion were found to be 17.6, 19.1, 18.0, and 19.3 kcal., respectively.[4] In the enolization of acetoacetic ester[5] and in the iodination of acetone[6] the measured energies of activation for different catalysts are practically the same. From the data it is evident that the statement of Lewis and Seaborg "The constancy of the heat of activation over the great range from chloroacetic acid to alcohol can hardly be explained by the theory of an activated complex" is hardly in accord with the facts for reactions showing general acid and basic catalysis.

Turning now to the alcohol reaction, Lewis and Seaborg state "Alcohol is itself an acid, and although its acid strength is not high

(1) Lewis and Seaborg, THIS JOURNAL, **61**, 1894 (1939).
(2) Lewis, *J. Franklin Inst.*, **226**, 293 (1938).
(3) Lewis and Seaborg, THIS JOURNAL, **61**, 1886 (1939).
(4) Kilpatrick and Kilpatrick, *Ibid.*, **53**, 3698 (1931).
(5) Pedersen, *J. Phys. Chem.*, **38**, 601 (1934).
(6) Smith, *J. Chem. Soc.*, 1774 (1934).

enough to cause the fading of the blue color to occur to any great extent before equilibrium is established, it does, in the presence of stronger acids, play an important and sometimes preponderating part in the mechanism of the fading process. This is due to the relatively large number of alcohol molecules present. Side by side, therefore, with the reaction we have considered so far, is this reaction with the solvent...." The reaction scheme therefore includes a reaction of the primary base with alcohol. In the new interpretation the blue form is already in equilibrium with B_P^-, and as soon as the acid is added the species B_P^- is removed and the change of B_S^- to B_P^- is catalyzed by two acids, the acid added, which is present in small concentration, and the acid alcohol. That is

$$-dC_{B_S^-}/dt = k'C_{B_S^-}C_{C_2H_5OH} + k''C_{B_S^-}C_{HA} \quad (4)$$

The molar catalytic constant k'' will be greater than k' because of the greater strength of the acid but the "preponderating" part played by the alcohol is due to its high concentration. In addition, since the concentration of alcohol is constant, the observed velocity constant should no longer be truly of the second order for the weaker acids, and this is in agreement with the experimental results. If the greater part of the reaction is by way of the alcohol, the last term in (4) becomes unimportant, and the rate of reaction will no longer be sensitive to change in concentration of the acid HA. This is also in accord with the experimental results.

The velocity constants range from 30 for the strongest acid (monochloroacetic acid) to 0.09 for phenol, and this difference in velocity is explained by the statement "It appears as though increasing polarization of the acid, by its orienting effect, increases the probability that a given collision between the acid and primary base will be effective." In terms of the catalytic mechanism a different velocity constant for each catalyst is expected. From the concentration of B_P^- in equilibrium with B_S^-, and from the velocity constant for the reaction between the blue ion and chloroacetic acid, Lewis and Seaborg compute that the molar velocity constant for the reaction between the primary base and chloroacetic acid is 6×10^{10}, time being expressed in seconds. This would mean that there was a high probability of reaction at each collision. Lewis regards this calculation as erroneous. Now the experimental

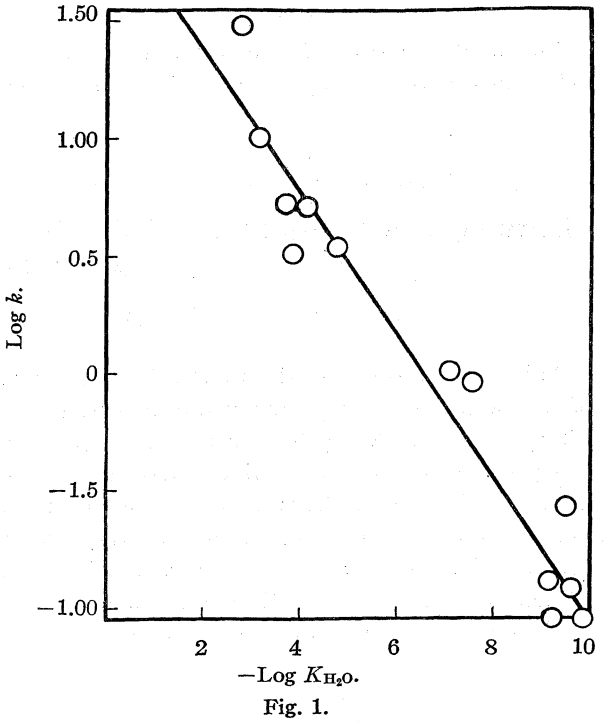


Fig. 1.

results for chloroacetic acid can be expressed by an equation of the Arrhenius type

$$\ln k = 27.5 - 10{,}200/RT \quad (5)$$

and the value 27.5 is in reasonable agreement with other acid–base catalyzed reactions. The corresponding values for the other catalysts range from 25.5 to 21.5. If the collision number were 10^{11} the value would be approximately 25.

The characteristic of all reactions showing general acid catalysis is the relation between the catalytic constant (k) and the acid strength constant (K)

$$k = GK^x \quad (6)$$

where G and x are constants for a series of catalysts of similar structure and charge type. For acids of different structure the relation is an approximate one. The following graph indicates that the relationship holds approximately in the present case. Lewis considers this relationship to be erroneous.[7] It should be pointed out that the velocity constants given in Table I of the paper by Lewis and Seaborg, and plotted here, include the alcohol reaction, so that the catalytic constants assigned to the weaker acids are somewhat too high.

(7) Lewis, *J. Franklin Inst.*, **226**, 293 (1938).

Summary

The neutralization of trinitrotriphenylmethide ion is interpreted as an acid-catalyzed reaction. The interpretation is in accord with the kinetic experiments.

PHILADELPHIA, PA. RECEIVED JANUARY 20, 1940

[CONTRIBUTION FROM THE MORLEY CHEMICAL LABORATORY, WESTERN RESERVE UNIVERSITY]

Thermodynamic Properties of the Hexyl Alcohols. IV. 3-Methylpentanol-1 and 2-Methylpentanol-5

BY FRANK HOVORKA, HERMAN P. LANKELMA AND ISADORE SCHNEIDER[1]

This paper represents the fourth[2,3,4] of a series of investigations being carried out in this Laboratory concerned with the relation between physical properties and chemical constitution of the hexyl alcohols, and deals with the preparation, purification and determination of the vapor pressure, viscosity, density, surface tension and refractive index of 3-methylpentanol-1 and 2-methylpentanol-5 (4-methylpentanol-1).

Experimental

Preparation of Materials.—Both alcohols were prepared in a manner similar to that described by Dreger[5] for the preparation of hexanol-1. 3-Methylpentanol-1 was made by the Grignard reaction using secondary butyl bromide and ethylene oxide. Similarly, 2-methylpentanol-5 was prepared from isobutyl bromide and ethylene oxide.

Purification.—The alcohols were allowed to stand over "Drierite"[6] for a period of two months, filtered from the drying agent and fractionally distilled. The fractionating columns used have been described previously.[3]

The alcohols were considered pure when the boiling point range did not exceed 0.02°.

Apparatus.—A complete description of the apparatus and technique used for the determination of the physical constants can be found in the paper by Hovorka, Lankelma and Stanford.[3]

All the instruments used in the surface tension, density, and viscosity measurements were recalibrated before determinations were made.

Discussion of Results

Vapor Pressure.—The vapor pressure data are tabulated in Table I, column 5.

The summary of the values calculated from the vapor pressure data is given in Table II. The temperature variation of the vapor pressure was found to be given very closely by the Rankine equation, whose constants A, B and C are listed.

The values of the Trouton constant are considerably higher than the normal value of 21. These high values correspond with those found for the hexanols previously reported.[2,3,4]

Viscosity.—The viscosity data are tabulated in Table I, column 3. The viscosity *vs.* temperature curves for the two hexanols cross at 65° although the values from 65–150° do not vary by more than 0.6%. This peculiar behavior has been noticed previously. Like hexanol-1, reported by Hovorka, *et al.*, these two alcohols have a small temperature coefficient of viscosity.

Plots of Raman's equation[7] and Andrade's equation[8] yielded perfectly symmetrical curves instead of the required straight lines. The constants of the two equations and the deviations of the calculated from the observed viscosities are listed in Table III. It is very interesting to note here that of all the hexyl alcohols so far studied, hexanol-1 gives the least deviation from Andrade's equation, and that it is closely followed by 2-methylpentanol-5 and 3-methylpentanol-1.

Values of the degree of association have been calculated from the fluidity using a formula proposed by Bingham, *et al.*[9,10] The association factor as determined by the fluidity method is the ratio of the temperature required to give a certain fluidity to the temperature calculated from the "atomic temperature" constants. The values obtained are listed in Table IV. Calculation of the association factor for hexanol-1 gave values of 1.59, 1.48 and 1.41.

Bingham further calculates the degree of association by application of the formula, n =

(1) Abstracted from a Thesis by I. Schneider, submitted to the Graduate School of Western Reserve University, in partial fulfillment of the requirements for the Degree of Master of Arts, May, 1937.

(2) Hovorka, Lankelma and Naujoks, THIS JOURNAL, **55**, 4820 (1933).

(3) Hovorka, Lankelma and Stanford, *ibid.*, **60**, 820 (1938).

(4) Hovorka, Lankelma and Axelrod, *ibid.*, **62**, 187 (1940).

(5) "Organic Syntheses," Coll. Vol. I, p. 299.

(6) Hammond and Withrow, *Ind. Eng. Chem.*, **25**, 1112 (1933).

(7) Raman, *Nature*, **111**, 532 (1923).

(8) Andrade, *Phil. Mag.*, **17**, 698 (1934).

(9) Bingham and Darrall, *J. Rheol.*, **1–2**, 174 (1929–31).

(10) Bingham and Spooner, *ibid.*, **3**, 228 (1932).

TABLE I

SURFACE TENSION, VISCOSITY, DENSITY, VAPOR PRESSURE AND REFRACTIVE INDEX

Temp., °C.	Surface tension, dynes	Absolute viscosity	Absolute density	Vapor press., mm.	Index of refraction	Parachor	Eötvös constant
			A. 3-Methylpentanol-1				
5.0	26.28	0.09615	0.83328	...	....	277.2	1.63
15.0	25.35	.06714	.82602	...	1.4208	277.2	1.61
25.0	24.65	.04755	.81870	1.3	1.4169	277.6	1.63
35.0	24.01	.03447	.81160	2.2	1.4136	278.2	1.66
45.0	23.21	.02574	.80484	4.4	1.4096	278.2	1.66
55.0	22.51	.01968	.79740	9.1		278.6	1.69
65.0	21.83	.01538	.78964	18.0		279.2	1.72
75.0	21.18	.01218	.78173	31.5		280.0	1.78
85.0	20.47	.00992	.77352	52.0		280.5	1.83
95.0	19.67	.00812	.76520	85.5		280.9	1.85
105.0	18.85	.00679	.75666	133.0		281.1	1.88
115.0	18.04	.00577	.74784	201.0		281.5	1.91
125.0	17.22	.00495	.73728	294.5		282.5	1.97
135.0	16.35	.00428	.72725	427.0		282.6	1.95
145.0	15.43	.00374	.71750	599.5		282.6	1.76
150.0	15.05	.....	.71260	702.5		282.9	..
154.0	...	.....	.....	797.5		...	..
			B. 2-Methylpentanol-5				
5.0	25.19	0.09091	0.82376	...	....	277.4	1.55
15.0	24.50	.06293	.81647	...	1.4172	277.9	1.56
25.0	23.84	.04604	.80940	1.3	1.4135	278.5	1.58
35.0	23.32	.03376	.80246	1.8	1.4092	279.3	1.65
45.0	22.58	.02547	.79493	4.0	1.4055	279.7	1.66
55.0	21.80	.01959	.78742	8.4		279.9	1.65
65.0	21.14	.01538	.77968	16.5		280.5	1.69
75.0	20.45	.01220	.77180	31.2		281.5	1.73
85.0	19.78	.00998	.76378	52.8		281.7	1.77
95.0	18.99	.00815	.75526	85.8		282.0	1.79
105.0	18.28	.00683	.74683	134.2		282.5	1.85
115.0	17.49	.00578	.73780	205.0		283.0	1.89
125.0	16.69	.00497	.72850	302.5		283.5	1.95
135.0	15.88	.00428	.71880	435.8		283.7	1.96
145.0	15.00	.00374	.70900	611.5		284.1	2.10
150.0	14.55	.....	.70392	721.5		284.1	..
154.0	...	.....	.....	816.5		...	..

TABLE II

SUMMARY OF VALUES CALCULATED FROM VAPOR PRESSURE DATA

$$\log P = A/T + B \log T + C$$

Substance		A	B	C	Deviation Maximum +	Deviation Average −
3-Methylpentanol-1	−4209.8	− 9.3605	37.3838	0.3	2.8	−0.43
2-Methylpentanol-5	−4778.8	−12.617	47.2894	.1	3.0	− .20

	Boiling point °C.[a]	Heat of vaporization[b]	Trouton's constant
3-Methylpentanol-1	152.44° ± 0.02	11,278	26.5
2-Methylpentanol-5	151.63° ± 0.02	11,124	26.2

[a] Boiling point values were obtained by interpolation from the vapor pressure curves.

[b] These values were calculated from the slope of the curve obtained by plotting log P against $1/T$.

$2.139 - 0.097\ N_c$, where N_c is the number of carbon atoms. This gives a value of 1.56 for the degree of association of the hexyl alcohols.

Refractive Index.—Using the values given by Eisenlohr[11] for the atomic refractive constants of carbon, hydrogen, and oxygen, the molecular refractive powers of 3-methylpentanol-1 and 2-methylpentanol-5 have been calculated. These values are compared with those calculated from the Lorenz–Lorentz equation in Table V.

(11) Eisenlohr, *Z. physik. Chem.*, **75**, 585 (1911).

TABLE III

CONSTANTS FOR RAMAN'S EQUATION $n = Ae^{B/T}$

	$A \times 10^6$	B	Maximum deviation +	Maximum deviation −
3-Methylpentanol-1	5.909	2675	5.8	7.4
2-Methylpentanol-5	6.759	2626	4.5	6.4

CONSTANTS FOR ANDRADE'S EQUATION $nv^{1/3} = Ae^{c/vT}$

	$A \times 10^6$	c	Maximum deviation +	Maximum deviation −
3-Methylpentanol-1	51.14	2503	6.9	10.5
2-Methylpentanol-5	56.13	2491	5.1	8.7

TABLE IV

CALCULATION OF ASSOCIATION FROM FLUIDITY

Rhes.	3-Methylpentanol-1 Calcd. temp., °A.	3-Methylpentanol-1 Obsd. temp., °A.	3-Methylpentanol-1 X	2-Methylpentanol-5 Obsd. temp., °A.	2-Methylpentanol-5 X
100	226.2	357.8	1.58	358.2	1.58
200	271.1	396.6	1.46	396.6	1.46
300	305.5	425.5	1.39	425.0	1.39

TABLE V

MOLECULAR REFRACTIVE POWER

	Lorenz–Lorentz equation	Summation of atomic constants
3-Methylpentanol-1	31.35	31.44
2-Methylpentanol-5	31.44	31.44

Surface Tension.—The surface tension data are listed in Table I, column 2.

The values of the Eötvös constant and the parachor were calculated over the entire temperature range and also are tabulated in Table I. The values listed are very similar to those calculated for the other hexanols. In all cases the values are those of associated substances.

The critical temperatures have been calculated from the Ramsay–Shields equation and are given in Table VI. A comparison of the surface tension of the two alcohols at equal distances from the critical point, so as to put the alcohols in corresponding states, showed that the values of the surface tension at one-third the critical temperature were identical, namely, 17.43 dynes. This may be ascribed to the fact that both alcohols seem to possess the same molecular aggregation at the higher temperatures.

TABLE VI

CRITICAL TEMPERATURES

Alcohol	T_c °C.	T_c °C.
3-Methylpentanol-1	403.9 (25–35)[a]	366.6 (145–150)
2-Methylpentanol-5	398.3 (25–35)	346.9 (145–150)

[a] The values in parentheses show the two temperatures used to calculate the critical temperature in question.

Summary

1. The preparation and purification of two hexyl alcohols, 3-methylpentanol-1 and 2-methylpentanol-5, have been described.

2. The surface tension, viscosity, density and vapor pressure have been determined over the temperature range from 5° to the boiling point. The refractive index has been determined from 15–45°.

3. The heat of vaporization, boiling point and the constants for Rankine's equation have been determined from the vapor pressure data. The vapor pressure values agreed very well with those calculated by the Rankine equation.

4. The viscosity values calculated from Raman's and Andrade's equation gave poor agreement with the experimental values. The two alcohols gave almost the same values for Andrade's constants and for degrees of association as obtained for hexanol-1.

5. The parachor, Eötvös constant and critical constants have been calculated from the surface tension data.

CLEVELAND, OHIO RECEIVED FEBRUARY 21, 1940

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE ETHYL GASOLINE CORPORATION]

The Redistribution Reaction. V. R_4Pb Compounds

BY GEORGE CALINGAERT, HAROLD A. BEATTY AND HAROLD SOROOS

Previous papers in this series[1,2,3] have described the redistribution reaction for the interchange of organic radicals, and have shown that this reaction takes place quantitatively and leads to the formation of random equilibrium mixtures. The present paper covers the experimental data relating to the redistribution of tetraalkyllead and tetraaryllead compounds. In view of the novelty of the reaction, it was desired to explore the field as widely as possible before attempting a systematic or detailed study, and the data submitted here should be evaluated accordingly. The present tests were limited to an investigation of the generality of the reaction in the R_4Pb field, and to a preliminary study of how the reaction is affected by some experimental variables such as catalysts, catalyst concentration, solvents, temperature, and time. Later reports will cover more quantitative investigations of the most promising parts of the field explored.

With a few exceptions, the reactions were carried out in the same general manner, which consisted of taking the R_4Pb compound or mixture with the desired catalyst and in many cases with an inert solvent, maintaining this mixture at a given temperature for a certain length of time, removing the catalyst by extraction with water or with a suitable solvent or reagent, and finally analyzing the product by fractional distillation[2] or some other suitable method. In some of the cases, the analysis was carried out only far enough to indicate clearly that the reaction had taken place.

Systems Investigated.—The various R_4Pb systems tested are listed in Table I, and comprise thirteen different compounds containing six different alkyl and two different aryl radicals. With the exception of tests 12 and 14, the reaction conditions used were, as is described in the Experimental Part, essentially the same for each test, and these conditions were usually more than adequate to bring the reaction to completion. In each of the fourteen systems listed, the redistribution occurred and was judged to be complete or nearly so.

As far as the data indicate, all the alkyl radicals tested showed a reactivity of the same order of magnitude, with the exception of the tertiary butyl radical. Indeed, the redistribution of trimethyl-*t*-butyllead was accomplished only under drastic conditions, and it was accompanied by decomposition, which is presumably due to the instability of the poly-*t*-butyllead compounds formed. Judging from tests 13 and 14, it appears that the reactivity of the aryl radicals is of an order equal to, if not greater than, that of the alkyl radicals. The result of test 14 is of interest in showing that in the case of aryl groups the presence of a catalyst is not essential, and this recalls the interchange of phenyl and tolyl radicals previously observed in triarylbismuth compounds.[4]

As shown in Table II, the products of eight of these reactions, for which complete analyses were obtained, corresponded as well as could be expected to random equilibrium mixtures. More careful analyses would doubtless have shown even closer correspondence.[2] In the other six tests, complete analyses were not obtained, but the results (described in the Experimental Part) were nevertheless sufficient to show that redistribution had occurred.

In the three different systems used in tests 1, 2, and 3, which contain the same proportions of methyl to ethyl radicals, the product of each is in accord with the predicted composition, namely, 6.25 mole per cent. tetramethyllead, 25 mole per cent. trimethylethyllead, 37.5 mole per cent. dimethyldiethyllead, 25 mole per cent. methyltriethyllead, and 6.25 mole per cent. tetraethyllead; whereas the compound used in test 4 containing a different proportion of methyl to ethyl radicals gave a product containing the above five methyl-ethyl-lead compounds in close to the predicted proportions of 31.6, 42.2, 21.1, 4.7, and 0.4 mole per cent. respectively. The system used in test 10 contained equal proportions of the three different radicals, methyl, ethyl and *n*-propyl, and gave a product for which the analyses and distillation curve agree very well with the data calculated for the expected mixture of the fifteen

(1) Calingaert and Beatty, THIS JOURNAL, **61**, 2748 (1939).
(2) Calingaert, Beatty and Neal, *ibid.*, **61**, 2755 (1939).
(3) Calingaert and Soroos, *ibid.*, **61**, 2758 (1939).
(4) Challenger and Ridgway, *J. Chem. Soc.*, **121**, 104 (1922).

TABLE I

REDISTRIBUTION OF R_4Pb SYSTEMS

Test	Composition Compounds	Moles	$AlCl_3$, Mole %	Solvent, ml.	Temp., °C.	Time, hr.
1	Me_4Pb	0.15	1.3	None	80	2
	Et_4Pb	.15				
2	Me_3EtPb	.215	3.5	None	80	1
	$MeEt_3Pb$	.215				
3	Me_2Et_2Pb	.3	2.5	Hexane (50)	80	5
4	Me_3EtPb	.3	2.5	Hexane (50)	85	6
5	Me_4Pb	.1	3.8	Hexane (50)	80	5
	n-Pr_4Pb	.1				
6	Me_4Pb	.295	1.7	None	80	5
	n-Pr_4Pb	.145				
7	Me_3-i-PrPb	.30	1.7	None	80	5
	Me_2-i-Pr_2Pb	.14				
8	Et_4Pb	.1	3.8	Hexane (50)	80	5
	n-Pr_4Pb	.1				
9	Et_2-n-Pr_2Pb	.16	3.7	Hexane (38)	80	5
10	Me_4Pb	.3	1.5	None	80	5
	Et_4Pb	.3				
	n-Pr_4Pb	.3				
11	Me_2-i-Bu_2Pb	.13	5.8	Hexane (25)	85	5
12	Me_3-t-BuPb	.08	9.4	Decalin (20)	100–130	5
13	Me_4Pb	.2	2.5	Hexane (75)	80	7
	Ph_4Pb	.1				
14	Ph_4Pb	.06	None	None	200	16
	(p-$MeC_6H_4)_4Pb$	.06				

TABLE II

OBSERVED AND CALCULATED[a] COMPOSITIONS OF THE REACTION PRODUCTS

Test	Compounds	r[b]		R_4Pb	$R_3R'Pb$	$R_2R'_2Pb$	RR'_3Pb	R'_4Pb
1	Me_4Pb	0.50	Obsd.	6.0	21.1	39.6	27.3	6.0
	Et_4Pb		Calcd.	6.25	25.0	37.5	25.0	6.25
2	Me_3EtPb	.50	Obsd.	4.4	25.4	44.4	17.8	8.0
	$MeEt_3Pb$		Calcd.	6.25	25.0	37.5	25.0	6.25
3	Me_2Et_2Pb	.50	Obsd.	3.5	20.4	42.7	27.4	6.0
			Calcd.	6.25	25.0	37.5	25.0	6.25
4	Me_3EtPb	.75	Obsd.	29.9	46.7	16.1	6.7	0.6
			Calcd.	31.6	42.2	21.1	4.7	.4
5	Me_4Pb	.50	Obsd.	5.0	20.6	45.4	23.0	6.0
	n-Pr_4Pb		Calcd.	6.25	25.0	37.5	25.0	6.25
6	Me_4Pb	.67	Obsd.	16.3	41.9	32.5	8.2	1.1
	n-Pr_4Pb		Calcd.	20.2	39.7	29.3	9.6	1.2
7	Me_3-i-PrPb	.67	Obsd.	13.2	49.2	32.7	4.5	0.4
	Me_2-i-Pr_2Pb		Calcd.	20.2	39.7	29.3	9.6	1.2
11	Me_2-i-Bu_2Pb	.50	Obsd.	8	22	48	18	4
			Calcd.	6.25	25.0	37.5	25.0	6.25

[a] Calculated mole percentages of compounds are obtained by the equations: Mole fraction $R_4Pb = r^4$; $R_3R'Pb = 4r^3(1-r)$; $R_2R'_2Pb = 6r^2(1-r)^2$; $RR'_3Pb = 4r(1-r)^3$; $R'_4Pb = (1-r)^4$. [b] r, the mole fraction of the smaller alkyl group, equals $[R_4Pb] + 0.75[R_3R'Pb] + 0.5[R_2R'_2Pb] + 0.25[RR'_3Pb]$, where the brackets denote the mole fraction of the compounds used.

possible compounds in their theoretical proportions, as shown in Table III and Fig. 1.

Tests 6 and 7, each of which contains the same relative proportion of methyl to propyl radicals, were made to determine whether the redistribution would be accompanied by the isomerization of i-propyl groups to n-propyl groups, an occurrence which might be anticipated in view of the

TABLE III

CALCULATED AND OBSERVED COMPOSITION OF RANDOM EQUILIBRIUM MIXTURE CONTAINING Me, Et, AND Pr RADICALS IN THE SAME PROPORTIONS

Carbon atoms	Compounds	Mole per cent. Calculated[a]	Observed[b]
4	Me_4Pb	1.23	1.3
5	Me_3EtPb	4.94	3.6
6	Me_2Et_2Pb	7.41	
	Me_3PrPb	4.94	12.35 13.0
7	$MeEt_3Pb$	4.94	
	$Me_2EtPrPb$	14.81	19.75 19.4
8	Et_4Pb	1.24	
	$MeEt_2PrPb$	14.81	
	Me_2Pr_2Pb	7.41	23.46 24.4
9	Et_3PrPb	4.94	
	$MeEtPr_2Pb$	14.81	19.75 22.6
10	Et_2Pr_2Pb	7.41	
	$MePr_3Pb$	4.94	12.35 8.6
11	$EtPr_3Pb$	4.94	5.9
12	Pr_4Pb	1.23	1.2
		100.00	100.0

[a] Calculated concentrations are given by the general formula previously presented,[1] which in the present case is:

Mole fraction $Me_aEt_bPr_{(4-a-b)}Pb = \frac{4!}{a!\,b!\,(4-a-b)!}\left(\frac{1}{3}\right)^a\left(\frac{1}{3}\right)^b\left(\frac{1}{3}\right)^{(4-a-b)}$

[b] Observed concentrations were calculated as described in the Experimental Part.

TABLE IV

LIST OF CATALYSTS

Conditions: 0.15 mole Me_4Pb, 0.15 mole Et_4Pb, 50 ml. solvent.

Catalyst	Mole %	Solvent	Temp., °C.	Time, hr.	Redistribution
ZnF_2	6.5	Decalin	170	5	Complete
$ZnCl_2$	4.9	Decalin	175	24	Partial[a]
$HgCl_2$	2.5	Decalin	170	6	Complete
BF_3 (gas)	..	Hexane	80	4	Complete
BF_3Et_2O	5.3	Hexane	85	5	Complete
$AlCl_3$	2.5	Hexane	80	5	Complete
$AlBr_3$	1.3	Hexane	80	5	Partial
AlI_3	1.6	Hexane	80	5	Slight
$MeAlCl_2$	3.0	Hexane	80	5	Complete
Me_2AlCl	7.2	Hexane	85	5	Complete
$Bu_3Al_2I_3$	2.9	Hexane	85	5	Slight
$ZrCl_4$	2.9	Decalin	175	5	Partial
$SnCl_4$	8.6	Decalin	160	5	Complete[a]
Et_3SnBr	2.3	Hexane	80	5	Partial
Et_3PbCl	5.1	Hexane	80	5	Complete[b]
Et_3PbBr	8.9	Hexane	80	5	Complete[b]
Me_3PbI	11.4	Hexane	80	5	Partial[b]
PCl_3	7.6	Decalin	160	5.5	Complete
$AsCl_3$	3.7	Decalin	170	5	Complete[c]
$BiCl_3$	2.1	Decalin	170	5	Complete
$FeCl_3$	2.1	Decalin	160	6	Complete
$PtCl_4$	2.0	Decalin	100	5	Complete

[a] Some decomposition occurred, with deposition of metallic lead. [b] The catalyst was not removed before distillation. [c] A moderate amount of side reaction occurred, with deposition of lead chloride.

greater stability of *n*-propyllead compounds. The distillation curves, which are illustrated in Fig. 2, clearly indicate that no isomerization takes place.

Catalysts.—The different catalysts for the redistribution reaction were tested with the system tetramethyllead–tetraethyllead. These catalysts are listed in Table IV, which also gives the concentrations and experimental conditions employed. It is believed that this list is by no means exhaustive. Bearing in mind that a large number of metallic halides have been shown to react with organo-metallic compounds to give organo-metallic halides[5] as, for example $Et_4Pb + AlCl_3 = Et_3PbCl + EtAlCl_2$, it will be noted that most of the catalysts either belong to the class of RMX compounds or will yield such compounds under the conditions of the reaction. For this reason, the list of catalysts probably could be enlarged quite readily by further tests. The different catalysts show a considerable variation in their activity, ranging from relatively weak catalysts such as the alkyllead halides and zirconium chloride, up to very

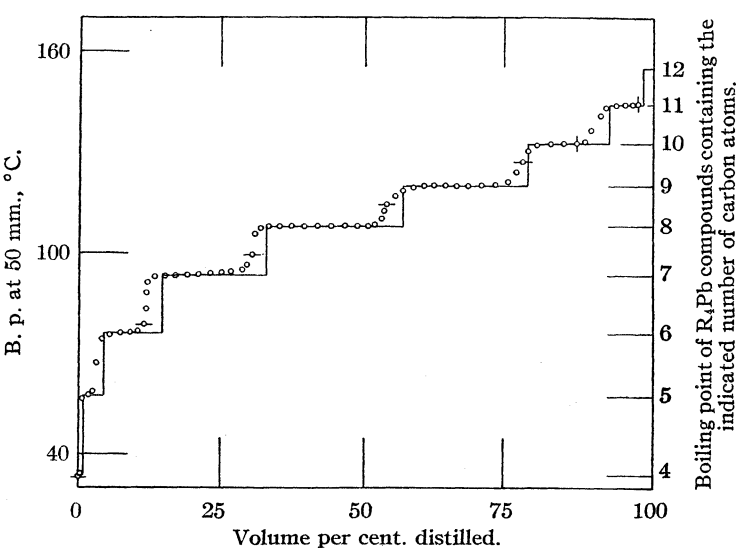


Fig. 1.—Distillation of the reaction product of $Me_4Pb + Et_4Pb + Pr_4Pb$: solid line calculated for random equilibrium mixture having [Me] = [Et] = [Pr] = 1/3; —o—, distillation cuts.

(5) Goddard, Ashley and Evans, *J. Chem. Soc.*, **121**, 978 (1922); Goddard and Goddard, *ibid.*, **121**, 260 (1922); Goddard, *ibid.*, **123**, 1172 (1923); Gilman and Apperson, *J. Org. Chem.*, **4**, 162 (1939).

effective catalysts such as the methylaluminum chlorides. A general idea of the influence of the kind and amount of catalyst on the reaction velocity is obtainable from the data in Table V. For the system tetramethyllead–tetraethyllead, with or without solvents, no reaction was detected in the absence of a catalyst even after a long time at a high temperature. Of the catalysts, the trialkyllead halides increase in activity in the order: iodide, bromide, chloride; but they are at best relatively weak catalysts, concentrations of five to ten mole per cent. being required to bring about complete reaction in five hours at 80°. The aluminum chloride catalysts are effective at a concentration of 0.5 mole per cent., even in thirty minutes at room temperature. With smaller concentrations there was some indication that the reaction proceeded for a time at about the normal rate but then came to a halt, probably owing to the disappearance of the catalyst through decomposition reactions.

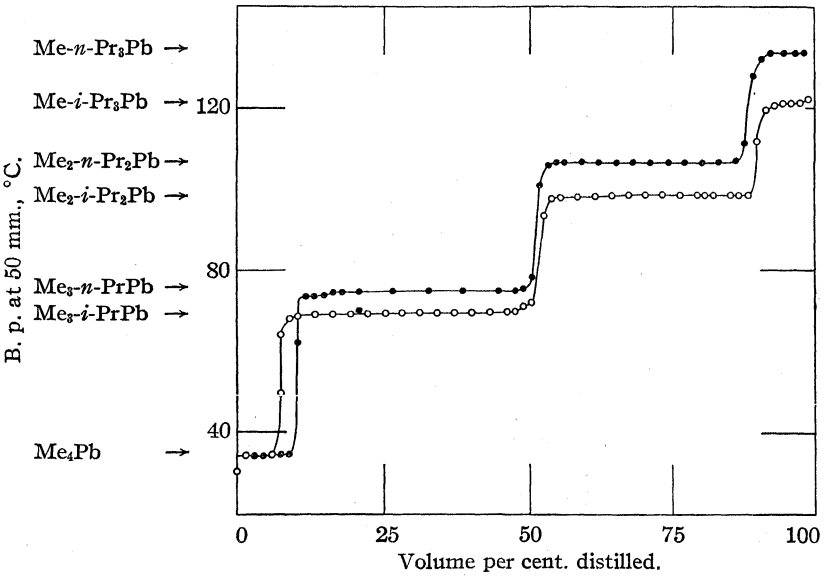


Fig. 2.—Distillation of the reaction products of test 6 (Me_3-*i*-PrPb + Me_2-*i*-Pr_2-Pb) and test 7 (Me_4Pb + *n*-Pr_4Pb): ○, *i*-Pr, ●, *n*-Pr.

Temperature.—The effect of temperature on the reaction velocity is marked, as can be seen from the data for the trialkyllead halide catalysts in Table V, but no quantitative measurement of the effect has been made as yet. On the other hand, there is not the slightest indication of any effect of tem-

TABLE V

THE EFFECT OF CATALYST CONCENTRATION, SOLVENTS AND TEMPERATURE[a]

Catalyst	Mole % of catalyst	Solvent	Ml.	Temp., °C.	Time, hr.	Redistribution
None	...	Decalin	50	160	28	None
None	...	Hexane	50	85	5	None
$AlCl_3$	2.5	Hexane	50	25	5	Complete
$AlCl_3$	2.5	Hexane	500	70	5	Complete
$AlCl_3$	1.3	Hexane	35	90	1	Complete
$AlCl_3$	0.3	Hexane	50	80	5	Partial
$AlCl_3$	1.02	None		25	0.25	Complete[b]
$AlCl_3$	0.61	None		25	.5	Complete[b]
Me_2AlCl	.51	None		25	.5	Complete[b]
Me_2AlCl	.44	None		25	.5	Complete[b]
Me_2AlCl	.38	None		25	1	Partial (stops)[b]
$AlCl_3$	.38	None		25	1	Partial (stops)[b]
$AlCl_3$	.32	None		20	24	Partial
Et_3PbCl	5.0	Hexane	50	80	5	Complete[c]
Et_3PbCl	3.0	Hexane	50	80	5	None[c]
Me_3PbCl + Et_3PbCl	5.1	None		25	24	None
Me_3PbCl + Et_3PbCl	2.6	Acetone	30	25	22	Trace[d]
Me_3PbCl + Et_3PbCl	5.1	Acetone	75	54	18	Partial[d]
Et_3PbBr	8.9	Hexane	50	80	5	Complete[c]
Et_3PbBr	4.4	Hexane	50	80	5	Partial[c]
Me_3PbI	11.4	Hexane	50	80	5	Partial[c]

[a] About 50 ml. of an equimolecular mixture of Me_4Pb and Et_4Pb was used in all cases. [b] The course of the reaction was followed by vapor pressure measurements. [c] The product was distilled directly without first extracting the catalyst. [d] The acetone was distilled and the catalyst extracted, prior to distillation.

perature on the relative proportions of the R_4Pb compounds in the product of the completed reaction of a given system.

Solvents.—The presence of any of several chemically inert solvents does not appear to exert any pronounced effect on the reaction velocity, and certainly does not alter the relative proportions of the R_4Pb compounds in the completely-reacted product. The data in Table V indicate that, for the aluminum chloride catalyst, the presence of hexane may have a moderate retarding effect on the reaction velocity, but that a ten-fold increase in the amount of hexane has no further perceptible effect.

Experimental

Tetramethyllead and Tetraethyllead with Aluminum Chloride Catalyst.—Into a three-neck flask equipped with a reflux condenser and thermometer was added successively 0.5 g. of aluminum chloride and a mixture of 0.15 mole each of tetramethyl- and tetraethyllead, while maintaining an atmosphere of nitrogen within the system and cooling the flask in ice water. The mixture was kept at 80° for two hours. After cooling, an equal volume of water was added and after shaking the alkyllead layer was separated, filtered, and fractionated.[2] Redistribution was complete, as shown in Table II.

Other Alkyllead Systems.—The other alkyllead systems were run in a similar manner, except for variations in temperature, kind and amount of solvent, and concentration of the particular catalyst used, as shown in Tables I, IV, and V. When a solvent was used, the catalysts, with the exception of the methylaluminum chlorides, were added directly to the solution of the lead alkyls. The methylaluminum chloride catalysts were added by breaking small sealed glass capsules of the materials beneath the surface of the liquid lead alkyls, while maintaining an atmosphere of nitrogen in the system. In the experiment using boron trifluoride catalyst, the gas was bubbled into the solution of lead alkyls for one to two minutes prior to heating. In the two tests (Table V) in which acetone was used as the solvent, after the reaction the acetone was first distilled and the mixture of trialkyllead chloride catalysts extracted from the residue of lead alkyls with concentrated ammonia solution, prior to distillation of the product. In all other tests (Tables IV and V) where the trialkyllead halides were used for catalysts (with the exception of one test (Table V) where no solvent was used) the products of the reaction were distilled without first removing the catalyst.

In five tests listed in Table V, the course of the redistribution reaction was followed by a vapor pressure method which consisted of removing samples of the reaction mixture at regular time intervals, extracting the catalyst from the samples with water and filtering, and measuring the vapor pressure of the mixtures at 60°. The apparatus used for these measurements consisted of a bulb of about 200-ml. capacity, fitted with a mercury manometer and with a side arm for evacuating the system and introducing a measured amount of the sample. The apparatus was contained in a bath maintained thermostatically at 60 ± 0.01°. The vapor pressure of samples thus measured varied from 67 mm., indicating no redistribution, to 31 mm., indicating complete redistribution.

Trimethylisopropyllead and Dimethyldiisopropyllead with Aluminum Chloride Catalyst.—The product of the reaction of 0.3 mole of trimethylisopropyllead, 0.14 mole of dimethyldiisopropyllead and 1 g. of aluminum chloride, at 80° for five hours, on distillation gave the fractions listed in Table VI. The observed and calculated composition of the equilibrium mixture based on the lead analyses of the various fractions and the distillation curve (Fig. 2) are compared in Table II, test 7. The reaction, under the conditions used, was not entirely complete.

TABLE VI

DISTILLATION AND ANALYTICAL DATA FOR TEST NO. 7

Fraction	B. p. at 50 mm.,[a] °C.	Weight, g.	Lead analysis	Compounds present
1	→ 30		3.1935 g.	Me_4Pb + hexane[b]
2	49.5	9.4	76.57%	Me_4Pb + hexane[b]
3	93.0	56.0	70.22%	Me_4Pb + Me_3-*i*-PrPb
4	111.5	41.8	64.39%	Me_3-*i*-PrPb + Me_2-*i*-Pr_2Pb
5	122.0	8.6	60.37%	Me_2-*i*-Pr_2Pb + Me-*i*-Pr_3Pb
Residue[c]			0.401 g.	Me-*i*-Pr_3Pb + *i*-Pr_4Pb

[a] The actual boiling points were converted to 50 mm. by the aid of a nomogram.[2] [b] Solvent hexane used for extraction of aqueous layer. [c] The residue was washed from the still with carbon tetrachloride. Its R_4Pb content was estimated to be 80% *i*-Pr_4Pb.

Tetraethyllead and Tetra-*n*-propyllead with Aluminum Chloride Catalyst.—The product of the redistribution of 0.1 mole each of tetraethyl- and tetra-*n*-propyllead in the presence of 1 g. of aluminum chloride and 50 ml. of hexane at 80° for five hours showed complete redistribution on distillation. The distillation, however, was not of such precision as to warrant making an analysis of the products.

Diethyldi-*n*-propyllead with Aluminum Chloride Catalyst.—The product of the redistribution of 0.16 mole of diethyldi-*n*-propyllead in 38 ml. of hexane in the presence of 0.8 g. of aluminum chloride at 80° for five hours was judged to be complete although the distillation was not precise enough to make an analysis of the products.

Tetramethyllead, Tetraethyllead and Tetra-*n*-propyllead with Aluminum Chloride Catalyst.—In the system tetramethyl-, tetraethyl-, tetra-*n*-propyllead, it was not possible to separate all fifteen constituents by fractionation since the boiling points of the compounds containing the same number of carbon atoms are almost identical. The analysis was therefore limited to separation into the nine groups of compounds containing, respectively, from 4 to 12 carbon atoms, as shown in Table III. This was accomplished by making eight sharp distillation cuts, and determining by lead analysis the relative amounts of two consecutive groups of isomers in each cut. These compositions are indicated in Table VII, and the quantitative summation for each group of isomers is given in Table III.

Trimethyl-*t*-butyllead with Aluminum Chloride Catalyst.—The products from the redistribution of 0.08 mole of trimethyl-*t*-butyllead with 1 g. of aluminum chloride in 20 ml. of decalin at 100–130° for five hours were 7 g. of

TABLE VII

DISTILLATION AND ANALYTICAL DATA FOR TEST NO. 10

Fraction	B. p. at 50 mm.,[a] °C.	Number of carbon atoms in R_4Pb compounds present	Weight, g.	Pb analysis
1[b]	→ 33	4	..	1.99 g.
2[c]	78.5	4 + 5 + 6	35.5	71.09%
3	99.0	6 + 7	54.0	67.33%
4	114.7	7 + 8	66.0	64.20%
5	127.3	8 + 9	59.7	61.59%
6	132.5	9 + 10	20.3	60.07%
7	145.5	10 + 11	29.6	57.82%
Residue[d]		11 + 12	..	4.04 g.

[a] The actual boiling points were converted to 50 mm. by use of a nomogram.[2] [b] Contained some solvent hexane used for extraction of aqueous layer. [c] Estimated to contain 0.25 ml. of Me_4Pb. [d] The residue was washed from the still with carbon tetrachloride and its R_4Pb content was estimated to be 50% $EtPr_3Pb$.

metallic lead and 6 g. of tetramethyllead. The other lead alkyls were not isolated.

Tetramethyllead and Tetraphenyllead in Hexane with Aluminum Chloride Catalyst.—To a solution of 0.1 mole of tetraphenyllead and 0.2 mole of tetramethyllead in 75 ml. of hexane contained in a three-necked flask equipped with a reflux condenser and thermometer was added 1 g. of aluminum chloride. The mixture was maintained at 80° for seven hours, after which the flask was cooled and the catalyst extracted by shaking with water. After filtering the organic lead layer, two distillations yielded: tetramethyllead, 9 g., b. p. →77° (3 mm.); trimethylphenyllead, 31 g., b. p. 77–78° (3 mm.), $n^{20}D$ 1.5837 (*Anal.* Calcd. for $C_9H_{14}Pb$: Pb, 62.90. Found: Pb, 63.32); dimethyldiphenyllead, 25 g., b. p. 151–152° (2 mm.), $n^{20}D$ 1.6263 (*Anal.* Calcd. for $C_{14}H_{16}Pb$: Pb, 52.93. Found: Pb, 53.11); and a residue of 10 g., from which was obtained, by three recrystallizations from *n*-hexane, 3.5 g. of triphenylmethyllead, m. p., 62–63° (*Anal.* Calcd. for $C_{19}H_{18}Pb$: Pb, 45.69. Found: Pb, 45.65). A few crystals of tetraphenyllead, m. p. 226–228°, mixed m. p. 226–228°, also precipitated out of the equilibrium mixture prior to the distillation.

Tetraphenyllead and Tetra-*p*-tolyllead without Catalyst.—A mixture of 3 g. of tetraphenyllead and 3.3 g. of tetra-*p*-tolyllead in an air-jacketed test-tube equipped with a thermometer and stirrer was heated to melting in an oil-bath and allowed to cool slowly with stirring. Two successive cooling curves showed initial freezing points of 204.5 and 201.5°, respectively. After remelting and maintaining the mixture at 200° for three successive five-hour periods, the mixture showed initial freezing points of 177, 152.5 and 150°, respectively. Attempts to isolate the constituents by fractional crystallization and use of selective solvents were unsuccessful.

Summary

Data presented for the redistribution reaction in various R_4Pb systems show that the reaction is a general one for these compounds, and give an indication of the influence of some of the factors affecting the reaction such as the R groups, catalysts, catalyst concentration, solvents, temperature and time.

DETROIT, MICHIGAN RECEIVED AUGUST 30, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE ETHYL GASOLINE CORPORATION]

The Redistribution Reaction. VI. Alkyl Lead Halides

BY GEORGE CALINGAERT, HAROLD SOROOS AND HYMIN SHAPIRO

It was stated in the first paper of this series[1] that the interchange of alkyl groups in trialkyllead halides appears to be a general reaction for which no catalyst is required other than the alkyl lead halide itself.

The present paper covers the experimental data for this interchange of alkyl groups between two trialkyllead halides, between trialkyllead halides and tetraalkyllead compounds, and in a single mixed trialkyllead halide. The six systems tested, together with the experimental conditions employed, are listed in Table I. In each system the alkyl groups involved were methyl and ethyl. In the tests involving trialkyllead halides alone, only the chlorides were used; in the systems comprising tetraalkyllead with trialkyllead halide, both the chlorides and bromides were investigated. An experimental difficulty encountered in these reactions was the instability of the salts, particularly the bromides, which tend to disproportionate to lead alkyls, dialkyllead dihalides, and even alkyllead trihalides, and yield in addition the decomposition products of the last two, namely, hydrocarbons, alkyl halides, and lead halides. These secondary reactions were minimized by operating at a relatively low temperature and, in two cases, by converting the trialkyllead halides to the stable lead alkyls by means of an appropriate Grignard reagent immediately upon completion of the redistribution reaction.

(1) Calingaert and Beatty, THIS JOURNAL, 61, 2748 (1939).

TABLE I

REDISTRIBUTION OF ALKYLLEAD HALIDES

No.	Compounds	Moles	Solvent	Ml.	Temp., °C.	Hours	Notes
1	$Me_2EtPbCl$	0.38	Acetone	240	60	5	*a*
2	Me_3PbCl	.30	Acetone	300	60	5	*a*
	Et_3PbCl	.30					
3	Me_4Pb	.15	Hexane	50	76	5	*b*
	Et_3PbCl	.15					
4	Me_4Pb	.15	Hexane	50	76	5	*b, c*
	Et_3PbCl	.15					
5	Me_4Pb	.15	Hexane	50	76	5	*d*
	Et_3PbBr	.15					
6	Et_4Pb	.15	Hexane	50	80	5	*c, d*
	Me_3PbBr	.15					

[a] Complete analysis showed the product to be a random equilibrium mixture. [b] Analysis showed that both the R_3PbCl and R_4Pb in the product contained methyl and ethyl radicals in about equal proportions. [c] Added 2.5 mole per cent. of aluminum chloride catalyst to the lead compounds. [d] Analysis of R_4Pb in the product indicated a random equilibrium mixture; the R_3PbBr salts were not analyzed.

In the first two systems involving only trialkyllead chlorides, four compounds are predicted by theory and, correspondingly, by appropriate treatment with a suitable Grignard reagent, four lead alkyls were obtained which were readily separated by fractional distillation.[2]

In the systems containing tetraalkyllead, the theory predicts the formation of five lead alkyls and four trialkyllead halides. These were first separated by distillation into two groups, the liquid lead alkyls and the solid trialkyllead halides. The lead alkyls were subsequently fractionated. Although no attempt was made to separate the constituents present in the mixture of trialkyllead halides, the melting point as well as the lead and chlorine analysis of the mixture indicated the presence of both methyl and ethyl radicals. Whenever the analysis was carried to completion, the composition of the groups of compounds analyzed corresponded to the predicted random equilibrium, and these equilibrium compositions were independent of the identity of the starting materials.

Material balances for the halides could not be established as quantitatively as in the case of the catalytic redistribution of the lead alkyl systems,[3] first, because of a certain amount of decomposition of these salts, and, second, because their conversion to lead alkyls by the Grignard reaction was not quantitative.

The reactions appeared to take place readily and to reach completion in a relatively short time.[4] The compounds themselves act as catalysts, and the presence of an additional catalyst did not materially affect the rate of the reaction or alter the composition of the final product. Analytical data for the composition of three of the equilibrium mixtures are given in Tables II, III, and IV, and the distillation curves for two of the products are shown in Figs. 1 and 2.

TABLE II

PRODUCTS FROM THE REDISTRIBUTION OF $Me_2EtPbCl$

Compound	Identified as	Composition, mole per cent. Found	Calcd.[a] for $r^b = 2/3$
Me_3PbCl	Me_4Pb	30.0	29.6
$Me_2EtPbCl$	Me_3EtPb	47.2	44.5
$MeEt_2PbCl$	Me_2Et_2Pb	18.4	22.2
Et_3PbCl	$MeEt_3Pb$	4.4	3.7

[a] Calculated mole percentages are given[1] by: $Me_3PbCl = r^3$; $Me_2EtPbCl = 3r^2(1 - r)$; $MeEt_2PbCl = 3r(1 - r)^2$; $Et_3PbCl = (1 - r)^3$. [b] r is the mole fraction of methyl radicals in the starting compound.

TABLE III

PRODUCTS FROM THE REDISTRIBUTION OF Me_3PbCl WITH Et_3PbCl

Compound	Identified as	Composition, mole per cent. Found	Calculated for $r^a = 0.46$	Calculated for $r^b = 0.50$
Me_3PbCl	Me_4Pb	8.6	9.7	12.5
$Me_2EtPbCl$	Me_3EtPb	34.9	34.3	37.5
$MeEt_2PbCl$	Me_2Et_2Pb	41.5	40.3	37.5
Et_3PbCl	$MeEt_3Pb$	15.0	15.7	12.5

[a] r is the mole fraction of methyl radicals found in the product. [b] r is the mole fraction of methyl radicals present in the starting mixture.

TABLE IV

R_4Pb PRODUCTS FROM THE REDISTRIBUTION OF Me_4Pb WITH Et_3PbBr

Compound	Composition, mole per cent. Found	Calculated[a] for $r^b = 0.66$	Calculated[a] for $r^c = 0.57$
Me_4Pb	17.6	19.0	10.6
Me_3EtPb	44.0	39.1	31.9
Me_2Et_2Pb	22.6	30.2	36.0
$MeEt_3Pb$ + Et_4Pb	15.8	11.7	21.5

[a] Calculated mole percentages are given[1] by: $Me_4Pb = r^4$; $Me_3EtPb = 4r^3(1 - r)$; $Me_2Et_2Pb = 6r^2(1 - r)^2$; $MeEt_3Pb = 4r(1 - r)^3$; $Et_4Pb = (1 - r)^4$. [b] r is the mole fraction of methyl radicals found in the R_4Pb portion of the product. [c] r is the mole fraction of methyl radicals present in the starting mixture.

Conclusion.—The data show that the redistribution reaction of the trialkyllead halides takes place readily in the absence of any additional catalyst other than the halides themselves. This fact elucidates several reports of anomalous be-

(2) Calingaert, Beatty and Neal, THIS JOURNAL, **61**, 2755 (1939).

(3) Calingaert and Soroos, *ibid.*, **61**, 2758 (1939); Calingaert, Beatty and Soroos, *ibid.*, **62**, 1099 (1940).

(4) Calingaert, Beatty and Hess, *ibid.*, **61**, 3300 (1939).

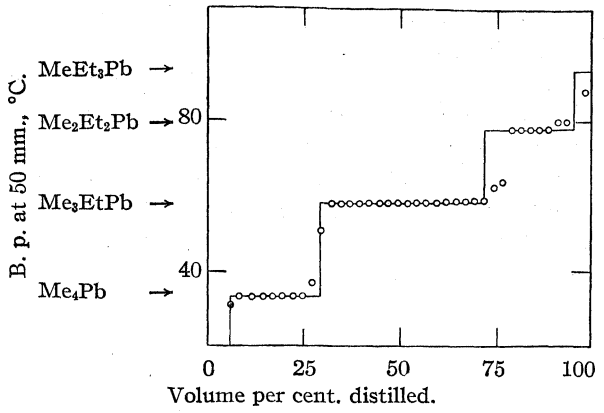


Fig. 1.—Distillation of R_4Pb compounds from reaction product of $Me_2EtPbCl$: solid line calculated for random equilibrium mixture with [Me] = 2/3.

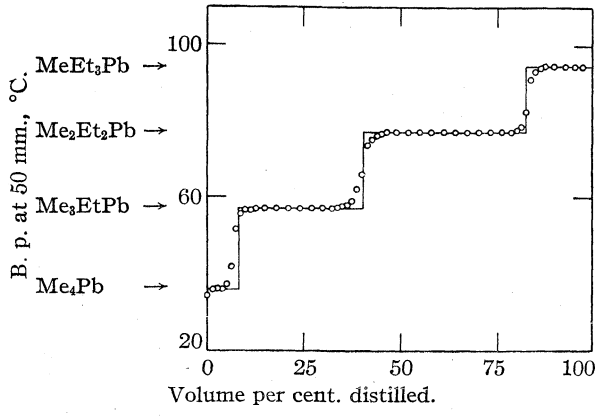


Fig. 2.—Distillation of R_4Pb compounds from reaction product of Me_3PbCl + Et_3PbCl: solid line calculated for random equilibrium mixture with [Me] = 0.46.

havior which have appeared in the literature, but which have received very little consideration from either their authors or others. Previous work in this Laboratory[5] has shown that in the synthesis of certain $R_3R'Pb$ compounds from the reaction of R_3PbX compounds with Grignard reagents, some R_4Pb and $R_2R'_2Pb$ compounds are also formed. Grüttner and Krause[6] have emphasized that in the preparation of $R_2R'R''Pb$ compounds from $R_2R'PbX$, great care must be exercised to use the halides only when freshly prepared, as storage for any length of time, especially of the bromides, leads to low yields and an impure product. On the basis of the disclosures made in the present paper, it seems certain that these previous results were due to the spontaneous redistribution of the trialkyllead halides containing different alkyl groups, with the result that the final lead alkyl product contained, in addition to the expected compound, the three compounds corresponding to this redistribution.

(5) Calingaert and Soroos, *J. Org. Chem.*, **2**, 535 (1938).
(6) Grüttner and Krause, *Ber.*, **50**, 202 (1917).

Experimental

Redistribution of Dimethylethyllead Chloride.—The salt was prepared by passing dry hydrogen chloride into a hexane solution of trimethyllead. The precipitated salt was filtered, and freed of small amounts of lead chloride and dialkyllead dichlorides by dissolving the product in benzene, filtering, and reprecipitating the salt by dilution with hexane. The material was finally filtered, washed with hexane, and dried by evacuation.

Anal. Calcd. for $C_4H_{11}PbCl$: Pb, 68.66; Cl, 11.75. Found: Pb, 68.62; Cl, 11.76.

The redistribution of dimethylethyllead chloride and the subsequent conversion of the resulting random equilibrium mixture of trialkyllead chlorides to the corresponding tetraalkyllead compounds was accomplished in the following manner. A solution of 0.38 mole of dimethylethyllead chloride in 240 ml. of dry acetone was refluxed at 60° for five hours. After cooling and filtering from 0.6358 g. of precipitated lead chloride, the acetone was distilled, the last traces being removed at reduced pressure and condensed in a dry-ice trap. The residue was washed with cold hexane. Fractionation of the acetone distillate and hexane washings yielded 2.234 g. of lead alkyls. The residue was next dissolved in 300 ml. of dry benzene, filtered from 0.1849 g. of dialkyllead chlorides, precipitated by dilution with hexane at −70°, and filtered. An additional small amount of the salts obtained by evaporation of the filtrate was combined with the main body of the material. The mixture of trialkyllead chlorides was finally suspended in 200 ml. of dry ether and treated with an ether solution of 0.7 mole of methylmagnesium bromide. After decomposing the reaction mixture with water and separating the ether layer, fractionation of the product indicated an 83% yield of tetraalkyllead compounds in the proportions corresponding to a random equilibrium mixture of the trialkyllead chlorides, as shown in Table II and Fig. 1.

Redistribution of Trimethyl- with Triethyllead Chloride.—A solution of 0.3 mole each of trimethyl- and triethyllead chloride in 300 ml. of dry acetone was refluxed at 60° for five hours. After filtering from a minute amount of lead chloride, the acetone was evaporated and the residue dried by suction. The mixture of trialkyllead chlorides was converted to the corresponding tetraalkyllead compounds by treating the salts, suspended in 300 ml. of dry ether, with an ether solution of 0.9 mole of methylmagnesium bromide. After decomposing the excess Grignard reagent with water, and separating the ether layer, fractionation of the product gave an 88% yield of lead alkyls corresponding to the random redistribution of the trialkyllead chlorides shown in Table III. The distillation curve is shown in Fig. 2. The observed 46% methyl radicals in the product agrees with the 50% taken in the starting materials as well as is to be expected.

That the redistribution of the two trialkyllead chlorides was not brought about by any catalytic effect of the Grignard reagent was demonstrated by treating an ether suspension of 0.2 mole each of trimethyl- and triethyllead chloride with an ether solution of 0.6 mole of methylmag-

nesium bromide. After decomposing the excess Grignard reagent with water and separating the ether layer, fractionation of the product gave only two lead alkyls, namely, 0.18 mole of tetramethyllead and 0.123 mole of methyltriethyllead. The yield of lead alkyls was 76%.

Redistribution of Triethyllead Chloride with Tetramethyllead. (a) **With no Catalyst.**—A mixture of 0.15 mole each of triethyllead chloride and tetramethyllead in 50 ml. of hexane was refluxed at 77° for five hours. The mixture of liquid lead alkyls was distilled rapidly at reduced pressure (2–50 mm.) from the mixture of solid alkyllead chlorides. The residue was washed with hexane, dried on a porous plate (wt. 40 g.), and analyzed. *Anal.* Calcd. for $Me_{1.5}Et_{1.5}PbCl$: Pb, 67.10; Cl, 11.48. Found: Pb, 65.96; Cl, 11.83. A sample of the solids recrystallized from hexane decomposed at 95°; triethyllead chloride decomposes at 170°. Fractionation of the distillate of liquid lead alkyls gave 2.3 ml. of tetramethyllead, 7.7 ml. of trimethylethyllead, 4.6 ml. of dimethyldiethyllead, and 2–3 ml. of residue containing the higher lead alkyls. Although the data obtained in this and the experiments given below were not of such accuracy as to permit a complete analysis of the products of the reaction, the results were nevertheless sufficient to indicate conclusively that redistribution of the alkyl groups had occurred.

(b) **With Aluminum Chloride Catalyst.**—A mixture of 0.15 mole each of triethyllead chloride and tetramethyllead with 1 g. of aluminum chloride in 50 ml. of hexane, treated in the same manner as in (a), gave 40.8 g. of a mixture of solid alkyllead chlorides. *Anal.* Calcd. for $Me_{1.5}Et_{1.5}PbCl$: Pb, 67.10; Cl, 11.48. Found: Pb, 65.59; Cl, 11.68. A sample of the solid mixture recrystallized from hexane decomposed at 90°. Fractionation of the liquid lead alkyls gave 2.5 ml. of tetramethyllead, 6.9 ml. of trimethylethyllead, 3.1 ml. of dimethyldiethyllead, and 4–5 ml. of residue containing the higher lead alkyls.

Redistribution of Triethyllead Bromide with Tetramethyllead.—A mixture of 0.15 mole each of triethyllead bromide and tetramethyllead in 50 ml. of hexane was refluxed at 77° for five hours. The liquid portion of the product was filtered from the undissolved salts and the solids were washed with hexane. The lead alkyl filtrate and hexane washings were distilled rapidly at reduced pressure (2–50 mm.) from a small amount of dissolved salts. Fractionation of the distillate gave 3.8 ml. of tetramethyllead, 10.6 ml. of trimethylethyllead, 6.0 ml. of dimethyldiethyllead, and 4.6 ml. of a mixture of methyltriethyllead and tetraethyllead. The analysis of the product is given in Table IV.

The data show that considerable decomposition of the trialkyllead bromides took place, forming lead alkyls and lead bromide, since the total recovery of lead alkyls (0.161 mole) is greater than the input (0.15 mole).

Redistribution of Trimethyllead Bromide with Tetraethyllead.—The redistribution of 0.15 mole each of trimethyllead bromide and tetramethyllead with 1 g. of aluminum chloride at 80° for five hours, followed by filtration and vacuum distillation from the solid alkyllead bromide salts, and by fractionation of the liquid lead alkyls, gave 45.5 g. of lead alkyl distillate. The fractionation, although not adequate for accurate analysis, indicated a random equilibrium mixture, showing that the redistribution was probably complete.

Summary

Trialkyllead halides containing methyl and ethyl radicals undergo the redistribution reaction spontaneously and yield a random equilibrium mixture containing all four possible trialkyllead halides. Mixtures of trialkyllead halides and tetraalkyllead containing these two radicals yield the five possible lead alkyls as well as the four halides.

DETROIT, MICHIGAN RECEIVED SEPTEMBER 27, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE ETHYL GASOLINE CORPORATION]

The Redistribution Reaction. VII. Alkyl Compounds of Mercury, Tin, Silicon and Zinc

BY GEORGE CALINGAERT, HAROLD SOROOS AND VINCENT HNIZDA

The first paper[1] of this series stated that the redistribution reaction takes place in a variety of metal alkyls and subsequent papers have described the reaction for R_4Pb compounds[2] and the trialkyllead halides.[3]

The present paper gives the experimental data relating to the interchange of alkyl groups in several other metal alkyls, namely, those of mercury, tin, silicon and zinc. The systems tested, together with the experimental conditions employed, are listed in Table I and comprise eleven compounds, four metals and three alkyl radicals. The results, except for zinc, were similar to those obtained for the lead compounds, the products being random equilibrium mixtures of all the possible metal alkyls for each metal and the two alkyl groups present.

Both methylethylmercury and an equimolecular mixture of dimethyl- and diethylmercury gave the same random equilibrium mixture of the three mercury alkyls, shown in Table II, when allowed to stand at room temperature in the presence of

(1) Calingaert and Beatty, THIS JOURNAL, **61**, 2748 (1939).
(2) Calingaert, Beatty and Soroos, *ibid.*, **62**, 1099 (1940).
(3) Calingaert, Soroos and Shapiro, *ibid.*, **62**, 1104 (1940).

TABLE I

ORGANO-METALLIC SYSTEMS TESTED

Composition Compd.	Moles	$AlCl_3$, mole per cent.	Solvent	Temp., °C.	Time, hours
Me_2Hg	0.11	1.7	None	25	18
Et_2Hg	.11				
MeEtHg	.07	4.0	None	25	66
Me_4Sn	.15	2.5	Pentane	60	5
Et_4Sn	.15		(50 ml.)		
Et_4Si	.14	2.5	None	173–181	5
Pr_4Si	.15				
Me_2Zn	.32	1.4[a]	None	About 60	5
Et_2Zn	.21				

[a] Also tested with 1.5% of a mixture of methylaluminum chlorides in addition to the aluminum chloride.

the aluminum chloride catalyst. The analytical distillation curves[4] are shown in Fig. 1. The redistribution of dimethylmercury with diethylmercury and the subsequent isolation of methylethylmercury is of particular interest, since reports in the literature[5] suggest that methylethylmercury is too unstable to exist as such for any length of time.

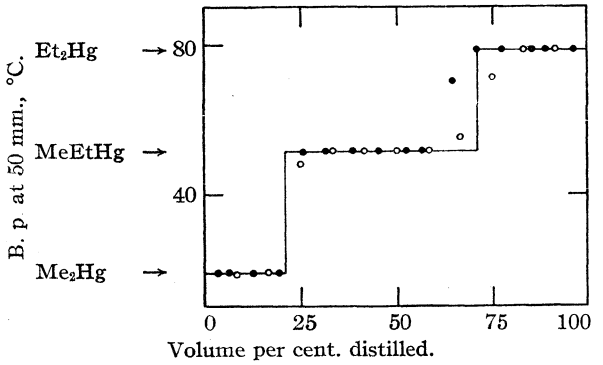


Fig. 1.—Distillation of reaction product from: ○, MeEtHg; ●, Me_2Hg + Et_2Hg; solid line calculated for random equilibrium in mixture having [Me] = 0.5.

Contrary to these reports, pure methylethylmercury appears to be a very stable compound, being unchanged on standing at room temperature for months, or on distillation at 127°, even after the addition of a small amount of iodine. Its isolation in a pure state can, therefore, be accomplished by fractional distillation of the random redistribution mixture of the three mercury alkyls obtained from the redistribution of a mixture of dimethylmercury with diethylmercury. In the light of the present study it now appears probable that Frankland's material contained catalytic amounts of alkylmercuric chloride which caused redistribution, and that the equilibrium was constantly displaced by the removal of dimethylmercury, thus resulting in the gradual disappearance of the methylethylmercury originally present.

(4) Calingaert, Beatty and Neal, THIS JOURNAL, **61**, 2755 (1939).

(5) Frankland, *Ann.*, **111**, 57 (1859), treated ethylmercuric chloride with dimethylzinc and stated that: "It is probable that mercuric ethomethide was formed in the above reaction; but subsequent distillations gradually transformed it, more or less perfectly, into a mixture of mercuric ethide and mercuric methide." Hilpert and Grüttner, *Ber.*, **48**, 906 (1915), state that RR'Hg compounds, sealed in glass and kept for a few weeks, decompose to R_2Hg and R'_2Hg; see also Kharasch and Marker, THIS JOURNAL, **48**, 3130 (1926).

TABLE II

PRODUCTS FROM THE REDISTRIBUTION OF Me_2Hg WITH Et_2Hg, AND OF MeEtHg

Original compounds		Composition, mole per cent. Me_2Hg	MeEtHg	Et_2Hg
Me_2Hg + Et_2Hg	Found	26	46	28
	Calcd.	25	50	25
MeEtHg	Found	28	47	25
	Calcd.	25	50	25

Random equilibrium mixtures containing the five possible metal alkyls were obtained from the redistribution reaction of tetramethyltin with tetraethyltin, and of tetraethylsilicon with tetrapropylsilicon. The analyses of the two products are given in Tables III and IV and the analytical distillations are shown in Figs. 2 and 3. The redistribution of tetraethylsilicon with tetrapropylsilicon was tested for convenience at the refluxing temperature of the mixture, and the possibility of reaction at a lower temperature was not investigated. These results for silicon recall the inter-

TABLE III

PRODUCTS FROM THE REDISTRIBUTION OF TETRAMETHYL- WITH TETRAETHYLTIN

	Mole per cent. Found	Calcd.[1] for r^a = 0.46
Me_4Sn, Me_3EtSn	24.6	25.3
Me_2Et_2Sn	38.4	37.0
$MeEt_3Sn$, Et_4Sn	37.0	37.7

[a] r is the estimated mole fraction of methyl radicals in the product.

TABLE IV

PRODUCTS FROM THE REDISTRIBUTION OF TETRAETHYL- WITH TETRAPROPYLSILICON

	Mole per cent. Found	Calcd.[1] for r^a = 0.464
Et_4Si	5	4.6
Et_3PrSi	21	21.4
Et_2Pr_2Si	40	37.1
$EtPr_3Si$	24	28.6
Pr_4Si	10	8.3

[a] r is the estimated mole fraction of methyl radicals in the product.

changes of radicals found at high temperatures (about 300°) by Dolgov and Volnov[6] in alkyl and alkyl–aryl $R_3R'Si$ compounds. These authors stated that the compounds rearranged according to the scheme $2R_3R'Si \rightarrow R_2R'_2Si + R_4Si$, and ascribed this to the greater stability of the symmetrical molecules. However, their analytical data are only sufficient for the identification of the new compounds so obtained, and are not adequate to determine the composition of the whole product or to demonstrate the existence of an equilibrium.

A mixture of dimethylzinc with diethylzinc did not undergo any redistribution at the boiling temperature (about 60°) in the presence of aluminum chloride or mixed methylaluminum chlorides as catalysts. The possibility that the reaction can be brought about at a higher temperature or under different operating conditions has not yet been tested.

Although only four metals and three alkyl radicals have been tested in the present study, it seems probable in the light of the results with lead[2] that the reaction will occur as well with other alkyl and aryl radicals of the present metals. It would at least with those metals which are known to form mixed compounds of the RR'M type. This supposition is borne out by the observation of Challenger and Ridgway,[7] who studied the transfer of aryl radicals in organo-metallic compounds, and stated that "a most interesting example of this type of reaction is afforded by the ready production of diphenyl-α-naphthylbismuth by the fusion of tri-α-naphthylbismuth and triphenylbismuth at 190°." Some amount of unchanged reactants was also found in the product, but the small quantities of materials and the methods of separation used obviously precluded an accurate analysis of the product, and no mention of phenyldi-α-naphthylbismuth is made. These authors also stated that "a preliminary experiment appeared to indicate that this reaction is reversible," without giving any experimental details. It would seem probable that this reaction is an example of redistribution and that a precise analysis would have shown a random equilibrium mixture of all four R_3Bi compounds.

Experimental

Dimethyl- with Diethylmercury.—A mixture of 0.11 mole each of dimethyl- and diethylmercury with 1.7 mole per cent. of aluminum chloride was allowed to stand in a stoppered flask at room temperature for eighteen hours. After extracting the catalyst by shaking with water, the distillation of the product, shown by the solid circles in Fig. 1, yielded the equilibrium mixture given in Table II.

Methylethylmercury.—The pure compound was obtained by fractional distillation of the random equilibrium mixture obtained from the redistribution of dimethylmercury with diethylmercury: b. p. 51.5 (50 mm.), d^{20} 2.71; $n^{20}D$ 1.5440. *Anal.* Calcd. for C_3H_8Hg: Hg, 81.98. Found: Hg, 81.24. The compound, after standing for seven months at room temperature, showed no evidence of spontaneous redistribution or decomposition to the symmetrical compounds, when redistilled at 50 mm. through a packed column in an atmosphere of nitrogen. Another sample distilled at atmospheric pressure (127.4° at 748 mm.) with no evidence of decomposition, even when the flask was almost dry. Repeating this high temperature distillation after the addition of a trace of iodine produced no change in boiling point or evidence of redistribution, although the iodine reacted immediately with the mercury compound.

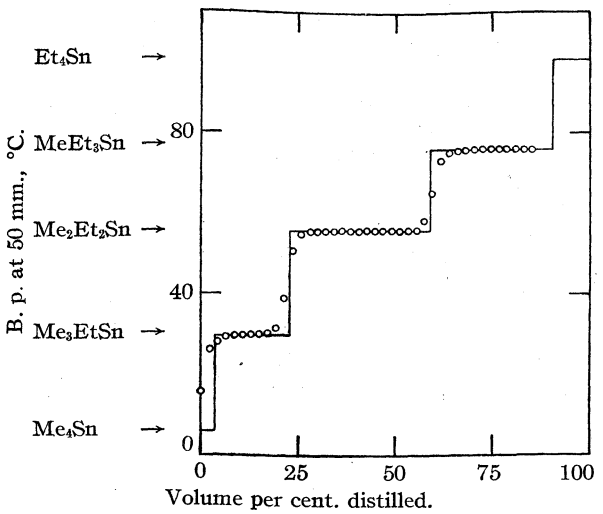


Fig. 2.—Distillation of the reaction product from $Me_4Sn + Et_4Sn$: solid line calculated for random equilibrium mixture having [Me] = 0.46.

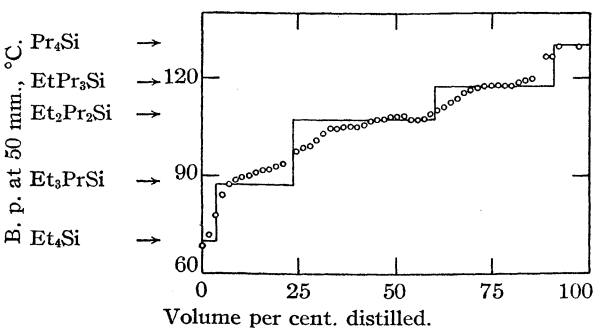


Fig. 3.—Distillation of the reaction product from Et_4Si and Pr_4Si: solid line calculated for random equilibrium mixture having [Et] = 0.464.

(6) Dolgov and Volnov, *Zhur. Obshchei Khim.*, **1**, 91 (1931); see also Ladenburg, *Ber.*, **7**, 387 (1874).

(7) Challenger and Ridgway, *J. Chem. Soc.*, **121**, 104 (1922).

The redistribution of the compound was effected by treating 0.07 mole with 3.5 mole per cent. of aluminum chloride at room temperature for sixty-six hours, followed by extraction of the catalyst with water. The analytical distillation of the product is shown by the open circles of Fig. 1, and its composition is given in Table II.

Tetramethyl- with Tetraethyltin.—The redistribution of a mixture of 0.15 mole each of the two tin alkyls with 2.5 mole per cent. of aluminum chloride was carried out in 50 ml. of pentane at the boiling point of the mixture, 60°, for five hours. The catalyst went into solution in the mixture and later there was formed about 1 ml. of heavy yellow oil, from which the product was decanted. After distilling off the solvent, there remained 61 g. of tin alkyls, whose analysis by distillation is given in Table III and Fig. 2.

Tetraethyl- with Tetrapropylsilicon.—The redistribution of a mixture of 0.14 mole of tetraethylsilicon and 0.15 mole of tetrapropylsilicon (48% ethyl radicals) with 2.5 mole per cent. of aluminum chloride was carried out at the boiling point of the mixture, 175–180°, for five hours. There was no visible reaction of the catalyst, which finally was extracted with water. The analytical distillation shown in Fig. 3, although not made carefully, showed that redistribution had occurred, and the estimated composition corresponded with the expected equilibrium mixture, as shown in Table IV.

Dimethyl- with Diethylzinc.—A mixture of 0.32 mole of dimethylzinc and 0.21 mole of diethylzinc, after refluxing for five hours in an atmosphere of nitrogen, was fractionated into the two original components without evidence of redistribution. After refluxing the same mixture at atmospheric pressure (temperature about 60°) for five hours in the presence of 1.4 mole per cent. of aluminum chloride, followed by vacuum distillation (20–50 mm.) from the catalyst, fractionation again gave only the symmetrical zinc alkyls. Repeating the experiment with the addition of 1.5 mole per cent. of a mixture of methylaluminum chlorides to the aluminum chloride still did not bring about redistribution.

The recovery of products in the above experiments was essentially quantitative, except for normal handling losses incurred during extraction of the catalyst, filtration, transfer, and distillation.

Summary

The alkyl compounds of mercury, tin and silicon readily undergo the redistribution reaction, yielding random equilibrium mixtures, while the zinc alkyls at 60° failed to react. Methylethylmercury was isolated and found to be stable on standing or distillation, in the absence of redistribution catalysts.

DETROIT, MICHIGAN RECEIVED OCTOBER 9, 1939

[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA, AND THE NATIONAL INSTITUTE OF HEALTH, WASHINGTON, D. C.]

Studies in the Phenanthrene Series. XXIV. Phenolic Amino Alcohols and Naphthisoquinolines Derived from 9,10-Dihydrophenanthrene[1]

BY ALFRED H. STUART AND ERICH MOSETTIG

Ethanolamine and propanolamine derivatives of 9,10-dihydrophenanthrene prepared in our laboratory[2] have been found to exhibit a relatively high analgesic activity, which, unfortunately, was accompanied by convulsant and emetic effects of similar or even higher degree.[3] In the hope of finding compounds with a more favorable ratio of desirable and undesirable physiological effects, it was decided to synthesize analogous amino alcohols of the dihydrophenanthrene series, containing besides the alkamine side chain also a phenolic hydroxyl group.

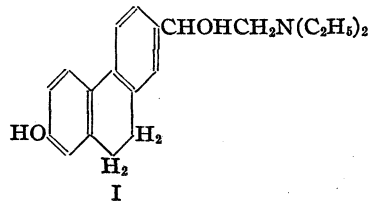
The choice of positions into which the phenolic hydroxyl group can be introduced appears to be limited, and the same holds true for the introduction of a second substituent that can be used for building up alkamine side chains or other desirable groups. Thus, the phenolic hydroxyl group can be conveniently introduced only into position 2 of 9,10-dihydrophenanthrene.[4] Also acyl groups enter chiefly position 2, and position 7 if 2 is already occupied by a phenolic hydroxyl group.[2,4b] We have described recently a practicable method for the preparation of 2-hydroxy-7-acetyl-9,10-dihydrophenanthrene,[4b] and this compound, indeed, became the key substance for the various syntheses described in this communication. The 2-hydroxy-7-[2-(diethylamino)-1-hydroxyethyl]-9,10-dihydrophenanthrene (I) was prepared by bromination of the above-mentioned hydroxy ketone, replacement of the bromine by the di-

(1) This work is part of a unification of effort by a number of agencies having responsibility for the solution of the problem of drug addiction. The organizations taking part are: The Rockefeller Foundation, the National Research Council, the U. S. Public Health Service, the U. S. Bureau of Narcotics, the University of Virginia, and the University of Michigan. Publication authorized by the Surgeon General, U. S. P. H. S.

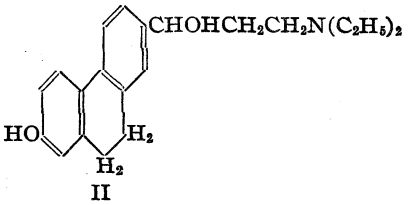
(2) Burger and Mosettig, THIS JOURNAL, **58**, 1857 (1936).

(3) Small, Eddy, Mosettig and Himmelsbach, "Studies on Drug Addiction," Supplement No. 138 to the Public Health reports, pp. 81–83 (1938).

(4) (a) Burger and Mosettig, THIS JOURNAL, **59**, 1302 (1937); (b) Mosettig and Stuart, *ibid.*, **61**, 1 (1939); (c) Krueger and Mosettig, *J. Org. Chem.*, **3**, 340 (1938).



I



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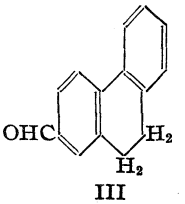

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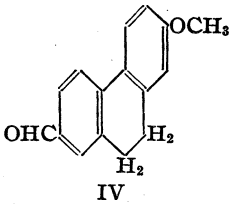

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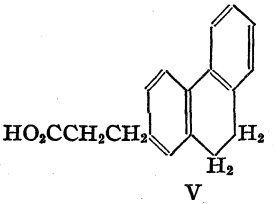

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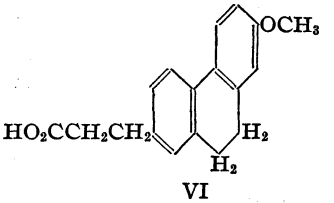

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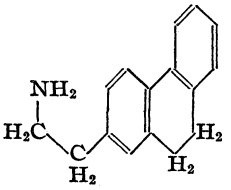
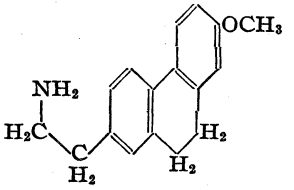


VII

N-acetyl derivative VIIa



VIII

N-acetyl derivative VIIIa

ethylamino group, and subsequent reduction of the resulting amino ketone. Actually, the reactions were carried out on the respective O-acetyl derivatives, with saponification as the last step of the synthesis. Similarly, application of the Mannich amino ketone synthesis to 2-acetoxy-7-acetyl-9,10-dihydrophenanthrene gave 2-acetoxy-7-[3-(diethylamino)-1-oxopropyl]-9,10-dihydrophenanthrene, from which the amino alcohol II was obtained by catalytic reduction. In this procedure, aqueous formaldehyde[5] was employed, the advantage over the use of paraformaldehyde and isoamyl alcohol[6] being that unreacted starting material can be recovered readily.[7]

Encouraged by the favorable reports on the pharmacological effectiveness of an isoquinoline derivative,[8] which was obtained by closing a nitrogen-containing ring onto the phenanthrene nucleus, we decided to synthesize analogous compounds derived from 9,10-dihydrophenanthrene and 2-methoxy-9,10-dihydrophenanthrene. The starting materials in these syntheses were the aldehydes III and IV, which were prepared *via* the corresponding acids by the Rosenmund method.[9] The phenanthroic acids themselves were readily obtained from 2-acetyl- and 2-methoxy-7-acetyl-9,10-dihydrophenanthrene by oxidation with sodium hypochlorite. This detour to the aldehydes was chosen because thereby better results were achieved than by the application of the direct method, involving the action of metal chlorides and hydrogen cyanide on 9,10-dihydrophenanthrene.[4a] Attempts to prepare the hydroxy aldehyde corresponding to IV by modified Gattermann syntheses[10] were unsuccessful. We did not succeed in preparing the β-phenanthrylethylamines VII and VIII by electrolytic reduction of the corresponding nitrovinyl derivatives, a method that we had applied previously to the preparation of other β-phenanthrylamines.[8a] Eventually we were able to synthesize VII and VIII in yields of from 60 to 80% by the Curtius method, starting from β-[2-(9,10-dihydrophenanthryl)]-propionic acid (V) and β-[7-(2-methoxy-9,10-dihydrophenanthryl)]-propionic acid (VI). Acid V had been prepared by us previously.[4a] The analogous preparation of acid VI did not offer any difficulties.

Attempts to produce tetrahydroisoquinoline derivatives by cyclization of the formaldehyde

(5) Mannich, Borkowsky and Wan Ho Lin, *Arch. Pharm.*, **275**, 54 (1937).

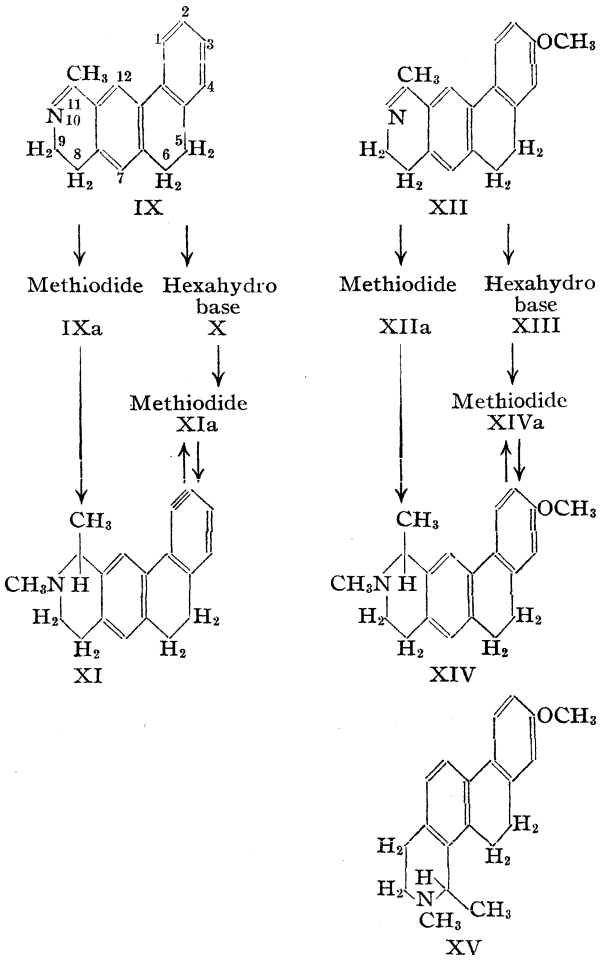
(6) *Cf.* van de Kamp and Mosettig, THIS JOURNAL, **58**, 1568 (1936).

(7) The possibility that the $-CH_2N(C_2H_5)_2$ group has entered a nuclear position activated by the acetoxy group, cannot be entirely excluded [*cf.* Auwers and Dombrowski, *Ann.*, **344**, 280 (1906)]. We had not enough material available to prove the structure of the amino ketone or the corresponding amino alcohol.

(8) (a) Mosettig and May, THIS JOURNAL, **60**, 2962 (1938). (b) Eddy, unpublished results.

(9) See Mosettig and van de Kamp, *ibid.*, **55**, 2995 (1933).

(10) Adams and co-workers, *ibid.*, **45**, 2373 (1923); **46**, 1518 (1924); Hinkel and co-workers, *J. Chem. Soc.*, 2793 (1932); 184, 339 (1936).



condensation products of VII and VIII[11] were completely unsuccessful, variations in experimental conditions leading either to starting material or to amorphous, insoluble, and non-basic condensation products. No satisfactory method for the preparation of the desired isoquinoline derivatives in adequate amounts was devised. Ring closure was effected eventually by the Bischler–Napieralski reaction. After investigating a number of modifications of this method,[12] we found that the best results were obtained by cyclizing the N-acetyl derivatives, VIIa and VIIIa, to the dihydroisoquinoline derivatives IX and XII by the action of phosphorus oxychloride in boiling toluene, in an average yield of less than 30%. In order to transform IX and XII into the corresponding N-methyltetrahydroisoquinoline derivatives XI and XIV, two routes were followed in each series. (a) The methiodides IXa and XIIa respectively were reduced catalytically. (b) The bases IX and XII were reduced catalytically to X and XIII, respectively. The latter two were completely methylated, and the resulting methiodides XIa and XIVa were decomposed by heating in an oil-pump vacuum. In each series, identical end-products, XI and XIV, were obtained by either route.

Because of the large number of steps involved in the synthesis of XI and XIV, and, in particular, on account of the relatively poor yield in the Bischler–Napieralski reaction, we eventually did not have enough material available to attempt a structural proof of the bases XI and XIV. By analogy,[13] we assume structure XI to be correct, *i. e.*, the ring closure of VIIa to have taken place in position 3 of the phenanthrene nucleus. There are no precedents in the 9,10-dihydrophenanthrene series that would justify speculations whether the methoxyl group in the terminal nucleus had any influence on the direction of ring closure of compound VIIIa. Formula XIV, therefore, can be suggested only tentatively, and an alternative structural formula, XV, must also be taken into consideration.

Compounds I, II, and XIV have been submitted to pharmacological investigation. As yet only results obtained with I are available. The analgesic activity of I (10 mg./kg., cat) shows, according to Dr. Eddy, a twofold increase over that of its analog carrying no phenolic hydroxyl group, the 2-[2-(diethylamino)-1-hydroxyethyl]-9,10-dihydrophenanthrene. The former was also more toxic and more convulsant, but the difference in these respects was relatively less.

Experimental

2-Acetoxy-7-ω-bromoacetyl-9,10-dihydrophenanthrene.—A saturated solution of 2-acetoxy-7-acetyl-9,10-dihydrophenanthrene[4b] in absolute ethanol was mixed at 0° in a quartz flask with an ice-cold solution of one molecular equivalent of bromine in absolute ether, and the mixture was exposed to a mercury vapor-lamp for five minutes. The hydrogen bromide formed in the reaction was neutralized with potassium carbonate, and the solution was evaporated to dryness. The product crystallized from ethanol in small white needles that melted at 123–124°.

Anal. Calcd. for $C_{18}H_{15}BrO_3$: C, 60.18; H, 4.21. Found: C, 60.68; H, 3.81.

2-Acetoxy-7-[2-(diethylamino)-1-oxoethyl]-9,10-dihydrophenanthrene.—A mixture of the above bromo ketone

(11) See ref. 8a and Decker and Becker, *Ann.*, **395**, 342 (1913); Buck, THIS JOURNAL, **56**, 1769 (1934).

(12) Pictet and Kay, *Ber.*, **42**, 1973 (1909); Späth and Mosettig, *Ann.*, **433**, 146 (1923); Haworth, *J. Chem. Soc.*, 2281 (1927); Späth, Berger and Kuntara, *Ber.*, **63**, 134 (1930); Kindler, Peschke and Plüddemann, *Arch. Pharm.*, **277**, 25 (1939).

(13) See ref. 4a and Mosettig and Krueger, *J. Org. Chem.*, **3**, 317 (1938).

and diethylamine (5–6 molecular equivalents) in dry benzene was allowed to stand at room temperature for five hours. The amino ketone was isolated in the customary manner and purified through its perchlorate. It melted at 89–90°.

Anal. Calcd. for $C_{22}H_{25}NO_3$: N, 3.99. Found: N, 3.93.

The **perchlorate** was recrystallized from an ethanol–ether mixture. It melted at 165–166°.

Anal. Calcd. for $C_{22}H_{26}ClNO_7$: N, 3.10; Cl, 7.84. Found: N, 3.39; Cl, 7.68.

No crystalline hydrochloride could be obtained.

2-Acetoxy-7-[2-(diethylamino)-1-hydroxyethyl]-9,10-dihydrophenanthrene.—A mixture of 2 g. of the amino ketone perchlorate, 70 cc. of absolute alcohol, and 0.1 g. of platinum oxide absorbed the calculated amount of hydrogen within six hours. The perchlorate of the resulting amino alcohol and the base itself were oily. The **hydrochloride** was recrystallized from an alcohol–ether mixture and melted at 154–155°.

Anal. Calcd. for $C_{22}H_{28}ClNO_3$: N, 3.59; Cl, 9.09. Found: N, 3.55; Cl, 9.32.

2-Hydroxy-7-[2-(diethylamino)-1-hydroxyethyl]-9,10-dihydrophenanthrene (I).—The above acetoxy compound was saponified readily. The base itself could be obtained only as an oil. The hydrochloride was recrystallized from an alcohol–ether mixture and melted at 202–203°.

Anal. Calcd. for $C_{20}H_{26}ClNO_2$: N, 4.03; Cl, 10.19. Found: N, 4.05; Cl, 10.23.

2-Acetoxy-7-[3-(diethylamino)-1-oxopropyl]-9,10-dihydrophenanthrene.—A mixture of 3 g. of 2-acetoxy-7-acetyl-9,10-dihydrophenanthrene, 1.4 g. of diethylamine hydrochloride, and 1.1 cc. of 36% aqueous formaldehyde was stirred mechanically in a nitrogen atmosphere for ten minutes at room temperature, and for one hour at 100°, during which the formaldehyde lost by evaporation was replaced by occasional additions. The mixture was diluted with water, and unchanged starting material was extracted with ether (1.6 g., after crystallization from ethanol). The amino ketone was precipitated in the aqueous layer with ammonia and extracted with ether. The recrystallized **hydrochloride** weighed 1.5 g. and melted at 132–134° (yield, calcd. on the basis of reacting material, 75%).

Anal. Calcd. for $C_{23}H_{28}ClNO_3$: Cl, 8.82. Found: Cl, 9.32.

In subsequent runs, the relative amounts of reacting material varied somewhat, but the yield of amino ketone was constant. When the reaction was carried out by boiling a mixture of ketone, diethylamine hydrochloride, and paraformaldehyde in isoamyl alcohol, the yield of crystalline amino ketone hydrochloride was approximately the same, but starting material could be recovered only with difficulty.

2-Hydroxy-7-[3-(diethylamino)-1-hydroxy-*n*-propyl]-9,10-dihydrophenanthrene (II).—The above compound, when reduced catalytically, absorbed smoothly one molecular equivalent of hydrogen (PtO_2, absolute alcohol), but no crystalline base or salt of the resulting amino alcohol could be obtained. Therefore, the crude reduction product was saponified, whereby a crystalline phenolic amino alcohol of m. p. 178–185° was formed. It crystallized readily from ethyl acetate and melted, after drying in the desiccator, at 129–130°. The analytical data agree approximately with values for a base containing two moles of ethyl acetate

Anal. Calcd. for $C_{21}H_{27}NO_2 + 2C_4H_8O_2$: C, 69.42; H, 8.63. Found: C, 70.70; H, 8.34.

When this compound was dried at 100° in an oil-pump vacuum, its m. p. rose to 182–183°. Satisfactory analytical data were obtained only after the base was sublimed in an oil-pump vacuum. It then melted at 185–186°.

Anal. Calcd. for $C_{21}H_{27}NO_2$: C, 77.50; H, 8.36. Found: C, 77.41; H, 8.69.

The hydrochloride melted after recrystallization at 180–181°.

Anal. Calcd. for $C_{21}H_{28}ClNO_2$: C, 69.69; H, 7.80. Found: C, 69.61; H, 7.68.

By allowing the pyridine solution of the above hydrochloride and the calculated amount of benzoyl chloride to stand for five hours, we obtained a dibenzoyl derivative whose hydrochloride melted unsharply at 157–159° after two crystallizations from an alcohol–ether mixture.

Anal. Calcd. for $C_{35}H_{36}ClNO_4$: Cl, 6.22. Found: Cl, 6.58.

9,10-Dihydrophenanthroyl-2-chloride.—2-Acetyl-9,10-dihydrophenanthrene[2] was oxidized readily by 1.5% aqueous sodium hypochlorite solution. The dried crude acid was suspended in thionyl chloride and the mixture was boiled under reflux for four hours. The solution was evaporated in a vacuum, and left an oily residue, which was distilled twice in an oil-pump vacuum. The distillate solidified slowly (yield, 95%). The analytical sample was sublimed slowly, and appeared as long, colorless needles, m. p. 50–51°.

Anal. Calcd. for $C_{15}H_{11}ClO$: C, 74.23; H, 4.57; Cl, 14.61. Found: C, 73.91; H, 4.51; Cl, 14.49.

9,10-Dihydrophenanthrene-2-aldehyde (III).—The acid chloride[14] was converted into the aldehyde by the method of Rosenmund, using an aged palladium–barium sulfate catalyst and decalin as solvent.[9] The yield was 70% (identified as semicarbazone).

2-Methoxy-9,10-dihydrophenanthroyl-7-chloride.—This compound was prepared from the corresponding acid[4a] in the manner described above. The crude crystalline residue from evaporation of the reaction mixture was used for catalytic reduction. For analysis, a sample was sublimed twice in an oil-pump vacuum; white needles, m. p. 87–88°.

Anal. Calcd. for $C_{16}H_{13}ClO_2$: C, 70.46; H, 4.80. Found: C, 70.84; H, 5.29.

2-Methoxy-9,10-dihydrophenanthrene-7-aldehyde (IV).—The catalytic replacement of the chlorine by hydrogen proceeded smoothly, and the aldehyde was formed in a yield of 67% (calculated on the basis of acid). It was recrystallized from methanol and melted at 100°.

Anal. Calcd. for $C_{16}H_{14}O_2$; C, 80.65; H, 5.92. Found: C, 80.42; H, 6.22.

(14) The thionyl chloride used in the preparation of the acid chlorides was purified according to the directions of Fieser's "Experiments in Organic Chemistry," 1935.

2-(2-Nitrovinyl)-9,10-dihydrophenanthrene.—Aldehyde III (4.5 g.) was condensed[8a,15] with nitromethane (2.6 cc.) in ethanolic solution (300 cc.) in the presence of sodium hydroxide (2.8 g.). When the reaction mixture was poured into 10% hydrochloric acid, the product separated as a yellow oil, which slowly became crystalline. It crystallized from ethanol in bright yellow needles, m. p. 77°; yield, 75%.

Anal. Calcd. for $C_{16}H_{13}NO_2$: C, 76.48; H, 5.21. Found: C, 76.13; H, 5.43.

The electrolytic reduction according to Slotta and Szyszka,[16] employing 4.1 g. of the compound, 52 cc. of ethanol, 80 cc. of glacial acetic acid, and 12 cc. of concd. hydrochloric acid, proceeded rather rapidly, the yellow color having disappeared within two hours. A large amount of insoluble sludge was produced and the expected amine VII could be isolated in a yield of only 16%. Similar experiences were encountered in the electrolytic reduction of 2-methoxy-7-(2-nitrovinyl)-9,10-dihydrophenanthrene.

Hydrazide of β-[2-(9,10-Dihydrophenanthryl)]-propionic Acid.—The acid V was prepared according to Burger and Mosettig[4a] and converted to the methyl ester by diazomethane. The oily methyl ester was heated under reflux in a mixture of 2.4 parts (by volume) of absolute ethanol and 2.4 parts of 42% aqueous solution of hydrazine hydrate for forty-two hours. The white hydrazide separated from the cooled reaction mixture. It was recrystallized from water and melted at 134–135°; yield, 85%.

Anal. Calcd. for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81. Found: C, 76.17; H, 6.80.

2-(2-Aminoethyl)-9,10-dihydrophenanthrene (VII).—The Curtius reaction was carried out, following in part the technique of Mayer and Schnecko.[17] To a cooled suspension (0 to 3°) of 8.5 g. of hydrazide in 250 cc. of 0.5 *N* hydrochloric acid was added in several portions a solution of 6 g. of sodium nitrite in 25 cc. of water. The mixture was stirred for one hour after the last portion of nitrite had been added. The azide formed was extracted with ether, the ether solution was dried and mixed with 180 cc. of absolute ethanol. The ether was distilled off and the ethanolic solution was kept boiling under reflux for five hours. No attempt was made to isolate the urethan, but a solution of 74 g. of potassium hydroxide in 300 cc. of absolute alcohol was added and the whole was kept boiling for twenty hours. The reaction mixture was concentrated to a small volume, water added, and the oil taken up in ether. The dried ether solution left, after evaporation, the desired amine, which was distilled in an oil-pump vacuum. The distillate consisted of 5.4 g. of colorless oil. A crystalline hydrochloride was obtained and purified in the customary manner; m. p. 229–230°.

Anal. Calcd. for $C_{16}H_{18}ClN$: C, 73.97; H, 6.98; Cl, 13.65. Found: C, 73.50; H, 7.08; Cl, 13.36.

Acidification of the aqueous alkaline layer (from the extraction of the amine with ether) yielded 0.8 g. of nearly pure dihydrophenanthrylpropionic acid. Taking this into account, the yield of amine in the Curtius reaction was about 75%.

Formyl Derivative.—The formate of VII was precipitated by addition of formic acid to an ethereal solution of the base. Heated at 150° for one-half hour, the salt slowly melted down to a brown oil, which solidified on cooling. It was recrystallized from a mixture of benzene and petroleum ether, and melted at 91°; yield, 80%.

Anal. Calcd. for $C_{17}H_{17}NO$: C, 81.24; H, 6.82. Found: C, 80.82; H, 7.38.

Acetyl Derivative (VIIa).—A mixture of base VII with half of its weight of acetic acid was heated with stirring at 150° for one hour. After cooling, the mass solidified, and was recrystallized from a benzene–petroleum ether mixture; m. p. 112°, yield 85%.

Anal. Calcd. for $C_{18}H_{19}NO$: C, 81.47; H, 7.22. Found: C, 81.08; H, 7.12.

β-[7-(2-Methoxy-9,10-dihydrophenanthryl)]-acrylic Acid.—A mixture of 19 g. of the aldehyde IV, 24 g. of malonic acid, 2 cc. of piperidine, and 60 cc. of pyridine was heated on the steam-bath for seventy-five minutes, and then kept boiling for ten minutes in order to complete the reaction. The acrylic acid derivative was purified by crystallization from methyl ethyl ketone; m. p. 192–193°, yield, 87%.

Anal. Calcd. for $C_{18}H_{16}O_3$: C, 77.12; H, 5.75. Found: C, 76.53; H, 5.73.

β-[7-(2-Methoxy-9,10-dihydrophenanthryl)]-propionic Acid (VI).—This acid was obtained nearly quantitatively by reducing the unsaturated acid catalytically (absolute alcohol, platinum oxide catalyst). It was recrystallized from dilute ethanol, and melted at 177°.

Anal. Calcd. for $C_{18}H_{18}O_3$: C, 76.57; H, 6.43. Found: C, 76.00; H, 6.62.

The **methyl ester** was prepared with diazomethane, and was recrystallized from methanol; m. p. 61–62°.

Anal. Calcd. for $C_{19}H_{20}O_3$: C, 77.00; H, 6.80. Found: C, 76.05; H, 6.70.

Hydrazide.—A mixture of crude methyl ester (prepared from 20 g. of the methoxy dihydrophenanthrylpropionic acid), 55 cc. of 42% hydrazine hydrate, and 60 cc. of absolute ethanol was heated under reflux for forty-four hours. The hydrazide precipitated from the cooled solution, and was recrystallized from dilute ethanol; m. p. 155–156°, yield, 90% (calculated on acid).

Anal. Calcd. for $C_{18}H_{20}N_2O_2$: C, 72.95; H, 6.80. Found: C, 72.85; H, 6.50.

2-Methoxy-7-(2-aminoethyl)-9,10-dihydrophenanthrene (VIII).—Seven and five-tenths grams of the hydrazide was degraded in the manner described for the analog without the methoxyl group. The end-product was distilled in an oil-pump vacuum, yielding 3.8 g. of a pale yellow oil, which partly solidified. The hydrochloride melted over a wide range, beginning to sinter at 240°.

Anal. Calcd. for $C_{17}H_{20}ClNO$: C, 70.45; H, 6.96. Found: C, 70.33; H, 6.75.

The **acetyl derivative** (VIIIa) was prepared like its methoxy-free analog. After crystallization from a benzene–petroleum ether solution, it melted at 125–126°.

(15) *Cf.* also Lange and Hambourger, THIS JOURNAL, **53**, 3865 (1931).

(16) Slotta and Szyszka, *J. prakt. Chem.*, [2] **137**, 339 (1933).

(17) Mayer and Schnecko, *Ber.*, **56**, 1408 (1923); *cf.* also Mayer and Krieger, *ibid.*, **55**, 1659 (1922).

Anal. Calcd. for $C_{19}H_{21}NO_2$: C, 77.26; H, 7.17. Found: C, 76.57; H, 7.58.

Ring Closure Experiments.—(a) According to the method of Decker and Becker. Numerous attempts were made to cyclize the formaldehyde condensation products of the amines VII and VIII. Condensation with formaldehyde took place readily with both, but no ring closure products could be obtained by heating the resulting products with hydrochloric acid. Variations in conditions of condensation extended from use of slightly more than one molecular equivalent of formaldehyde to use of a large excess of this reagent, and from five minutes to one hour of heating. The residues remaining after the removal of the excess of formaldehyde in each case were heated with 23% hydrochloric acid for times varying from five minutes to four hours. Under the mildest conditions, amine VII was isolated almost unchanged. When only one molecular equivalent of formaldehyde was used and the time of heating the condensation product did not exceed thirty minutes, small amounts of unchanged amine VII still remained. Under stronger conditions, and when using amine VIII under all conditions, only amorphous white products were obtained, which were insoluble in acids as well as in organic solvents.

(b) According to the method of Bischler–Napieralski. Attempts to bring about ring closure of the formyl derivatives of VII by the action of phosphorus pentoxide were unsuccessful. No reaction occurred in boiling benzene, while in xylene and in tetralin only tarry products were produced. In subsequent experiments the N-acetyl derivatives VIIa and VIIIa were used. Small amounts of IX were obtained by the action of phosphorus pentoxide on the acetyl derivative VIIa in boiling toluene or xylene. The use of phosphorus oxychloride as condensing agent in xylene gave similar results. The use of phosphorus oxychloride in boiling toluene appeared to be relatively most favorable.

11-Methyl-5,6,8,9-tetrahydronaphth[2,1-g]isoquinoline (IX).[18]—A typical reaction was carried out by boiling a solution of 1.6 g. of the N-acetyl derivative VIIa and 1.6 cc. of phosphorus oxychloride in 40 cc. of dry toluene for thirty-five minutes. After two minutes the solution became cloudy and oily material slowly began to separate. The isoquinoline derivative was isolated by extracting the reaction mixture repeatedly with small portions of 5 *N* hydrochloric acid. The base was liberated, extracted with ether, and reconverted to the hydrochloride. The salt melted at 230–232°.

Anal. Calcd. for $C_{18}H_{18}ClN$: Cl, 12.50. Found: Cl, 12.44.

Methiodide (IXa).—On addition of methyl iodide to an acetone solution of the base IX, the methiodide precipitated rapidly. It crystallized from absolute ethanol in long, pale yellow needles, m. p. 267–268°.

Anal. Calcd. for $C_{19}H_{20}IN$: I, 32.60. Found: I, 32.67.

(18) The nomenclature policy of *Chemical Abstracts* has been followed in numbering the naphthisoquinoline derivatives. Formula-pictures of IX, XI, XII, and XIV have been oriented accordingly. For the sake of emphasizing the direction of ring closure, formula XV (a naphth[1,2-*h*]isoquinoline derivative) has been oriented incorrectly (see also ref. 8a).

11-Methyl-5,6,8,9,10,11-hexahydronaphth[2,1-g]isoquinoline (X).—The hydrochloride of base IX, dissolved in absolute ethanol, absorbed readily one molecular equivalent of hydrogen when reduced catalytically (platinum oxide catalyst). The hydrochloride of the reduction product was recrystallized from an ethanol–ether mixture and melted at 239–241°.

Anal. Calcd. for $C_{18}H_{20}ClN$: C, 75.64; H, 7.05. Found: C, 75.06; H, 7.05.

Methiodide of 10,11-Dimethyl-5,6,8,9,10,11-hexahydronaphth(2,1-g)isoquinoline (XIa).—To a solution of 0.25 g. of base X in 3 cc. of acetone was added 0.15 g. of powdered potassium hydroxide and 0.4 cc. of methyl iodide. A white methiodide precipitated rapidly. It was filtered off, washed with water (0.3 g.) and recrystallized from absolute ethanol; m. p. 231°.

Anal. Calcd. for $C_{20}H_{24}IN$: I, 31.31. Found: I, 29.81.

10,11-Dimethyl-5,6,8,9,10,11-hexahydronaphth[2,1-g]-isoquinoline (XI).—(a) The methiodide IXa was reduced catalytically (absolute ethanol, platinum oxide). The oily base of the reduction product was liberated and distilled in an oil-pump vacuum. Its **hydrochloride** melted at 234–236°.

Anal. Calcd. for $C_{19}H_{22}ClN$: C, 76.11; H, 7.40; Cl, 11.83. Found: C, 75.39; H, 7.39; Cl, 11.80.

A sample of the base was dissolved in acetone, and methyl iodide was added. The white methiodide which precipitated immediately was identical (melting point, and mixture melting point) with the methiodide (XIa) that was obtained from 11-methyl-5,6,8,9,10,11-hexahydronaphth[2,1-g]isoquinoline (X), as described above.

(b) The methiodide XIa (from either source) decomposed smoothly when heated above 200° in an oil-pump vacuum. The oily base thus formed was redistilled and converted to the hydrochloride which melted at 232–235°. The mixture melting point with the hydrochloride of the base obtained in the catalytic reduction of methiodide IXa was 233–236°.

3-Methoxy-11-methyl-5,6,8,9-tetrahydronaphth[2,1-g]-isoquinoline-(?)(XII).—A solution of 2 g. of the acetyl derivative VIIIa and 2 cc. of phosphorus oxychloride in 50 cc. of dry toluene was boiled for thirty-five minutes. The reaction product was extracted with 5 *N* hydrochloric acid. The base was liberated and purified by crystallization of the hydrochloride (28%). The salt melted at 249–250°.

Anal. Calcd. for $C_{19}H_{20}ClNO$: Cl, 11.30. Found: Cl, 10.96.

Methiodide (XIIa).—This was precipitated from an acetone solution of the base by addition of methyl iodide. It was recrystallized from absolute ethanol, in which it is but slightly soluble; yellow, m. p. 287–288°.

Anal. Calcd. for $C_{20}H_{22}INO$: I, 30.27. Found: I, 30.43.

3-Methoxy-11-methyl-5,6,8,9,10,11-hexahydronaphth-[2,1-g]isoquinoline (XIII).—The hydrochloride of XII was hydrogenated rapidly in absolute ethanol solution (platinum oxide). The hydrochloride was precipitated with ether from the filtered solution, and melted at 261–263° after recrystallization from an ethanol–ether mixture.

Anal. Calcd. for $C_{19}H_{22}ClNO$: Cl, 11.23. Found: Cl, 11.73.

Methiodide of 3-Methoxy-10,11-dimethyl-5,6,8,9,10,11-hexahydronaphth[2,1-g]isoquinoline (XIVa).—The base from 0.2 g. of the above hydrochloride was dissolved in 3 cc. of acetone, and 0.3 cc. of methyl iodide and 0.1 g. of powdered potassium hydroxide were added. After one hour the white methiodide was filtered, and washed free of alkali with cold water. It was recrystallized from absolute ethanol; m. p. 256–258°.

Anal. Calcd. for $C_{21}H_{26}INO$: I, 29.15. Found: I, 29.47.

3-Methoxy-10,11-dimethyl-5,6,8,9,10,11-hexahydronaphth[2,1-g]isoquinoline (XIV).—(a) The methiodide XIIa (m. p. 287–288°) absorbed one mole of hydrogen rapidly when catalytically reduced. After removal of the catalyst, the ethanol solution was concentrated, and a white **hydriodide** was precipitated by addition of ether. It was recrystallized from ethanol, and melted at 236–238°.

Anal. Calcd. for $C_{20}H_{24}INO$: I, 30.12. Found: I, 29.75.

The **base** was liberated with ammonium hydroxide and slowly distilled at about 100° in an oil-pump vacuum; m. p. 97–98°.

Anal. Calcd. for $C_{20}H_{23}NO$: C, 81.87; H, 7.90. Found: C, 81.70; H, 7.72.

The **hydrochloride** was prepared and purified in the usual way, and melted at 200–202°.

Anal. Calcd. for $C_{20}H_{24}ClNO$: C, 72.82; H, 7.33. Found: C, 72.71; H, 7.53.

Addition of methyl iodide to an acetone solution of the base precipitated the quaternary methiodide, XIVa, identical (melting point, mixture melting point) with that obtained by the action of methyl iodide and potassium hydroxide on 3-methoxy-11-methyl-5,6,8,9,10,11-hexahydronaphth[2,1-g]isoquinoline (XIII).

(b) Base XIV was also obtained by heating the methiodide XIVa to 250° in an oil-pump vacuum. It was identified by melting point and mixture melting point.

Summary

The synthesis of two new phenolic amino alcohols, 2-hydroxy-7-[2-(diethylamino)-1-hydroxyethyl]-9,10-dihydrophenanthrene and 2-hydroxy-7-[3-(diethylamino)-1-hydroxy-*n*-propyl]-9,10-dihydrophenanthrene, is described.

The synthesis of two isoquinoline derivatives of the 9,10-dihydrophenanthrene series, 10,11-dimethyl-5,6,8,9,10,11-hexahydronaphth[2,1-g]isoquinoline and 3-methoxy-10,11-dimethyl-5,6,8,-9,10,11-hexahydronaphth[2,1-g]isoquinoline (?), is described.

The starting materials, 9,10-dihydrophenanthrene-2-aldehyde and 2-methoxy-9,10-dihydrophenanthrene-7-aldehyde, were obtained by the Rosenmund method from the corresponding phenanthroic acid chlorides, while the intermediate products, 2-(2-aminoethyl)-9,10-dihydrophenanthrene and 2-methoxy-7-(2-aminoethyl)-9,10-dihydrophenanthrene, were prepared by the Curtius reaction from the corresponding β-dihydrophenanthrylpropionic acids.

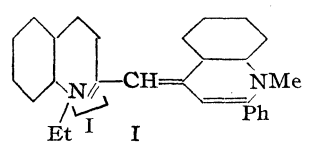
WASHINGTON, D. C. RECEIVED FEBRUARY 23, 1940

[JOINT CONTRIBUTION FROM THE KODAK RESEARCH LABORATORIES AND THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

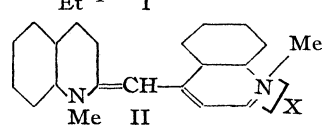
Color and Constitution. I. Halochromism of Anhydronium Bases Related to the Cyanine Dyes[1]

BY L. G. S. BROOKER, R. H. SPRAGUE, C. P. SMYTH AND G. L. LEWIS

In their work on the structure of the isocyanines, Kaufmann and Vonderwahl[2] brought forward evidence which they interpreted as indicating the static configuration I for 1-ethyl-1′-methyl-2′-phenyl-2,4′-cyanine iodide. They heated the dye in a high vacuum and obtained ethyl iodide and a base having the composition of a methylphenylquinolylidenequinaldine, and this was considered to prove that the iodine atom was attached to the nitrogen atom of the quinaldine nucleus.



I



II

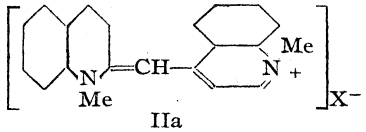
On the other hand, as a result of their experiments on the oxidation of 1,1′-dimethyl-2,4′-cyanine acetate, Mills and Wishart[3] felt that it was justifiable to accept II as the formula of this substance rather than the alternative structure in

(1) Communication No. 755 of the Kodak Research Laboratories. Presented in part before the Organic Section of the American Chemical Society at the September, 1937, meeting at Rochester, New York.

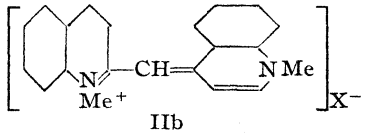
(2) Kaufmann and Vonderwahl, *Ber.*, **45**, 1407 (1912).

(3) Mills and Wishart, *J. Chem. Soc.*, **117**, 579 (1920).

which the nitrogen atom of the quinaldine nucleus is quaternary, but they recognized that the two forms might be virtually tautomeric. Since then, much evidence has been accumulated in favor of such tautomerism.[4] This conception has been amplified by the theory of resonance[5] according to which the molecule of a cyanine dye such as II is considered to be a resonance hybrid between two extreme states, the intense colors of the cyanines being attributed to such resonance. Thus, in the case of II, which is highly colored, we have the resonance scheme IIa ⟷ IIb.



IIa

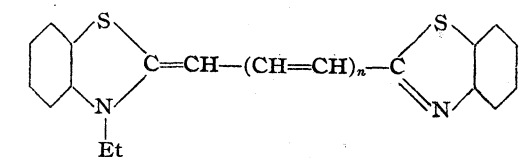


IIb

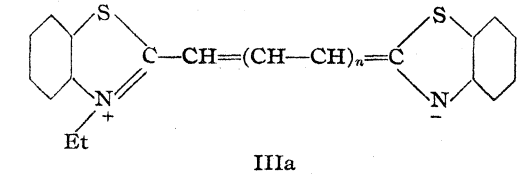
There can be no doubt that resonance of this type is very closely related to the occurrence of color in many organic compounds, and resonance structures have been assigned to practically all the principal dye types.[5] The subject has been particularly well worked out for dyes of the triphenylmethane series where it has been shown that so treating a dye that a possible mode of resonance is restricted results in the characteristic absorption of the dye being profoundly modified.[6]

In the present work, we have endeavored to throw further light on the nature of resonance in the cyanines by comparing the series of three symmetrical cyanines derived from benzothiazole (IV, n = 0, 1, 2) with the series of tertiary bases (III, n = 0, 1, 2) obtained from them by removal of the elements of ethyl halide by heating with diethylaniline according to the method of Schwarz.[7]

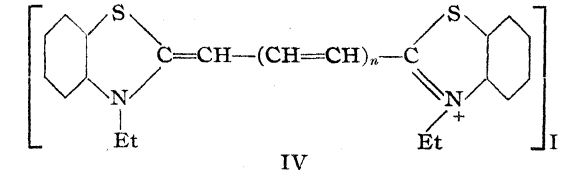
Of the three bases, that with the shortest chain (n = 0) was first prepared using another method by Mills,[8] who obtained it as a pale yellow



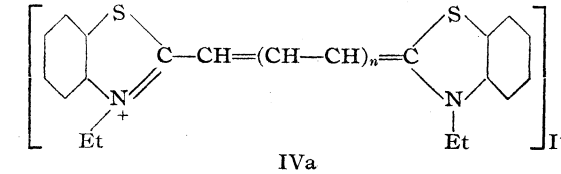
III



IIIa



IV



IVa

crystalline substance. Its methyl alcoholic solution has an extremely pale yellow color. The next higher vinylene homolog (n = 1) was made by Schwarz and Gevaert Photo-Producten, N. V.,[7] who describe it as slightly yellow colored and add that it absorbs only the short wave end of the visible spectrum without having a distinct maximum. We find, however, that its methyl alcoholic solution absorbs in the blue part of the spectrum and shows a well-defined maximum. The base with the longest chain (n = 2) has not hitherto been described. It forms lustrous reddish needles which dissolve in methyl alcohol to give a rather dull brownish-red solution.

In every case, a solution of one of these bases in methyl alcohol is markedly lighter in color than a solution of the cyanine with the same length of chain, the colors of the cyanines in solution being yellow (n = 0), bluish-red (n = 1) and blue (n = 2).

The absorptions of all six compounds in methyl alcohol are given in Fig. 1, and these curves reveal striking relationships. The positions of the absorption maxima are given in Table I, differences also being shown.

From Fig. 1 and Table I, it can be seen that in every case, a base (III) absorbs nearer the shorter waves than the cyanine with a chain of the same

(4) (a) Mills and Braunholtz, *J. Chem. Soc.*, **121**, 1489 (1922); (b) Hamer, *ibid.*, 206 (1928); (c) Kuhn, Winterstein and Balser, *Ber.*, **63**, 3176 (1930); (d) Ogata, *Proc. Imp. Acad. Tokyo*, **8**, 119 (1932); (e) Ogata, *Bull. Inst. Phys. and Chem. Research, Tokyo*, **13**, 549 (1934); (f) Brooker and Keyes, THIS JOURNAL, **57**, 2488 (1935).

(5) Bury, *ibid.*, **57**, 2115 (1935).

(6) Taylor and Baker, Sidgwick's "Organic Chemistry of Nitrogen," Oxford Univ. Press, New York, N. Y., 1937, p. 88.

(7) Schwarz and Gevaert Photo-Producten, N. V., United States Patent 2,169,434.

(8) Mills, *J. Chem. Soc.*, **121**, 455 (1922).

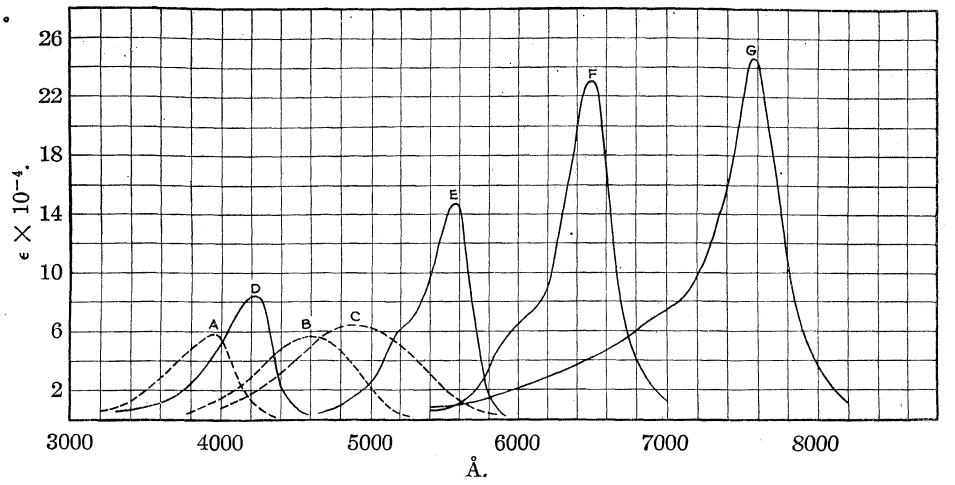


Fig. 1.—Absorption curves in methyl alcohol: A, B, C, = III, n = 0, 1, 2, respectively; D, E, F, G = IV, n = 0, 1, 2, 3, respectively.

TABLE I

Compound	Absorption max. Å.	Differences		Max. value of $\epsilon \times 10^{-4}$
III, n = 0	3960			5.85
III, n = 1	4580	> 620		5.65
III, n = 2	4900	> 320	270	6.4
IV, n = 0	4230		995	8.45
IV, n = 1	5575	> 1345	1600	14.8
IV, n = 2	6500	> 925		22.9
IV, n = 3	7580	> 1080		24.6

length. Furthermore, whereas it has been amply demonstrated that increasing the length of the polymethine chain joining the nuclei in a cyanine dye shifts the absorption toward the longer waves,[9] it can be seen that a similar relationship also holds in the series of tertiary bases. Here also lengthening the conjugated chain joining the nitrogen atoms shifts the absorption toward the red, but the amounts of the shifts are considerably smaller than with the cyanines. Whereas addition of a vinylene group to the cyanine IV, n = 0, produces a shift of 1345 Å., addition of vinylene to the base III, n = 0, produces a shift of only 620 Å., and addition of a further vinylene results in shifts of 925 and 320 Å. in the cyanine and base series, respectively. It follows that the difference in absorption between a cyanine and a base of the same chain length becomes greater with increasing length of the vinylene chain. There is only a difference of 270 Å. between base and cyanine in the series n = 0, this difference increasing to 995 Å. where n = 1 and to 1600 Å. where n = 2.

(9) *Cf.* in particular, (a) Fisher and Hamer, *Proc. Roy. Soc.* (London), **A154**, 703 (1936); (b) Beilenson, Fisher and Hamer, *ibid.*, **163**, 138 (1937).

In the cyanine series, the value of $\epsilon_{max.}$ increases continuously as the series is ascended, this being in agreement with the findings of Kuhn and Hausser[10] in series of polyene compounds that they examined. The difference between the values of $\epsilon_{max.}$ for IV, n = 1 and IV, n = 2 is, however, much greater than that between IV, n = 2 and IV, n = 3.

In the series of bases, the values of $\epsilon_{max.}$ are very close together, and the first member actually has a slightly higher value than the second, although the value for the third member is the highest of the three. However, these values are decidedly lower than those for the corresponding cyanines.

In the cyanine series, the two extreme resonance states IV and IVa are identical and have the same internal energy. The mobility of the linkages in the conjugated chain is therefore very great, and since there is a full ionic charge available for resonance, this reaches a high level of perfection. These conditions appear to give rise to absorption curves which rise, in the first few members, to a high value of $\epsilon_{max.}$, and which are widely separated with respect to wave length.

On the other hand, the bases III are not ionized structures, and no alternative formula for III can be written in which the sequence of single and double linkages of the conjugated chain between the nuclei is reversed and in which the nitrogen atoms are in the normal tri- or tetra-covalent states. However, there is a certain amount of probability for the alternative configuration IIIa.

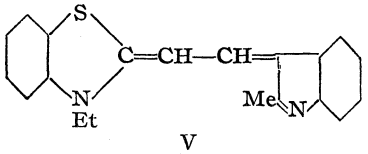
(10) Hausser, *Z. tech. Physik.* **15**, 10 (1934); note especially Fig. 20.

In particular, this gives an explanation of why addition of alkyl halide takes place solely at the right-hand benzothiazole nucleus. The negatively charged nitrogen atom is free to accept a proton or alkyl while the nitrogen of the left-hand nucleus will not do so because it is already quaternary. The resonance scheme III←→IIIa is, therefore, suggested for these bases which thus resemble the anhydronium bases of Robinson and coworkers.[11] Since III and IIIa are not identical, the actual state of the molecule will tend to approach the more stable of the two configurations, thereby becoming, in corresponding measure, less of a resonance hybrid. Resonance will therefore be more restricted in the bases than in the cyanines, and this accords with the observed lighter colors of the former.

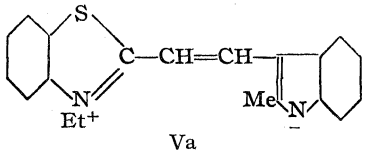
Of the two configurations III and IIIa, it seems probable that the former is the more stable, so that the actual state of the molecule will be closer to III than to IIIa. In the latter, the negatively charged nitrogen atom seems likely to be the least stable part (the quaternary nitrogen is a normal structure), and it would follow that if the negatively charged nitrogen could be rendered more stable, the whole configuration IIIa would become more stable. This would result in resonance being increased in the base which, in turn, would be accompanied by a deepening of color.

Now pyrroles and indoles with hydrogen attached to nitrogen will in general yield potassium derivatives and hence show a strong tendency to form negatively charged ions in which $>\overline{N}$ is stable.

We have accordingly prepared the base 3-[(3-ethyl-2(3)-benzothiazolylidene)-ethylidene]-2-methyl-indolenine (V) by condensing 2-methyl-3-indolealdehyde with 2-methylbenzothiazole ethiodide in acetic anhydride solution. This base dissolves in methyl alcohol to give a yellowish orange solution which is actually deeper in color

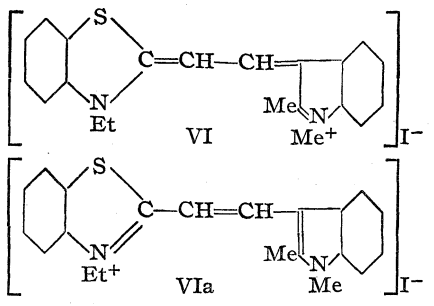


V



Va

(11) *Cf.* Freak and Robinson, *J. Chem. Soc.*, 2013 (1938).



than the solution of its methiodide VI made either by the addition of methyl iodide to V or by condensing 1,2-dimethyl-3-indolealdehyde with 2-methylbenzothiazole ethiodide. The absorption curves are shown in Fig. 2. The maximum

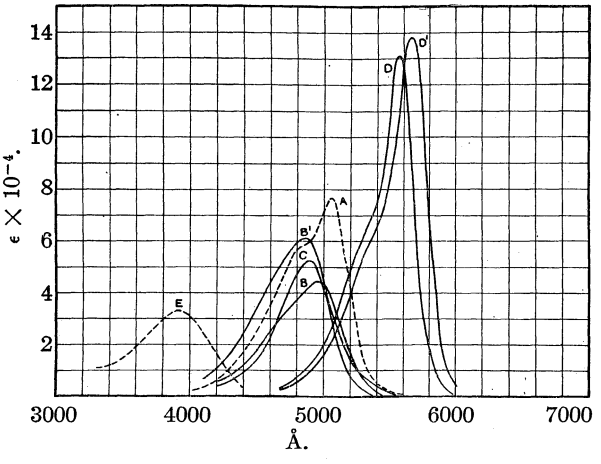


Fig. 2.—Absorption curves: A, 3-[(3-ethyl-2(3)-benzothiazolylidene)-ethylidene]-2-methyl-indolenine (V) in pyridine; B and B′, [3-ethyl-benzothiazole-(2)]-[1,2-dimethyl-indole-(3)]-di-methine-cyanine iodide (VI) in pyridine and nitromethane, respectively; C, bis-[1,2-dimethyl-indole-(3)]-methine-cyanine iodide (VIII) in nitromethane; D and D′, 3,3′-diethyl-thiacarbocyanine iodide in nitromethane and pyridine, respectively; E, 3-(β-2-benzothiazolyl-vinyl)-1,2-dimethyl-indole (IX) in pyridine.

absorption of V determined in pyridine is at 5060 Å., there being an inflection at shorter wave length and the maximum of VI in the same solvent is at 4970 Å. (Pyridine was chosen for the absorptions because in dilute methyl alcoholic solution there was a tendency on the part of V to develop a maximum at 4830 Å. corresponding to the acidified form. Addition of a few drops of piperidine deepened the color so that the maximum moved to 5070 Å., corresponding closely with the maximum developed in pyridine alone.)

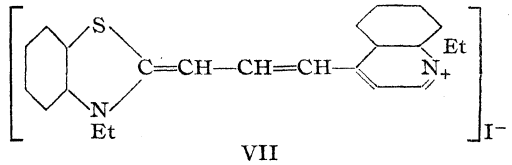
König[12] already has prepared several bases of the type of V, and he noted that they showed a "kind of reversed halochromism" in that they

(12) König, *J. prakt. Chem.*, [2] **85**, 514 (1912).

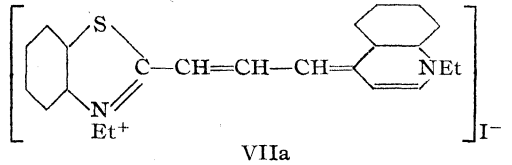
were deeper in color than their salts, but no explanation of this unusual state of affairs has so far appeared.

We now suggest that the known tendency of indole to yield an indolyl anion renders the configuration Va relatively more stable than the corresponding configuration IIIa and hence the actual state of the compound represented by the resonance scheme V ⟷ Va is closer to an intermediate position, *i. e.*, the base is more truly a resonance hybrid, than a base represented by III ⟷ IIIa. We consider, then, that V ⟷ Va represents a relatively high degree of resonance but, even so, it is remarkable that this base is deeper colored than its methiodide, in which a full ionic charge is available for resonance. The explanation of this apparent anomaly appears to lie in the fact that the methiodide VI, considered as an unsymmetrical cyanine, is exceptionally light in color.

Most of the unsymmetrical cyanines studied by Dr. Hamer and her colleagues[9b] have absorption maxima which agree fairly well with the calculated mean values of the related parent dyes, agreement being rather better in the carbocyanine than in the simple cyanine or dicarbocyanine series. This would seem to indicate that the internal energies of the two extreme resonance states of such unsymmetrical cyanines are very nearly the same. For example, the two extreme states in the case of 1′,3-diethylthia-4′-carbocyanine iodide (VII and VIIa) must have nearly



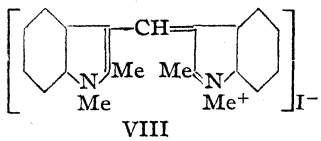
VII



VIIa

equal probability. This is understandable in view of the fact that although benzothiazole is considered to be somewhat less basic than quinoline, these bases are nevertheless comparable types, so that no very marked preference for the positive charge will be shown by either of the nitrogen atoms in dyes of this type, *i. e.*, VII will not be appreciably favored over VIIa or *vice versa*.

In the present case, the methiodide VI (or VIa) is a dimethine cyanine which may be considered as a cross between the two symmetrical dyes, *bis*-[1,2-dimethylindole-(3)]methine-cyanine iodide (VIII) and 3,3′-diethylthiacarbocyanine



VIII

iodide (IV, $n = 1$), but unlike the unsymmetrical cyanines hitherto described,[9b] the absorption of VI lies at markedly shorter wave length than the mean of the absorptions of the parent symmetrical dyes, and in fact, its absorption maximum in nitromethane actually lies at shorter wave length than that of the lighter of the parent dyes (VIII) (Fig. 2), and this constitutes the first recorded instance of an unsymmetrical cyanine absorbing in this way. (Nitromethane was chosen as solvent for the comparison because VIII was unstable in pyridine or in alcoholic solution.)

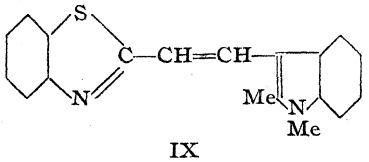
Since indoles are very weak bases and form salts with difficulty, it seems likely that of the two extreme resonance configurations VI and VIa, that in which the indole nitrogen is quaternary (VI) will be appreciably less stable than that in which the positive charge is associated with the more strongly basic benzothiazole nitrogen (VIa). Thus the actual state of the compound will tend to approach VIa in the resonance scheme VI ⟷ VIa with consequent diminution of resonance which will cause the color to be lightened.

The "reversed halochromism" of V may be attributed, therefore, to a combination of two related factors. The first is that the base is deeply colored because it resonates strongly according to the scheme V ⟷ Va, this being traceable to the stability of $\rangle\overset{+}{N}$ in the indole ring in Va. The second is that the methiodide is unusually light in color because in it resonance is inhibited due to the relative instability of one of the resonance configurations (VI) traceable in turn to the weak basicity of the indole nitrogen. The net result is that the base is more deeply colored than its methiodide.

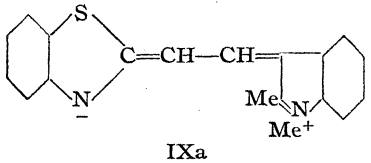
Since in some cases salt formation causes deepening of color and in others lightening of color, it is clear that it is theoretically possible for salt formation to bring about no color change at all. Actually, those instances appear to be more numerous in which a deepening of color occurs, and the term halochromism usually im-

plies this, but a lightening of color is no less significant from a theoretical standpoint.

That the mere presence of an indole nucleus in an anhydronium base does not give rise to unusually deep colors may be deduced from the following consideration. The base 3-(β-2-benzothiazolyl-vinyl)-1,2-dimethylindole (IX) was prepared by condensing 1,2-dimethyl-3-indolealdehyde with 2-methylbenzothiazole in the presence of hydrochloric acid and basifying the product.



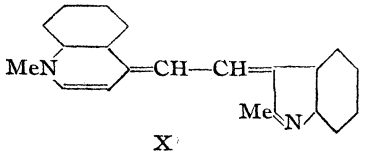
IX



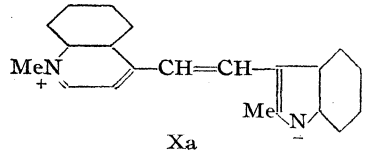
IXa

The second extreme resonance configuration of this substance, IXa, contains a negatively charged benzothiazole nitrogen which we have suggested is not as stable as the corresponding negatively charged nitrogen in Va, and also a quaternary indole nitrogen which we have argued above is also unstable. It will be concluded, therefore, that IXa is an especially unstable configuration and consequently the base will tend strongly to approach IX with corresponding loss of its resonance-hybrid character, and this will result in its having a relatively light color. This argument is supported by the facts, for IX is almost colorless in solution, its absorption maximum in pyridine being at 3920 Å. (Fig. 2, Curve E). Its structure was confirmed by the fact that it gave VI (or VIa) on treatment with ethyl iodide.

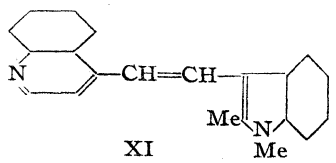
In a further set of comparisons, two isomeric bases were compared, 2-methyl-3-[(1-methyl-4(1)-quinolylidene)-ethylidene]-indolenine (X) and 1,2-dimethyl-3-(β-4-quinolyl-vinyl)-indole (XI).



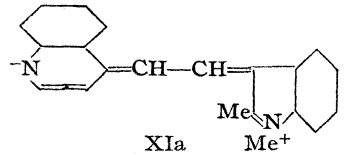
X



Xa



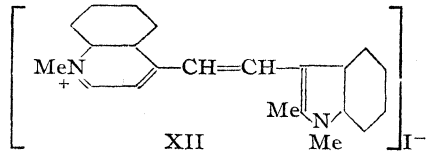
XI



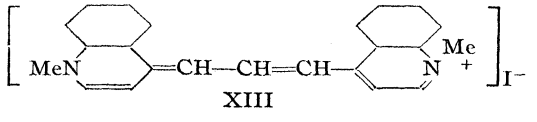
XIa

The first of these was prepared by condensing lepidine methiodide with 2-methyl-3-indolealdehyde in acetic anhydride solution and basifying the product, and the second by condensing lepidine with 1,2-dimethyl-3-indolealdehyde in the presence of hydrochloric acid and basifying the product. Of these bases, X is much the deeper colored of the two, its bluish purple pyridine solution having two absorption maxima of comparable strength at 5710 and 6160 Å., the former being somewhat the stronger (Fig. 3, A). On the other hand, XI gives only a pale yellow solution in pyridine which absorbs very weakly indeed with its maximum at 3940 Å. (Fig. 3, B), and these results can be correlated with the probability of much greater resonance mobility in X ⟷ Xa than in XI ⟷ XIa for precisely similar reasons to those advanced in the case of V and IX, respectively.

Both X and XI add methyl iodide readily to give the same methiodide XII, and this has $\lambda_{max.}$ at 5390 Å. in pyridine (Fig. 3, C) so that it is lighter in color than X but much deeper in color than XI. In this case XII may be regarded as



XII



XIII

the cross between the two symmetrical dyes VIII and 1,1′-dimethyl-4,4′-carbocyanine iodide XIII, and once again XII absorbs at markedly shorter wave length than the mean of the wave lengths of maximum absorption of these two,[13] for, it

(13) For this comparison, it was hoped to obtain the absorptions of all three substances in the same solvent. Curves D and C′ (Fig. 3) are those of VIII and XII in nitromethane but dilute solutions of XIII in this solvent proved to be extremely unstable, and

is suggested, a reason similar to that advanced in the case of VI.

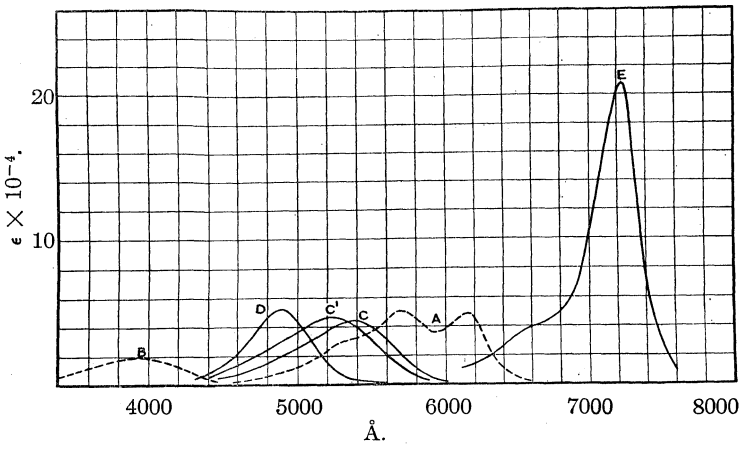


Fig. 3.—Absorption curves: A, 2-methyl-3-[(1-methyl-4(1)-quinolyl-idene)-ethylidene]-indolenine (X) in pyridine; B, 1,2-dimethyl-3-(β-4-quinolyl-vinyl)-indole (XI) in pyridine; C, [1,2-dimethylindole-(3)]-[1-methylquinoline-(4)]-dimethinecyanine iodide (XII) in pyridine, C′ in nitromethane; D, bis-[1,2-dimethylindole-(3)]-methinecyanine iodide (VIII) in nitromethane; E, 1,1′-dimethyl-4,4′-carbocyanine iodide (XIII) in pyridine.

Independent confirmation of the theories developed here to account for the colors of the anhydronium bases III (n = 1), V, IX, X and XI has been provided by a study of their dipole moments. If the suggested dipolar configurations were significant in defining the structures of these bases, then the dipole moments would be expected to be much higher than those calculated from the classical formulas. Further, since it has been argued that the dipolar configurations Va and Xa play more important parts in the resonance schemes V ⟷ Va and X ⟷ Xa than IXa and XIa do in the schemes IX ⟷ IXa and XI ⟷ XIa, it should follow that the dipole moments of the first pair of bases should be markedly higher than those of the latter. These expectations have been fully realized. Not only were the dipole moments of the bases in all cases markedly higher than those calculated from the classical formulas, but those of the deeply colored bases V ⟷ Va and X ⟷ Xa were much higher than those of the corresponding lighter colored bases IX ⟷ IXa and XI ⟷ XIa.

Curve E was determined in pyridine. In the three cases in this paper where absorptions have been determined in the two solvents (Fig. 2, B and B′, D and D′; Fig. 3, C and C′) nitromethane gives somewhat the lower value for $\lambda_{max.}$, so that by analogy, $\lambda_{max.}$ of XIII in nitromethane should lie at shorter wave length than that in pyridine. Even if an allowance of as much as 200 Å. is made for this effect, XII still absorbs at much shorter wave length than the mean of the absorptions of VIII and XIII. The value of $\lambda_{max.}$ for curve C′ (Fig. 3) is 5240 Å., and for E it is 7230 Å.

The dielectric constants of very dilute solutions of the bases in benzene were measured at a frequency of 520 kilocycles and a temperature of 25° with a heterodyne beat apparatus described elsewhere[14] and have been used, together with the densities measured with an Ostwald–Sprengel pycnometer, to calculate the dipole moments by the usual method.[15]

In Table II there are given the mole fraction c_2 of each substance in benzene solution, the dielectric constant D and density d of the solution, and the polarization P_2 of the substance calculated from these data. As the color of several of the solutions made impossible an accurate determination of refractive index, the molar refractions, MR_D, were calculated as the sums of the atomic refractions with due regard to constitutive influences. The uncertainties in these calculated values of MR_D given in the first column of Table II are small in comparison with the errors in the values of the polarization at infinite dilution, P_∞, obtained by extrapolation of the P_2 values. The probable errors in these P_∞ values are unusually large as the result of the high dilutions at which the measurements had to be made because of the low solubilities of the substances. The resulting experimental values of the moments given in the eighth column of Table II have probable errors of about 1% except in the case of X(Xa), where it is 5%.

The last column of Table II gives the values of the dipole moments μ calcd. which the molecules should have in the absence of resonance contributions from ionic structures other than those normally found in the bonds involved. These moment values are necessarily extremely approximate, having a probable error 0.5×10^{-18}. They are calculated[16] from bond moments and from the moments of groups obtained from molecular moments in the literature, rotation around single bonds being taken into account as far as possible.[17] Uncertainty as to rotation or orientation of large groups around single bonds and, in some cases, the question of *cis* or *trans*

(14) Lewis and Smyth, *J. Chem. Phys.*, **7**, 1085 (1939).
(15) Lewis and Smyth, THIS JOURNAL, **61**, 3063 (1939).
(16) Smyth, *J. Phys. Chem.*, **41**, 209 (1937); THIS JOURNAL, **60**, 183 (1938).
(17) See Smyth and Walls, *ibid.*, **54**, 2261 (1932).

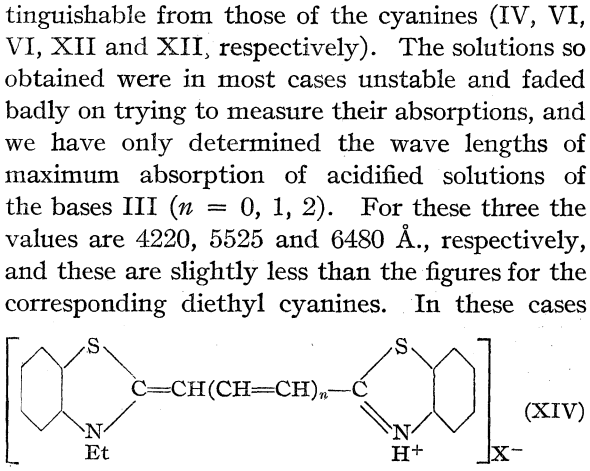
TABLE II

MOLE FRACTIONS (C_2), DIELECTRIC CONSTANTS (D), DENSITIES OF SOLUTIONS IN BENZENE (d), POLARIZATIONS AT 25° (P_2), MOLAR REFRACTIONS (MR_D), POLARIZATIONS AT 25° (P_∞), OBSERVED MOMENT (μ) AND CALCULATED MOMENT (μ CALCD.)

Compound	C_2	D	d	P_2	MR_D	P_∞ (25°)	μ(× 10^{18})	μcalcd. (× 10^{18})
III ⟷ IIIa	0.000000	2.2760	0.87334	(P_1 = 26.668)				
(n = 1)	.001617	2.3258	.87531	521				
	.004340	2.4115	.87872	500	103	525	4.51	1.6
	.005760	2.4526	.88046	511				
	.007401	2.5010	.88230	506				
V ⟷ Va	.000000	2.2760	.87334	(P_1 = 26.668)				
	.000710	2.3364	.87405	1304				
	.001299	2.3860	.87473	1285	100	1350	7.68	2.2
	.001581	2.4097	.87515	1280				
IX ⟷ IXa	.00000	2.2751	.87275	(P_1 = 26.672)				
	.00169	2.3154	.87429	424				
	.00322	2.3513	.87581	422	94	434	4.06	2.2
	.00488	2.3889	.87754	416				
	.00673	2.4332	.87971	408				
X ⟷ Xa	.000000	2.2760	.87334	(P_1 = 26.668)				
	.000076	2.2875	.87337	2303	96	2450	10.6	2.5
	.000144	2.2958	.87345	2090				
XI ⟷ XIa	.000000	2.2751	.87275	(P_1 = 26.672)				
	.001557	2.3390	.87418	670				
	.002623	2.3773	.87503	637	93	705	5.43	2.5
	.003546	2.4083	.87569	615				

configurations contribute to the uncertainty of these calculated values. Moments calculated for dipolar structures are subject to far greater errors because of these uncertainties. The values estimated for these structures lie, for the most part, between 20 and 30 × 10^{-18}. As it seems probable that values thus calculated for such dipolar structures without knowledge of the reduction of the moments by induced shifts of charge are much too high,[16] they are omitted from Table II as misleading.

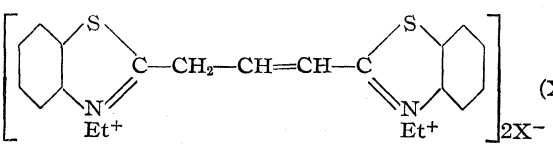
Addition of mineral acid to dilute alcoholic solutions of the anhydronium bases (III, V, IX, X and XI) gave colors which were visually indistinguishable from those of the cyanines (IV, VI, VI, XII and XII, respectively). The solutions so obtained were in most cases unstable and faded badly on trying to measure their absorptions, and we have only determined the wave lengths of maximum absorption of acidified solutions of the bases III (n = 0, 1, 2). For these three the values are 4220, 5525 and 6480 Å., respectively, and these are slightly less than the figures for the corresponding diethyl cyanines. In these cases



(XIV)

addition of a proton gives XIV and this can resonate in similar fashion to that postulated for IV.

Addition of excess of mineral acid to solutions of the cyanines or of the bases discharges the color completely, indicating destruction of the conjugated system as suggested in XV.



(XV)

Acknowledgment.—We wish to thank Mr. E. E. Richardson and Dr. L. A. Jones for the absorptions and Dr. L. T. Hallett for the analyses.

Experimental

2 - [(3 - Ethyl - 2(3) - benzothiazolylidene) - methylene] - benzothiazole (III, n = 0).—3,3'-Diethylthiacyanine iodide[18] (1.3 g.) was heated to refluxing with diethylaniline (100 cc.) for two hours. The mixture was then steam distilled and the residue extracted with 500 cc. methyl alcohol and the extract concentrated to 40 cc. The base separated and was purified by two recrystallizations from methyl alcohol (charcoal) (145 cc. per g.); yield 46%, m. p. 163–164° with darkening.

2 - [3 - (3 - Ethyl - 2(3) - benzothiazolylidene) - propenyl] - benzothiazole (III, n = 1).—3,3'-Diethylthiacarbocyanine iodide[19] (30 g.) was heated under dry carbon dioxide with diethylaniline (600 cc.) for two hours with mechanical

(18) Fisher and Hamer, *J. Chem. Soc.*, 2502 (1930).
(19) Hamer, *ibid.*, 2796 (1927).

stirring, some of the solvent being slowly distilled off. After concentration *in vacuo* as far as possible 300 cc. of ether was added and the base separated on chilling, and was purified by recrystallization from absolute ethyl alcohol (30 cc. per g.); yield 65%. The base formed reddish-brown crystals with double green and blue reflex; m. p. 138–140° with some decomposition.

Anal. Calcd. for $C_{19}H_{16}N_2S_2$: C, 67.79; H, 4.80. Found: C, 67.62; H, 5.09.

2 - [5 - (3 - Ethyl - 2(3) - benzothiazolylidene) - 1,3-pentadienyl]-benzothiazole (III, $n = 2$).—3,3'-Diethylthiadicarbocyanine iodide[9a] (10 g.) was heated under dry carbon dioxide with diethylaniline (500 cc.) for one hour with mechanical stirring, some of the solvent (200 cc.) being slowly distilled off during the reaction. After filtration to remove a small residue of unchanged cyanine the liquid was concentrated *in vacuo* to 25 cc. The oily residue so obtained was extracted with 50 cc. hot methyl alcohol and separated as an oil from the extract on chilling. Crystals were obtained on stirring with cold acetone (15 cc.) and were purified by recrystallization from this solvent (50 cc. per g.); yield 4%; m. p. 161–162° with some decomposition.

Anal. Calcd. for $C_{21}H_{18}N_2S_2$: C, 69.55; H, 5.01. Found: C, 69.46; H, 5.15.

3 - [(3 - Ethyl - 2(3) - benzothiazolylidene) - ethylidene]-2-methyl-indolenine (V).—The hydriodide of this base was prepared by condensing 2-methylbenzothiazole ethiodide (5.75 g.; 1 mol) with 2-methyl-3-indolealdehyde (3 g., 1 mol) in acetic anhydride (30 cc.), refluxing for two minutes; yield 93%. After two recrystallizations from methyl alcohol (190 cc. per g.) the dye formed minute reddish-brown needles with a blue reflex and had m. p. 283–284°, dec.

Anal. Calcd. for $C_{20}H_{19}IN_2S$: I, 28.45. Found: I, 28.31.

The hydriodide (2 g., 1 mol) was stirred mechanically with a mixture of 50 cc. of 20% aqueous sodium hydroxide and 75 cc. of acetone at room temperature for one-half hour. The hydriodide slowly dissolved and crystals of the base separated. The aqueous layer was drawn off and more base was obtained by concentrating the acetone layer; yield 91%. After recrystallization from acetone (50 cc. per g.) the base formed beautiful reddish-brown prisms with a bright green reflex and had m. p. 286–288° dec.

Anal. Calcd. for $C_{20}H_{18}N_2S$: C, 75.43; H, 5.70. Found: C, 75.08; H, 5.84.

[3 - Ethyl - benzothiazole - (2)] - [1,2 - dimethyl - indole-(3)]-dimethine-cyanine Iodide (VI).—**(a).** 2-Methylbenzothiazole etho-*p*-toluenesulfonate[20] (3.5 g., 1 mol) and 1,2-dimethyl-3-indolealdehyde (1.73 g., 1 mol) were refluxed for five minutes in acetic anhydride (15 cc.). Dye separated on chilling; yield 91%. This was converted directly into the iodide using sodium iodide; yield 95% for the conversion. The dye separated in scarlet prisms from methyl alcohol (310 cc. per g.); m. p. 269–271°, dec.

Anal. Calcd. for $C_{21}H_{21}IN_2S$: I, 27.57. Found: I, 27.52.

(b) The dye was obtained in theoretical yield when the base V (1.6 g., 1 mol) was heated under reflux with methyl iodide (2.8 g., 4 mols) in nitrobenzene (25 cc.) for four hours. The base first dissolved and then the iodide separated rapidly, crystallization being subsequently promoted by adding ether. After recrystallization analysis gave I, 27.37.

(c) When the base IX (0.5 g., 1 mol) was refluxed with ethyl iodide (1.6 g., 6 mols) for six hours, the iodide separated slowly; yield 39%. After recrystallization analysis gave I, 27.34.

The identity of specimens obtained in a, b and c was established by m. p. and mixed m. p. determinations. The absorptions were also identical.

3-(β-2-Benzothiazolyl-vinyl)-1,2-dimethylindole (IX).—2-Methylbenzothiazole (3 g., 2 mols), 1,2-dimethyl-3-indolealdehyde (1.73 g., 1 mol) and concd. hydrochloric acid (2.3 g., 2 mols) were heated together at 100° for sixteen hours. The solid mass was dissolved in hot methyl alcohol (100 cc.), basified with triethylamine, chilled and the product filtered off; yield 50%. After recrystallization from methyl alcohol (46 cc. per g.) the canary yellow crystals had m. p. 150–151° with slight decomposition.

Anal. Calcd. for $C_{19}H_{16}N_2S$: C, 74.94; H, 5.30. Found: C, 74.68; H, 5.37.

bis-[1,2-Dimethylindole-(3)]-methine-cyanine Iodide (VIII).—1,2-Dimethylindole (2.9 g., 1 mol) and 1,2-dimethyl-3-indolealdehyde (3.46 g., 1 mol) were fused together and concentrated hydrochloric acid (2 cc., 1 mol) added. Much heat was generated and the mixture was stirred without further heating for five minutes. The product was dissolved in ethyl alcohol (15 cc.) and precipitated by adding excess of aqueous sodium iodide (6 g.). The dye was washed (water then ether) and was recrystallized from methyl alcohol (30 cc. per g.); yield 35%. The brown crystals had m. p. 221–222°, dec.

Anal. Calcd. for $C_{21}H_{21}IN_2$: I, 29.65. Found: I, 29.62.

2 - Methyl - 3 - [(1 - methyl - 4(1) - quinolylidene) - ethylidene]-indolenine (X).—The hydriodide of this base was prepared by condensing lepidine methiodide (14.3 g., 1 mol) with 2-methyl-3-indolealdehyde (8 g., 1 mol) by refluxing in acetic anhydride (50 cc.) for three minutes. Dye separated from the hot solution; yield 72%. After recrystallization from methyl alcohol (600 cc. per g.) the dye formed brownish coppery crystals with m. p. 319–320°, dec.

Anal. Calcd. for $C_{21}H_{19}IN_2$: I, 29.79. Found: I, 29.60.

The hydriodide was basified in similar fashion to V; yield quantitative. The base separated from acetone (330 cc. per g.) as dark blue needles m. p. 249–251° dec.

Anal. Calcd. for $C_{21}H_{18}N_2$: C, 84.50; H, 6.08; N, 9.40. Found: C, 83.91; H, 6.35; N, 9.21.

König[12] gives m. p. 240°. His analysis is that of $C_{21}H_{18}N_2 \cdot 2CHCl_3$.

1,2-Dimethyl-3-(β-4-quinolyl-vinyl)-indole (XI).—An excess of lepidine (3 g., 2 mols) was heated with 1,2-dimethyl-3-indolealdehyde (1.73 g., 1 mol) and concentrated hydrochloric acid (1.1 g., 1 mol) at 100° for sixteen hours. The hydrochloride of the base which resulted was purified by recrystallization from methyl alcohol (120 cc. per g.); yield 2 g. of red needles, and was suspended in cold methyl alcohol and basified by the addition of triethylamine. A

(20) Brooker and White, THIS JOURNAL, **57**, 550 (1935).

yellow solid separated and was recrystallized from methyl alcohol (160 cc. per g.); yield 43%. The yellow needles had m. p. 192–193° slight dec.

Anal. Calcd. for $C_{21}H_{18}N_2$: C, 84.50; H, 6.08; N, 9.40. Found: C, 83.84; H, 6.10; N, 9.29.

[1,2 - Dimethylindole - (3)] - [1 - methylquinoline-(4)]-dimethine-cyanine Iodide (XII).—(a) Lepidine methiodide (1.43 g., 1 mol) was condensed with 1,2-dimethyl-3-indolealdehyde (0.86 g., 1 mol) by refluxing in acetic anhydride (15 cc.) for three minutes. Dye separated from the hot mixture; yield 68%. After recrystallization from methyl alcohol (230 cc. per g.) the dye formed dull brownish crystals with m. p. 297–298° dec.; yield 59%.

Anal. Calcd. for $C_{22}H_{21}IN_2$: I, 28.83. Found: I, 28.82.

(b) The dye was obtained when the base X (0.5 g., 1 mol) was heated on a steam-bath to refluxing with methyl iodide (2 g., 8 mols) in nitrobenzene (10 cc.) for two hours; yield 88%. Found: I, 28.88 after recrystallization.

(c) XII was similarly obtained from XI; yield 81%. Found: I, 28.95 after recrystallization. The identity of the specimens from a, b and c was established by m. p. and mixed m. p. determinations and by absorptions.

Summary

A number of cyanine dyes have been compared with respect to absorption with the bases derived from them by removal of the elements of alkyl halide. In most cases the bases are lighter in color than the corresponding cyanines, but this is not invariably the case. These facts may be explained on the basis of the resonance theory. Certain of the arguments used have been confirmed by dipole moment determinations.

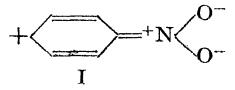
ROCHESTER, N. Y.
PRINCETON, N. J. RECEIVED FEBRUARY 15, 1940

[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY OF THE UNIVERSITY OF CHICAGO]

The Steric Inhibition of Resonance in Aromatic Nitro Compounds[1]

BY G. W. WHELAND AND A. A. DANISH[1a]

From a study of dipole moments, Birtles and Hampson have concluded[1b] that, in the aromatic nitro compounds, the resonance with quinoid structures of the type I[2] is sterically inhibited



I

when the nitro group lies between methyl groups in the two ortho positions. The work described in the present paper was undertaken in order to obtain chemical evidence bearing upon this hypothesis.[3]

The particular problem investigated was that presented by the striking effect of para nitro groups upon the acid strengths of the phenylmethanes. While triphenylmethane has been assigned[4] a pK value greater than 33, its trinitro derivative, 4,4′,4″-trinitrotriphenylmethane (hereafter called simply trinitrotriphenylmethane) is sufficiently acidic for its salts to be stable in aqueous alcohol.[5] It seems probable that resonance of the sort considered is at any rate partially responsible for this greater acidity of the trinitro derivative, since the quinoid structures increase the positive electrostatic potential at the position of the ionizable hydrogen atom, and since, moreover, the negative ion can be stabilized by resonance with these quinoid structures to a greater extent than the undissociated molecule.

If the above reasoning is correct, and if the contention of Birtles and Hampson is justified, it follows that 3,3′,3″,5,5′,5″-hexamethyl-4,4′,4″-trinitrotriphenylmethane (hereafter called simply trinitrotrixylylmethane) should be appreciably less acidic than trinitrotriphenylmethane. The former compound was, accordingly, prepared, and its acid strength was investigated in a manner analogous to that employed by Conant and Wheland[6] and by McEwen.[4] The sodium salts of both trinitrotriphenylmethane and trinitrotrixylylmethane are characterized by intense purple colors, and, consequently, the position of the equilibrium between either methane and its salt can be estimated colorimetrically. Since

(1) Abstract of a thesis presented by A. A. Danish to the faculty of the Division of the Physical Sciences of the University of Chicago in partial fulfilment of the requirements for the degree of Master of Science, December, 1938.

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(1b) R. H. Birtles and G. C. Hampson, *J. Chem. Soc.*, 10 (1937), see also C. E. Ingham and G. C. Hampson, *ibid.*, 981 (1939).

(2) L. E. Sutton, *Proc. Roy. Soc.* (London), **A133**, 668 (1931); *Trans. Faraday Soc.*, **30**, 789 (1934).

(3) Since the present research was started, several papers have appeared dealing with the steric inhibition of resonance from the chemical point of view. These have provided strong support for the existence of such an effect in various types of compounds, but apparently little work of this sort has been done with nitro compounds. See for example, W. G. Brown, A. H. Widiger and N. J. Letang, THIS JOURNAL, **61**, 2597 (1939); G. Baddeley, *Nature*, **144**, 444 (1939).

(4) W. K. McEwen, THIS JOURNAL, **58**, 1124 (1936).

(5) V. v. Richter, *Ber.*, **21**, 2475 (1888).

(6) J. B. Conant and G. W. Wheland, THIS JOURNAL, **54**, 1212 (1932).

only qualitative results were desired, no attempt was made to put the experiments upon a quantitative basis or to determine the values of the dissociation constants. It was considered sufficient to establish the relative stabilities of the two salts in a series of weakly acidic solvents.

The results of the experiments can be summarized as follows. The sodium salt of trinitrotrixylylmethane is stable in acetophenone and aniline, and in cyclohexylamine containing up to about 15% of methyl alcohol or 30% of ethyl alcohol; it is solvolyzed completely in methyl alcohol, ethyl alcohol and water–dioxane mixtures. The sodium salt of trinitrotriphenylmethane, on the other hand, is stable in all of the solvents named but is decomposed by phenol. Thus, it is evident that trinitrotrixylylmethane is a weaker acid than trinitrotriphenylmethane by several pK units. This conclusion is consistent with, and lends support to, the theory of Birtles and Hampson. However, since the observed difference in acidity is apparently not very great, the evidence is insufficient to establish the theory beyond question.[7] The problem is being investigated further.

Experimental. I

All melting points given below are uncorrected.

3,3′,3″,5,5′,5″-Hexamethyl Triphenylmethyl Chloride.—*sym*-Bromoxylene[8] was transformed into the Grignard reagent and treated with ethyl chlorocarbonate in the usual way. The resulting trixylylcarbinol was not purified but was transformed directly into the corresponding trixylylmethyl chloride by the action of dry hydrogen chloride in absolute ether.[9] The yield of crude chloride was 46%, based upon the amount of bromoxylene used. A small portion, after crystallization from high-boiling ligroin saturated with dry hydrogen chloride, formed colorless needles melting at 210°.

Anal. Calcd. for $C_{25}H_{27}Cl$: Cl, 9.77. Found: Cl, 9.83.

3, 3′, 3″, 5, 5′, 5″ - Hexamethyltriphenylmethane.—The crude trixylylmethyl chloride was reduced[10] with zinc dust in acetic acid solution under an atmosphere of carbon dioxide, and the resulting trixylylmethane was purified by crystallization from alcohol and water. The yield was 72% of the theoretical, based upon the amount of crude chloride used. The pure methane was colorless and melted at 108°.

Anal. Calcd. for $C_{25}H_{28}$: C, 91.41; H, 8.59; mol. wt., 328.2. Found: C, 91.52; H, 8.43; mol. wt. (camphor), 310.

3,3′,3″,5,5′,5″ - Hexamethyl - 4,4′,4″ - trinitro - triphenylmethane.[11]—The trixylylmethane prepared as above was nitrated with fuming nitric acid in a mixture of acetic acid and acetic anhydride in accordance with the method given by Powell and Johnson[12] for the nitration of mesitylene. After the completion of the reaction, the mixture was poured into an excess of ice water. The product, which then precipitated, was separated from the aqueous solution and washed free of acid. After one crystallization from glacial acetic acid and two from alcohol, the trinitrotrixylylmethane melted at 247°. The yield was only 16% of the theoretical. An attempt to obtain further material by adding water to the mother liquor from the original crystallization provided only a reddish oil, which changed to a resinous solid after a few hours of standing, and the composition of which could not be determined.

Anal. Calcd. for $C_{25}H_{25}N_3O_6$: N, 9.07; mol. wt., 463. Found: N, 9.06; mol. wt. (camphor), 465.

3,3′,3″,5,5′,5″ - Hexamethyl - 4,4′,4″ - triaminotriphenylmethane by Reduction of the Nitro Compound.—The trinitrotrixylylmethane was reduced with zinc dust in boiling glacial acetic acid.[13] The product, obtained in 64% yield after crystallization from dioxane and water, had no definite melting point. It darkened at 190° and decomposed completely at 275–280°.

Anal. Calcd. for $C_{25}H_{31}N_3$: N, 11.25. Found: N, 11.11.

3,3′,3″,5,5′,5″ - Hexamethyl - 4,4′,4″ - triaminotriphenylmethane by the Method of Giacalone.[14]—This preparation, which was undertaken in order to obtain material for comparison with that prepared as above, proceeded in two steps. First, 2,2′,2″,6,6′,6″-hexamethyltrianilidomethane was made by condensation of 2-amino-*m*-xylene with ethyl orthoformate, and then this was rearranged to the triaminotrixylylmethane. The reactions went much less readily than those reported by Giacalone, and more vigorous conditions were necessary.

(a) Forty-five grams of the xylidine and 30 g. of the ortho ester were refluxed together for twenty-four hours. From the resulting mixture, there was obtained 7 g. of the trianilido compound, melting at 179° (from benzene).

Anal. Calcd. for $C_{25}H_{31}N_3$: N, 11.25. Found: N, 11.26.

(b) One and one-half grams of the above trianilido compound, 3 g. of 2-amino-*m*-xylene, and 3 g. of 2-amino-*m*-xylene hydrochloride were heated together in an oil-bath at 170–175° for forty-eight hours and then at 140° for an additional fifty-three hours. The resulting mixture was steam distilled until no more volatile matter came over. From the residue in the flask was obtained 0.052 g. of the triaminotrixylylmethane. No unreacted starting material could be recovered, since extensive decomposition had occurred. In two preliminary runs, in which the heating was continued for only twenty-five and forty-two hours, respectively, the starting materials were recovered

(7) The correction for the direct inductive effect of the methyl groups is probably not significant, because the effect of the analogously situated methyl group in *m*-cresol upon the acidity of the substance appears to be quite small; *cf.* D. R. Boyd, *J. Chem. Soc.*, **107**, 1538 (1915).

(8) E. Fischer and A. Windaus, *Ber.*, **33**, 1967 (1900).

(9) M. Gomberg, *ibid.*, **35**, 2401 (1902).

(10) M. Gomberg, *ibid.*, **36**, 383 (1903).

(11) The proof that the three nitro groups occupy the 4,4′,4″ positions is given later.

(12) W. W. Hartman, "Organic Syntheses," Vol. XIV, John Wiley and Sons, Inc., N. Y., 1934, p. 68.

(13) J. B. Shoesmith, C. E. Sosson and A. C. Hetherington, *J. Chem. Soc.*, 2221 (1927).

(14) A. Giacalone, *Gazz. chim. ital.*, **62**, 577 (1932).

unchanged, but no rearrangement product was obtained. The triaminotrixylylmethane, after crystallization from dioxane, darkened at 190° and decomposed completely at 275–280°.

Anal. Calcd. for $C_{25}H_{31}N_3$: N, 11.25. Found: N, 11.04.

Comparison of the Samples of 3,3′,3″,5,5′,5″-Hexamethyl-4,4′,4″-triaminotriphenylmethane from the Two Sources.—The two samples of triaminotrixylylmethane, prepared, respectively, by the reduction of the corresponding trinitro compound and by the method of Giacalone, exhibited the same behavior on melting, as did also a mixture of the two. This evidence of their identity was not conclusive, however, since the substances had merely decomposition points and not true melting points. A crystallographic comparison was accordingly made,[15] and this showed the two to be identical.

The fact that the same substance was obtained by the two methods establishes its structure; the preparation from the trinitro compound shows that it is a derivative of 3,3′,3″,5,5′,5″-hexamethyltriphenylmethane, and the preparation from 2-amino-*m*-xylene shows that each amino group lies between two methyl groups in one of the benzene rings. Thus, the substance can only be 3,3′,3″,5,5′-5″-hexamethyltriphenylmethane. The proof of the structure of the corresponding trinitro compound now follows at once.

II

The solvents used in the following tests were purified as stated.

Water: distilled water was used.

Methyl and ethyl alcohols: the commercial absolute alcohols were distilled over magnesium methoxide and ethoxide, respectively.

Acetophenone, aniline, cyclohexylamine, and dioxane: the Eastman Kodak Co. products were distilled and fractions boiling over a 1° range were retained. The dioxane was kept over sodium.

Some difficulty was encountered at the outset in devising an experimental procedure for the comparison of acid strengths, and many of the preliminary results were neither reproducible nor consistent. The procedures described below, however, were entirely satisfactory. All the tests were made as rapidly as possible, since the colors were discharged in a few minutes as a result of oxidation by the air.

Water as Solvent.—To approximately 1 mg. of trinitrotriphenylmethane dissolved in 1/4 g. of dioxane was added slowly 10 cc. of a 1 *N* solution of sodium hydroxide in water. The intense bluish-purple color of the salt appeared immediately with the first few drops of the aqueous solution. The color became fainter and more reddish as the remainder of the base was added, but it was still distinctly perceptible even after dilution of the solution with a further 10 cc. of water. The fading of the color presumably was due to the decreasing solubility of the methane, which precipitated from the solution.

When this experiment was carried out with trinitrotrixylylmethane, the color of the corresponding salt was not perceptible at any time.

Methyl or Ethyl Alcohol as Solvent.—When trinitrotriphenylmethane was added to a methyl alcoholic solution of sodium methoxide, or to an ethyl alcoholic solution of sodium ethoxide, the intense purple color of the salt was formed immediately. The concentrations used were not critical. If the solutions were diluted with water, the color persisted as long as an appreciable quantity of the methane remained dissolved, but if an excess of phenol were added, the color was discharged immediately.

Approximately 1 mg. of trinitrotrixylylmethane was dissolved in 5 g. of the alcohol in question, and a solution of the corresponding sodium alkoxide was prepared from 0.5 g. of sodium and 10 g. of the alcohol. When 1 cc. of each of these two solutions were mixed, no color appeared in either the methyl or the ethyl alcoholic solution. Cyclohexylamine was now added slowly. The color of the salt became just perceptible after the addition of about 10 cc. of cyclohexylamine to the methyl alcoholic solution, or of about 4 cc. to the ethyl alcoholic solution.

Cyclohexylamine as Solvent.—A dilute solution of sodium cyclohexylamide in cyclohexylamine was prepared by the action of sodium upon a large excess of the amine in the presence of naphthalene.[16] The concentration of the amide solution was not critical. When about 1 mg. of either trinitrotriphenylmethane or trinitrotrixylylmethane was added to 2–4 cc. of the solution, the intense purple color of the corresponding salt developed immediately.

Acetophenone or Aniline as Solvent.—A small amount of the solution of sodium cyclohexylamide in cyclohexylamine, prepared as above, was added to a larger quantity of acetophenone or aniline. The addition of about 1 mg. of either of the two methanes to 2–4 cc. of the resulting solution again produced immediately the color of the salt. The color was not discharged on the addition of further quantities of acetophenone or aniline, as the case might be, although it did become less intense as a result of dilution.

The authors wish to express their appreciation to Mr. Kurt Eder for making the elementary analyses reported in this paper, to Mr. George Monk, Jr., for carrying out the crystallographic comparison, and to Mr. R. D. Kleene for helping with some of the preliminary experiments upon the trinitrotrixylylmethane.

Summary

In order to obtain evidence bearing upon the hypothesis of Birtles and Hampson that methyl groups in the two ortho positions can inhibit the resonance of a nitro group with an aromatic ring, 3,3′,3″,5,5′,5″-hexamethyl - 4,4′4″ - trinitrotri - phenylmethane has been prepared and its acid strength compared with that of the corresponding trinitrotriphenylmethane. It was found, in agreement with the hypothesis of Birtles and Hampson, that the former substance is somewhat less acidic than the latter.

CHICAGO, ILLINOIS RECEIVED FEBRUARY 9, 1940

(15) By Mr. George Monk, Jr.

(16) K. Ziegler, *Chem. Abs.*, **29**, 6250 (1935).

[CONTRIBUTION FROM THE SCHOOL OF CHEMICAL TECHNOLOGY, NORTH DAKOTA AGRICULTURAL COLLEGE]

Apparent and Partial Molal Volumes of Sodium Chloride and Hydrochloric Acid in Mixed Solutions[1]

BY HENRY E. WIRTH[2]

In a previous paper[3] it was shown that the partial molal volumes of potassium chloride, potassium bromide and potassium sulfate in sodium chloride solutions depend on the total volume ionic strength. The slopes of the partial molal volume–square root of concentration curves for these salts in aqueous solutions are near the values predicted by the Debye–Hückel theory.[4] A few electrolytes (*i. e.*, hydrochloric acid, lithium chloride and nitric acid) give slopes that are less than the theoretical value.[5] The effect of hydrochloric acid on the partial molal volumes of sodium chloride, and the effect of sodium chloride on the partial molal volumes of hydrochloric acid have therefore been investigated.

Methods.—In general the same apparatus and methods were employed. Pyrex tubes were substituted for the silver plated containers previously used as the latter were attacked by acid solutions.

C. P. grade chemicals were used without attempt at further purification.

The partial molal volumes of sodium chloride were determined in water and in approximately 0.04, 0.16, 0.36, 1.0, 2.18 and 4.23 *N* hydrochloric acid solutions. Enough hydrochloric acid solution for each series was prepared and the concentration determined by base titration as described below for the stock acid solution. As a check the concentrations were also calculated from the determined densities. Weighed amounts of sodium chloride were added to weighed portions of the acid solution to give the solutions used in the density determinations.

The partial molal volumes of hydrochloric acid were determined in water and in approximately 0.04, 0.16, 0.36, 1.0 and 2.25 *N* sodium chloride solutions. To meet the requirement that the ratio of moles of water to moles of sodium chloride remain constant throughout a given series, weighed stock acid solution was added to a weighed amount of water and to this solution was added an amount of sodium chloride calculated from the total water present.

The stock acid solution was analyzed by adding a weighed excess of approximately 0.25 *N* carbonate-free base to a sample and titrating the excess with approximately 0.01 *N* acid in a carbon dioxide-free atmosphere. Phenolphthalein was used as the indicator. The base was standardized against potassium acid phthalate. The average of six analyses was 0.21975 g. of hydrochloric acid per g. of solution (average deviation 0.00005). The average of five determinations using the weight Volhard method for chloride was 0.21960 (average deviation 0.00002).

Results[6]

The experimental values of the density for the solutions studied are presented in Tables I, II and III. Each series of results was represented by an equation of the form

$$-F_3 = a + b(\mu_v^{1/2} - C_2^{0\,1/2}) + c(\mu_v^{1/2} - C_2^{0\,1/2})^2 \quad (1)$$

The values for the constants a, b and c are given in Table IV. The apparent and partial molal volumes were calculated from this equation using the methods previously employed.[3] Values of the apparent and partial molal volumes are given in Tables I, II and III for the actual concentrations studied. Tables V[1] and VI[1] present values of $\overline{V}_3$ for various even concentrations.

It is possible to compare the values of the apparent molal volumes of the solutes in aqueous solutions with values which have previously appeared in the literature. In Fig. 1 values of Φ_3 for sodium chloride at 25° as determined in the present study are compared with those reported by Kruis.[7] The apparent molal volume at infinite dilution ($\overline{V}_3^0$) found by Kruis is 16.60$_5$ as compared with 16.67$_0$. This difference arises in

(1) Tables V, VI, VII and VIII referred to in this paper may be obtained from the American Documentation Institute, 2101 Constitution Ave., Washington, D. C., by remitting 24¢ for microfilm or 60¢ for photoprints.

(2) Present address: Department of Chemistry, The Ohio State University, Columbus, Ohio.

(3) H. E. Wirth, THIS JOURNAL, **59**, 2549 (1937).

(4) O. Redlich and P. Rosenfeld, *Z. physik. Chem.*, **A155**, 65 (1931).

(5) F. T. Gucker, Jr., *Chem. Rev.*, **8**, 111 (1933).

(6) The symbols used have the following significance:

d_1, d_2, d_3 = Density of water, of solution containing one solute and of solution containg two solutes, resp.

M_1, M_2, M_3 = Molecular weight of water, of first solute and of second solute, resp.

n_1, n_2, n_3 = Moles of water, moles of first solute and moles of second solute, resp. In a given series the ratio n_1/n_2 was maintained constant while n_3 varied.

C_2, C_3 = Volume concentration of first and second solute, resp., expressed as moles per liter of solution.

V = Volume of solution containing $n_1 + n_2 + n_3$ moles.

$\overline{V}_1 = \partial V/\partial n_1$, $\overline{V}_2 = \partial V/\partial n_2$, $\overline{V}_3 = \partial V/\partial n_3$. Partial molal volumes of water, of first solute and of second solute, resp.

$\overline{V}_1^0$ = Molal volume of pure water.

$\overline{V}_3^0$ = Partial molal volume of second solute when $C_3 = 0$, $C_2 = C_2^0$.

Φ_3 = $[V - (n_1\overline{V}_1^0 + n_2\Phi_2)]/n_3$. Apparent molal volume of second solute, where Φ_2 is the apparent molal volume of the first solute in a solution containing n_1 moles of solvent and n_2 moles of solute only.

F_3 = $1000(d_2 - d_3)/C_3$.

μ_V = $\omega_2C_2 + \omega_3C_3$. Volume ionic strength, where ω is one-half the summation of the number of ions times the square of the valence of the ion.

(7) A. Kruis, *Z. physik. Chem.*, **B34**, 1 (1936).

TABLE I

APPARENT AND PARTIAL MOLAL VOLUMES OF SODIUM CHLORIDE AND HYDROCHLORIC ACID IN WATER SOLUTION (25°)

C_3	$\mu_V^{1/2}$	$(d_3 - d_1)1000$	$-F_3$	Φ_3	$\overline{V}_3$
		Sodium Chloride			
0	0	0	(41.83$_3$)	16.67$_0$	16.67$_0$
0.03986	0.1997	1.654	41.50	17.00	17.17
.03986	.1997	1.655	41.52		
.1591$_1$	.3989	6.547	41.15	17.35	17.70
.1591$_1$	.3989	6.546	41.14		
.3567$_3$	.5973	14.552	40.79$_2$	17.71	18.26
.3567$_3$	.5973	14.553	40.79$_6$		
.9792$_0$	.9895	39.205	40.037	18.48	19.47
.9791$_8$	.9895	39.201	40.03$_5$		
2.251$_2$	1.5004	87.653	38.937	19.57	21.19
2.251$_2$	1.5004	87.668	38.94$_3$	19.57[a]	21.11[a]
5.411$_5$	2.3263	200.88	37.12$_1$	21.39[a]	23.68[a]

[a] Calculated from equation: $\Phi_3 = 16.435 + 2.010\ C_3^{1/2} + 0.052\ C_3$

		Hydrochloric Acid			
0	0	0	(18.44$_5$)	18.07$_2$	18.07$_2$
0.04023	0.2006	0.735	18.27	18.26	18.36
.04007	.2002	0.731	18.23		
.1565$_1$	.3956	2.830	18.08	18.45	18.63
.1551$_6$	.3939	2.806	18.09		
.3487$_0$	.5905	6.238	17.89		
.3589$_8$	.5992	6.421	17.89	18.63	18.90
.6330$_7$	.7957	11.207	17.70$_3$	18.81	19.17
.6299$_3$	.7937	11.154	17.70$_7$		
.9875$_7$	.9938	17.311	17.52$_9$	18.99	19.42
1.033$_1$	1.0164	18.083	17.50$_5$		
2.257$_8$	1.5026	38.606	17.09$_9$		
2.244$_9$	1.4983	38.393	17.10$_2$	19.43	20.04
3.897$_5$	1.9742	65.061	16.69$_3$		
4.001$_9$	2.0005	66.715	16.67$_1$	19.85	20.61

TABLE II

APPARENT AND PARTIAL MOLAL VOLUMES OF SODIUM CHLORIDE IN HYDROCHLORIC ACID SOLUTION (25°)

C_2	C_3	$\mu_V^{1/2}$	$(d_3 - d_2)1000$	$-F_3$	Φ_3	$\overline{V}_3$
		$C_2^0 = 0.041543$, $d_2 = 0.997832$				
0.04154	0	0.2038$_2$	0	(41.34)	17.15	17.15
.04151	0.04996	.3024$_4$	2.058	41.20	17.29	17.41
.04151	.04967	.3019$_6$	2.047	41.21		
.04146	.1153$_9$	.3960$_4$	4.738	41.06	17.43	17.65
.04146	.1148$_4$	.3953$_5$	4.717	41.07		
.04131	.3139$_7$	.5960$_6$	12.789	40.73$_3$	17.75	18.20
.04107	.6309$_8$	.8197$_9$	25.448	40.33$_1$	18.16	18.89
		$C_2^0 = 0.1558_2$, $d_2 = 0.999885$				
0.1558$_2$		0.3947$_4$	0	(40.93)	17.53	17.53
.1555$_7$	0.0891$_6$	.4947$_0$	3.635	40.77	17.69	17.83
.1555$_8$	.0887$_2$	.4942$_7$	3.617	40.77		
.1552$_7$	.1972$_0$	.5936$_9$	8.006	40.60	17.85	18.13
.1552$_7$	.1992$_9$	.5954$_5$	8.093	40.61		
.1544$_8$	.4705$_7$	.7906$_0$	18.949	40.26$_8$	18.19	18.71
.1534$_3$	.8268$_8$	.9901$_1$	32.995	39.90$_2$	18.55	19.33
		$C_2^0 = 0.35964$, $d_2 = 1.003507$				
0.3596$_4$		0.5997$_0$	0	(40.45)	17.94	17.94
.3588$_0$	0.1294$_5$	.6987$_5$	5.214	40.28	18.10	18.26
.3588$_0$	.1287$_2$	.6982$_2$	5.187	40.29		

TABLE II (*Concluded*)

C_2	C_3	$\mu_V^{1/2}$	$(d_3 - d_2)1000$	$-F_3$	Φ_3	$\overline{V}_3$
0.3578_2	0.2771_4	0.7968_4	11.118	40.12	18.27	18.57
$.3578_3$	$.2762_6$	$.7963_0$	11.084	40.12		
$.3554_4$	$.6265_0$	$.9909_3$	24.908	39.75_7	18.63	19.22
$.3524_8$	1.0476	1.1832	41.249	39.37_6	19.01	19.90
		$C_2^0 = 0.9891_0$, $d_2 = 1.014416$				
0.9891_0	0	0.9945_4	0	(39.39)	18.80	18.80
$.9852_2$	0.2068_5	1.0918	8.111	39.21	18.97	19.13
$.9852_0$	$.2079_0$	1.0923	8.153	39.22		
$.9810_2$	$.4268_6$	1.1865	16.661	39.03	19.14	19.48
$.9809_6$	$.4295_1$	1.1876	16.767	39.04		
$.9712_5$	$.9239_8$	1.3766	35.706	38.64_3	19.53	20.23
		$C_2^0 = 2.1789$, $d_2 = 1.034366$				
2.1789		1.4762	0	(37.92)	19.85	19.85
2.1659	$.2972_5$	1.5694	11.214	37.73	20.04	20.23
2.1659	$.2979_0$	1.5696	11.239	37.73		
2.1510	$.6331_8$	1.6686	23.751	37.51_1	20.25	20.62
2.1509	$.6352_1$	1.6692	23.826	37.50_9		
2.1190	1.330_8	1.8574	49.366	37.09_3	20.65	21.38
		$C_2^0 = 4.2338$, $d_2 = 1.067394$				
4.2338	0	2.0576	0	(36.02)	21.02	21.02
4.1980	0.3981_9	2.1439	14.261	35.82	21.20	21.37
4.1981	$.3977_1$	2.1438	14.252	35.84		
4.1590	$.8267_6$	2.2329	29.454	35.62_6	21.38	21.73
4.1588	$.8291_1$	2.2334	29.542	35.63_2		

TABLE III

APPARENT AND PARTIAL MOLAL VOLUMES OF HYDROCHLORIC ACID IN SODIUM CHLORIDE SOLUTION (25°)

C_2	C_3	$\mu_V^{1/2}$	$(d_3 - d_2)1000$	$-F_3$	Φ_3	$\overline{V}_3$
		$C_2^0 = 0.0398_61$, $d_2 = 0.998728$				
0.03986	0	0.1996_5	0	(18.04)	18.45	18.45
.03982	0.05052	$.3005_6$	0.908	17.97	18.50	18.55
.03982	.04999	$.2996_9$	0.900	18.01		
.03977	$.1217_5$	$.4019_0$	2.185	17.94	18.56	18.66
.03977	$.1179_1$	$.3971_0$	2.113	17.92		
.03964	$.2983_6$	$.5813_8$	5.306	17.79	18.70	18.91
.03964	$.2992_1$	$.5821_1$	5.321	17.78		
.03941	$.5964_3$	$.7974_0$	10.500	17.60_5	18.90	19.29
		$C_2^0 = 0.1591_1$, $d_2 = 1.003621$				
0.1591_1		0.3988$_9$	0	(17.61)	18.79	18.79
.1588$_4$	0.0878_1	.4966$_4$	1.542	17.56	18.84	18.89
.1588$_3$	.0929$_3$	.5017$_6$	1.632	17.56		
.1584$_9$	.1960$_3$	.5954$_1$	3.429	17.49	18.90	19.00
.1584$_9$	.1993$_2$	.5981$_7$	3.488	17.50		
.1576$_3$	.4826$_3$	.8001$_6$	8.377	17.36	19.04	19.28
.1576$_3$	.4723$_5$	.7937$_1$	8.198	17.36		
.1565$_3$	.8433$_0$	.9999$_1$	14.492	17.18_4	19.21	19.60
		$C_2^0 = 0.3567_3$, $d_2 = 1.011626$				
0.3567_3		0.5972_7	0	(17.07)	19.18	19.18
.3558$_7$	0.1258_0	.6940$_2$	2.142	17.03	19.22	19.25
.3558$_1$	.1345$_4$	.7002$_5$	2.290	17.02		
.3540$_6$	.2785$_5$	.7953$_7$	4.732	16.99	19.26	19.35
.3547$_7$	.2853$_9$	.8001$_0$	4.844	16.97		
.3523$_9$	.6281$_9$	.9902$_4$	10.599	16.87_2	19.37	19.56
.3524$_3$	.6226$_5$	.9874$_6$	10.503	16.868		
.3494$_1$	1.0539	1.1846	17.645	16.74_2	19.50	19.81

TABLE III (*Concluded*)

C_2	C_3	$\mu_v^{1/2}$	$(d_3 - d_2)1000$	$-F_3$	Φ_3	$\overline{V}_3$
		$C_2^0 = 0.97918$, $d_2 = 1.036277$				
0.97918	0	0.98953	0	(15.85)	19.90	19.90
.97546	0.19075	1.0799	3.016	15.81	19.93	19.95
.97484	.22262	1.0943	3.522	15.82		
.97088	.42460	1.1813	6.696	15.77	19.96	20.04
.97081	.42911	1.1832	6.773	15.78		
.96104	.92486	1.3733	14.505	15.683	20.06	20.24
		$C_2^0 = 2.2512$, $d_2 = 1.08473$				
2.2512		1.5004	0	(13.91)	20.79	20.79
2.2375	0.29181	1.5904	4.040	13.84	20.82	20.84
2.2231	.59933	1.6800	8.305	13.86	20.84	20.88
2.1907	1.2864	1.8647	17.760	13.81	20.89	20.97
2.1592	1.9514	2.0275	26.853	13.76	20.93	21.05

TABLE IV

CONSTANTS IN THE EQUATION:

$$-F = a + b(\mu_v^{1/2} - C_2^{0\,1/2}) + c(\mu_v^{1/2} - C_2^{0\,1/2})^2$$

$C_2^{0\,1/2}$	a	b	c	Average Deviation	d_2	$\partial C_2/\partial C_3$
		NaCl (58.454) in H_2O and in HCl Solution				
0 (0–2.25 N)	41.833	−1.609	−0.213	0.003	0.997074	
(1 N-Sat.)	42.067	−2.004	− .052	.002	.997074	
.2038	41.343	−1.345	− .477	.005	.997832	−0.000754
.3974	40.926	−1.552	− .281	.003	.999885	− .00306
.5997	40.451	−1.610	− .401	.003	1.003507	− .00684
.9945	39.388	−1.728	− .590	.002	1.014416	− .0193
1.4762	37.924	−2.097	− .216	.001	1.034366	− .0450
2.0576	36.017	−2.213	.....	.007	1.067394	− .0905
		HCl (36.465) in H_2O and in NaCl Solution				
0	18.445	−0.952	0.033	0.008	0.997074	
.1997	18.042	− .466	− .484	.014	.998728	−0.000754
.3989	17.611	− .499	− .359	.002	1.003621	− .00306
.5973	17.065	− .373	− .305	.004	1.011626	− .00694
.9895	15.845	− .277	− .383	.005	1.036277	− .0196
1.5004	13.910	− .285	.....	.011	1.08473	− .0471

the extrapolation to infinite dilution and does not represent a great variation in reported densities. Densities calculated from the equation in Table IV agree with those reported by Jones and Christian[8] with an average deviation of 0.0008% which is within the experimental error of their results. $\overline{V}_3^0$ calculated from the equation given by Jones and Christian is 16.62_1.

For comparison values of the apparent molal volumes at 18.55° as determined by Kohlrausch and Hallwachs[9] are also given in Fig. 1. The results of Prang[10] for concentrations below 0.015 N are in essential agreement and indicate that the value found by Kohlrausch and Hallwachs in the most dilute solution is probably in error.

The apparent molal volumes of hydrochloric acid in aqueous solutions are compared with the values determined by Hedestrand as reported by Geffcken[11] in Fig. 1. These are apparently the only values in the literature for the concentrations and temperature studied here. Hedestrand's value for $\overline{V}_3^0$ is 18.20 as compared with 18.07. The equation of Åkerlöf and Teare[12] derived from data at much higher concentrations and at other temperatures yields a value of 17.98_0 for $\overline{V}_3^0$ at 25°. Values of the apparent molal volumes at 17.15° as reported by Kohlrausch and Hallwachs[9] are also plotted in Fig. 1.

The partial molal volumes of sodium chloride are much less in the acid solutions than in solutions of the same volume ionic strength containing sodium chloride alone (Fig. 2). In the five cases ($\mu_v^{1/2}$ = 0.4, 0.6, 0.8, 1.0 and 1.2) where it is pos-

(8) G. Jones and S. M. Christian, THIS JOURNAL, **59**, 484 (1937).
(9) F. Kohlrausch and W. Hallwachs, *Wild, Ann. Physik*, **53**, 14 (1894).
(10) W. Prang, *ibid.*, **31**, 681 (1938).
(11) W. Geffcken, *Z. physik. Chem.*, **A155**, 1 (1931).
(12) G. Åkerlöf and J. W. Teare, THIS JOURNAL, **60**, 1226 (1938).

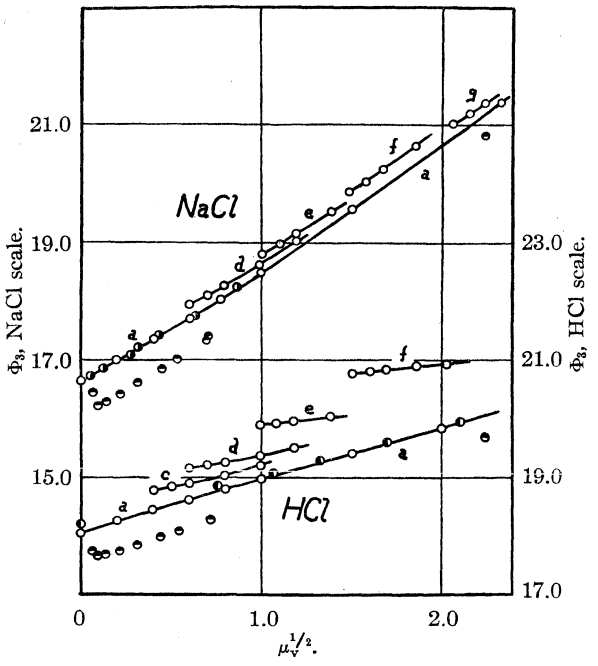


Fig. 1.—Apparent molal volumes of sodium chloride in water (a), and in 0.36 *N* (d), 0.99 *N* (e), 2.18 *N* (f) and 4.23 *N* (g) hydrochloric acid solutions (upper curves). Apparent molal volumes of hydrochloric acid in water (a), and in 0.16 *N* (c), 0.36 *N* (d), 0.98 *N* (e) and 2.25 *N* (f) sodium chloride solutions (lower curves). ◑, Kruis (25°); ◓, Kohlrausch and Hallwachs (18°); ◐, Hedestrand (25°); ○, Wirth (25°).

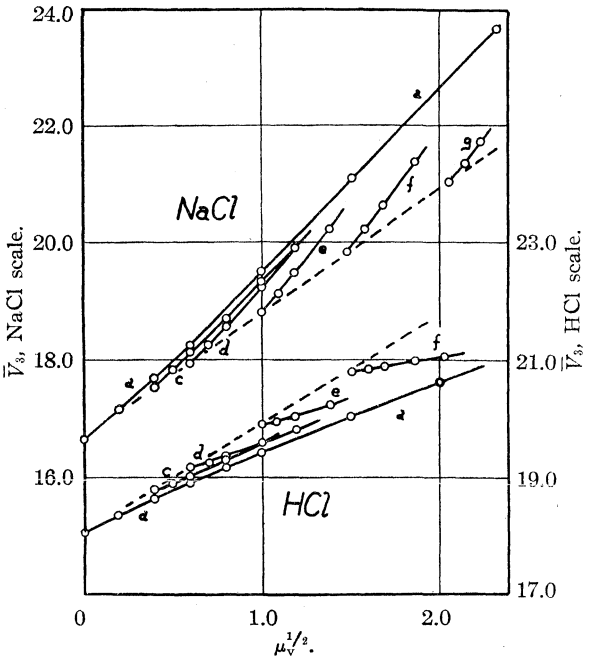


Fig. 2.—Partial molal volumes of sodium chloride in water (a), and in 0.16 *N* (c), 0.36 *N* (d), 0.99 *N* (e), 2.18 *N* (f) and 4.23 *N* (g) hydrochloric acid solutions (upper curves). Partial molal volumes of hydrochloric acid in water (a), and in 0.16 *N* (c), 0.36 *N* (d), 0.98 *N* (e) and 2.25 *N* (f) sodium chloride solutions (lower curves) (25°).

sible to make a comparison it was found that at constant total volume ionic strength the decrease in the partial molal volume is very accurately a linear function of the concentration of the acid (Fig. 3).

The partial molal volumes of hydrochloric acid are greater in solutions containing sodium chloride than in solutions of the same volume ionic strength containing acid alone (Fig. 2). Although there are two exceptions (the highest concentrations studied in 0.04 and 0.16 *N* sodium chloride solutions) it appears that at constant total volume ionic strength the increase in the partial molal volumes of hydrochloric acid is a linear function of the concentration of sodium chloride (Fig. 3).

In both cases presented in Fig. 2 it is possible to draw straight lines through the limiting values of the partial molal volumes ($\overline{V}_3^0$). All possible values of $\overline{V}_3$ are included between this line and the curve for $\overline{V}_3$ in aqueous solution. The slopes of the limiting lines are 1.81 for hydrochloric acid and 2.06 for sodium chloride. These values may be compared with a slope of 1.28 for hydrochloric acid and a slope of 3.12 for sodium chloride in water solutions at a concentration of 1 *N*.

The independent determination of the partial molal volumes of the two solutes in the mixed solutions makes possible the calculation of the partial molal volumes of water in most of the solutions studied.

In solutions containing only one solute, $\overline{V}_1$ can be calculated from the relation

$$\overline{V}_1 = \frac{(1000 - C_3\overline{V}_3)\,M_1}{1000d_3 - C_3M_3} \qquad (2)$$

For two solutes, $\overline{V}_1 = (1000 - C_2\overline{V}_2 - C_3\overline{V}_3)/n_1$. But since $n_1 = C_2K$ for all solutions of a given series and $K = (1000\ d_2 - C_2^0M_2)/C_2^0M_1$, the equation used in calculation becomes

$$\overline{V}_1 = \frac{(1000 - C_2\overline{V}_2 - C_3\overline{V}_3)\,M_1C_2^0}{C_2(1000d_2 - C_2^0M_2)} \qquad (3)$$

Values of $\overline{V}_3$ for even volume ionic strengths were taken directly from Table V[1] or VI,[1] while values of $\overline{V}_2$ were interpolated from Table VI[1] or V,[1] respectively. The calculated values of $\overline{V}_1$ are given in Tables VII[1] and VIII[1] and in Fig. 4.

In aqueous solutions $\overline{V}_1$ is decreased less by hydrochloric acid than by sodium chloride, and in mixed solutions the values are intermediate between those for the single solutes.

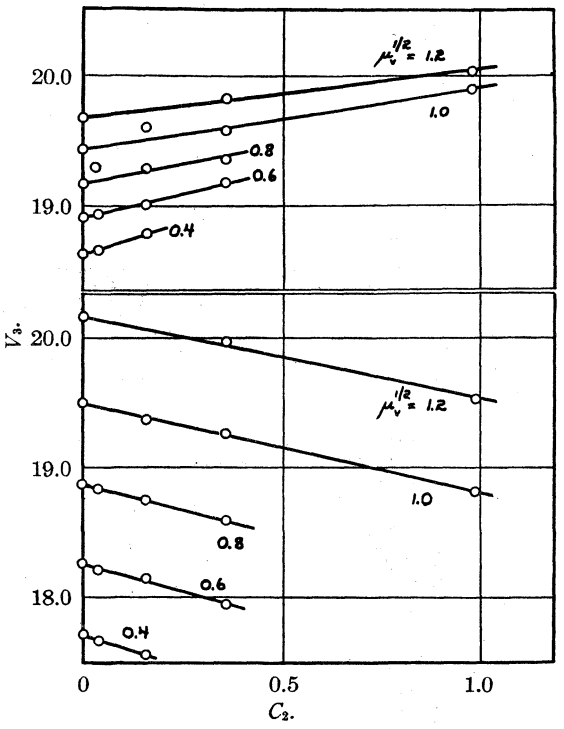


Fig. 3.—Partial molal volumes of hydrochloric acid *vs.* concentration of sodium chloride at constant total volume ionic strengths (upper graph), and partial molal volumes of sodium chloride *vs.* concentration of hydrochloric acid at constant total volume ionic strengths (lower graph) (25°).

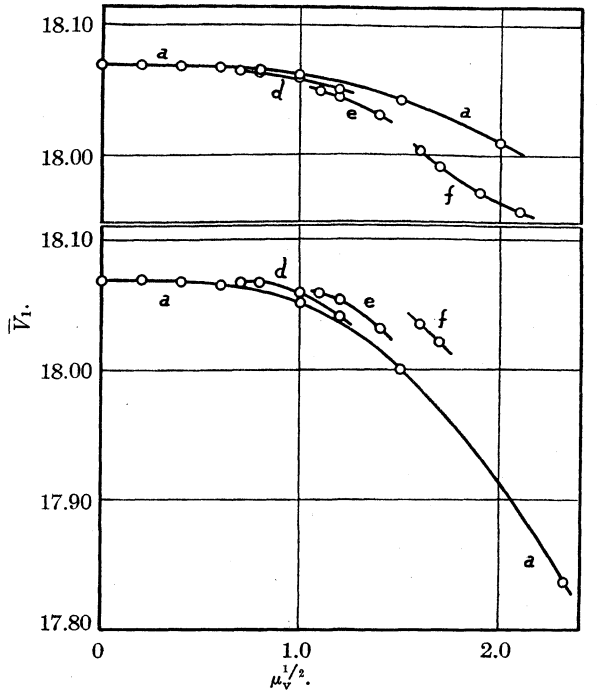


Fig. 4.—Partial molal volumes of water in hydrochloric acid solutions (a), and in hydrochloric acid solutions 0.36 *N* (d), 0.98 *N* (e) and 2.25 *N* (f) in sodium chloride (upper graph). Partial molal volumes of water in sodium chloride solutions (a), and in sodium chloride solutions 0.36 *N* (d), 0.99 *N* (e) and 2.18 *N* (f) in hydrochloric acid (lower graph) (25°).

Discussion

The slope of the apparent molal volume–square root of concentration curve for hydrochloric acid in water is less than for any highly ionized, uni-univalent electrolyte with the possible exception of nitric acid.[12,13,14] While the results obtained here do not exclude the possibility of $\partial\Phi/\partial C^{1/2}$ attaining the theoretical limiting value, this would require an abrupt change at concentrations below 0.04 *N*.

Since $\partial\Phi/\partial C^{1/2}$ is apparently least for substances containing hydrogen or lithium ions, the effect may be related to ion size. The second approximation derived by Redlich and Rosenfeld[4] from the Debye–Hückel expression involving ionic radii predicts however that $\partial\Phi/\partial C^{1/2}$ will be increased as the ionic size is decreased. The breakdown of the Debye–Hückel theory in other cases where small ions are involved has been attributed to ion association.[15]

The relationship between $\partial\Phi/\partial C^{1/2}$ and the partial molal volume of the solvent is of significance. For a single solute, the relations $(1000 - n_1\overline{V}_1^0)/C_3 = \Phi_3 = \overline{V}_3^0 + k_1C_3^{1/2}$, $\overline{V}_3 = \overline{V}_3^0 + kC_3^{1/2}$, and $k_1 = {}^2/_3k$(Geffcken[11]) can be combined with the equation $V = 1000 = n_1\overline{V}_1 + C_3\overline{V}_3$ to give the expression

$$\overline{V}_1 = \frac{\overline{V}_1^0(1000 - C_3\overline{V}_3^0 - kC_3^{3/2})}{1000 - C_3\overline{V}_3 - {}^2/_3kC_3^{3/2}} \qquad (4)$$

This equation holds with considerable accuracy at least up to concentrations of 1 *N* and shows that the partial molal volume of the solvent at a given concentration is determined by $\partial\Phi/\partial C^{1/2}$ $(= k)$, or *vice versa*.

Since $\partial\Phi/\partial C^{1/2}$ for moderately concentrated solutions cannot now be predicted accurately from theory, it may be convenient to take the view of Stewart[16] and others that the change in structure of water through decrease in coördination number in the presence of ions is the controlling factor.[17]

(13) D. O. Masson, *Phil. Mag.*, [7] **8**, 218 (1929).

(14) G. Åkerlöf and G. Kegeles, THIS JOURNAL, **61**, 1027 (1939).

(15) H. Falkenhagen, "Electrolytes," translated by R. P. Bell, Oxford University Press, New York, N. Y., 1934, p. 257.

(16) G. W. Stewart, *J. Chem. Phys.*, **7**, 869 (1939).

(17) This should be done without discarding the Debye–Hückel theory, since this theory correctly predicts the choice of variable ($C^{1/2}$ or $\mu_v^{1/2}$), the order of magnitude of $\partial\Phi/\partial C^{1/2}$, and the effect of valence on $\partial\Phi/\partial C^{1/2}$.

From this standpoint, the low value for $\partial\Phi/\partial C^{1/2}$ for hydrochloric acid is due to the ease with which the hydrogen ion fits into the existing structure of water, and only the chloride ion is effective in changing that structure.

The observed increase in the partial molal volume of hydrochloric acid at constant total volume ionic strength when the hydrogen ion is replaced by sodium ion must be due to the greater effect of the sodium ion on the water structure. The fact that the increase is a linear function of the amount of sodium ion added is in harmony with this view. The decrease in the partial molal volume of sodium chloride on replacing the sodium ion with hydrogen ion is explained in the same manner.

Summary

The apparent and partial molal volumes of sodium chloride and hydrochloric acid have been determined in water and in mixed solutions.

The partial molal volumes of sodium chloride are decreased at constant total volume ionic strength by the addition of hydrochloric acid. The decrease is a linear function of the acid concentration.

The partial molal volumes of hydrochloric acid are increased at constant total concentration by the addition of sodium chloride. The increase is a linear function of the sodium chloride concentration.

The partial molal volumes of water have been determined in the mixed solutions. At a given concentration they are largest in solutions of pure hydrochloric acid and least in pure sodium chloride solutions.

The observed behavior may be interpreted in terms of changes in the structure of water caused by ions in solution.

RECEIVED DECEMBER 11, 1939

[CONTRIBUTION FROM THE CHEMICAL AND METALLURGICAL ENGINEERING DEPARTMENT, UNIVERSITY OF MICHIGAN]

An X-Ray Investigation of the System Cr_2O_3–NiO[1]

BY L. THOMASSEN

The present work has for its purpose to investigate the phases that are present in the above system. This equilibrium diagram is of considerable practical interest since the scale formed on the common electric resistance wires of nominal composition 80% Ni 20% Cr mainly consists of these oxides.

An earlier investigation[1a] has shown that the compound $NiO{\cdot}Cr_2O_3$ is formed when mixtures of this composition are heated with a mineralizer such as potassium chloride. This compound crystallizes in the widely distributed spinel type of structure.[2] Regarding the rest of the system, no information seems to be available. Similar systems with ferric oxide as the trivalent metal oxide have been investigated.[3]

Experimental Procedure

Most of the samples were made by mixing the oxides in the proper proportions, grinding them intimately and heating them with potassium chloride in platinum crucibles at 1000° for one to two hours. An electric furnace with automatic temperature control was used for the heating. After fusion, the crucibles were taken out and allowed to cool rapidly in the air. Unless changes take place very rapidly, the material as investigated would represent equilibrium conditions at 1000°.

The chromic oxide used was obtained by heating C. P. ammonium chromate to 900°. Upon heating a sample to 1000° for ten hours, a loss of 0.2% was obtained. According to Wretblad[4] there is no danger of forming CrO_2 when heating Cr_2O_3 to 1000° in oxygen and there should be still less chance of forming such a compound in air.

The nickel oxide was obtained by heating C. P. nickel nitrate, cobalt free, to 400°. The oxide obtained analyzed 77.3% Ni instead of 78.5% theoretically. Both the weight loss of the chromic oxide and this deviation from the theoretical composition were taken into account when making up mixtures to be fused.

After fusion the samples were washed carefully to remove all the potassium chloride present. Invariably, the first wash water was yellow, showing that some chromic oxide was oxidized to chromate.

Boric oxide was also tried as a mineralizer but with the straight $NiO{\cdot}Cr_2O_3$ composition, a number of extra lines appeared on the X-ray diagram. This observation confirmed the doubts expressed by Holgersson[1a] regarding the advisability in using boric oxide in this synthesis.

(1) Original manuscript received July 31, 1939.

(1a) S. Holgersson, *Z. anorg. allgem. Chem.*, **204**, 382 (1932).

(2) See for instance S. Holgersson, "Lunds Universitetets Arsskrift," N. F. Avd. 2. Vol. 23, Nr. 9; G. L. Clark, *Am. J. Sci.*, **22**, 539 (1931).

(3) A. E. van Arkel, E. J. W. Verwey and M. G. van Bruggen, *Rec. trav. chim.*, **55**, 331, 340 (1936).

(4) Wretblad, *Z. anorg. allgem. Chem.*, **189**, 329 (1930).

The method of grinding and pressing together the oxides in the proportions to form spinel and heating them at 1000° for two hours did not produce complete combination since both the nickel and chromium oxide lines were present besides the spinel lines.

Some of the samples used were produced by co-precipitation of nickel carbonate and chromium hydroxide with sodium carbonate. Proper proportions were taken out of solutions of known contents of $NiCl_2$ and Cr_2Cl_6, precipitated out of hot diluted solutions, filtered, washed carefully, dried and ignited, keeping the samples at 1000° for ten hours.

The porportions used may be seen from Table I. The samples with an asterisk are those prepared by co-precipitation. The sample of straight spinel composition was analyzed for nickel and gave 33.0% NiO instead of theoretically 32.6%.

The phases present were identified by X-ray diffraction patterns, using filtered chromium radiation. The X-rays were produced by a modified Siegbahn–Hadding tube with a plated chromium target. The samples were made up by mixing the powders with Duco Household Cement and rolling them out into rods of about $^3/_{10}$ mm. diameter. For lattice parameter determinations C. P. sodium chloride was mixed with the sample to provide a variable correction factor. The lattice constant of sodium chloride was taken to be 5.626 Å.[5]

Computations of lattice parameters are not given in this work since the lattice constants of the substances investigated are all known, and the precision determinations did not differ much from those in the literature. For more detailed information on the method of computation, see for instance L. Thomassen, *Z. physik. Chem.*, **135**, 388 (1928); *ibid.*, **B2**, 340 (1929).

Discussion of Results

The results obtained are shown in Table I. It will be seen that the only compound in the system is the spinel. A separate experiment shows that this compound remains cubic when cooled slowly from 1000° in the electric furnace. It also will be noticed that chromic oxide on one side of the spinel composition and nickel oxide on the other side appear when present in small excess over the 1:1 ratio. This means that if solid solubility exists, the amounts dissolved are small at the temperature of formation.

In order to investigate whether solid solubility could be detected in lattice dimensions, diffraction diagrams of the samples 0.95 $NiO{\cdot}Cr_2O_3$, $NiO{\cdot}Cr_2O_3$ and 1.1 $NiO{\cdot}Cr_2O_3$ were made, using sodium chloride as reference substance. Within experimental error, the measurements gave the same results, namely, 8.282, 8.282 and 8.284 Å., respectively, with an error of ±0.003 Å. This compares to the lattice constant given by Holgersson[1a] of 8.30 Å., also using sodium chloride as a reference substance. Since the lines were comparatively broad, no precision back reflection pictures were taken.

(5) T. Barth and G. Lunde, *Z. physik. Chem.*, **126**, 417 (1927).

TABLE I

Mols of NiO per Mol Cr_2O_3	Phases present
0.25	Cr_2O_3
* .25	Cr_2O_3 + spinel
* .30	Cr_2O_3 + spinel
.375	Cr_2O_3 + increasing amount of spinel on increasing NiO
.50	
.75	
.87	
.95	
1.0	Spinel only
1.1	NiO + decreasing amount of spinel on increasing NiO
1.25	
1.50	
1.75	
2.0	
4.0	
8.0	
*20	
*50	
*100	NiO

From the table it will be seen that the samples with high chromic oxide content give conflicting results regarding phases present, depending on whether they are produced by co-precipitation or by fusion. The meaning of this observation is not clear and this question of the solubility of nickel oxide in chromium oxide will be treated in another paper.

Among the samples with high nickel oxide content, the one with 100 mols of nickel oxide is the only one which does not show spinel lines. By the technique used in this investigation the diffraction method will not detect phases present below one to three per cent. The one mol spinel which would be formed would hardly register in a diffraction diagram when diluted with 99 mols of NiO. Taking into account that the spinel lines were hardly discernible when present in the double concentration and in amounts which are at the threshold of detection, it seems probable that the solubility of Cr_2O_3 in NiO is very small.

As is well known, the nickel oxide crystallizes in the sodium chloride type of structure, and several investigators have found a lattice constant $a = 4.17$ Å.[6,7] The present investigation also gave $a = 4.170 \pm 0.003$Å.

(6) G. Lunde, *Z. anorg. allgem. Chem.*, **163**, 345 (1927).

(7) S. B. Hendricks, M. E. Jefferson and J. F. Schultz, *Z. Krist.*, **73**, 376 (1930).

It is a pleasure to acknowledge the assistance of Mr. George Manning who made up most of the preparations and also took some of the X-ray diagrams.

Summary

1. In the equilibrium diagram Cr_2O_3–NiO the spinel $NiO \cdot Cr_2O_3$ is the only compound present.

2. At 1000° the solubility of nickel and chromium oxide in the spinel is small.

3. Nickel oxide does not dissolve chromium oxide.

ANN ARBOR, MICH. RECEIVED MARCH 4, 1940

[CONTRIBUTION FROM THE WILLIAM H. CHANDLER CHEMISTRY LABORATORY OF LEHIGH UNIVERSITY]

The Acid Catalyzed Esterification of Aliphatic Acids

BY HILTON A. SMITH

In two previous papers the effect of the alkyl chain of an aliphatic organic acid on its velocity of esterification in methanol was discussed. The first[1] dealt with normal acids only, and the second included simple methyl substituted acids.[2] The present paper reports a study of the velocity of esterification of certain other branched-chain aliphatic acids, together with a discussion of the general effect of alkyl substitution on reaction velocity.

Experimental

Methanol was obtained in a pure dry state, as in previously reported work, by careful fractionation of 99.5% methyl alcohol using a 5-foot (1.5-meter) spiral column. The material used distilled at a constant head temperature.

Trimethylacetic acid and **diethylacetic acid** were obtained by fractionation of the Eastman Kodak Co. acids in a 5-ft. (1.5-meter) Vigreux type column. The former analyzed 99.5% by titration with standard base and melted at 35.4°. The latter analyzed 99.9%.

β-Methylvaleric acid[3] was prepared by the malonic ester synthesis from diethyl malonate, *s*-butyl bromide and sodium ethylate. Ethyl *s*-butylmalonate was prepared by the method indicated in "Organic Syntheses" for its normal isomer,[4] and this ester converted to β-methylvaleric acid by hydrolysis and decarboxylation. The crude acid was purified by fractionation in a 5-ft. Vigreux type column. The sample used for esterification purposes distilled at constant head temperature (±0.05°) and analyzed 100.0% by titration with standard base.

Dipropylacetic acid, dibutylacetic acid, and **di-isobutylacetic acid** were prepared in a manner similar to that used for β-methylvaleric acid. The di-alkyl substituted ethyl malonates were prepared by introducing two alkyl groups into the ester using sodium ethylate and the necessary alkyl iodide. The substituted malonic ester was hydrolyzed and decarboxylated, and the crude acids purified by reduced pressure distillation in a 5-ft. Vigreux column. Each of the samples used in the esterification studies analyzed at least 99.6% by titration with standard base.

The method employed to obtain the rate constants for the hydrion-catalyzed esterification of these acids was similar to that previously described[1] with the exception that the glass-stoppered bottles were replaced by small Pyrex vials the openings of which were fitted with a glass plug. A rubber sleeve around the opening and the plug prevented possible loss of solvent by evaporation. This was necessary because of the slowness of the runs, some of them lasting for several weeks.

Experimental Results and Calculations

The rate constants were calculated from Goldschmidt's equation

$$k = \frac{(r + a) \ln [a/(a - x)] - x}{(\text{catalyst})rt}$$

where a is the original concentration of organic acid, x is the concentration of ester formed after time t, and the catalyst is hydrogen chloride. The values of the constant r used were those obtained in earlier work for normal aliphatic acids.[1]

The values of the reaction velocity constant, k, were quite constant for reactions run at the lower temperatures. This is illustrated in Table I for the esterification of trimethylacetic acid at 20°.

TABLE I

ESTERIFICATION OF CH_3OH AND $(CH_3)_3CCOOH$ AT 20°
$a = 0.500$, (HCl) = 0.005

t, min.	$(a - x)$	k (liters × moles^{-1} × sec.$^{-1}$)
190	0.465	0.00139
1047	.361	.00141
1897	.298	.00140
3304	.227	.00141
5611	.157	.00139
11593	.073	.00133

For the slower runs at elevated temperatures, the rate constants fall off consistently with increasing reaction. The greatest falling off oc-

(1) Smith, THIS JOURNAL, **61**, 254 (1939).

(2) Smith, *ibid.*, **61**, 1176 (1939).

(3) The author is greatly indebted to Mr. A. S. Raff for his aid in the preparation of this compound.

(4) "Organic Syntheses," Coll. Vol. I, p. 245.

curred with di-isobutylacetic acid at 50°, this being the slowest high temperature run. The results of such a run are presented in Table II.

TABLE II

ESTERIFICATION OF CH_3OH AND DI-ISOBUTYLACETIC ACID AT 50°

$a = 0.500$, (HCl) = 0.005

t, min.	$(a - x)$	k (liters × moles^{-1} × sec.$^{-1}$) k (simple)	k (correct)
407	0.436	0.00121	0.00123
1130	.370	.00103	.00108
1842	.323	.000970	.00104
3376	.255	.000882	.00099
5415	.193	.000834	.00100
7130	.159	.000794	.00100
11297	.106	.000726	.00103

Inspection of column three of this table shows the extent of the falling off of the reaction velocity constant. The value of r at this temperature is 0.42. The falling off of the rate constants might be prevented by changing the value of r for the slow reactions, but this is not permissible since r is theoretically defined by the equation

$$r = \frac{(CH_3OH_2^+)(H_2O)}{(H_3O^+)}$$

and at any given temperature should be the same for all acids.

Hinshelwood[5] already has demonstrated that, at elevated temperatures, the reaction of methanol with hydrogen chloride is appreciable. For the purpose of correcting the rate constants for reaction of the catalyst with the solvent, the rate of reaction of a 0.005 N solution of hydrogen chloride in methanol was studied. The solution was placed in a thermostat in one of the reaction vials, and the disappearance of the acid followed by titration with dilute (0.00229 N) base. Figure 1 gives the results obtained at 30, 40 and 50°. It demonstrates the fact that, while this reaction is negligible in the study of esterification of normal or simple substituted aliphatic acids (80% reaction in a few hours), it must be taken into account for the slower reactions under consideration here.

The rate of reaction of hydrogen chloride with methanol as shown in Fig. 1 is somewhat faster than that found by Hinshelwood.[5] The reason for this difference is not apparent, but may be due to the different concentrations used.

Unfortunately it is impossible to make an absolute correction for the reaction of the catalyst with solvent since one cannot predict the effect of the

(5) Hinshelwood, *J. Chem. Soc.*, 599 (1935).

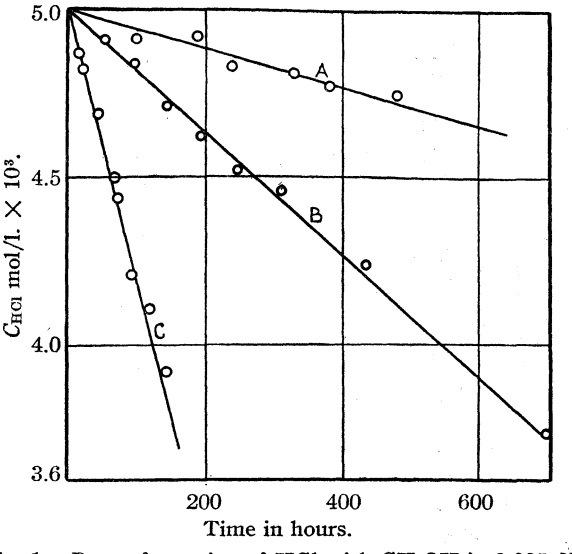


Fig. 1.—Rate of reaction of HCl with CH_3OH in 0.005 N solution: A, $T = 30°$; B, $T = 40°$; C, $T = 50°$.

acid and ester present on its rate. The corrected values of k in column 4 of Table II were calculated by substituting in equation (1) not the original concentration of hydrogen chloride for (catalyst) but rather the concentration present at time t, thus assuming the reaction of hydrogen chloride and methanol in the reaction mixture to proceed at the same rate as that found for the pure solutions. This correction results in reasonably constant values of the reaction velocity constants. Such a correction was applied for studies involving diethyl-, dipropyl-, dibutyl-, and di-isobutylacetic acids at temperatures of 30, 40, and 50°. With the exception of di-isobutylacetic acid at 50°, these corrections are not more than some 10% at as much as 80% reaction, and are usually considerably less.

The values of the specific reaction rate constants for esterification of the acids studied are given in Table III. They represent averages of the individual values of k over the range covered by 20 to 80% reaction. The ± deviations are generally of the order of 2–3%.

Figure 2 shows the plot of log k against inverse temperature for the acids studied. The activation energy for each acid is given in the last column of Table III. These were calculated from the slopes of the lines in the figure, and were checked by the method of least squares.

Discussion

The effect of the length of an alkyl chain of an aliphatic acid on its esterification velocity

TABLE III

REACTION RATE CONSTANTS FOR ESTERIFICATION OF ALIPHATIC ACIDS IN METHYL ALCOHOL CATALYZED BY H^+ IONS

In all cases a = 0.500,[a] (HCl) = 0.005[b]

Acid	k (liters × moles^{-1} × sec.$^{-1}$) t = 20°	t = 30°	t = 40°	t = 50°	E
β-Methylvaleric	0.00461	0.00808	0.0142	0.0239	
	.00465	.00802	.0144	.0242	
Av.	.00463	.00805	.0143	.0240	10,400
Trimethylacetic	.00141	.00267	.00488	.00867	
	.00140	.00269	.00497	.00849	
Av.	.00140	.00268	.00493	.00858	11,400
Diethylacetic	.000348	.000699	.00132	.00254	
	.000354	.000722	.00132	.00252	
Av.	.000351	.000711	.00132	.00253	12,400
Dipropylacetic	.000297	.000630	.00122	.00227	
	.000296	.000632	.00122	.00227	
Av.	.000297	.000631	.00122	.00227	12,400
Dibutylacetic	.000272	.000547	.00111	.00203	
	.000262	.000558	.00108	.00210	
Av.	.000267	.000553	.00110	.00207	12,900
Di-isobutylacetic	.000141	.000282	.000550	.00102	
	.000140	.000278	.000547	.00105	
Av.	.000140	.000280	.000547	.00105	12,600

[a] For trimethylacetic acid at 50°, a = 0.486, (HCl) = 0.00486. [b] For β-methylvaleric acid at 20°, (HCl) = 0.00386.

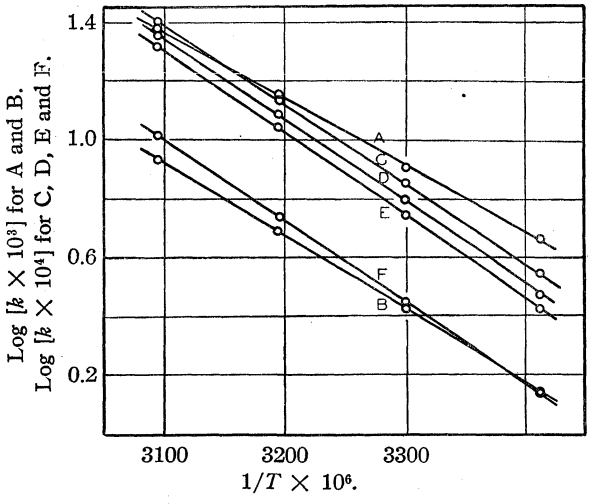


Fig. 2.—Temperature coefficients of hydrogen ion catalyzed esterification of substituted alkyl acids in methanol: A, β-methylvaleric acid; B, trimethylacetic acid; C, diethylacetic acid; D, dipropylacetic acid; E, dibutylacetic acid; F, di-isobutylacetic acid.

already has been discussed.[1,6] It was demonstrated that the velocity constants decreased from formic to butyric acids, and thereafter remained constant with increasing chain length. It was also demonstrated that the activation energy was constant throughout the series. It is now possible to consider the results of lengthening two chains simultaneously. Table IV gives a summary of the pertinent data.

TABLE IV

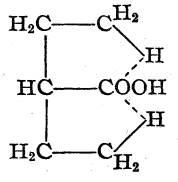
Acid	$k_{20°}$	E
Acetic[1]	0.0440	10,000
Isobutyric[2]	.0147	9,800
Diethylacetic	.000351	12,400
Dipropylacetic	.000297	12,400
Dibutylacetic	.000267	12,900

The results shown in this table are quite parallel with those found when the length of a single chain is increased. In each case a relatively small drop in the reaction velocity constant occurs on the first methyl substitution, a much larger one on an ethyl substitution, and little change occurs as the chain length is subsequently increased. For the disubstituted acids, some falling off does occur beyond diethylacetic acid, but this change is insignificant when compared to previous changes. In contrast to the normal acids, the change from dimethylacetic to diethylacetic acid is accompanied by a large change in activation energy.

The results of increasing the chain length of a normal aliphatic acid on its velocity of esterification were explained by postulating ring formation in butyric and higher acids. Similar rings have been postulated by Palomaa and co-workers in

(6) Smith and McReynolds, THIS JOURNAL, 61, 1963 (1939).

their studies of the ether-type linkage.[7] The results for disubstituted acids which are presented here are not readily explainable either by inductive effect[8] or by the mechanical model studies of Fairclough and Hinshelwood.[9] They are, however, readily explainable by the ring theory. The postulated ring structure of diethylacetic acid is



A similar structure might be expected even were no chelation to occur, since from stereochemical considerations alone the zig-zag structure usually assigned to a hydrocarbon chain is improbable for both chains of this acid. The slow esterification of diethylacetic acid is in accord with the explanation already advanced[6] for its high dissociation constant.[10] The fact that only minor changes in esterification rate are found when the alkyl chains are lengthened to form dipropyl and dibutylacetic acids is also expected from the ring theory.

The slow esterification of β-methylvaleric acid was predicted from previous results with impure isocaproic acid.[2] These predictions are now confirmed. The rate of esterification of this acid ($k_{20°} = 0.00463$) compared with that of isovaleric acid ($k_{20°} = 0.00488$) gives further evidence that substitution in the γ position ordinarily has little effect.

The results with di-isobutylacetic acid are interesting since k for this acid is considerably lower than those for diethyl, dipropyl and dibutylacetic acids. In the single chain series, the corresponding compound, isocaproic acid, esterified at the same rate as the corresponding normal acids. The slower rate for di-isobutylacetic acid is in line with the fact that some falling off of the esterification rate does occur when the chains in the di-substituted acids are longer than those in diethylacetic acid, and with the fact that β-methylvaleric acid esterifies a little slower than isovaleric acid.

(7) *Cf.* Palomaa and Siitonen, *Ber.*, **69B**, 1338 (1936).

(8) *Cf.* Evans, Gordon and Watson, *J. Chem. Soc.*, 1439 (1938); see also Smith and Levenson, THIS JOURNAL, **61**, 1172 (1939).

(9) Fairclough and Hinshelwood, *J. Chem. Soc.*, 593 (1939).

(10) Dippy, *ibid*, 1222 (1938). In this connection the attention of the author has been called to the fact that direct credit was not given to Dippy for the form of Fig. 3 in the publication of Smith and McReynolds.[6] A similar figure was presented by Dippy.

Complete data are now available for discussing the effect of substitution of methyl groups in the α position of acetic acid. This material is summarized in Table V.

TABLE V

Acid	$k_{20°}$	E
Acetic[1]	0.0440	10,000
Propionic[1]	.0400	9,800
Isobutyric[2]	.0147	9,800
Trimethylacetic	.00140	11,400

From this table it is evident that successive methyl substitution in the α position of acetic acid causes a decrease in the velocity of esterification of the acid, the decrease per methyl group becoming greater with increased substitution. This is in accord with the idea of geometrical steric hindrance. The activation energy is changed only when the third methyl group is introduced, in which case a considerable increase occurs. The high activation energy for trimethylacetic acid corresponds with the results of Hinshelwood and Legard[11] for the catalyzed esterification of this acid in ethanol. The increase in activation energy accompanying considerable substitution already has been discussed.[6]

In general, the results of the esterification studies with alkyl substituted acetic acids may be summed up as follows.

Substitution must ordinarily take place in the α or β position from the carboxyl group if the reaction velocity is to be affected, and substitution in either of these positions has approximately the same net effect. The so-called "ethyl effect" is the result of simultaneous substitution in the α and β positions.

One substituent in these positions has little effect on the esterification velocity and none on the activation energy, *e. g.*, propionic acid.

Two substituents have a considerably greater effect on the reaction velocity, but none on the activation energy, *e. g.*, isobutyric acid, butyric and higher normal acids.

Three substituents have a still greater effect on the esterification velocity, and result in a somewhat increased value of E, *e. g.*, methylethylacetic acid, isovaleric acid, β-methylvaleric acid, and trimethylacetic acid.

Four substituents have a large effect on the reaction velocity, and result in a greatly increased activation energy, *e. g.*, diethylacetic acid, dipropylacetic acid, etc.

(11) Hinshelwood and Legard, *ibid*, 1588 (1935).

Acids which have more than four substituents in the α or β positions should be practically unesterifiable under ordinary conditions.[12]

Finally, if considerable substitution in the α or β positions has already been made, substitution in the γ position may have some effect on esterification rate.

It has been demonstrated already that the effect of lengthening the alkyl chain of the acid portion of ethyl esters on the rate of saponification of these esters is the same as that observed in esterification.[8] In a subsequent paper it will be shown that the general effect of α and β substitution is the same for these two processes.

(12) *Cf.* Braun and Fischer, *Ber.*, **66B**, 101 (1933).

Summary

The kinetics of the hydrogen ion catalyzed esterification of the following organic acids have been studied: β-methylvaleric acid, trimethylacetic acid, diethylacetic acid, dipropylacetic acid, dibutylacetic acid and di-isobutylacetic acid.

The velocity of esterification of β-methylvaleric acid is similar to that of isovaleric acid. Trimethylacetic acid esterifies slowly, and has a greater activation energy than normal acids. The other four acids esterify very slowly, and have a considerably increased activation energy.

The general results of esterification studies of alkyl substituted acetic acids have been discussed

BETHLEHEM, PENNA. RECEIVED FEBRUARY 14, 1940

[CONTRIBUTION FROM THE METCALF RESEARCH LABORATORY OF BROWN UNIVERSITY]

Some Unusual Hydrates of Quaternary Ammonium Salts

BY D. L. FOWLER, W. V. LOEBENSTEIN, D. B. PALL AND CHARLES A. KRAUS

Introduction

In concentrating a solution of tetra-*n*-butylammonium hydroxide for the purpose of preparing as nearly anhydrous a product as possible, it was observed that crystals appeared at room temperature in comparatively dilute solutions and that the entire mass solidified at this temperature while a large quantity of water was still present. On investigating this phenomenon further, it was found that tetra-*n*-butylammonium hydroxide forms a hydrate, containing 31 molecules of water, which melts at 30.2°. On examining solutions of tetra-*n*-butylammonium fluoride, a similar hydrate was found containing 18 molecules of water and melting at 37°. Somewhat later, tetramethyl-, tetra-*n*-propyl-, tetra-*n*-amyl- and tetraisoamylammonium hydroxides were investigated. It was found that only tetraisoamylammonium hydroxide forms a high hydrate. More recently, a considerable number of quaternary ammonium salts has been investigated in a preliminary fashion in order to determine whether they form hydrates and approximately of what composition. All the tetra-*n*-butylammonium salts having a high solubility in water were found to form hydrates, as did also tetraisoamylammonium formate, the one tetraisoamylammonium salt investigated. No salts of ions other than tetra-*n*-butylammonium and tetraisoamylammonium have been found that form high hydrates.[1]

Experimental

Method.—In determining the composition of these salt hydrates, a weighed sample of solution, which had previously been analyzed, was introduced into a suitable cell which was either cylindrical or of Erlenmeyer form and which was provided with a stopcock. The weight of the cell was known so that the composition of the solution could be obtained at any time by weighing the cell and its contents. The cell was attached to a vacuum system which was provided with a mercury manometer; an oil manometer, which had a higher sensitivity than the mercury manometer; a flask, containing water; a small pipet, graduated to 0.1 cubic centimeter; and a closed, drying tube for absorbing water vapor as desired. In most cases, the cell was attached to the apparatus by means of a short length of pressure tubing so that the contents of the cell could be shaken conveniently in determining melting points or in adjusting for pressure equilibrium. The entire apparatus was carefully exhausted so as to remove the permanent gases.

Most of the salts were prepared by titrating acids with solutions of the desired quaternary bases. The bases were prepared from the corresponding iodides by means of silver oxide. In preparing these bases, it is very essential to guard against carbon dioxide. All solutions must be made up with carbon dioxide-free water and the apparatus must

(1) The experimental work in connection with tetra-*n*-butylammonium hydroxide and fluoride was carried out by D. L. Fowler; that of the other hydroxides by W. V. Loebenstein; that of the remaining salts by David B. Pall. Since it is not planned to continue the investigation of these hydrates at this time, the results are presented as far as they have been obtained.

be filled with carbon dioxide-free air or nitrogen. Traces of carbon dioxide are immediately absorbed by the bases to form carbonates, thus introducing an additional component which renders a study of the desired phase relations impossible.

In determining the precise composition of the hydrates, several methods were employed, depending upon the nature of the hydrate. In some cases, the initial melting point and the point of disappearance of the last crystal were observed as the temperature was slowly raised, while in others the vapor pressure curve was followed and the break point observed in passing from one phase system to another. In still other cases, the melting point curves were determined.

Tetra-*n*-butylammonium Hydroxide, $(C_4H_9)_4NOH \cdot 31H_2O$.—A quantity of tetra-*n*-butylammonium hydroxide was prepared as described under careful exclusion of carbon dioxide. Several samples of the solution were taken for analysis and the remainder was introduced into the cell and attached to the vacuum system. Melting temperatures were determined until a maximum was reached at 30.2° where the mass melted homogeneously. The weight of the cell and homogeneously melting solid was taken and the results computed as follows: weight hydrated base, 2.7681; anhydrous base, 0.8780; moles anhydrous base, 0.003386; moles water, 0.1050; moles base/moles water, 1/31.01.

$(C_4H_9)_4NOH \cdot 4H_2O$.—On withdrawing water from the hydrate described above, the entire mass liquefied and on continued withdrawal of water, a new solid phase separated. This phase had a sharp melting point at 26°. Its composition was determined as follows: wt. hydrated base, 1.1225; anhydrous base, 0.8780; moles anhydrous base, 0.003386; moles water, 0.01358; moles base/moles water, 1/4.01.

$(C_4H_9)_4NOH \cdot 2H_2O$.—On dehydration of the tetrahydrate, another solid appeared which approximated the dihydrate in composition. However, the base is not stable when this hydrate is subjected to the action of a vacuum pump. With the sample used in the preceding experiments, most of the material was lost in the course of pumping, and upon opening the tube the presence of tributylamine was detectable. Accordingly, another sample was prepared and when no perceptible liquid was left in the solid mass, the tube was weighed. The results follow: wt. hydrated base, 1.6301; anhydrous base, 1.4200; moles anhydrous base, 0.00549; moles water, 0.01167; moles anhydrous base/moles water, 1/2.12.

Tetra-*n*-butylammonium Fluoride, $(C_4H_9)_4NF \cdot {}_{18}H_2O$.—A quantity of tetra-*n*-butylammonium fluoride was prepared by titrating a solution of the hydroxide with hydrofluoric acid. After taking samples of the solution for analysis, the remainder was introduced into the cell and the composition of the hydrate determined as in the case of the hydroxide. The homogeneously melting hydrate had a melting point of 37°. The tube was weighed and the composition of the hydrate determined as follows: wt. hydrated fluoride, 8.9582; anhydrous fluoride, 3.9832; moles anhydrous fluoride, 0.01526; moles water, 0.2764; moles fluoride/moles water, 1/18.11. On further dehydration of the octadecahydrate, the whole mass liquefied and there was no evidence of the formation of any other hydrate on continued dehydration down to the pure salt.

Tetraisoamylammonium, Hydroxide, $(C_5H_{11})_4NOH \cdot 32H_2O$.—A solution of this hydroxide was prepared as described above and introduced into a cell of the Erlenmeyer form. The advantage of a container of this type is that the thickness of the liquid layer is small and the surface large and it is, therefore, easier to establish equilibrium than in the case of a narrower tube with a greater depth of liquid. To determine the composition of the hydrate in this case, pressures were observed somewhat above and somewhat below the point at which the entire mass in the tube appeared to be solid, the water content of the cell being determined after each observation. Water was then withdrawn or introduced and the range between the upper and lower pressures gradually narrowed until it approximated the composition of the hydrate. The pressures observed at 20° in millimeters of oil and the mean composition of the system in moles of water per mole of base follow:

Moles of water/base	38.5*	44.3	31.4*	34	32.9
p, mm. of oil	277	274	<228	267	264
Moles of water/base	31.4	32.3*	31.99*	32.01*	
p, mm. of oil	218	266	217	>259	

The pressure readings on the oil manometer may be converted to millimeters of mercury by multiplying by the factor 0.0633.

Not all the pressures as read are precise equilibrium values but observations in any one case were continued long enough to ensure that the pressures corresponded either to the equilibrium of higher or of lower pressure. The upper pressure, which is in the neighborhood of 265 mm., is the vapor pressure of the more dilute solution in equilibrium with the base hydrate, while the lower pressure of approximately 218 mm. is the pressure of the more concentrated solution in equilibrium with the same base hydrate (at 25°). The composition of all the starred values was directly determined by weighing the cell and is, therefore, accurate. The other values were determined by taking account of the amount of water introduced or removed and although sufficiently accurate for the purpose, they are not as precise as the starred values. The data for the last two values are given: wt. of hydrated base, 5.8587, 5.8602; anhydrous base, 2.0717; moles water/moles base, 31.99, 32.01. The hydrate melts homogeneously at 31°.

$(C_5H_{11})_4NOH \cdot 4H_2O$.—On dehydrating the hydrate described above, the entire mass liquefied and upon further dehydration, crystals appeared which were evidently the tetrahydrate and which melted at 57.5°. They were not entirely stable at room temperature under the action of the pump. Assuming that the base decomposes to tertiary amine, olefin and water[2] and that the tertiary amine remains behind when the hydrate decomposes, the composition of the hydrate may be determined by titrating the strong base and weighing the cell and its contents. The correction due to decomposition was of the order of 10%. Following are the results for a typical determination: mmoles. base original sample, 6.659; mmoles. base after

(2) Meyer and Jacobson, "Lehrbuch der organischen Chemie," Vol. I, part 1, Leipzig, 1907, p. 378.

decomposition, by titration, 6.124; mmoles. base decomposed, 0.4568; wt. final product (hydrate and amine), 2.4571; wt. of amine (equivalent to 0.4568 mmoles.), 0.1038; wt. hydrated base, 2.3533; wt. anhydrous base (6.124 mmoles.), 1.9254; wt. water, 0.4279; mmoles. water, 23.75; moles base/moles water, 1/3.88.

Tetra-*n*-amylammonium Hydroxide, $(C_5H_{11})_4NOH \cdot 4H_2O$. —With this base there was found no evidence of the existence of a high hydrate. A solid ultimately was formed whose composition approximated that of the tetrahydrate and which proved unstable under the action of the pump. Making corrections for the amount of the base decomposed, and assuming that the free amine resulting was not lost, the following results were obtained: mmoles. original base, 8.273; mmoles. after decomposition, 7.676; mmoles. of water in final hydrate, 29.5; moles base/moles water, 1/3.9.

Tetramethylammonium Hydroxide, $(CH_3)_4NOH \cdot 5H_2O$. —On concentrating a solution of this base, the first hydrate that appeared was the already known pentahydrate.[3] The results follow: wt. anhydrous base, 0.6402; hydrated base, 1.2590; hydrate water, 0.6188; moles base/moles water, 1/4.9.

Tetra-*n*-propylammonium Hydroxide.—Although the existence of a heptahydrate of this base is reported in the literature,[4] all attempts to obtain a crystalline product with this base failed. In one case, the liquid having a composition closely approximating that of the heptahydrate was left at sub-zero temperature overnight without the appearance of crystals. On further concentrating the solution, the product decomposed rather suddenly at room temperature.

Ethyltri-*n*-butylammonium Hydroxide.—The behavior of a solution of this base resembled that of tetra-*n*-propylammonium hydroxide on concentration. No crystals could be obtained and when the concentration of the solution approximated that of three moles of water per mole of base, decomposition occurred.

Tetra-*n*-butylammonium Oxalate, $[(C_4H_9)_4N]_2C_2O_4 \cdot 38H_2O$.—The salt was prepared by metathesis of silver oxalate and tetrabutylammonium iodide. It was purified by recrystallizing three times from water at 0°. The composition of the hydrate was determined by the vapor pressure method; three determinations gave the following values for the number of moles of water per mole of salt: 37.5, 37.6, 37.9. The hydrate melted between 20 and 25°.

Tetra-*n*-butylammonium Formate, $(C_4H_9)_4NCHO_2 \cdot 33H_2O$.—This salt has a very flat melting point curve with a maximum near 12.5° and 33 moles of water. The composition was also checked by the vapor pressure method which yielded the same value but the difference between the upper and the lower vapor pressures was extremely small.

Tetra-*n*-butylammonium Bromide, $(C_4H_9)_4NBr \cdot 26H_2O$. —The salt was prepared by digesting tetra-*n*-butylammonium iodide with an excess of silver bromide in aqueous solution. After evaporating the solution, the salt was recrystallized from ethyl acetate, melting point 113°. The melting point curve of solutions of this salt is much less flat than that of the formate and has a maximum at 14.5° at a composition corresponding to 26 molecules of water.

(3) Walker and Johnston, *J. Chem. Soc.*, **87**, 958 (1905).
(4) Crichton, *ibid.*, **91**, 1796 (1907).

Other Hydrated Salts.—Rough determinations were made with some other salts. Tetraisoamylammonium formate yielded a product melting at 15–20° with a composition in the neighborhood of 50 moles of water per mole of salt. Tetra-*n*-butylammonium acetate yielded a hydrate melting at 10–15° and containing 60 molecules of water. Tetra-*n*-butylammonium propionate yielded a hydrate melting at 17° and containing 50 molecules of water. Tetra-*n*-butylammonium benzoate yielded a hydrate melting at 3.5° and containing approximately 35 molecules of water. Tetra-*n*-butylammonium nitrate yielded a hydrate melting at 5.8° and containing 27 molecules of water. Tetra-*n*-butylammonium chloride yielded a hydrate melting at 15° and containing 30 molecules of water. Tetra-*n*-butylammonium sulfate and tetra-*n*-butylammonium chromate both yielded hydrates but their approximate composition was not determined.

Tetra-*n*-butylammonium thiocyanate, picrate and cyanide were found to be difficultly soluble in water and yielded no hydrates. Tetra-*n*-propylammonium formate, tetra-*n*-amylammonium formate, tetra-*n*-amylammonium acetate, methyltri-*n*-butylammonium formate and propyltri-*n*-butylammonium formate yielded no hydrates. Tetra-*n*-propylammonium fluoride deposited a solid from fairly concentrated aqueous solution, apparently in anhydrous form.

Summary

The highly soluble salts of tetra-*n*-butylammonium and tetraisoamylammonium ions quite generally form hydrates containing above 15 molecules of water and having relatively high melting points. The following hydrates have been accurately determined: $(n\text{-}C_4H_9)_4NOH \cdot 31H_2O$, m. p. 30.2°; $(n\text{-}C_4H_9)_4NF \cdot 18H_2O$, m. p. 37°; $(i\text{-}C_5H_{11})_4NOH \cdot 32H_2O$, m. p. 31°; $[(n\text{-}C_4H_9)_4N]_2C_2O_4 \cdot 38H_2O$, m. p. 20–25°; $(n\text{-}C_4H_9)_4NCHO_2 \cdot 33H_2O$, m. p. 12.5°; $(n\text{-}C_4H_9)_4NBr \cdot 26H_2O$, m. p. 14.5°.

Other salts yielding high hydrates whose composition and melting points have been less accurately determined are the following: $(i\text{-}C_5H_{11})_4NCO_2 \cdot 50H_2O$, m. p. 15–20°; $(n\text{-}C_4H_9)_4NCH_3CO_2 \cdot 60H_2O$, m. p. 10–15°; $(n\text{-}C_4H_9)_4NC_2H_5CO_2 \cdot 50H_2O$, m. p. 17°; $(n\text{-}C_4H_9)_4NC_6H_5CO_2 \cdot 35H_2O$, m. p. 3.5°; $(n\text{-}C_4H_9)_4NNO_3 \cdot 27H_2O$, m. p. 5.8°; $(n\text{-}C_4H_9)_4NCl \cdot 30H_2O$, m. p. 15°. Tetra-*n*-butylammonium sulfate and tetra-*n*-butylammonium chromate both yield high hydrates but their approximate composition was not determined.

Higher hydrates could not be found in the case of tetramethylammonium hydroxide, tetra-*n*-propylammonium hydroxide, tetra-*n*-amylammonium hydroxide and ethyltri-*n*-butylammonium hydroxide.

PROVIDENCE, RHODE ISLAND RECEIVED JANUARY 18, 1940

[CONTRIBUTION FROM THE METCALF RESEARCH LABORATORY OF BROWN UNIVERSITY]

Quaternary Ammonium Salts with Anions Containing Triphenylboron

BY D. LEIGH FOWLER* AND CHARLES A. KRAUS

Introduction

In solvents other than liquid ammonia, it is difficult to obtain negative ions with more than one organic group attached to the central atom. Nevertheless, salts of such ions are highly desirable for study in determining the influence of constitutional factors on the properties of electrolytes. Hawes found that sodium and potassium amides react with triphenylboronammine in liquid ammonia to form salts in which the NH_2^- ion is joined to boron by a coördinated linkage.[1] He measured the conductance of these salts in liquid ammonia[2] and found that the ammidotriphenylboron ion has a very low mobility and that its salts are exceptionally highly dissociated, the sodium salt having a dissociation constant of 150×10^{-4}. In solvents other than ammonia, it is necessary that the electrolytes have a high degree of stability, which is not the case with the ammidotriphenylboron salts. It seemed probable, however, that other small ions, particularly the fluoride and the hydroxyl ions, would coördinate with triphenylboron and that the resulting salts would be stable. It is well known that the lower alkyl boranes are absorbed by sodium or potassium hydroxide.

The general procedure in preparing the desired salts was to treat the quaternary ammonium fluoride or hydroxide with triphenylboronammine in alcohol solution. The ammonia is replaced by the fluoride or the hydroxyl ion and the salts are recovered from the solvent by crystallization.

Experimental

Tetramethylammonium Triphenylborofluoride, $(CH_3)_4NF \cdot B(C_6H_5)_3$.—The triphenylboronammine used was a stock sample which had been prepared in this Laboratory. Its preparation has been described by Hawes.[1] Tetramethylammonium hydroxide was prepared from the bromide by means of freshly precipitated silver oxide and the resulting base was titrated with hydrogen fluoride after separating from the solid material. The fluoride is very soluble in water but it may be obtained in anhydrous form by concentrating the aqueous solution and thereafter gradually heating to 115° while exhausting the system with a pump. The solid which is formed under these conditions reaches constant weight and is evidently anhydrous since a small sample of the salt was found to decompose at 180° in accordance with the earlier observations of Lawson and Collie.[3]

Equivalent quantities of tetramethylammonium fluoride and triphenylboronammine are introduced into alcohol, in which both are soluble, and the solution is refluxed for several hours during which time ammonia is evolved and crystals are formed. After cooling, the crystals are separated from the supernatant liquid and recrystallized from alcohol; melting point 175–177°.

The compound was analyzed for boron by the method of Booth.[4] The sample was warmed with a few cubic centimeters of concentrated sulfuric acid in a distilling flask. Thereafter, approximately 50 cc. of carefully dried methyl alcohol was added and the mixture was warmed for a few minutes to permit the reaction between the alcohol and the boric acid to complete itself. Thereafter, successive fractions of about 10 cc. of the methyl alcohol were distilled through a fractionating column into a suitable receiver until no further boron was carried over. Two or three fractions were generally sufficient. The boron was determined after hydrolysis of the methyl borate by titration with sodium hydroxide in the presence of mannitol. Sample, 0.2192, 0.1870; cc. 0.04413 *N* sodium hydroxide, 14.86, 12.62; % B found, 3.237, 3.222; calcd. for $C_{22}H_{27}BNF$, 3.229. The fluorine content of the compound was determined by the method of Allen and Furman[5] in which triphenyltin chloride is used as the precipitant. In order to break the fluorine–boron linkage, the compound was first hydrolyzed with sodium hydroxide solution, in which process it dissolved completely. However, when the solution was neutralized with hydrochloric acid, a precipitate appeared which was removed by filtration. The neutralized solution was then treated with triphenyltin chloride according to the directions of Allen and Furman. Sample, 0.3144, 0.3037; triphenyltin fluoride, 0.3445, 0.3398; % F found, 5.645, 5.764; calcd. for $C_{22}H_{27}BNF$, 5.671.

Tetrabutylammonium Triphenylborofluoride, $(C_4H_9)_4NF \cdot B(C_6H_5)_3$.—Tetrabutylammonium fluoride was prepared from tetrabutylammonium iodide in the same manner as was tetramethylammonium fluoride from the corresponding bromide. The anhydrous salt, together with triphenylboronammine, was dissolved in alcohol where reaction took place readily with the formation of crystals of the desired compound. After separating, these were recrystallized from ethyl alcohol and were found to melt at 161–162°. The compound was found to be stable in air.

Analyses were carried out as in the case of the tetramethylammonium compound. B: sample, 0.1932, 0.2101; cc. 0.04413 *N* sodium hydroxide, 8.68, 9.76; % B found,

* This paper is based on a portion of a thesis presented by D. L. Fowler in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Graduate School of Brown University, 1935.

(1) W. W. Hawes, Master's Thesis, Brown University, 1928.

(2) W. W. Hawes, THIS JOURNAL, **55**, 2776 (1933).

(3) Lawson and Collie, *J. Chem. Soc.*, **53**, 627 (1888).

(4) R. B. Booth, Thesis, Brown University, 1934.

(5) Allen and Furman, THIS JOURNAL, **54**, 4425 (1932).

2.145, 2.218; calcd. for $C_{34}H_{51}BNF$, 2.150. F: sample, 0.3133, 0.3171; triphenyltin fluoride, 0.2275, 0.2285; % F found, 3.741, 3.712; calcd. for $C_{34}H_{51}BNF$, 3.776.

Tetramethylammonium Triphenylborohydroxide Monoalcoholate, $(CH_3)_4NOH\cdot B(C_6H_5)_3\cdot C_2H_5OH$.—Tetramethylammonium hydroxide was prepared by treating an aqueous solution of tetramethylammonium bromide with moist silver oxide. After separating from the silver bromide and excess silver oxide, the solution was concentrated. The residual water was removed by pumping through a phosphorus pentoxide tube while at the same time placing the tube containing the base in a bath whose temperature was gradually raised to 100°. A small sample of the final product was found to decompose at 125–130°, which corresponds to the range given by Walker and Johnston[6] for the monohydrate. All attempts to remove the last molecule of water were unsuccessful. It should be stated that all operations described above were carried out under strict exclusion of carbon dioxide. The reaction between the monohydrate of tetramethylammonium hydroxide and triphenylboronammine was carried out in ethyl alcohol, as in the case of the fluoride. The product formed immediately on warming the solution. After separating from the alcohol, it was recrystallized from the same solvent. When heated to 230°, it puffed up slightly but did not melt until the temperature reached 359–360°, where it decomposed upon melting. This compound was not analyzed directly but was quantitatively converted to the corresponding monohydrate which was analyzed as will be described in the following section.

Tetramethylammonium Triphenylborohydroxide Monohydrate, $(CH_3)_4NOH\cdot B(C_6H_5)_3\cdot H_2O$.—When the alcoholate described in the preceding paragraph was treated with water for a few minutes and immediately pumped dry, a substance resulted which melted at 185–187°. When this, in turn, was dissolved in absolute alcohol and dried, the compound again melted at 360°. Evidently the alcoholate and the hydrate may be converted one to the other by treatment with the appropriate solvent. That the conversion is quantitative is shown by the following figures: wt. original alcoholate, 0.0937, 0.0910; wt. hydrate, 0.0870, 0.0845; observed loss in wt., 0.0067, 0.0065; calcd. loss, 0.0069, 0.0067. Wt. original hydrate, 0.2504; wt. alcoholate, 0.2705; observed gain in wt., 0.0201; calcd. gain, 0.0200.

Samples of the hydrated compound were analyzed for boron as described above. The results were: sample, 0.1915, 0.2182; cc. sodium hydroxide (0.04413 *N*), 12.30, (0.0657 *N*), 9.32; % B found, 3.067, 3.036; calcd. for $C_{22}H_{30}BNO_2$, 3.082.

In order to determine the amount of the base present in the compound, a known quantity of dilute hydrochloric acid, slightly in excess of that required to neutralize the base, was added to the salt and the resulting solution was refluxed for a couple of hours. At the end of this process, the salt had broken down and dissolved completely in the hot acid solution. Upon cooling, some solid precipitated, which was filtered off, after which the solution was titrated with standard alkali. Sample, 0.2501, 0.3279; cc. hydrochloric acid (0.0577 *N*), 12.38, (0.1084 *N*), 8.84; % OH found, 4.858, 4.970; calcd. for $C_{22}H_{30}BNO_2$, 4.845.

(6) Walker and Johnston, *J. Chem. Soc.*, **87**, 958 (1905).

Tetrabutylammonium Triphenylborohydroxide, $(C_4H_9)_4NOH\cdot B(C_6H_5)_3$.—This compound was prepared by two methods; the first was similar to that used in the case of the tetramethylammonium salts. This method, however, is disadvantageous because of the difficulty experienced in dehydrating tetrabutylammonium hydroxide. Accordingly, the base was prepared in absolute alcohol solution by allowing equivalent quantities of tetra-*n*-butylammonium chloride and potassium hydroxide to react. After the potassium chloride had been separated by filtration, an equivalent amount of the triphenylboronammine was added. The product, after recrystallization from alcohol, was found to melt at 143.5–145.5°. This compound, like those previously described, was perfectly stable in the atmosphere.

Analyses were carried out as in the case of the tetramethylammonium salt. B: sample, 0.1980, 0.1476; cc. 0.04413 *N* sodium hydroxide, 9.01, 6.88; % B found, 2.173, 2.226; calcd. for $C_{24}H_{52}BNO$, 2.159. Base: sample, 0.2205, 0.2916; cc. 0.0577 *N* hydrochloric acid, 7.49, 10.05; % OH found, 3.333, 3.382; calcd. for $C_{34}H_{52}BNO$, 3.393.

Some Other Salts.—In general, it is only the small ions, such as NH_2^-, OH^- and F^-, which form stable complexes with triphenylboron. Neither tetramethylammonium chloride nor tetramethylammonium bromide forms complexes with triphenylboron. Alcohol solutions of these salts brought together with amminotriphenylboron show no reaction and the original materials are recovered from solution unchanged.

Potassium cyanide reacts with amminotriphenylboron in alcohol solution. On addition of petroleum ether, hair-like crystals are precipitated which decompose in the neighborhood of 300°. They react vigorously with water. Sodium phenolate shows little reaction with amminotriphenylboron in liquid ammonia solution. Most of the reactants are recoverable. Sodium benzhydrolate reacts with amminotriphenylboron in liquid ammonia. The white solid which results upon evaporation of the solvent oxidizes slowly in air and is unstable in organic solvents at higher temperatures. Sodium triphenylcarbinolate reacts with amminotriphenylboron in liquid ammonia. The product may be recrystallized from benzene and it seems to be stable in air and in organic solvents at ordinary temperatures. The potassium salt exhibits similar properties. Sodium phenylacetylate reacts with amminotriphenylboron in liquid ammonia with the formation of a white solid which shows low stability when dissolved in organic solvents under ordinary conditions; the solutions develop color.

Summary

On treating amminotriphenylboron with quaternary ammonium hydroxides or fluorides, complex ions are formed in which the hydroxyl or the fluoride ion is coördinated with triphenylboron. The salts are stable in air. The following salts have been prepared: $(CH_3)_4NF\cdot B(C_6H_5)_3$, $(n\text{-}C_4H_9)_4NF\cdot B(C_6H_5)_3$, $(CH_3)_4NOH\cdot B(C_6H_5)_3\cdot C_2H_5OH$, $(CH_3)_4NOH\cdot B(C_6H_5)_3\cdot H_2O$, $(n\text{-}C_4H_9)_4NOH\cdot B(C_6H_5)_3$.

PROVIDENCE, R. I. RECEIVED JANUARY 18, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF NOTRE DAME]

Alkylation of Benzene with Alcohols, Boron Fluoride and Assistants[1]

BY N. F. TOUSSAINT AND G. F. HENNION

Introduction

The alkylation of benzene with monohydric alcohols has received relatively little attention. The reactions proceed only in the presence of strong dehydrating agents such as zinc chloride,[2] sulfuric acid,[3] aluminum chloride,[4] and boron fluoride.[5]

Disadvantages of the reported procedures are a frequent need for autoclave or sealed tube methods and/or excessive amounts of condensing agent; products are often impure and yields unsatisfactory. Furthermore, these methods have not been applied to the higher alcohols now available from the hydrogenolysis of fats.

Because long-chain alkylbenzenes have possible utility in the field of detergents and wetting agents the authors have reinvestigated alcohol–benzene reactions with boron fluoride.[5] It was desired particularly to apply the method to various primary alcohols and to improve yields of monoalkyl products. It was soon observed that boron fluoride is assisted remarkably in these reactions by various acidic dehydrating agents as phosphorus pentoxide, sulfuric acid and benzenesulfonic acid. The effect of these secondary condensing agents is particularly marked with the primary alcohols. Data for a number of experiments are given in Table I.

Alkylation apparently occurs without carbon skeleton rearrangement. However, only secondary and tertiary alkyl benzenes have been made in this manner. While the reaction mechanism is in doubt, the products are those which would be formed by dehydration of the alcohol to olefin and addition of benzene according to Markownikoff's rule. The dialkyl derivatives are the para compounds.[5] Methylation and ethylation were unsuccessful.

(1) Paper XXIII on organic reactions with boron fluoride; previous paper, THIS JOURNAL, **61**, 1463 (1939).

(2) Goldschmidt, *Ber.*, **15**, 1066, 1425 (1882).

(3) Brochet and Le Boulenger, *Compt. rend.*, **117**, 235 (1898); Verley, *Bull. soc. chim.*, [3] **19**, 67 (1898); Boedker, *ibid.*, [3] **31**, 966 (1904); Meyer and Bernhauer, *Monatsh.*, **53**, 721 (1929); Kirrmann, *Bull. soc. chim.*, [4] **51**, 451 (1932); Kirrmann and Graves, *ibid.*, [5] **1**, 1494 (1934).

(4) Huston, *et al.*, THIS JOURNAL, **38**, 2531 (1916); **40**, 785 (1918); **48**, 1955 (1926); **56**, 2432 (1934); Tzukervanik, *J. Gen. Chem.* (*U. S. S. R.*), **5**, 117, 764 (1935); **31**, 5779 (1937); Norris and Ingraham, THIS JOURNAL, **60**, 1421 (1938).

(5) Sowa and McKenna, *ibid.*, **59**, 470 (1937).

Physical properties for the compounds are given in Table II. Analyses for octyl- and dodecylbenzene are given in Table III.

Procedure

Reagents.—Boron fluoride was purchased from the Harshaw Chemical Co. *n*-Octyl and *n*-dodecyl alcohols were furnished by the du Pont Co. Other alcohols were from Eastman Kodak Co. Benzenesulfonic acid was prepared as previously described.[6]

***s*-Butylbenzene (Expt. 10).**—Two moles (156 g.) of benzene and 0.5 mole (37 g.) of *n*-butyl alcohol were placed in a one-liter three-necked flask equipped with a reflux condenser and motor-driven mercury-sealed stirrer. The solution was cooled in a bath of cold water and boron fluoride admitted, with stirring, until 0.5 mole (34 g.) had been absorbed. Then 0.125 mole (17.7 g.) of phosphorus pentoxide was added quickly. The mixture was warmed *slowly*, with stirring, to reflux temperature and soon became homogeneous. On continued heating the solution became turbid and stratified into two layers when agitation was discontinued. Further heating caused gradual diminution in the volume of the lower layer. After heating for three hours the layers were separated and the upper one washed, neutralized, dried and fractionally distilled. There was obtained 50 g. (74.5%) of *s*-butylbenzene and 3 g. (6.3%) of *p*-di-*s*-butylbenzene.

***s*-Amylbenzene (Expt. 32).**—Sulfuric acid (25 g., 94% acid) was added to a solution of *n*-amyl alcohol (44 g., 0.5 mole) in benzene (312 g., 4.0 moles) previously saturated with boron fluoride (34 g., 0.50 mole). After heating for five and one-half hours the upper layer was separated and treated as above. Distillation gave 59.2 g. (80%) of *s*-amylbenzene.

Miscellaneous.—All experiments with phosphorus pentoxide gave homogeneous solutions after brief heating. Upon further reaction these separated into two layers, except in cases where dodecyl alcohol was used. Dodecylbenzene was distilled, *in vacuo*, from the crude reaction mixture, then washed, dried and redistilled.

In the sulfuric acid experiments with *n*-butyl alcohol (Expts. 25–29) three layers appeared after heating. The lowest layer was removed in each case and water added to the remaining layers. The hydrocarbon was then removed and treated in the conventional manner.

A condition of temporary homogeneity was observed only in experiments with phosphorus pentoxide. With sulfuric acid and benzenesulfonic acid separate phases persisted throughout the reaction periods.

Frequently dodecylbenzene gave troublesome emulsions when first washed with water. The emulsions were broken by addition of ether.

In the experiments with benzenesulfonic acid it was

(6) Thomas, Anzilotti and Hennion, *Ind. Eng. Chem.*, **32**, 408 (1940).

TABLE I

ALKYLATION OF BENZENE WITH ALCOHOLS IN THE PRESENCE OF BORON FLUORIDE

Expt.	Moles ROH	Moles C_6H_6	Moles BF_3	Moles Asst. reagent	Time, hr.	Yield, % Mono	Yield, % Di
	A. Assisted by Phosphorus Pentoxide						
1	0.5 *n*-C_3	2.0	0.5	0	5	5.4	0
2	.5 *n*-C_3	2.0	.5	.12	3	58.5	13
3	.5 *i*-C_3	2.0	.5		3	40.0	19.8
4	.5 *i*-C_3	2.0	.5	.12	3	37.5	19.8
5	.5 *n*-C_4	1.0	.5		4	0	0
6	.5 *n*-C_4	2.0	.4	.12	3	37.4	6.3
7	.5 *n*-C_4	2.0	.33	.17	3	55.3	10.5
8	.5 *n*-C_4	2.0	.5	.12	3	73.2	8.3
9	.5 *n*-C_4	1.0	.5	.12	2.5	73.2	14.7
10	.5 *n*-C_4	2.0	.5	.12	3	74.5	6.3
11	.5 *s*-C_4	2.0	.5		3	51.5	11.8
12	.5 *s*-C_4	2.0	.5	.12	3	46.2	12.7
13	.5 *i*-C_4	2.0	.5		3	47.8	14.7
14	.5 *i*-C_4	2.0	.5	.12	3	56.7	11.8
15	.5 *t*-C_4	2.0	.25		3	28.4[a]	..
16	.5 *t*-C_4	2.0	.25	.12	3	24.6[a]	..
17	.25 *n*-C_5	2.0	.25		5.5	0	0
18	.25 *n*-C_5	2.0		.07	5.5	0	0
19	1.0 *n*-C_5	1.0	1.0	.25	1	19.6	10.5
20	0.5 *n*-C_5	0.5	0.5		2	32.2	26.8
21	2.0 *n*-C_5	4.0	2.0	.5	2	66.4	14.2
22	0.5 *n*-C_5	4.0	0.5	.12	6	85.0	0
23	1.0 *n*-C_8	8.0	1.0	.25	3	79.0	0
24	0.5 *n*-C_{12}	4.0	0.5	.25	16	33.3	0
	B. Assisted by Sulfuric Acid						
25	0.5 *n*-C_4	1.0	0.5	0.5	4	12.7	11.0
26	.5 *n*-C_4	2.0	.75[b]	1.0	4	22.4	4.2
27	.5 *n*-C_4	2.0	.5	1.5	4	19.5	0
28	.5 *n*-C_4	2.0	.5	0.5[c]	3	37.4	0
29	.5 *n*-C_4	2.0	.5	1.0[c]	3	7.5	0
30	1.0 *n*-C_5	1.0	.5	0.5	2	30.2	9.1
31	0.5 *n*-C_5	4.0		.75	5.5	20.2[d]	0
32	.5 *n*-C_5	4.0	.5	.25	5.5	80.0	0
33	.5 *n*-C_{12}	2.0	.5	1.0	10	46.4	0
	C. Assisted by Benzenesulfonic Acid						
34	0.5 *n*-C_4	2.0	0	0.5	4	0	0
35	1.0 *n*-C_4	4.0	1.5[e]	1.0	4	68.5	0
36	0.5 *n*-C_4	2.0	0.5	0.5	4	63.0	0
37	.5 *n*-C_5	2.0	.5	.5[f]	5.5	19.5	7.3
38	.5 *n*-C_{12}	2.0	.5	.5	10	44.6	0

[a] Contains polymer, presumably triisobutylene. [b] Added H_2SO_4 before BF_3. [c] 100% H_2SO_4, others were 94% H_2SO_4. [d] After first distillation. [e] Includes $BF_3 \cdot H_2O$ from preparation of benzenesulfonic acid. [f] Recovered from Exp. no. 35.

TABLE II

PHYSICAL CONSTANTS OF PRODUCTS

Expt.	Alkylbenzene	Boiling point, °C.	Mm.	d^{20}	$n^{20}D$
2	*i*-C_3	151–2	744	0.8619	1.4912
10	*s*-C_4	170–2	744	.8624	1.4900
13	*t*-C_4	165–9	746	.8660	1.4918
22	*s*-C_5	189–90	744	.8621	1.4890
23	*s*-C_8	123–5	20	.854	1.4837
24	*s*-C_{12}	182–4	20	.855	1.4818
2	*p*-di-*i*-C_3	200–8	744	.860	1.490
8	*p*-di-*s*-C_4	236–8	744	.862	1.489
13	*p*-di-*t*-C_4	234–6	746	m. p., 77°	
21	*p*-di-*s*-C_8	141–6	20	.863	1.495

TABLE III

ANALYSES

Expt.	Alkylbenzene	%, C Calcd.	%, C Found	% H Calcd.	% H Found	Mol. wt. Calcd.	Mol. wt. Found
23	*i*-C_8H_{17}	88.4	88.6	11.6	11.0	190	182
24	*i*-$C_{12}H_{25}$	87.6	88.0	12.3	12.2	246	243

found possible to recover boron fluoride, as the dihydrate, from the acid layers by addition of the calculated amount of water and distillation.[6] Boron fluoride was thus recovered as $BF_3 \cdot 2H_2O$, b. p. 91° at 25 mm., from Expt. 35 in 95% yield.

Further work is in progress.

Summary

1. Certain acidic dehydrating agents assist boron fluoride as a condensing agent in the alkylation of benzene with primary alcohols.

2. Data are given for thirty-eight experiments, showing the influence of conditions upon yields of products.

3. Normal and secondary alcohols give secondary alkylbenzenes. Iso and tertiary butyl alcohol gave *t*-butylbenzene. Dialkylation proceeds mainly para.

4. Alcohols as high as dodecyl have been used successfully.

NOTRE DAME, INDIANA RECEIVED FEBRUARY 23, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

The Chlorination and the Structure of Acetylketene

BY CHARLES D. HURD AND J. L. ABERNETHY

The recent paper[1] by Boese on "diketene" mentions that this substance "rapidly absorbs chlorine at low temperatures to yield γ-chloroacetoacetyl chloride" and states that it is "stable only at low temperatures and cannot be purified by distillation." Since no details were listed, this note is submitted in view of our similar work on the same compound.

Chlorine was passed into an ice-cold, vigorously-stirred solution of 7 cc. of acetylketene in 20 cc. of carbon tetrachloride until there was a 6-g. increase in weight. The mixture was slightly yellow in color. Distillation of the solvent with a steam-bath left an orange-colored residue of chloroacetoacetyl chloride, $ClCH_2COCH_2COCl$, which was vacuum distilled. Extensive decomposition occurred, but 1.5 cc. of the acid chloride was obtained at 93–96° (8 mm.), or 117–119° (17 mm.). The distillate was orange colored and fumed in moist air. A black tar remained in the distilling flask. These physical constants were obtained for the chloroacetoacetyl chloride: d^{20}_4 1.4397; $n^{20}D$ 1.4860; mol. rotation, calcd. 30.77, found 30.89.

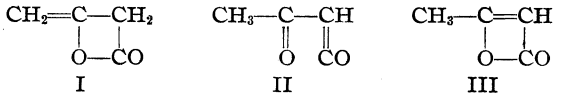
Anal. Calcd. for $C_4H_4O_2Cl_2$: Cl, 45.7. Found: Cl, 45.2, 45.1.

Chloroacetoacetyl chloride was converted to ethyl chloroacetoacetate, $ClCH_2COCH_2COOC_2H_5$, as follows. Five cc. of acetylketene in 30 cc. of carbon tetrachloride was treated with chlorine until 4.5 g. had been absorbed. Then, without distillation, the solution was poured slowly into an excess of absolute alcohol at 0°. On distillation, 6 cc. of the ethyl ester was collected at 117–119° (17 mm.). This ester has been made in other ways by several investigators.[2]

Chloroacetoacetanilide, $ClCH_2COCH_2CONHC_6H_5$, was obtained by mixing pure chloroacetoacetyl chloride with an equivalent amount of aniline in benzene. The aniline hydrochloride was removed by washing with water. Then the benzene was distilled off and the resulting anilide was crystallized from ether. The melting point was 140–141°.

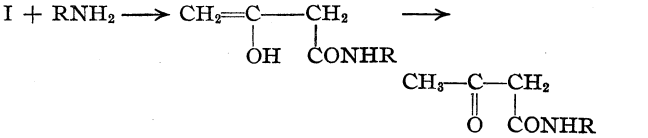
Anal. Calcd. for $C_{10}H_{10}O_2NCl$: N, 6.61. Found: N, 6.75, 6.71.

Boese adopts vinylaceto-β-lactone (I) as a preferred structure for ketene dimer. With



I II III

(I) addition reactions with alcohols or amines may be explained by assuming reaction at the lactone position, followed by tautomerization



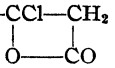
Hydrogenation to butyro-β-lactone must involve addition at the double bond. Neither of these reactions are critical for purposes of structure

(1) Boese, *Ind. Eng. Chem.*, **32**, 20 (1940).

(2) Lespieau, *Compt. rend.*, **138**, 422 (1904); Picha, Doht and Weisl, *Monatsh.*, **27**, 1247 (1906); Schlotterbeck, *Ber.*, **42**, 2570 (1909); Alexandrow, *ibid.*, **46**, 1022 (1913).

proof because they may be explained also from acetylketene (II) or its resonance isomer crotono-β-lactone (III).

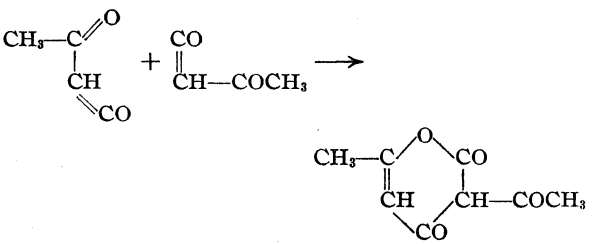
When the dimer is halogenated, chlorine presumably adds to the double bond. If structure II is selected then a subsequent rearrangement is involved to explain the formation of chloroacetoacetyl chloride which is actually produced. Since ethyl acetobromoacetate, $CH_3COCHBrCOOC_2H_5$, is known[3] to rearrange to ethyl bromoacetoacetate, $CH_2BrCOCH_2COOC_2H_5$, such a rearrangement for the corresponding acid chloride also seems plausible. Indeed it may be assumed that the COCl or COBr groups promote a more rapid rearrangement than the $COOC_2H_5$ group.

Formula I, in the halogenation reaction, also calls for rearrangement because  would represent the initial addition product at the double bond. Less readjustment is necessary than with II, however, because chlorine alone is involved, instead of hydrogen and chlorine. This seems to be the strongest evidence in favor of I. Unfortunately for its case, halogenation evidence is unreliable so frequently that one hesitates to trust it unless it is supported by other and better evidence.

An example in point is furfuryl chloride. By rules of metathesis, one would expect it to yield furylacetonitrile in its reaction with sodium cyanide. Instead, the substance obtained[4] is 5-methyl-2-furonitrile. Again, isobutylene and chlorine[5] yield chiefly methallyl chloride instead of isobutylene dichloride. Many other instances of irregularity with halogens might be cited.

The recently determined[6] value for the parachor of ketene dimer is more favorable to the equilibrium mixture of II $\rightleftarrows$ III than to I, II or III taken individually. The observed parachor at 25° is 188.0. The calculated parachors for I, II and III, respectively, are 182.4, 197.2, and 182.4.

Polymerization of ketene dimer to dehydroacetic acid (ketene tetramer) is far more simply explained from II than from I. From II, it is but an addition of the Diels–Alder type



From I, it is necessary to assume an initial condensation of the Claisen type, followed by several tautomeric shifts, and finally ring-closure.

One of the most powerful tools for structural proof is ozonolysis. By this approach, compound I should give rise to malonic acid, II to pyruvic aldehyde or acetic acid, III to pyruvic aldehyde or acetic acid. In the actual ozonolysis,[7] ketene dimer gave rise to pyruvic aldehyde and acetic acid. Malonic acid was sought for but not found.

This accumulation of critical evidence favors II and III as the correct structure for ketene dimer, and discredits formula I.

Summary

Evidence is reviewed for the structure of ketene dimer. An equilibrium mixture of the resonance isomers acetylketene and crotono-β-lactone best fits the evidence. Vinylaceto-β-lactone, which has been proposed recently, fails to explain the behavior on ozonolysis. Also, this structure does not satisfy the parachor, nor does it lend itself to a simple explanation of the polymerization to dehydroacetic acid.

Chlorine and acetylketene give rise to chloroacetoacetyl chloride. The latter reacts with alcohol and aniline to yield the ester and anilide, respectively.

EVANSTON, ILLINOIS RECEIVED MARCH 4, 1940

(3) Hantzsch, *Ber.*, **27**, 355, 3168 (1894).

(4) Runde, Scott and Johnson, THIS JOURNAL, **52**, 1284 (1930); Reichstein, *Ber.*, **63**, 749 (1930).

(5) Burgin, Engs and Hearne, *Ind. Eng. Chem.*, **31**, 1413 (1939).

(6) Hurd and Roe, THIS JOURNAL, **61**, 3358 (1939).

(7) Hurd and Williams, *ibid.*, **58**, 964, 968 (1936).

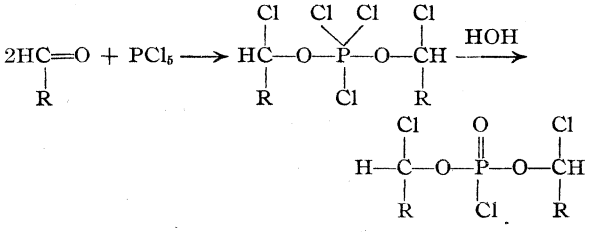
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

The Action of Phosphorus Pentachloride upon *aldehydo*-Galactose Pentaacetate. The 1,1-Dichloride of *aldehydo*-Galactose Pentaacetate

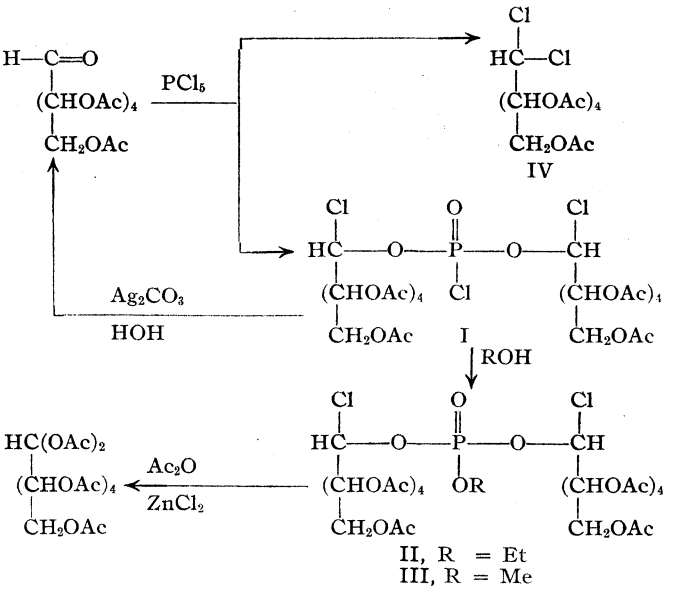
BY M. L. WOLFROM AND D. I. WEISBLAT

The action of phosphorus pentachloride upon aldehydes to produce the 1,1-dichlorides[1] is a well-known reaction. We were interested in its extension to an *aldehydo*-sugar acetate and were successful in obtaining a crystalline product in the galactose structure. The product, 1,1-dichloro-*aldehydo*-*d*-galactose pentaacetate (IV) is the first substance of this type in the sugar series. It is a very stable substance and reduces Fehling solution only on prolonged boiling. It does not reduce neutral copper acetate solution on boiling. We have found that the reduction of neutral copper acetate solution is a general property of *aldehydo*-sugar acetates and also of the very reactive acetyl chloride carbonyl addition compound of *aldehydo*-galactose pentaacetate.[2] The behavior of a number of significant sugar structures toward this reagent is tabulated in Table I. We believe that this lack of reduction toward neutral copper acetate confirms our assigned structure for substance IV.

If the reaction of phosphorus pentachloride with *aldehydo*-galactose pentaacetate is carried out in ether solution, an insoluble reaction product separates which is assigned structure I. This may be considered as a carbonyl addition compound of phosphorus pentachloride with two moles of the aldehyde in which two of the chlorine atoms attached to phosphorus have been hydrolyzed.



The structure of substance I, designated di-(1-chloro-*aldehydo*-*d*-galactose pentaacetate) chlorophosphate, is made probable by its analysis, its hydrolysis with water and silver carbonate to *aldehydo*-galactose pentaacetate and by the fact that it contains one reactive chlorine extremely readily replaceable by an alkoxyl group. On recrystallization from ethanol, I yields the substance II, designated di-(1-chloro-*aldehydo*-*d*-galactose pentaacetate) ethyl phosphate. II exhibits the predicted molecular weight and on acetylation with acetic anhydride and zinc chloride, yields *aldehydo*-galactose heptaacetate. The



compound III, analogous to II but containing a methoxyl group, also was synthesized.

It is probable that the substance I represents a general structure for the initial reaction stages of aldehydes with phosphorus pentachloride. In the cyclic sugar structures, Freudenberg and Braun[3] have reported a crystalline reaction product of 2,3,6-trimethylglucose with phosphorus pentachloride which on analysis proved to be $(C_6H_8O_3(OCH_3)_3)_2PCl_3$. Helferich and du Mont[4] have obtained a crystalline tri-(β-*d*-glucopyranose tetraacetate)-6-phosphate by the reaction of phosphorus oxychloride with β-*d*-glucose 1,2,3,4-tetraacetate.

Experimental

Di-(1-chloro-*aldehydo*-*d*-galactose pentaacetate) Chlorophosphate (I).—*aldehydo*-*d*-Galactose pentaacetate[5] (10 g.,

(1) C. Friedel (A. Wurtz), *Compt. rend.*, **45**, 1015 (1857); A. Wurtz and C. Frapolli, *ibid.*, **47**, 418 (1858); A. Geuther, *Ann.*, **105**, 321 (1858).

(2) M. L. Wolfrom, THIS JOURNAL, **57**, 2498 (1935).

(3) K. Freudenberg and E. Braun, *Ann.*, **460**, 303 (1928).

(4) B. Helferich and H. du Mont, *Z. physiol. Chem.*, **181**, 300 (1929).

(5) M. L. Wolfrom, THIS JOURNAL, **52**, 2464 (1930).

TABLE I

REDUCTION OF *d*-GALACTOSE DERIVATIVES BY COPPER ACETATE[a]

Substance	Time at b. p., sec.[b]	Reduction
d-Galactose	0	+
β-*d*-Galactopyranose pentaacetate	120	−
α-*d*-Galactopyranose pentaacetate	120	−
aldehydo-*d*-Galactose pentaacetate	15	+
aldehydo-*d*-Galactose isopropyl hemiacetal	45	+
d-Galactose heptaacetate	50	+
1-Chloro-*d*-galactose hexaacetate	60	+
1-Methoxy-*d*-galactose hexaacetate	90	+
1-Chloro-1-ethoxy-*d*-galactose pentaacetate	30	+
d-Galactopyranose tetraacetate	90	+
1,1-Dichloro-*aldehydo*-*d*-galactose pentaacetate[c]	120	−
Di-(1-chloro-*aldehydo*-*d*-galactose pentaacetate) chlorophosphate[c]	120	−

[a] One mole equivalent of 0.05 g. *d*-galactose in 5 cc. of saturated aqueous cupric acetate solution. [b] In the case of a positive reduction, the time of boiling recorded is that at which visible reduction was initiated. *d*-Galactose gave a visible reduction before the boiling point was attained. [c] No reduction also on addition of ethanol.

1 mol) and powdered phosphorus pentachloride (5 g., 0.9 mol) were suspended in 200 cc. of anhydrous ether and refluxed for twelve hours in an all-glass apparatus equipped with a drying tube. The product began to separate from the reaction mixture within the first hour of reflux. At the end of this period of refluxing an equal volume of petroleum ether (b. p. 65–110°) was added and the mixture kept overnight at icebox temperature. The product was removed by filtration and washed three to four times with ether–petroleum ether (1:1); yield 4.5–6 g., m. p. 145–155°. The product was immediately recrystallized from about 80 parts of hot ethyl acetate; yield 3.5 g., m. p. 190° (dec.), spec. rot. −20° (26°; *c*, 2.2; $CHCl_3$).[6]

The substance was very soluble in chloroform, moderately so in acetone and practically insoluble in ether, petroleum ether and cold water. It showed no reduction toward copper acetate (see Table I) but slowly reduced boiling Fehling solution. It gave a positive Schiff test very slowly on standing. The material is very unstable unless of maximum purity, in which condition a sample in a desiccator over soda lime has shown no decomposition over a period of one year.

The substance was also formed by shaking the reaction mixture at room temperature over a period of several days. No appreciable difference was noted on starting with the aldehydrol form of *aldehydo*-*d*-galactose pentaacetate.

By working up the mother liquor material from the ethyl acetate recrystallizations by means of alcohol–water, a very small amount of 1,1-dichloro-*aldehydo*-*d*-galactose pentaacetate (see below) could be obtained in very high purity. No conditions could be found for converting compound I into the dichloride (IV).

Anal. Calcd. for $C_{32}H_{42}O_{23}Cl_3P$: Cl, 11.41; P, 3.32; saponification value (15 equivalents), 16.1 cc. 0.1 *N* NaOH per 100 mg. Found: Cl, 11.3; P, 3.34; saponification value (Kunz and Hudson procedure[7]), 16.0 cc.

Hydrolysis of Di-(1-chloro-*aldehydo*-*d*-galactose pentaacetate) Chlorophosphate (I) to *aldehydo*-*d*-Galactose Pentaacetate.—I (2 g.) was suspended in 100 cc. of toluene and 4 g. of freshly prepared silver carbonate and 0.5 cc. of water added. The mixture was refluxed for twenty-one hours with vigorous mechanical stirring. The silver salts were then removed by filtration and crystalline material was obtained by solvent removal under reduced pressure. The crystalline material was recrystallized from absolute ethanol and 0.3 g. of pure *aldehydo*-*d*-galactose pentaacetate ethyl hemiacetal was obtained which was identified by melting point (133–135°), mixed melting point and optical behavior in chloroform solution.[8]

Di-(1-chloro-*aldehydo*-*d*-galactose pentaacetate) Ethyl Phosphate (II).—When di-(1-chloro-*aldehydo*-*d*-galactose pentaacetate) chlorophosphate (I) was recrystallized from 75 parts of boiling absolute ethanol, hydrogen chloride was evolved and on cooling, filtering, and concentrating the mother liquors, a practically quantitative yield of the di-(1-chloro-*aldehydo*-*d*-galactose pentaacetate) ethyl phosphate (II) was obtained; m. p. 156–158°, spec. rot. −24° (21°; *c*, 1.3; $CHCl_3$).

The product was similar to substance I in solubility and behavior toward copper acetate, Fehling solution and the Schiff reagent.

Anal. Calcd. for $C_{32}H_{44}O_{23}(OC_2H_5)Cl_2P$: Cl, 7.53; P, 3.29; OC_2H_5, 4.79; saponification value (15 equivalents), 15.9 cc. of 0.1 *N* NaOH per 100 mg.; mol. wt., 941.6. Found: Cl, 7.60; P, 3.30; OC_2H_5, 5.0; saponification value,[7] 15.9 cc.; mol. wt. (Rast), 950.

Conversion of Di-(1-chloro-*aldehydo*-*d*-galactose pentaacetate) Ethyl Phosphate (II) to *aldehydo*-*d*-Galactose Heptaacetate.—II (1 g.) was dissolved in a solution of 0.3 g. of freshly fused zinc chloride in 10 cc. of acetic anhydride and the solution heated for one hour at 98°. The black solution was poured on a mixture of sodium bicarbonate and crushed ice. This mixture was extracted with chloroform and the extract washed with an aqueous solution of sodium bicarbonate and finally with water. The dark sirup obtained on solvent removal of the dried (decolorizing charcoal) extract was dissolved in benzene and petroleum ether added to incipient opalescence. After standing overnight at icebox temperature the supernatant liquid was removed by decantation and the separated sirup was crystallized from 50% ethanol; yield 0.32 g., m. p. 95°. Pure material was obtained on recrystallization from ethanol and from methanol; yield 0.10 g., m. p. 100–102° (mixed m. p. unchanged), spec. rot. +10° (20°; *c*, 2, abs. EtOH). Micheel and co-workers[9] report for *aldehydo*-*d*-galactose heptaacetate m. p. 103°, spec. rot. +10° (EtOH).

Di-(1-chloro-*aldehydo*-*d*-galactose Pentaacetate) Methyl Phosphate (III).—This substance was prepared according

(6) All specific rotations are recorded to the D-line of sodium light; 26° is the temperature; *c* is the concentration in grams per 100 cc. of solution.

(7) A. Kunz and C. S. Hudson, THIS JOURNAL, **48**, 1982 (1926).

(8) M. L. Wolfrom, *ibid.*, **53**, 2275 (1931).

(9) F. Micheel, H. Ruhkopf and F. Suckfüll, *Ber.*, **68**, 1523 (1935).

to the procedure described for the corresponding ethyl compound (II) except that 150 parts of methanol was used in place of the ethanol. A good yield was obtained; m. p. 187–188° (dec.), spec. rot. −19° (30°; *c*, 4.2; $CHCl_3$). The substance crystallized in rod-shaped prisms and showed solubilities and behavior similar to II.

Anal. Calcd. for $C_{32}H_{44}O_{23}(OCH_3)Cl_2P$: OCH_3, 3.35. Found: OCH_3, 3.97.

1,1-Dichloro-*aldehydo-d*-galactose Pentaacetate (IV).—*aldehydo-d*-Galactose pentaacetate (10 g., 1 mol) was dissolved in 100 cc. of pure benzene, 15 g. of Drierite (anhydrous calcium sulfate) added and the whole refluxed in an all-glass apparatus equipped with a drying tube. Powdered phosphorus pentachloride (6.8 g., 1.3 mol) was introduced quickly and the reflux maintained for twelve hours, whereupon the pale yellow solution was filtered and the filtrate washed with ice water and with an aqueous solution of sodium bicarbonate until halogen free (eight to twelve washings). Solvent removal from the dried (decolorizing charcoal) solution left 3 to 5 g. of a pale yellow sirup. This sirup was dissolved in the minimum quantity of hot ethanol and was crystallized on the addition of an equal volume of water. Pure material was obtained on further recrystallization from 80% ethanol; yield 0.8–1.6 g. of m. p. 148–150°; spec. rot. +11° (20°; *c*, 3.2; $CHCl_3$).

The substance was soluble in the common solvents except petroleum ether and cold water. It showed no reduction toward copper acetate (see Table I) and reduced Fehling solution only on long boiling. It gave a positive Schiff test very slowly on standing.

It was found that a reflux period less than specified above (twelve hours) yielded compound I while a longer period yielded only sirups which could not be crystallized and which readily decomposed.

Anal. Calcd. for $C_6H_7O_5(CH_3CO)_5Cl_2$: C, 43.2; H, 4.98; Cl, 15.9. Found: C, 43.3; H, 5.07; Cl, 15.6.

We are indebted to Mr. John Walker (W. P. A. Project 18062) for assistance rendered in the analytical determinations. We also acknowledge the general assistance of Mr. Irving Auerbach (N. Y. A. Project O. S. U. 167).

Summary

1. The action of phosphorus pentachloride upon *aldehydo-d*-galactose pentaacetate in dry benzene produces a crystalline substance (IV) which is shown to be 1,1-dichloro-*aldehydo-d*-galactose pentaacetate.

2. The action of phosphorus pentachloride upon *aldehydo-d*-galactose pentaacetate in ether leads to the isolation of a crystalline substance (I) designated di-(1-chloro-*aldehydo-d*-galactose pentaacetate) chlorophosphate.

3. From I is obtained di-(1-chloro-*aldehydo-d*-galactose pentaacetate) ethyl (and methyl) phosphate, II, and III.

4. The structure assigned to I is made probable by its hydrolysis to *aldehydo-d*-galactose pentaacetate and by its reaction with ethanol to form II, from which *aldehydo-d*-galactose heptaacetate is obtained on acetylation.

COLUMBUS, OHIO RECEIVED MARCH 2, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

Crystalline Phenylurethans (Carbanilates) of Sugar Glycosides

BY M. L. WOLFROM AND D. E. PLETCHER

A well-established procedure in organic chemistry is the characterization of carbinols as N-aryl urethans prepared by the reaction of N-aryl isocyanates with the carbinol. Maquenne and Goodwin[1] investigated the extension of this reaction, using phenyl isocyanate, to a number of unsubstituted sugars but obtained only amorphous powders. Jolles and Botrini,[2] likewise employing phenyl isocyanate, obtained as amorphous powders the phenylurethans or carbanilates of several naturally occurring glycosides. Crystalline fully substituted carbanilates of some of the sugar alcohols have been reported.[1,3]

We have now been successful in obtaining in crystalline form the carbanilates of four of the methyl glycosides of the sugars, in which derivatives all of the free hydroxyls have been brought into reaction. These substances melt with decomposition at high temperatures and exhibit correspondingly low solubilities. Under certain conditions they show a pronounced tendency to separate as gels and are in general rather difficult to manipulate.

These polyurethans or polycarbanilates were not sufficiently soluble in chloroform for satisfactory polarizations. Rotations are recorded in acetone solution for all except β-methyl-*d*-glucoside tetracarbanilate, for which pyridine was found to be the only suitable polarization sol-

(1) L. Maquenne and W. Goodwin, *Bull. soc. chim.*, [3] **31**, 430 (1904).

(2) E. Jolles and M. Botrini, *Gazz. chim. ital.*, **65**, 1217 (1935).

(3) H. Tessmer, *Ber.*, **18**, 968 (1885).

vent. It is of interest to note that the tetracarbanilate of α-methyl-*d*-mannoside (+ 79°, water) exhibits a specific rotation in acetone solution of eighteen degrees to the left. Such a reversal of rotation had been noted by Jolles and Botrini[2] for the amorphous tetracarbanilates of arbutin and esculin in pyridine solution.

Crystalline carbanilates and thionocarbanilates on carbon one of glucose and other sugars have been synthesized through the Fischer[4] procedure of treating acetobromosugars with silver cyanate or silver thiocyanate and subsequent treatment with an alcohol.[5]

When the work herein reported was practically completed, we were pleased to note the publication of Salmon and Powell.[6] These workers found that phenyl isocyanate formed readily crystallizable, easily purified, derivatives with two partially substituted glucose structures in which only one or two hydroxyl groups remained free and which failed to form crystalline acetates or tosylates (*p*-toluenesulfonates). In fact, they were able to crystallize 5,6-dimethyl-monoacetoneglucose only by seeding with crystals obtained by the hydrolysis of the corresponding urethan (carbanilate). The sodium methylate hydrolysis procedure of Salmon and Powell was applied to one of our derivatives and the parent glycoside was regenerated. We did not find any of the N,N-diphenylallophanate derivatives mentioned by these workers when pyridine was used as a reaction catalyst.

It would appear that the carbanilates (phenylurethans) are worthy of further consideration by investigators in the carbohydrate field, especially when derivatives are desired of structures containing only one or two free hydroxyl groups.

Experimental

β-Methyl-*d*-glucoside Tetracarbanilate.—β-Methyl-*d*-glucoside (5.0 g., 1 mol, previously dried over phosphorus pentoxide in a vacuum desiccator) was dissolved by heating in 30 cc. of dry pyridine in an apparatus equipped with a reflux condenser and a drying tube. To the solution, cooled to room temperature, was added 12.5 cc. (4.5 mols) of phenyl isocyanate. A reaction was immediately initiated with the liberation of considerable heat. The solution was refluxed for three hours and on cooling a crystalline product separated which was removed by filtration and washed with cold pyridine and finally with ether or petroleum ether; yield 4.5 g., m. p. 223–225°[7] (dec.), preliminary softening at 220°. Pure material could be obtained on recrystallization from pyridine, acetone or ethyl acetate; m. p. 225° (dec.), mixed m. p. with diphenyl urea (m. p. 235°), 210–211°, spec. rot. +13° (23°; *c*, 0.7; pyridine).[8]

The substance crystallized in long, fine needles. It was slightly soluble hot in acetone, chloroform, alcohol, ethyl acetate and pyridine. It was practically insoluble in water, ether and petroleum ether. It was not sufficiently soluble in acetone or chloroform for a satisfactory polarization.

Anal. Calcd. for $C_{35}H_{34}O_{10}N_4$: C, 62.67; H, 5.07; N, 8.35. Found: C, 62.68; H, 5.21; N, 8.38.

β-Methyl-*d*-xyloside Tricarbanilate.—β-Methyl-*d*-xyloside (5 g.) was treated exactly as described for the synthesis of β-methyl-*d*-glucoside tetracarbanilate and the crystalline reaction product was isolated in the same manner; yield 2.5 g., m. p. 233–235° (dec.). Pure material could be obtained on recrystallization from pyridine or alcohol–acetone (1:1); m. p. 234° (dec.), spec. rot. −23° (22°; *c*, 1; acetone).

The substance crystallized in long, fine needles and exhibited solubilities similar to those of the corresponding β-glucoside derivative except that it was more acetone-soluble.

Anal. Calcd. for $C_{27}H_{27}O_8N_3$: C, 62.19; H, 5.18; N, 8.06. Found: C, 62.00; H, 5.10; N, 8.24.

α-Methyl-*d*-glucoside Tetracarbanilate.—α-Methyl-*d*-glucoside (5 g.) was treated as described for the synthesis of the corresponding β-glucoside derivative except that the reaction product did not separate on cooling. The pyridine was then removed under reduced pressure and the amorphous residue washed repeatedly with warm ether; yield 11.5 g. The product was dissolved in a hot mixture of two parts of ethanol and one part of acetone, most of the acetone was then removed by boiling and to the residual hot ethanol solution water was added to incipient turbidity. The product crystallized on standing at room temperature and was removed by filtration. A second crop of approximately the same purity was obtained on mother liquor concentration; total yield 8 g., m. p. 210–214° (dec.). Pure material was obtained by repeating the above process several times; m. p. 227° (dec.), spec. rot. +73° (23°; *c*, 3; acetone).

The substance crystallized in long, fine needles and was somewhat more soluble in organic solvents than the corresponding β-glucoside derivative.

Anal. Calcd. for $C_{35}H_{34}O_{10}N_4$: C, 62.67; H, 5.07; N, 8.35. Found: C, 62.63; H, 5.10; N, 8.38.

α-Methyl-*d*-mannoside Tetracarbanilate.—α-Methyl-*d*-mannoside (5 g.) was treated with phenyl isocyanate as described for the β-methyl-glucoside but was isolated and crystallized by the procedure described for the α-methyl-glucoside derivative. The substance also could be recrystallized from absolute ethanol or isopropyl alcohol by the addition of water to the hot solution until incipient turbidity was produced; yield 3.4 g. of m. p. 189–190° (dec.); spec. rot. −18° (20°; *c*, 3; acetone).

The substance crystallized in long, fine needles and was

(4) E. Fischer, *Ber.*, **47**, 1377 (1914).

(5) T. B. Johnson and W. Bergmann, THIS JOURNAL, **54**, 3360 (1932); **60**, 1916 (1938).

(6) M. R. Salmon and G. Powell, *ibid.*, **61**, 3507 (1939).

(7) All melting points are uncorrected and were taken on a 360° thermometer with immersion to the −10° mark.

(8) All rotations are recorded to the D-line of sodium light; 23° is the temperature; *c* is the concentration in g. per 100 cc. soln.

somewhat more soluble in organic solvents than the corresponding β-glucoside derivative.

The α-methyl mannoside was regenerated from this tetracarbanilate according to the procedure of Salmon and Powell[6] and was identified by melting point and mixed melting point.

Anal. Calcd. for $C_{35}H_{34}O_{10}N_4$: C, 62.67; H, 5.07; N, 8.35. Found: C, 62.60; H, 5.05; N, 8.29.

We are indebted to Mr. John Walker (W. P. A. Project 18062) and to Mr. H. S. Clark for all analytical determinations. We also acknowledge the assistance and counsel of Dr. John C. Sowden.

Summary

1. The tetracarbanilates of α-methyl-*d*-mannoside, α-methyl-*d*-glucoside, β-methyl-*d*-glucoside and the tricarbanilate of β-methyl-*d*-xyloside have been synthesized in crystalline condition.

COLUMBUS, OHIO RECEIVED MARCH 9, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

aldehydo-Maltose Octaacetate

BY M. L. WOLFROM AND M. KONIGSBERG

The crystalline octaacetate of maltose diethyl mercaptal was reported[1] from this Laboratory some time ago. At the time, efforts to demercaptalate this substance yielded no crystalline product but the application of certain recent improvements[2] in the demercaptalation procedure has yielded the *aldehydo*-maltose octaacetate in crystalline form. A preliminary report[2] to this effect has been made and the details will now be communicated. The substance gives a positive Schiff aldehyde test and readily forms a crystalline oxime without loss of acetyl.

aldehydo-Maltose octaacetate exhibits no detectable mutarotation in ethanol solution but crystallizes as a compound with one mole of ethanol. This ethanol compound shows no detectable mutarotation in chloroform or ethanol solution and thus differs from the ethanol addition compounds of the *aldehydo*-acetates of galactose,[3] fucose[4] and mannose,[2] which have been demonstrated clearly to be true carbonyl addition compounds or ethyl hemiacetals. Table I indicates that the molecular rotations of *aldehydo*-maltose octaacetate and its ethanol compound are identical within the limits of experimental error. The ethanol compound is thus apparently not an ethyl hemiacetal but is a secondary valence compound with one mole of ethanol of crystallization. An alternative view would be that a change in the configuration of carbon one in this open chain derivative of maltose has little effect upon the rotation of the compound as a whole. This viewpoint receives some support in that the diethyl mercaptal of maltose octaacetate has practically the same rotation (specific, +88°; molecular, +69,000) in chloroform as the *aldehydo*-acetate. The fact that these maltose derivatives are α-glucosides might lead to the lactol carbon of the glucosidic portion making the controlling contribution to the rotation.

aldehydo-Maltose octaacetate is the first crystalline *aldehydo*-acetate in the disaccharide series.

TABLE I

ROTATIONS OF *aldehydo*-MALTOSE OCTAACETATE AND ITS ETHANOL COMPOUND

	$[\alpha]^{21}D$, $CHCl_3$ (alcohol free)	Mol. rotn.	$[\alpha]^{25}D$, EtOH	Mol. rotn.
aldehydo-Maltose octaacetate	+93.5°	+63,000	+96°	+65,000
The monoethyl alcoholate	+85	+62,000	+90	+65,000

Experimental

***aldehydo*-Maltose Octaacetate.**—Maltose diethyl mercaptal octaacetate[1] (20 g.) was dissolved in 300 cc. of acetone and added to a mixture of 60 g. of mercuric chloride, 70 g. of cadmium carbonate, and 7 cc. of water in 500 cc. of acetone. This mixture was stirred vigorously and refluxed for eight hours. The cold solution was filtered into a flask containing 75 g. of cadmium carbonate and the filtrate was concentrated under reduced pressure (35–40°) in the presence of the cadmium carbonate. The residue was extracted with warm chloroform (alcohol free) and the extract washed free of halogen, treated with decolorizing charcoal, dried over calcium chloride and concentrated to a thick sirup under reduced pressure. The sirup was dissolved in ether, one-fourth its volume of low boiling petroleum ether added, and cooled. The crystalline product was filtered and washed with cold ether; 8.5 g., m. p. 112–113°. A second crop was obtained from the mother liquors; 4.9 g. or 13.4 g. (78%) total, m. p. 105–113°. Pure material was obtained on two recrystallizations from absolute ether; m. p. 116–117°, spec. rot.

(1) M. L. Wolfrom and E. E. Stahly, THIS JOURNAL, **53**, 4379 (1931).
(2) M. L. Wolfrom and M. Konigsberg, *ibid.*, **61**, 574 (1939).
(3) M. L. Wolfrom, *ibid.*, **53**, 2275 (1931).
(4) M. L. Wolfrom and J. A. Orsino, *ibid.*, **56**, 985 (1934).

+93.5° (22°; *c*, 5; abs. $CHCl_3$),[5] spec. rot. +96° (25°; *c*, 1; EtOH; no mutarotation).

The compound crystallized as elongated prisms and was very soluble in chloroform and acetone and was moderately soluble in ether, alcohol and boiling water. It reduced Fehling solution on warming and reduced a neutral solution of copper acetate. In aqueous solution at room temperature it quickly restored the color to Schiff reagent.

Anal. Calcd. for $C_{12}H_{14}O_{11}(CH_3CO)_8$: C, 49.56; H, 5.64; CH_3CO, 11.8 cc. 0.1 *N* NaOH per 100 mg. Found: C, 49.49; H, 5.63; CH_3CO, 11.8 cc.

***aldehydo*-Maltose Octaacetate Monoethyl Alcoholate.**—This substance was obtained on recrystallization of *aldehydo*-maltose octaacetate from absolute ethanol or on working up the demercaptalation reaction with absolute ethanol in place of ether and petroleum ether. Pure material was obtained on several recrystallizations from absolute ethanol; m. p. 66–67°, spec. rot. +85° (21°; *c*, 5; abs. $CHCl_3$; no mutarotation), spec. rot. +90° (25°; *c*, 1; abs. EtOH; no mutarotation).

The substance was not very stable and slowly decomposed on long standing, with the liberation of alcohol and acetic acid. The product crystallized as long, lustrous needles and was very soluble in chloroform and acetone, moderately so in alcohol and warm ether, and was practically insoluble in water and ligroin. It reduced Fehling solution.

Anal. Calcd. for $C_{12}H_{14}O_{11}(CH_3CO)_8(C_2H_5OH)$: C, 49.7; H, 6.12; OC_2H_5, 6.22; CH_3CO, 11.0 cc. 0.1 *N* NaOH per 100 mg. Found: C, 49.5; H, 6.14; OC_2H_5, 6.16; CH_3CO, 11.0 cc.

***aldehydo*-Maltose Oxime Octaacetate.**—*aldehydo*-Maltose octaacetate (4 g.) was dissolved in 400 cc. of boiling water, filtered and a solid mixture of 0.9 g. of hydroxylamine hydrochloride and 1.8 g. of potassium acetate was added to the filtrate. A crystalline product separated on cooling; yield 1.5 g., m. p. 89–92°, spec. rot. +100° ($CHCl_3$). Pure material was obtained on two recrystallizations from water; yield 0.7 g., m. p. 93–94°, spec. rot. +107° (24°; *c*, 3; U. S. P. $CHCl_3$), spec. rot. +100° (24°; *c*, 3; EtOH). Recrystallization of the product from ether or aqueous alcohol did not alter the constants.

The product crystallized as fine rectangular rods and was soluble in chloroform, acetone, alcohol, ether and boiling water. It was insoluble in the hydrocarbon solvents.

Anal. Calcd. for $C_{12}H_{15}O_{11}N(CH_3CO)_8$: N, 2.02; CH_3CO, 11.5 cc. 0.1 *N* NaOH per 100 mg. Found: N, 2.00; CH_3CO,[6] 11.5 cc.

(5) All rotations are recorded to the D-line of sodium light, 22° is the temperature, *c* is the concentration in g. per 100 cc. soln.

We are indebted to Mr. John Walker (W. P. A. Project 18062) for assistance rendered in the analytical determinations. We also acknowledge assistance rendered by Mr. F. B. Moody.

Summary

1. The synthesis of the first crystalline *aldehydo*-acetate in the disaccharide series, *aldehydo*-maltose octaacetate, is reported.

2. *aldehydo*-Maltose octaacetate forms a crystalline oxime and a crystalline compound containing one mole of ethanol.

3. *aldehydo*-Maltose octaacetate shows no detectable mutarotation in ethanol solution and its ethanol compound shows no detectable mutarotation in chloroform or ethanol solution.

(6) M. L. Wolfrom, M. Konigsberg and S. Soltzberg, THIS JOURNAL, **58**, 490 (1936).

COLUMBUS, OHIO RECEIVED MARCH 11, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NEW YORK UNIVERSITY]

Disproportionation in Aryloxymalonic Acid Syntheses

BY JOSEPH B. NIEDERL AND ROSLYN T. ROTH[1]

In the course of the studies of substituted phenylmalonic acids[2,3] studies of various phenoxymalonic acids were undertaken as well. Mono- and di-phenoxymalonic acids, with and without substituents in the phenyl or the malonyl radical, were prepared.

In the preparation of the mono-phenoxymalonic acids from the diethyl mono-bromomalonate by the Williamson synthesis, a "disproportionation" phenomenon was encountered. Thus it was found that the di-phenoxy compounds result in about equal quantities with the monophenoxy products despite the use of equimolar quantities of sodium phenolate and diethyl mono-bromomalonate. On the other hand, no such disproportionation took place when the diethyl mono-chloromalonate was used instead of the bromo compound.

Although the mono- and diphenoxy-malonic acid esters had been prepared previously by Conrad and Brueckner[4] and the mono- and di-*p*-

(1) The material presented in this paper is taken from Part III of the thesis presented by Roslyn T. Roth to the Faculty of the Graduate School of New York University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) J. B. Niederl, R. T. Roth and A. Plentl, THIS JOURNAL, **59**, 1901 (1937).

(3) J. B. Niederl and R. T. Roth, *ibid.*, **60**, 2140 (1938).

(4) M. Conrad and C. A. Brueckner, *Ber.*, **24**, 2993 (1891).

nitrophenoxy malonic acid esters and acids by C. A. Bischoff[5] from the respective mono- and di-bromomalonic acid esters, neither one had reported the simultaneous formation of mono- and di-phenoxy derivatives from the mono-bromo ester. Formation of di-substituted malonic acid esters from equimolecular reactants of the mono-sodium salt of methyl malonate, or ethyl acetoacetate and mono-bromomalonic acid ester, while mono-substituted malonic acid derivatives were formed using the corresponding mono-chloromalonic acid ester, have previously been reported.[6,7]

While it is simple enough to state the formation of the mono phenoxymalonic acid esters from the respective sodium phenolates and the diethyl mono-bromomalonate (reaction A), interpretation of the disproportionation process (reaction B) is certainly more complicated and might be expressed in its simplest form as follows.

Reaction A

$$ROOC_2CH\boxed{Br + Na}OC_6H_4R \longrightarrow NaBr + (ROOC)_2CH\cdot O\cdot C_6H_4R$$

Reaction B

$$2(ROOC)_2CHBr + 2NaOC_6H_4R \longrightarrow 2NaBr + (ROOC)_2C(OC_6H_4R)_2 + (ROOC)_2CH_2$$

In the course of this investigation there were prepared the ethyl esters of the mono- (Ia) and the di-phenoxymalonic acids, the mono- (IIa) and di-*m*-cresoxymalonic acids (IIIa), the mono- and di-*p*-nitrophenoxy-malonic acids and the *p*-nitrophenoxy-methylmalonic acid (IVa), then several of the free acids (I, II, III, IV) and some of the amides (Ib, IIb). The various mono- as well as di-phenoxymalonic acid esters were subjected to rearrangement processes according to J. B. Niederl[8] and E. Wallis.[9] These attempts proved to be negative inasmuch as no carbon-arylated malonic acid could be obtained, the respective phenoxyacetic acids resulting from the mono derivatives. Of particular interest in this respect is the *p*-nitrophenoxy-methyl-malonic acid (IV) and ester (IVa), on account of its being a tertiary alkyl phenyl ether and yet being unable to undergo any rearrangement.

Experimental

Diethyl Aryloxymalonates.—These esters were prepared by refluxing until neutral 0.125 mole of diethyl mono-chloromalonate and the respective sodium phenolate, or cresylate, in absolute alcohol. The mixture was then poured into water and extracted with ether. The ether extract was fractionally distilled under reduced pressure. In this manner were prepared: diethyl phenoxymalonate (Ia) (yield 60%, the crystals were crystallized from methyl alcohol), and diethyl *m*-cresoxymalonate (IIa) (yield 60%). The diethyl di-*m*-cresoxymalonate (IIIa) was prepared by the method of M. Conrad and C. A. Brueckner[4] (yield 50%): the diethyl *p*-nitrophenoxy-methylmalonate was prepared according to the method of C. A. Bischoff[5] using xylene as the solvent (yield, 50–60%; the crystals were recrystallized from methyl alcohol).

Mono-aryloxymalonic Acids.—The individual free acids were prepared by hydrolyzing the respective esters with 5% alcoholic potassium hydroxide solution. The potassium salts which usually precipitated out were redissolved in water and the free acids were precipitated out of these solutions by subsequent acidification. Purification of the acids was effected by dissolving the acids in ether, extracting the ether solution with 5% aqueous sodium carbonate solution, precipitating the acids from the carbonate solution and re-extracting with ether. Upon concentration of the ether extracts at room temperature, the acids crystallized out on standing. The phenoxy and *m*-cresoxymalonic acids (I, II) were recrystallized from toluene, the *p*-nitrophenoxy-methylmalonic acid (IV) from a mixture of ether and petroleum ether. The free acids were hygroscopic. Upon heating and also on prolonged standing the acids lost carbon dioxide and were converted into the respective aryloxyacetic acids.

Di-aryloxymalonic Acids.—These acids also were prepared by hydrolysis of the corresponding esters. Usually only a short period of refluxing was required for the saponification of the ester. The di-*m*-cresoxymalonic acid (III) precipitated out on acidification in a partially hydrated state. The acid was recrystallized from hot water in the form of a tri-hydrate (III_1). On further heating or on long standing it lost water, forming the anhydrous acid (III). The anhydrous acid also was obtained from the ether solution of the acid or by precipitation by petroleum ether from the solution of the acid in benzene.

The di-aryloxymalonic acids upon heating underwent decomposition yielding the respective phenol, carbon dioxide, water and a non-volatile resin.

Mono-aryloxymalonic Acid Amides.—One gram of the aryloxymalonic acid ester (Ia, IIa) was shaken with 10 cc. of concentrated aqueous ammonium hydroxide solution for five minutes. The amide crystallized out in about 80% yield and was recrystallized from 30% alcohol (Ib, IIb).

Disproportionation.—The reactions between the sodium salts of the respective phenols (phenol, *m*-cresol, *p*-nitrophenol) and diethyl mono-bromomalonate (b. p. 125–127° (15 mm.)) were carried out with and without solvents. The solvents were ethyl alcohol (85%, 95% and absolute) and xylene. The mixtures were refluxed until they reacted neutral to litmus paper. They were then poured into water and the resulting aqueous mixtures were extracted with ether. The ether extract was separated and subjected to fractional distillation *in vacuo* (phenol and *m*-cresol). The fraction boiling above 140° (4 mm.) (a)

(5) C. A. Bischoff, *Ber.*, **40**, 3134, 3150 (1907).
(6) C. A. Bischoff, *ibid.*, **29**, 1276 (1896).
(7) A. Gault and L. Klees, *Bull. soc. chim.*, [4] **39**, 1000 (1926).
(8) J. B. Niederl and co-workers, THIS JOURNAL, **53**, 1928 (1931); **54**, 1063 (1932).
(9) E. Wallis and co-workers, *ibid.*, **56**, 1715 (1934).

TABLE I

CHEMICAL CONSTANTS AND ANALYSES OF COMPOUNDS

Compound	M. p. or b. p. °C. (uncor.)	Formula	Carbon % Calcd.	Carbon % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen % Calcd.	Nitrogen % Found	Neut. equiv. Calcd.	Neut. equiv. Found
Phenoxymalonic acid										
I Acid	124 (dec.)	$C_9H_8O_5$	55.07	55.19	4.08	4.12			98	97
(a) Ethyl ester	52–53	$C_{13}H_{16}O_5$	61.88	61.94	6.37	6.24				
(b) Amide	214–215	$C_9H_{10}N_2O_3$	55.67	55.65	5.15	5.20	14.42	14.43		
***m*-Cresoxymalonic acid**										
II Acid	138 (dec.)	$C_{10}H_{10}O_5$							105	103
(a) Ethyl ester	154–156 (4 mm.)	$C_{14}H_{18}O_5$	63.16	63.11	6.77	6.94				
(b) Amide	216–217	$C_{10}H_{12}N_2O_3$	57.69	57.60	5.76	5.80	13.46	13.54		
Di-*m*-cresoxymalonic acid										
III Acid	148 (dec.)	$C_{17}H_{16}O_6$							158	158
(1) Acid-hydrate	87	$C_{17}H_{22}O_9$							185	183
(a) Ethyl ester	202–205 (3 mm.)	$C_{21}H_{24}O_6$	67.70	67.85	6.46	6.67				
***p*-Nitrophenoxymethylmalonic acid**										
IV Acid	142 (dec.)	$C_{10}H_9NO_7$	47.04	46.88	3.57	3.39	5.49	5.52	128	128
(a) Ethyl ester	50–51	$C_{14}H_{17}NO_7$	54.07	53.95	5.47	5.59	4.50	4.59		

and 150° (4 mm.) (b) were reserved for examination. In the case of the *p*-nitrophenol (c) the esters crystallized out of the reaction mixture upon dilution with water when alcohol was used as the solvent; otherwise the solvent (xylene) had to be distilled off first.

(a) **Mono- and Di-phenoxymalonic Acids.**—The weighed esters as obtained above were first hydrolyzed with 20% aqueous potassium hydroxide solution and the solution acidified afterward. The di-phenoxymalonic acid (m. p. 173°) (the acetal) precipitated out and was weighed, while the monophenoxymalonic acid (I) (the ether) remained in solution. The second method for the determination of the proportion of mono- (ether) to the di-phenoxymalonic acid (acetal) involved treatment of the weighed ester mixture with concd. aqueous ammonium hydroxide solution. Only the mono acid (the ether) yielded an amide (Ib) which alone crystallized out and was then weighed.

The proportion of ether to acetal was two to three in absolute alcohol, xylene and no solvent. In 95 and 85% alcohols it changed to a one to one and a three to two ratio.

(b) **Mono- and Di-*m*-cresoxymalonic Acids.**—The proportion of mono- (ether) to the di-acid (acetal) was ascertained by determining the saponification equivalent of a weighed amount of the distillate. The second method involved determination of the refractive index of the ester mixture and comparing the value obtained with those of standard mixtures of the two components. Diethyl mono-*m*-cresoxymalonate: n^{23}°D 1.4895; sapon. equiv., 133. Diethyl di-*m*-cresoxymalonate: n^{22}°D 1.5221; sapon. equiv., 186. The proportion of ether to acetal was three to one using 95% alcohol as solvent.

(c) **Mono and Di-*p*-nitrophenoxymalonic Acid.**—The crude ester mixture was recrystallized from methyl alcohol. The melting point range of the mixture was then compared with those of a series of standard mixtures of the two components, which were prepared according to C. A. Bischoff[5] using diethyl mono-chloromalonate (b. p. 118–119° (16 mm.)) for the ether and diethyl di-bromomalonate (b. p. 140–143° (18 mm.)) for the acetal. The two esters were also separated by fractional crystallization from methyl alcohol in which solvent the ether compound is much more soluble than the acetal. Diethyl mono-*p*-nitrophenoxymalonate: m. p. 86°; diethyl di-*p*-nitrophenoxymalonate: m. p. 144°. The proportion of ether to acetal was two to three in absolute and 95% alcohol, three to two in 85% alcohol and one to one in xylene and without a solvent.

Summary

1. A disproportionation phenomenon involving abnormal aryloxylation has been described.

2. Various mono- and di-aryloxymalonic acids, their esters and amides have been prepared and their behavior on heating as well as under conditions which normally would lead to carbon arylation has been studied.

WASHINGTON SQUARE COLLEGE
NEW YORK, N. Y. RECEIVED JANUARY 31, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF NEW YORK UNIVERSITY]

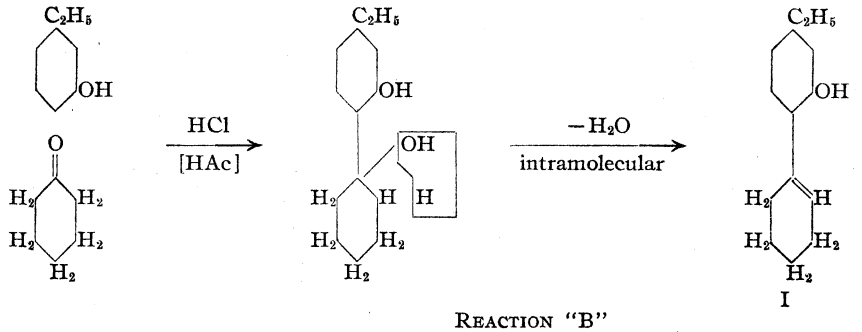
Flavans

BY JOSEPH B. NIEDERL AND ALBERT ZIERING

The condensation of cyclohexanone and *m*-ethylphenol to a cyclohexenylphenol (I)[1] takes place in glacial acetic acid, hydrogen chloride being used as the catalyst. It has now been found that, if the reaction is run without a solvent, the product is entirely different. The new compound is saturated and has twice the molecular weight of the cyclohexenylphenol (I). It has been assigned structure II, 2′-hydroxy-4′,7-diethyl-2,3-tetra-4,4-pentamethylene-flavan.

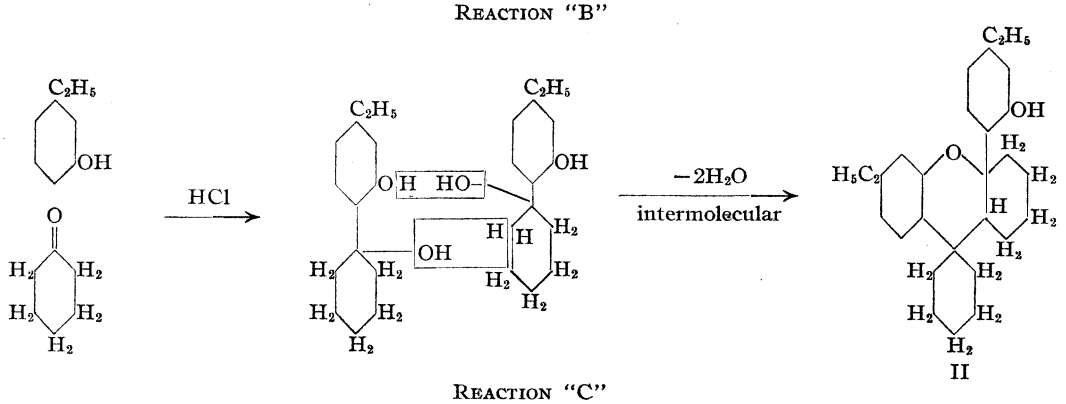
That this structure is correct was shown by an independent synthesis. *m*-Ethylphenol condensed with cyclohexylidenecyclohexanone gave the same flavan (II). Thus the probable mechanisms of these condensations can be represented as follows:

REACTION "A"



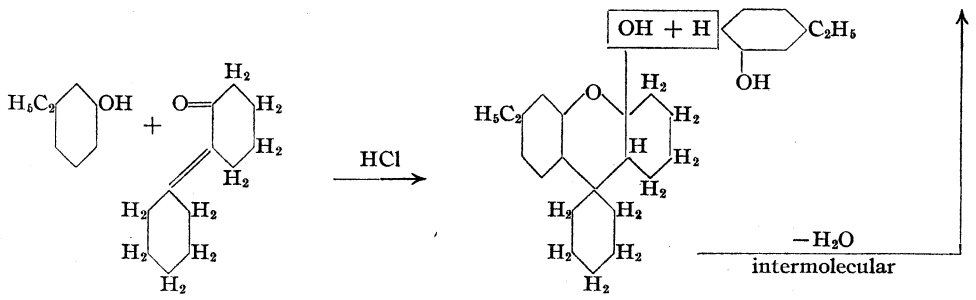
I

REACTION "B"



II

REACTION "C"



This reaction scheme would first of all suggest condensation of the cyclohexanone in the ortho position to the phenolic hydroxyl group, an assumption which is now well substantiated by spirochroman formation of the *m*-ethylphenol[2] and by coumaran formation of the same phenol when condensed with the alpha methylcyclohexanone.[1] That the cyclohexenyl radical is in the ortho position in the condensation product obtained in reaction "A" can be further inferred by the fact that its aryloxyacetic acid derivative,

(1) J. B. Niederl and co-workers, THIS JOURNAL, **61**, 1785 (1939).

(2) J. B. Niederl and co-workers, *ibid.*, **62**, 324 (1940).

despite being unsaturated, upon bromination gives a saturated monobromo derivative, while under the same condition the isomeric *o*-ethylphenol compound yields a dibromo derivative,[1] a fact which suggests cyclization in the former, yielding the respective coumaran compound (6-ethyl-2-carboxy-3,3-(2′-bromo)-pentamethylene-coumaran).

Thus in the last analysis the difference between condensation "A," involving the formation of the unsaturated phenol, and condensation "B" is that in the first case dehydration of the intermediate "phenol-hydrin" takes place "intramolecularly," whereas the second case, which involves the loss of two molecules of water from two molecules of the "phenol-hydrin," points to "intermolecular" dehydration.[3]

Experimental

Condensation Methods

Cyclohexanone and *m*-Ethylphenol.—One mol of *m*-ethylphenol was added to 1 mol of cyclohexanone in a 3-necked flask into which was inserted a thermometer, reflux condenser, and a gas inlet tube reaching to the bottom of the flask. A stream of dry hydrogen chloride gas was passed into the mixture for six hours. The temperature rose to 50° and was kept at that level for one hour. The flask was stoppered and set aside for five days, after which time crystals had formed. The mixture was filtered through a fritted glass filter, the crystals washed with benzene and recrystallized repeatedly from alcohol until colorless crystals were obtained; yield, 15% (five days condensation time).

Cyclohexylidene-cyclohexanone and *m*-Ethylphenol.—Eighteen grams, 0.1 mol, of cyclohexylidene-cyclohexanone (b. p. 143–146° at 15 mm.) prepared according to C. Mannich[4] was added to 24.6 g. (0.20 mol) of *m*-ethylphenol in a 3-necked flask equipped with a thermometer, reflux condenser, and a gas inlet tube. Hydrogen chloride gas was passed in for six hours, at the end of which time the flask was stoppered and let stand for a week. The crystals were washed with benzene and crystallized from alcohol; yield, 9% (one week condensation time).

2′ - Hydroxy - 4′,7 - diethyl - 2,3 - tetra - 4,4 - pentamethylene-flavan.—Soluble in organic solvents, but insoluble in Claisen solution; diazotization reactions positive. M. p., 195–196° (uncor.).

Anal. Calcd. for $C_{28}H_{36}O_2$: C, 83.17; H, 8.91; mol. wt., 404. Found: C, 82.77; H, 8.92; mol. wt., 404, 409.

Derivatives

Di-bromo Derivative.—One-half gram of the flavan compound was dissolved in 30 cc. of carbon tetrachloride and 0.4 g. of bromine in 10 cc. of the same solvent added drop by drop. The solvent was evaporated at room temperature and the crystals were recrystallized from alcohol; m. p. 180–181° (uncor.).

Anal. Calcd. for $C_{28}H_{34}O_2Br_2$: C, 59.78; H, 6.05; Br, 28.43. Found: C, 59.45; H, 6.25; Br, 28.47.

Benzoate.—One-half gram of the flavan was dissolved in 7 cc. of pyridine and 0.5 cc. of benzoyl chloride added. After the mixture had refluxed for one hour, it was poured with stirring into 20 cc. of water. The precipitate formed was taken up in ether and the solution washed with 3 cc. of 5% sodium carbonate solution and then with 5 cc. of water. After drying over calcium chloride and filtering, the ether was allowed to evaporate and colorless crystals of the benzoate remained; m. p. 169–170° (uncor.).

Anal. Calcd. for $C_{35}H_{40}O_3$: C, 82.68; H, 7.87. Found: C, 82.81; H, 8.18.

3,5-Dinitrobenzoate.—The procedure employed was the same as for the benzoate except that 3,5-dinitrobenzoyl chloride was used. The pale yellow crystals were recrystallized from alcohol; m. p. 176° (uncor.).

Anal. Calcd. for $C_{35}H_{38}O_7N_2$: C, 70.23; H, 6.35. Found: C, 70.20; H, 6.01.

Acetate.—One-half gram of the flavan was added to 20 cc. of acetic anhydride and the mixture refluxed for three hours. On pouring the cooled solution into water an oil separated which on standing solidified. The acetate was recrystallized from alcohol; m. p. 118–119° (uncor.).

Anal. Calcd. for $C_{30}H_{38}O_3$: C, 80.72; H, 8.52. Found: C, 80.90; H, 8.28.

Summary

Formation of a "flavan" type of crystalline condensation product from a cyclic ketone and a meta alkylated phenol was observed. The structure of the compound was proved by its synthesis from a cyclic alkylidene ketone and the same phenol. This as well as previous investigations seem to indicate that in condensations with ketones meta alkylated phenols appear to undergo alkylation in the *ortho* position to the phenolic hydroxyl group.

WASHINGTON SQUARE COLLEGE
NEW YORK, N. Y. RECEIVED MARCH 7, 1940

(3) M. E. McGreal and J. B. Niederl, "Abstracts of Papers, 97th meeting Am. Chem. Soc.," Baltimore, Md., 1939, pp. M 5–7.

(4) C. Mannich, *Ber.*, **40**, 157 (1907).

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

The Dehydration of *cis*- and *trans*-2-Phenylcyclohexanols

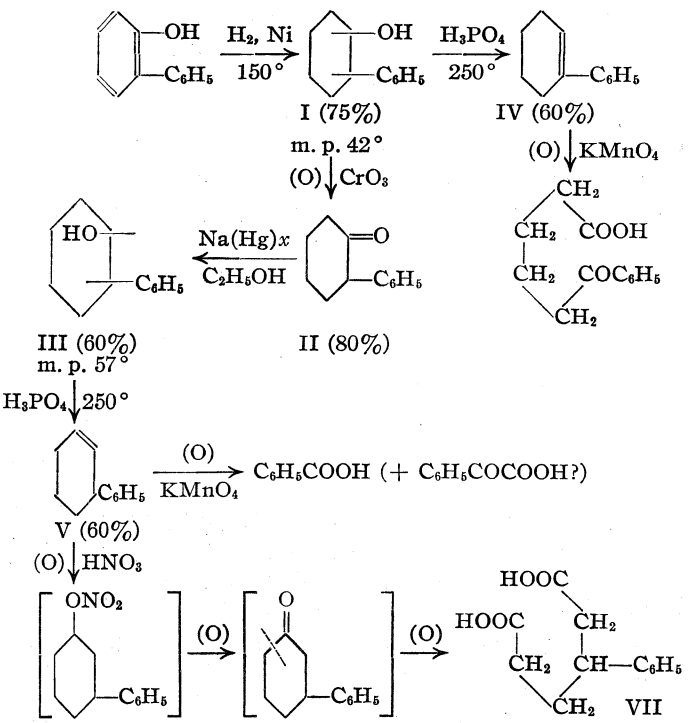
BY CHARLES C. PRICE AND JOSEPH V. KARABINOS

An investigation of the dehydration of *cis*- and *trans*-2-phenylcyclohexanols has been undertaken in order to obtain further evidence concerning the *trans*-elimination of water in such reactions. Vavon and Barbier[1] have observed that *cis*-2-alkylcyclohexanols are more easily dehydrated thermally or chemically than their *trans*-isomers, indicating that hydroxyl and hydrogen are more readily removed as water when they are in the *trans*-positions. They did not, however, determine the nature of the olefin formed in each case; it was with this purpose in view that the dehydration of the 2-phenylcyclohexanols has been investigated.

Only one of these two alcohols previously has beeen characterized and identified. From the catalytic reduction of *o*-phenylphenol with a nickel catalyst at temperatures above 200°, von Braun, Gruber and Kirschbaum[2] obtained a mixture of phenylcyclohexanol, cyclohexylcyclohexanol, cyclohexylbenzene and bicyclohexyl. The two alcohols were separated by oxidation to the ketones and subsequent reduction by sodium and alcohol; the 2-phenylcyclohexanol melted at 54–55°. Bedos[3] treated cyclohexene oxide with phenylmagnesium bromide and obtained a poor yield of a liquid which he suggested was a stereoisomer of the alcohol above, although it gave the same phenylurethan and phthalate. Cook, Lawrence and Hewitt,[4] however, pointed out that Bedos' alcohol may be contaminated by products of ring contraction. Using phenyllithium they obtained excellent yields of the alcohol, melting at 56–57° and identical with that reported by von Braun, Gruber and Kirschbaum.[2]

By the hydrogenation of *o*-phenylphenol with Raney nickel catalyst at 150° we have obtained an excellent yield of 2-phenylcyclohexanol melting at 41–42°. Since the compound crystallized only on standing for several days, the "viscous liquid" described by Ranedo and Leon[5] from a similar hydrogenation using platinum black in the cold may have been a slightly less pure sample of this isomer. The fact that this low-melting isomer has the *cis*-configuration is indicated by its method of preparation.[6]

Oxidation of the new low-melting *cis*-2-phenylcyclohexanol (I) with chromic acid yielded 2-phenylcyclohexanone (II) which was reduced to the high-melting isomer (III) by sodium amalgam and ethanol.



Dehydration of these two phenylcyclohexanols with phosphoric acid or anhydride gave chiefly 1-phenylcyclohexene (IV) from the *cis*-isomer (I) and 3-phenylcyclohexene (V) from the *trans* (III), another example of the well-known fact

(1) Vavon and Barbier (*Bull. soc. chim.*, [4] **49**, 567 (1931)) and Hückel and Neunhoeffer (*Ann.*, **477**, 135 (1930)) found that *cis*-2-cyclohexylcyclohexanol was dehydrated readily to Δ^1-cyclohexylcyclohexene while the *trans*-isomer was dehydrated with difficulty to give this same olefin contaminated by a small amount of an isomer which they suggested was Δ^1-hexahydrobenzylcyclopentene. A similar study with *trans*-2-methylcyclohexanol[3] gave no evidence for such a ring contraction, but the formation of both Δ^1- and Δ^2-methylcyclohexenes was demonstrated.

(2) Von Braun, Gruber and Kirschbaum, *Ber.*, **55**, 3668 (1922).

(3) Bedos, *Compt. rend.*, **177**, 111 (1923); *Bull soc. chim.*, **39**, 292 (1926).

(4) Cook, Lawrence and Hewitt, *J. Chem. Soc.*, 71 (1936).

(5) Ranedo and Leon, *Añales soc. espan. fis. quim.*, **22**, 222 (1924).

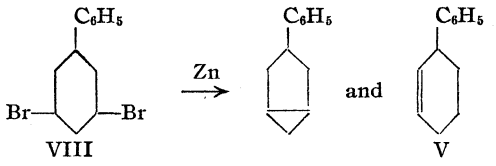
(6) See, *e. g.*, Vavon, *Bull. soc. chim.*, **41**, 1401 (1925); Bourguel, *Compt. rend.*, **180**, 1753 (1925); **187**, 383 (1928); Aronstein and Holleman, *Ber.*, **22**, 1181 (1899); Ott, *ibid.*, **61**, 2124 (1928).

that elimination to form a multiple link takes place most readily when the elements lost are *trans* to each other.[7]

In each case a small amount of the isomeric cycloölefin was obtained (Table I). In the second case (III) this could not have been due to isomerization after dehydration since the olefin (V) was unaffected when refluxed with phosphoric acid. The formation of a mixture must therefore be due either to the fact that some of the alcohol was isomerized before dehydration occurred or else *cis*- and *trans*-elimination must be competitive reactions; the first possibility seems the more likely.

The results differ somewhat from those with *trans*-2-methylcyclohexanol,[8] which gave nearly equivalent amounts of the two possible isomeric olefins. The *cis*-isomer of this compound has not yet been studied.

Of the two olefins above only 1-phenylcyclohexene (IV) has been reported previously in the literature.[9] Uspenski,[10] however, found that the treatment of 3,5-dibromo-1-phenylcyclohexane (VIII) with zinc yielded an olefin as well as the expected bicyclo compound. This olefin is identical in physical properties with the 3-phenylcyclohexene (V) above and is also similar in that no satisfactory products were obtained by permanganate oxidation (Uspenski obtained benzoic acid; we obtained benzoic, and possibly benzoylformic, acids).



VIII V

Oxidation of 3-phenylcyclohexene with dilute nitric acid gave a good yield of β-phenyladipic acid (VII). The formation of this acid was rather surprising; evidently the nitric acid attacks the double bond first by addition as indicated above.

Experimental

***cis*-2-Phenylcyclohexanol (I).**—*o*-Phenylphenol[11] was treated with hydrogen and Adams platinum catalyst in alcohol at 3–4 atmospheres at temperatures up to 70° but no hydrogen was absorbed.[5] When 680 g. of *o*-phenylphenol in 400 cc. of alcohol was treated with hydrogen at 135 atmospheres and 140–150° in the presence of Raney nickel until the theoretical amount of hydrogen had been absorbed, the product washed with 5% sodium hydroxide and distilled, 480 g. (75%) of *cis*-2-phenylcyclohexanol was obtained as a colorless, viscous oil, crystallizing after standing several days, b. p. 140–141° (16 mm.), m. p. 41–42°.[12]

Anal. Calcd. for $C_{12}H_{16}O$: C, 81.77; H, 9.14. Found: C, 81.44; H, 9.42.

Acidification of the alkaline extract above yielded 40 g. of starting material.

The **phenylurethan** was recrystallized readily from petroleum ether, m. p. 127.5–128°.

Anal. Calcd. for $C_{19}H_{21}O_2N$: N, 4.75. Found: N, 4.77.

Mixed with the phenylurethan from the *trans*-isomer (m. p. 136–137°) the melting point was 110–125°.

2-Phenylcyclohexanone (II).—The oxidation of the *cis*-cyclohexanol (I) was carried out by a modification of the method used by Cook, Lawrence and Hewitt.[4] To a solution of 31 g. of I in 50 cc. of glacial acetic acid, 14 g. of chromic oxide in 50 cc. of 80% acetic acid was added dropwise with vigorous stirring so that the temperature did not rise above 50°. After standing at room temperature for twenty-four hours, the mixture was poured into 250 cc. of water and extracted with one 200-cc. and two 100-cc. portions of benzene. The combined extracts were washed with sodium bicarbonate and with water, dried and distilled. The yield of 2-phenylcyclohexanone (II) was 25 g. (80%); b. p. 155–160° (16 mm.); m. p. 52.5–54.5°. The pure ketone melts at 63°[2,13]; the product reported by Cook, Lawrence and Hewitt[4] melted at 50–53°. The low-melting products are undoubtedly contaminated by a small amount of the unoxidized alcohol. The **semicarbazone** melted at 189–190°.[2,13]

***trans*-2-Phenylcyclohexanol (III).**—The ketone (II, 25 g.) was reduced by shaking with 433 g. of sodium amalgam (10 g. of sodium) in 175 cc. of alcohol for several hours. The mixture was partially evaporated, diluted with water and extracted with ether. The ether was washed, dried and distilled, yield, 15 g. (60%) of III, b. p. 152–155° (16 mm.), m. p. 52–54°. Recrystallized from petroleum ether, it melted at 56–57°.[2,4]

The **phenylurethan** had a melting point of 136–137°, in agreement with reports by other investigators.[2,3,4]

Dehydration.—Dehydration of the two alcohols was accomplished by refluxing with an equal weight of sirupy phosphoric acid for four hours. Ether and water were added and the ether washed, dried and distilled under diminished pressure. The composition of the fractions boiling from 115–130° (16 mm.) was determined by refractive index. These results are summarized in Table I. The physical constants of the purest samples of the two olefins are recorded in Table II.

One dehydration using phosphoric anhydride gave results very similar to those with phosphoric acid. The

(7) Michael, *Ber.*, **34**, 4225 (1901); Pfeiffer, *Z. physik. Chem.*, **48**, 40 (1904); Chavanne, *Bull. soc. chim. Belg.*, **26**, 287 (1912); **28**, 234, 240 (1914); Van der Walle, *ibid.*, **27**, 209 (1913); **28**, 369 (1914).

(8) Price, THIS JOURNAL, **61**, 1847 (1939).

(9) Sabatier and Mailhe, *Compt. rend.*, **138**, 1323 (1904).

(10) Uspenski, *J. Russ. Phys.-Chem. Soc.*, **51**, 245 (1920).

(11) Dow Chemical Company, Midland, Michigan.

(12) All melting points are corrected.

(13) Le Brazidec, *Compt. rend.*, **159**, 774 (1914).

TABLE I

DEHYDRATION OF *cis*- AND *trans*-2-PHENYLCYCLOHEXANOLS

Product	Expt.....1	% Yield from *cis*-Isomer 2	3[a]	4	*trans*-Isomer 5	6
1-Phenylcyclohexene (IV)	61.8	56	62	17.5	10	15.9
3-Phenylcyclohexene (V)	16.8	14.9	8.9	58.5	61	68.2

[a] Phosphoric anhydride.

TABLE II

PHYSICAL CONSTANTS OF 1- AND 3-PHENYLCYCLOHEXENES

	B. p. °C.	Mm.	$n^{20}D$	d^{20}_4	$M^{20}D$ (calcd. 51.36)
1-Phenyl- (IV)	126-128	16	1.5670	0.9939	51.95
1-Phenyl-[9]	128	16	1.569 (14°)	.9939	
3-Phenyl-[a]	115-117	16	1.5530	.9800	51.62
3(?)-Phenyl-[10]	101	9.5	1.5528	.9801	51.60

[a] *Anal.* Calcd. for $C_{12}H_{14}$: C, 91.08; H, 8.92. Found: C, 90.81; H, 9.32.

dehydration mixture was heated so that the product would distil at 16 mm. This crude olefin was washed, dried and redistilled as above.

3-Phenylcyclohexene (V, 1 g., $n^{20}D$ 1.5528) and 1 g. of phosphoric acid were refluxed for four hours and 75% of the hydrocarbon was recovered unchanged ($n^{20}D$ 1.5529), indicating that the dehydration conditions are not sufficient to cause isomerization of the double bond, in spite of the fact that in this case the isomer should be more stable due to conjugation. This conjugation, incidentally, leads to a slight exaltation in the molecular refraction for the 1-phenylcyclohexene (Table II).

Oxidation of 1-Phenylcyclohexene (IV).—Five grams of (IV) and 10 g. of potassium permanganate were stirred for twenty-four hours, initially at 0° but gradually warming to room temperature. Filtration and acidification gave an acid which was recrystallized from water as plates, 2 g., m. p. 75–76°. This corresponds to δ-benzoylvaleric acid (VI), the expected product. Its semicarbazone melted at 183–185°.[4,14]

Oxidation of 3-Phenylcyclohexene (V).—This hydrocarbon (4.75 g.) was refluxed with 100 cc. of 5% nitric acid for six days with the addition of a total of 7 cc. of concentrated nitric acid at intervals. On cooling, 3 g. of solid acid was obtained. Recrystallization from water gave β-phenyladipic acid (VII), m. p. 147–148°.[15] The permanganate (20.7 g.) oxidation of this olefin (4.5 g.) was not very satisfactory. Only benzoic acid precipitated on acidifying the filtrate. Semicarbazide gave a semicarbazone melting at 178–180° (the mixture with the semicarbazone of benzoylvaleric acid melted below 110°), which was hydrolyzed to an acid melting at 64–65° (benzoylformic acid is reported as melting at 66°).[16]

Summary

cis-2-Phenylcyclohexanol has been prepared in 75% yield by hydrogenation of *o*-phenylphenol.

Oxidation of this alcohol with chromic acid is an easy and economical method for the preparation of 2-phenylcyclohexanone.

cis-2-Phenylcyclohexanol and the *trans*-isomer yield chiefly 1- and 3-phenylcyclohexene, respectively, on dehydration, products corresponding to the *trans*-elimination of the elements of water in each case.

URBANA, ILLINOIS RECEIVED FEBRUARY 14, 1940

(14) Von Auwers and Treppmann, *Ber.*, **48**, 1217 (1915), report a melting point of 77–78° for the acid and 187° for the semicarbazone.

(15) Case, THIS JOURNAL, **55**, 2927 (1933), reported α-phenyladipic acid, m. p. 132–133°. Manske, *ibid.*, **53**, 1104 (1931), gives the melting point of β-phenyladipic acid as 146°. We found the neutral equivalent to be 109 (calcd.: 111).

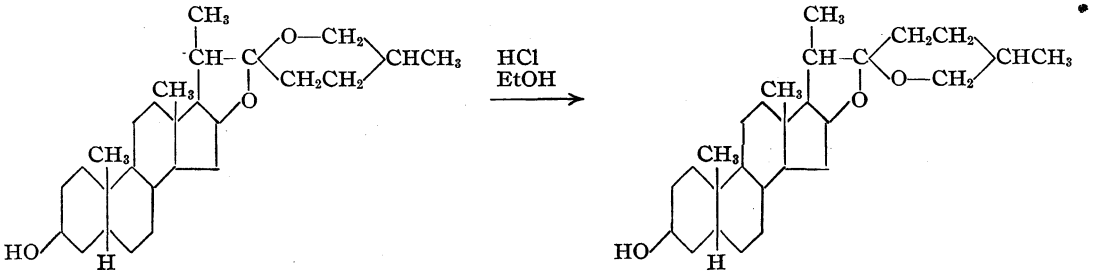
(16) Claisen, *Ber.*, **10**, 431 (1877); Bougault, *Ann. chim.* [9], **5**, 341 (1916), reported the melting point of the semicarbazone as 200°, dec.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE]

Sterols. XCVIII. Conversion of Isosarsasapogenin (Smilagenin) to Tigogenin

BY RUSSELL E. MARKER, EWALD ROHRMANN AND ELDON M. JONES

There has been considerable evidence presented recently indicating that sarsasapogenin differs from tigogenin not only in its configuration at C-5 but also in the configuration of the side chain,[1] the most significant evidence in this connection being the conversion of sarsasapogenin (I) to neotigogenin (III).[1,2] The fact that this transformation yielded neotigogenin rather than tigogenin suggested that the side chain of tigogenin possibly has the configuration of isosarsasapogenin[3,4] rather than of sarsasapogenin.



I. Sarsasapogenin

II. Isosarsasapogenin (Smilagenin)

III. Neotigogenin

IV. Tigogenin

We have now completely substantiated these predictions by effecting the conversion of isosarsasapogenin (II) to tigogenin (IV) by the procedure used for the conversion of sarsasapogenin to neotigogenin.[1] Isosarsasapogenone, prepared by the isomerization of sarsasapogenone with ethanolic hydrochloric acid, was converted to dibromo-isosarsasapogenone which upon treatment with pyridine yielded bromodehydro-$\Delta^{4,5}$-isosarsasapogenone. Reduction of this product with sodium and ethanol yielded tigogenin.

(1) Marker and Rohrmann, THIS JOURNAL, **62**, 647 (1940).
(2) Goodson and Noller, *ibid.*, **61**, 2420 (1939).
(3) Marker and Rohrmann, *ibid.*, **61**, 846 (1939).
(4) Marker and Rohrmann, *ibid.*, **62**, 898 (1940).

As might be anticipated, neotigogenin upon treatment with aqueous ethanolic hydrochloric acid readily passes into tigogenin.

Experimental Part

Dibromo-isosarsasapogenone.—To a solution of 21 g. of isosarsasapogenone, m. p. 186–188°, in 1 liter of acetic acid containing 2 cc. of 48% hydrobromic acid was added 101.5 cc. of 1.05 *N* bromine in acetic acid over a period of fifteen minutes with stirring at 20°. Much hydrogen bromide came off and the solution turned a deep violet color. Water was added and the precipitate filtered, dried and recrystallized from acetone containing 10% ethyl acetate to give white crystals, m. p. 184–188° dec.; yield 14 g.

Anal. Calcd. for $C_{27}H_{40}O_3Br_2$: C, 56.7; H, 7.1. Found: C, 57.1; H, 7.2.

Bromo-dehydro-$\Delta^{4,5}$-isosarsasapogenone.—A solution of 14 g. of dibromo-isosarsasapogenone in 140 cc. of dry pyridine was refluxed for eight hours. The solution was cooled and the precipitated material collected, washed well with ether and water, and dried. It melted with decomposition at 245–246° and was probably a pyridinium salt.

Anal. Calcd. for $C_{32}H_{45}O_3NBr$: C, 59.0; H, 7.0. Found: C, 58.7; H, 6.5.

The filtrate from the above was dissolved in ether and the pyridine removed by shaking with dilute sulfuric acid.

The ether solution was treated with Norit and the product crystallized from ether to give a product with m. p. 200–205°, dec.; yield 4.2 g.

Anal. Calcd. for $C_{27}H_{39}O_3Br$: C, 66.0; H, 8.0. Found: C, 65.8; H, 8.1.

Reduction of Bromo-dehydro-$\Delta^{4,5}$-isosarsasapogenone with Sodium and Ethanol.—To a boiling solution of 4 g. of bromo-dehydro-$\Delta^{4,5}$-isosarsasapogenone in 400 cc. of absolute ethanol was added 20 g. of sodium in small pieces over a period of one hour. Water was added and the precipitated solid taken up in ether, washed well with water and the ether evaporated. The residue was dissolved in a small amount of ethanol and to this was added a solution of 8 g. of digitonin in 400 cc. of 80% ethanol. After standing overnight the digitonide was collected, washed and dried; yield 6.2 g. This was decomposed with pyridine in the usual manner. The product was treated with Norit in methanol and crystallized from ether and methanol to give white crystals, m. p. 202–204°. A mixture with neotigogenin, m. p. 198–200°, melted at 174–185°. A mixture with sarsasapogenin, m. p. 199–201°, melted at 165–174°.

Anal. Calcd. for $C_{27}H_{44}O_3$: C, 77.8; H, 10.6. Found: C, 77.8; H, 10.5.

With boiling acetic anhydride the product gave an acetate which crystallized from methanol as white plates, m. p. 202–204°. When mixed with tigogenin acetate, m. p. 203–204° it gave no depression in melting point.

Anal. Calcd. for $C_{29}H_{46}O_4$: C, 75.9; H, 10.1. Found: C, 75.6; H, 9.9.

Isomerization of Neotigogenin into Tigogenin.—A solution of 100 mg. of neotigogenin in 20 cc. of ethanol and 2 cc. of concentrated hydrochloric acid was refluxed for eighty hours. Water was added and the product was crystallized from methanol–acetate, methanol and ethanol to give a product, m. p. 202–204°. When mixed with tigogenin, m. p. 204–206°, it melted at 203–206°. When mixed with neotigogenin of m. p. 199–201°, it melted at 180–186°.

Anal. Calcd. for $C_{27}H_{44}O_3$: C, 77.8; H, 10.6. Found: C, 77.7; H, 10.6.

When refluxed with acetic anhydride it gave an acetate which when crystallized from methanol melted at 202–204°. When mixed with tigogenin acetate, m. p. 203–205°, it melted at 203–205°.

Anal. Calcd. for $C_{29}H_{46}O_4$: C, 75.9; H, 10.1. Found: C, 75.8; H, 10.1.

We wish to thank Parke, Davis and Company for their generous help and assistance in the various phases of this work.

Summary

Isosarsasapogenin has been converted to tigogenin, indicating that the tigogenin side chain is of the "iso- configuration."

Neotigogenin upon isomerization with hydrochloric acid is converted into tigogenin.

STATE COLLEGE, PENNA. RECEIVED FEBRUARY 2, 1940

[CONTRIBUTION FROM THE CHEMISTRY LABORATORY OF THE JOHNS HOPKINS UNIVERSITY]

Divalent Nitrogen. I. The Rate of Dissociation of Tetraphenylhydrazine[1]

BY C. K. CAIN[2] AND F. Y. WISELOGLE

The successive substitution of the hydrogen atoms of ethane by phenyl groups weakens the ethane carbon–carbon linkage to such an extent that hexaphenylethane in solution undergoes rapid dissociation into free radicals at 0°. This marked decrease in the bond strength has been attributed in part to stabilization of the resulting triphenylmethyl radicals through resonance of the odd electrons in the aromatic nuclei, resonance which is not possible in hexaphenylethane.[3]

If stabilization of triarylmethyl radicals through increased resonance is responsible for dissociation in hexaarylethanes,[4] then it seems reasonable to predict that substitution by aryl groups of the hydrogen atoms of any simple dimeric molecule would weaken the central bond of the compound. An accumulation of aryl groups could lead to compounds which would dissociate at moderate temperatures to give relatively stable radicals. Indeed Wieland has attributed many of the reactions of tetraarylhydrazines, $R_2N\text{-}NR_2$, to preliminary dissociation into free radicals, R_2N-, in which the nitrogen atom is divalent.[5] We have now undertaken a study of substituted hydrazines in order to determine the energetics of this dissociation process and thereby to determine the effect on the strength of the N-N bond of substituting various groups for hydrogen atoms. In this paper we report measurements of the rate of dissociation of tetraphenylhydrazine and from these data a calculation of the activation energy for the formation of diphenylnitrogen radicals.

(1) From a dissertation submitted by C. K. Cain in partial fulfillment of the requirements for the degree of Doctor of Philosophy in the Johns Hopkins University.

(2) E. I. du Pont de Nemours and Co. Fellow, 1938–1939.

(3) Pauling and Wheland, *J. Chem. Phys.*, **1**, 367 (1933).

(4) Recently the importance of resonance as a factor in promoting dissociation of polyarylethanes has been questioned. See, for example, Marvel, Mueller and Ginsberg, THIS JOURNAL, **61**, 2008 (1939). That resonance plays some part in stabilizing the radicals, however, is not disputed.

(5) Wieland, "Die Hydrazine," Ferdinand Enke, Stuttgart, 1913, pp. 71–78.

Properties and Reactions of Tetraphenylhydrazine.—Tetraphenylhydrazine, prepared from diphenylamine by oxidation, is a colorless crystalline product melting with decomposition at 165–170° to a greenish-brown liquid. Solutions give the same color when heated to approximately 70°; at this temperature tetraphenylhydrazine rapidly undergoes disproportionation (Equation 1).[6]

$$2(C_6H_5)_2N{-}N(C_6H_5)_2 \longrightarrow \text{(9-phenylcarbazole)} + 2(C_6H_5)_2NH \quad (1)$$

Solutions of tetraphenylhydrazine absorb nitric oxide at 100° to give quantitative yields of N-nitrosodiphenylamine, a product which is also obtained by the action of nitrous acid on diphenylamine (Equation 2).[6] The formation of N-nitrosodiphenylamine

$$(C_6H_5)_2N{-}N(C_6H_5)_2 + 2NO \rightleftharpoons 2(C_6H_5)_2N{-}NO + 2(C_6H_5)_2NH + 2HONO \quad (2)$$

from nitric oxide is a reversible reaction since at 130° the nitric oxide is evolved in yields up to 95% of the theoretical. Although tetraphenylhydrazine does not react with gaseous oxygen, a reagent for trivalent carbon radicals, further evidence for dissociation was reported in the reaction with triphenylmethyl to give a coupling product of the two radicals (Equation 3)[6]

$$(C_6H_5)_2N{-}N(C_6H_5)_2 + 2(C_6H_5)_3C{-} \xrightarrow{100°} 2(C_6H_5)_3C{-}N(C_6H_5)_2 \quad (3)$$

Rate of Dissociation of Tetraphenylhydrazine.—In order to measure the rate of dissociation of tetraphenylhydrazine it was necessary to find a reagent which would react rapidly and irreversibly with the free diphenylnitrogen radicals but at a negligible rate with the undissociated tetraphenylhydrazine. The rate of the over-all reaction would thus be limited to that of the slowest step and therefore a measure of the rate of the dissociation process. Ziegler, Orth and Weber used nitric oxide successfully to measure the rate of dissociation of hexaphenylethane at temperatures from −20° to +10°[7]; if the partial pressure of nitric oxide was greater than about 0.2 atmosphere the rate of absorption was independent of the pressure and identical with the rate of reaction of hexaphenylethane with iodine or oxygen, proof that the rate-controlling step in each case was the dissociation process. Accordingly, we first selected the reaction of tetraphenylhydrazine with nitric oxide to determine whether the rate-controlling step in this case was the dissociation process.

(6) Wieland, *Ann.*, **381**, 200 (1911). ϕ represents the phenyl radical.

(7) Ziegler, Orth and Weber, *ibid.*, **504**, 131 (1933).

Experimental

The gas absorptions were carried out in an air thermostat of inside dimensions 16″ × 19″ × 30″ (64 × 79 × 120 cm.) provided with rapid air circulation and containing a bimetallic thermoregulator capable of maintaining temperatures from 50 to 120° constant to within ±0.05°. Temperature control was achieved by using two electrical heating units of which one, carrying 75 to 500 watts, was manually operated to give the approximate temperature and the other, carrying 50 to 200 watts, was operated by the thermoregulator. The temperatures were read on a short stem thermometer graduated to 0.2° and calibrated against a thermometer certified by the Bureau of Standards.

A 200-cc. round-bottomed flask provided with an interchangeable ground glass joint was fastened by a spring clamp to an oscillating shaking mechanism. The thermometer was fastened to the thermostat so that the bulb was a few cm. from the center of the flask. The flask was connected by means of heavy rubber and glass capillary tubing through a T-stopcock to the top of a 100-cc. gas buret (Fig. 1). The buret communicated with a parallel glass leveling tube open at the top and leading through a stopcock into a reservoir of diethyl phthalate which was used as the retaining liquid. The glass leveling tube was connected to the buret by means of a rubber stopper which was protected from the retaining liquid by a layer of mercury. The diethyl phthalate was forced up into the buret and leveling tube by applying air pressure to the reservoir and temporarily opening the stopcock. When the level of liquid was the same in the buret and leveling tube the pressure within the system was equal to that outside. By varying the air pressure on the reservoir and by manipulating the stopcock this condition was maintained throughout each run. This design allowed the use of a light organic liquid sensitive to pressure changes within the system but avoided any direct contact between the organic liquid and rubber. The tedious manipulation of a leveling bulb also was eliminated.

***o*-Dichlorobenzene** was used as the solvent for the reaction. Preliminary experiments indicated that *o*-dichlorobenzene did not react with nitric oxide at any of the temperatures used in the rate studies. The technical product containing 5% of the para isomer was fractionated and the portion distilling at 180–181° (760 mm.) was retained.

Tetraphenylhydrazine was prepared according to the general directions in Gattermann.[8] Mechanical stirring was used during the addition of the potassium permanganate and the product was recrystallized from benzene and

(8) Gattermann, "Laboratory Methods of Organic Chemistry," The Macmillan Co., New York, N. Y., 1937, p. 355.

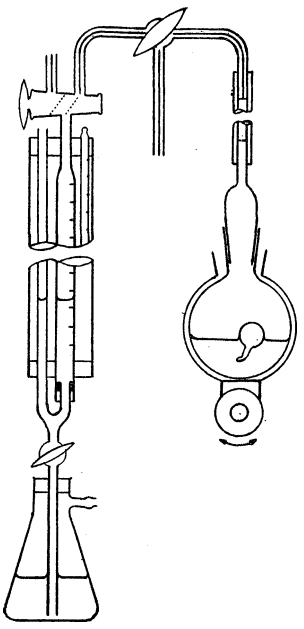


Fig. 1.—Apparatus for measuring rate of absorption of gas at constant pressure.

alcohol. The color on the surface of the crystals was removed by washing the filtered product on the funnel with cold ether. The recorded melting point (144°) is not significant. If the melting point tube was plunged into a preheated bath at this temperature there was a lag of about thirty seconds before the solid suddenly melted. This time lag was reduced at higher temperatures until at 165–170° essentially instantaneous melting took place. The product was dried at 50° under reduced pressure and was used at once for the rate measurements since the solid slowly acquired a green color on standing.

Nitric oxide was prepared by the action of diluted sulfuric acid (1/1) on a solution of sodium nitrite, the nitrogen dioxide being removed by washing the gases with 10% sodium hydroxide solution. The nitric oxide was stored in a gasometer over 1% sodium hydroxide solution, and was dried before use by passage through a tube containing soda-lime. Synthetic mixtures of known volumes of nitric oxide and nitrogen were prepared and stored in gasometers.

In a typical run the flask containing 25 cc. of solvent and a few glass beads was placed in the thermostat at the desired temperature. In order to remove any oxygen dissolved in the solvent the flask was repeatedly evacuated and filled with nitrogen. In the meantime approximately 0.34 g. of tetraphenylhydrazine was introduced into a previously weighed thin-walled glass bulb. The bulb was weighed, then evacuated, filled with nitrogen and sealed. After the flask and solvent had attained the temperature of the thermostat the sample was carefully introduced. Any air which entered the system at this time was removed by evacuation and displacement by nitrogen. The nitrogen was immediately displaced by nitric oxide of known partial pressure and the gas buret was filled with nitric oxide at a pressure of one atmosphere. The T-stopcock was turned to shut off the nitric oxide supply and to open the system to the buret.

As soon as the buret reading remained constant for two minutes while the flask was gently shaken, an indication of thermal equilibration, the bulb was broken by increasing the speed and eccentricity of shaking to that maintained throughout the run. The initial buret reading was taken the instant the bulb broke and was usually 0.3 cc. greater than the reading immediately before breaking. The increase in volume undoubtedly arose from the pressure built up within the bulb at the elevated temperature. Absorption of gas began immediately and buret readings were taken at regular, convenient time intervals.

The theoretical absorption was calculated from the equation

$$V = 370.8w(t + 273)/P$$

where w is the weight of the sample, t the temperature of the gas buret and P is the corrected barometric pressure in mm. The coefficient 370.8 is the value of $2 \times 760R/M$, where R is the gas constant, 82.07, M the molecular weight of tetraphenylhydrazine, 336.2, and the factor 2 arises from the absorption of two moles of nitric oxide by one mole of tetraphenylhydrazine.

In Table I, columns 1, 2 and 3, are recorded typical data obtained in a representative experiment.

Results and Discussion

Nature of the Reaction.—In Fig. 2 are plotted the time rates of absorption of nitric oxide at 95.15° by 0.04 molar solutions of tetraphenylhydrazine in *o*-dichlorobenzene at various nitric oxide pressures. From an inspection of the

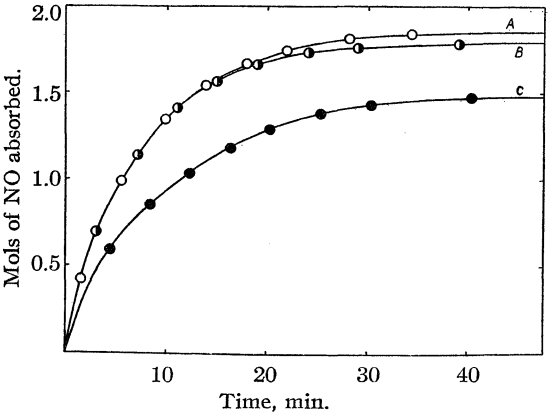


Fig. 2.—Rate of absorption of nitric oxide by solutions of tetraphenylhydrazine in *o*-dichlorobenzene at 95.15°: Curve A, pNO = 1.0 atm.; curve B, pNO = 0.2 atm.; curve C, pNO = 0.1 atm.

curves it is evident that the absorption of nitric oxide did not approach two moles, required for the formation of N-nitrosodiphenylamine, but stopped at 75–95% of this value. We were first inclined to attribute this apparent incomplete

absorption to redissociation of the N-nitrosodiphenylamine and attainment of equilibrium (Equation 2). Although Wieland has established the dissociation of N-nitrosodiphenylamine into nitric oxide at 130°, a sample of the reaction product dissolved in *o*-dichlorobenzene at 100° proved perfectly stable and no nitric oxide was evolved.

TABLE I

ABSORPTION OF NITRIC OXIDE BY TETRAPHENYLHYDRAZINE: TYPICAL DATA OBTAINED IN REPRESENTATIVE EXPERIMENT

Tetraphenylhydrazine, 0.3949 g.; 25 cc. of *o*-dichlorobenzene; barometer, cor., 760.7 mm.; buret temp., 23.0°; *p*NO, 0.20 atm.; temp. of thermostat, 95.15°; theoretical absorption, 57.0 cc.; rate constant, from slope of curve in Fig. 3, 0.1285 min.$^{-1}$.

Time, min.	Buret reading, cc.	Absorption, cc.	Volume yet to be absorbed, cc.	$-\text{Log}\ (1 - Z)$	$= kt/2.3$
0.00	85.2	0.0	51.5	0.000	0.000
.73	80.6	4.6	46.9	.041	.041
1.73	74.9	10.3	41.2	.097	.097
2.73	69.9	15.3	36.2	.153	.153
3.73	65.5	19.7	31.8	.209	.208
4.73	61.6	23.6	27.9	.266	.264
5.73	58.2	27.0	24.5	.323	.320
6.73	55.2	30.0	21.5	.379	.376
7.73	52.7	32.5	19.0	.433	.432
8.73	50.4	34.8	16.7	.489	.488
9.73	48.4	36.8	14.7	.543	.543
11.73	45.1	40.1	11.4	.655	.655
13.73	42.6	42.6	8.9	.762	.767
15.73	40.6	44.6	6.9	.873	.879
17.73	39.1	46.1	5.4	.979	.991
19.73	37.8	47.4	4.1	1.100	1.103
24.73	35.9	49.3	2.2	1.369	1.414
29.73	35.1	50.1	1.4	1.566	1.661
39.73	34.3	50.9	0.6	1.934	2.220
∞	33.7	51.5	0.0		

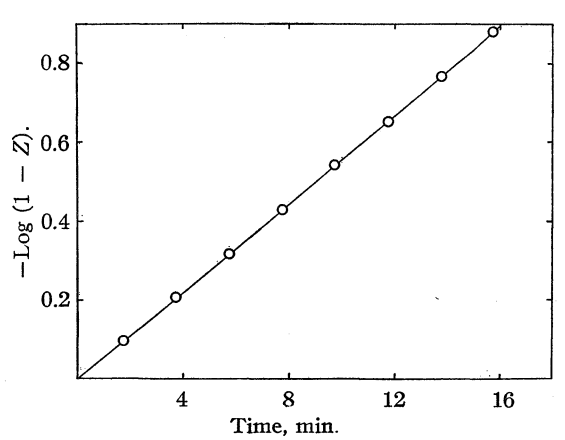


Fig. 3.—Rate of nitric oxide absorption by tetraphenylhydrazine. A plot of data in Table I.

Moreover, the fraction of the theoretical absorption of nitric oxide decreased as the time increased between the introduction of the sealed sample into the reaction flask and the beginning of the reaction. In an extreme case a bulb containing solid tetraphenylhydrazine in a nitrogen atmosphere was maintained at 100° for one hour; at the end of this period the sample was colored dark green and had partially liquefied, indicating extensive decomposition. When the bulb was broken in the absorption flask and the sample dissolved, the total absorption of nitric oxide was only 5.7% of the theoretical. It is evident, therefore, that tetraphenylhydrazine in the solid state undergoes extensive thermal decomposition at 100° to give products which do not react with nitric oxide.

That the reaction between nitric oxide and tetraphenylhydrazine was quantitative was shown in another experiment by dissolving a weighed sample of tetraphenylhydrazine in *o*-dichlorobenzene at 18°, a temperature at which no reaction took place; the solution, in the presence of nitric oxide, was warmed to 100° and maintained at this temperature for one hour. When the reaction mixture was again cooled to 18° the decrease in volume indicated an absorption of 99% of the theoretical amount of nitric oxide. A 94% yield of N-nitrosodiphenylamine was isolated from the reaction mixture on removal of the solvent; the product was identified through a determination of the melting point of a mixture with an authentic sample prepared from diphenylamine.

The reaction between tetraphenylhydrazine and nitric oxide, therefore, is stoichiometric and irreversible at temperatures up to 100°; moreover, the rate of absorption of nitric oxide, at 1 atm. pressure, is greater than the rate of thermal decomposition in *o*-dichlorobenzene. Because solid tetraphenylhydrazine also undergoes a fairly rapid pyrolysis, however, the true concentration of material present at the start of the reaction, *i. e.*, when the bulb was broken, was considerably less than that calculated from the weight of the sample. This initial concentration of tetraphenylhydrazine was calculated from the total absorption of nitric oxide at the completion of the reaction, using the equation given in the experimental section for calculating the theoretical absorption.

It was, of course, impossible to prevent the undesired pyrolysis of the solid tetraphenylhydrazine in our rate experiments but we reduced to a minimum the time between the introduction of the sample and the breaking of the bulb. This

period was rarely more than twenty minutes and under these conditions the absorption approached 85–95% of the theoretical at the higher temperatures and 100% of the theoretical at the lower temperatures.

Mechanism of the Reaction.—If the rate-controlling step involves a direct reaction between tetraphenylhydrazine and nitric oxide, regardless of the mechanism, then the rate must be a function of the nitric oxide concentration. Conversely, if the rate of absorption proves to be independent of the nitric oxide concentration, the nitric oxide cannot be involved in the rate-controlling step. Under the conditions of our experiments the partial pressure of nitric oxide was maintained constant throughout a run; the concentration of dissolved nitric oxide, proportional to the partial pressure, also remained constant since the gas–solution equilibrium was maintained by vigorous shaking. In order to determine the effect of changing the concentration of nitric oxide, therefore, several runs were made at different nitric oxide pressures.

From an inspection of the curves A and B of Fig. 2 it is apparent that the initial rate of absorption is independent of the nitric oxide pressure if this is greater than 0.2 atm. At these relatively high pressures, therefore, the rate-controlling step is a first-order reaction and a direct reaction between tetraphenylhydrazine and nitric oxide is precluded. For very low pressures, however, both the rate and extent of absorption of nitric oxide decrease (Curve C, Fig. 2).

These data, then, parallel those obtained by Ziegler, Orth and Weber for the reaction between hexaphenylethane and nitric oxide at 0°[7]; we believe the mechanisms in the two cases are analogous. The first step in the formation of N-nitrosodiphenylamine is a slow, unimolecular dissociation of tetraphenylhydrazine into free radicals (Equation 4).

$$(C_6H_5)_2N{-}N(C_6H_5)_2 \xrightarrow{\text{slow}} 2(C_6H_5)_2N{-} \quad (4)$$

In the absence of any reagent these radicals may undergo recombination to form tetraphenylhydrazine (Equation 5) or they may undergo an irreversible thermal decomposition (Equation 6). In

$$2(C_6H_5)_2N{-} \longrightarrow (C_6H_5)_2N{-}N(C_6H_5)_2 \quad (5)$$

$$x(C_6H_5)_2N{-} \xrightarrow{\text{fast}} \text{disproportionation products} \quad (6)$$

the presence of nitric oxide at pressures above 0.2 atm., however, the radicals react exclusively with nitric oxide as fast as they are formed (Equation 7). The rate of absorption of nitric

$$(C_6H_5)_2N{-} + NO \xrightarrow{\text{very fast}} (C_6H_5)_2N{-}NO \quad (7)$$

oxide, therefore, depends only upon the rate of formation of the diphenylnitrogen radicals and the over-all reaction is of the first order with respect to tetraphenylhydrazine.

At low partial pressures the small concentration of dissolved nitric oxide results in a decrease in the rate of formation of N-nitrosodiphenylamine (Equation 7); diphenylnitrogen radicals accumulate in the solution and may undergo reactions (5) and (6) as well as (7); the over-all rate becomes a function of the nitric oxide pressure and is less than the rate of dissociation.

For a first-order reaction the time rate of change of concentration may be expressed in the form: $-\log(1 - Z) = kt/2.3$, where Z is the fraction of tetraphenylhydrazine or nitric oxide reacted in time, t, and k is the specific reaction rate constant. In our work the fraction, Z, was determined by dividing the decrease in volume at time t by the total decrease in volume at the completion of the reaction. For such a reaction a plot of $-\log(1 - Z)$ against t should give a straight line the slope of which multiplied by 2.3 is the rate constant. Figure 3 shows such a plot from the data of Table I, and represents a typical evaluation of the rate constant. The precision of the data may be evaluated by comparing columns 5 and 6 of Table I.

Table II shows the effect of changing conditions on the rate constant at 95.15°. It will be noted that the rate constant is independent of the concentration of tetraphenylhydrazine, and of the partial pressure of nitric oxide except at very low values.

TABLE II

VELOCITY OF NITRIC OXIDE ABSORPTION BY TETRAPHENYLHYDRAZINE AT 95.15°

Concn. of tetraphenylhydrazine in moles per liter	Nitric oxide pressure, atm.	Per cent. of theoretical absorption	Rate constant k
0.046	1	82	0.131
.033	1	76	.132
.025	1	89	.127
.042	0.2	90	.128
.019	.2	88	.114
.028	.1	74	.088
Average of all reliable runs made			.130

We have repeated the absorption rate studies at five-degree intervals from 75 to 100° and have

verified this unimolecular character of the rate-controlling step at all temperatures; the results are collected in Table III. At the lower temperatures it was inconvenient to allow the reaction to proceed to completion and a more practicable method was adopted for calculating the rate constant. The reaction was carried to approximately 75% of completion and the total absorption of nitric oxide at infinite time was used as a parameter in plotting $-\log (1 - Z)$ against t; that value was chosen which gave no appreciable departure from a straight line and the rate constant was calculated from the slope of this line. This method is illustrated in Fig. 4 where three curves are plotted selecting values for the total absorption 2.5% too high and too low from the value which gave the best straight line. In a few experiments the two methods were compared; the agreement of the rate constants was usually within 2%.

TABLE III

VELOCITY OF NITRIC OXIDE ABSORPTION BY TETRAPHENYLHYDRAZINE

Temp., °C.	Av. vel. constant k, min.$^{-1}$	Half-life, min.	No. of runs	Mean error of mean, %
75.20	0.0119	58.3	2	1.7
80.20	.0230	30.2	4	1.7
85.20	.0397	17.5	4	2.5
90.2	.0670	10.4	4	1.8
95.15	.130	5.35	4	1.0
100.10	.222	3.13	5	2.0

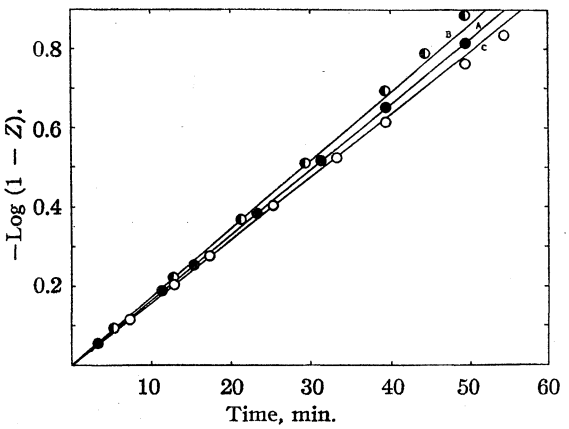


Fig. 4.—Rate of absorption of a 0.04 molar solution of tetraphenylhydrazine in *o*-dichlorobenzene at 85.20° showing alternative method of calculating rate constant: pNO = 1.0 atm.; Curve A, filled circles, total absorption assumed to be 40.0 cc.; Curve B, half-filled circles, total absorption assumed to be 39.0 cc.; Curve C, open circles, total absorption assumed to be 41.0 cc. It is apparent that the curves on either side of A diverge; rate "constants" for the three curves are: for C, 0.0365; for A, 0.0382; for B, 0.0401. The curves are exaggerated to illustrate the principle of the method; in practice absorptions of 39.5 cc. and 40.5 cc. would be assumed. The rate constant was determined from the slope of curve A, which shows no perceptible deviation from a straight line.

The energy of activation, E, for the rate-controlling step was calculated from the Arrhenius equation, $\log k = E/2.3RT + C$, where R is the gas constant, T the absolute temperature and C the integration constant. A plot of $\log k$ against the reciprocal of the absolute temperature gave a straight line (Fig. 5) the slope of which multiplied by 2.3 R gave 30 kcal. as the heat of activation. We consider that this value is accurate to ±1.5 kcal.

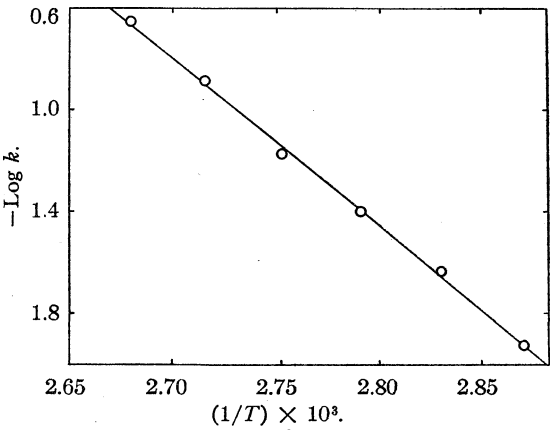


Fig. 5.—The rate of dissociation of tetraphenylhydrazine at different temperatures.

The energy of activation for a dissociation process, E_d, is of considerable significance since it represents a maximum value for the strength of the bond broken and is related to the bond strength, ΔH, by the equation $\Delta H = E_d - E_a$, where E_a is the activation energy for the association of the resulting radicals. The carbon–carbon bond strength in hexaphenylethane, 11.5 kcal.,[9] represents a marked decrease from the normal carbon–carbon bond strength of ethane, 58.6 kcal.,[10] an average reduction of 8 kcal. per phenyl group. The activation energy for the dissociation process likewise decreases as phenyl groups are substituted for hydrogen atoms. The activation energies for the dissociation of pentaphenylethane and hexaphenylethane are, respectively, 27.6 kcal.[11] and 19.5 kcal.[6] It will be noted that the difference, 8 kcal., is identical with

(9) Ziegler and Ewald, *Ann.*, **473**, 163 (1929).

(10) Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1939.

(11) Bachmann and Wiselogle, *J. Org. Chem.*, **1**, 359 (1936).

the average effect on the bond strength of replacing a hydrogen atom by a phenyl group.

Recently Hughes, Corruccini and Gilbert[12] have redetermined the heat of combustion of hydrazine, H_2N-NH_2, making possible a calculation of the strength of the normal N–N bond from thermochemical data. From the energy of formation of gaseous hydrazine from the elements, 22.25 kcal., the energy of dissociation of hydrogen, 103.8 kcal.,[13] and the energy of dissociation of nitrogen, 170.2 kcal., the energy of formation of gaseous hydrazine from the atoms may be calculated. This energy, 355.6 kcal., may be considered to be composed of two terms, one involving four N–H bonds and the other involving the N–N bond. If we assume that the average N–H bond strength in hydrazine is the same as in ammonia, 83.9 kcal., the energy of dissociation of hydrazine into divalent nitrogen radicals is 20 kcal. (Equation 8).[14]

$$N_2H_4(g) \longrightarrow 2NH_2^{\cdot}(g) \qquad \Delta H = 20 \text{ kcal.} \quad (8)$$

The energy of activation for the dissociation of tetraphenylhydrazine is greater than the energy of dissociation of hydrazine, in marked contrast to the lowering of bond strength and activation energy by substituting phenyl groups for hydrogen atoms in the ethane series. If the substitution of an aryl group for a hydrogen atom in hydrazine lowers the bond strength, then the energy of activation for the coupling of two divalent nitrogen radicals must be inordinately high. A rigorous test of this must await a determination of the energy of dissociation of tetraphenylhydrazine.

Acknowledgment.—We are indebted to E. I. du Pont de Nemours and Company for a fellowship held by one of us (C. K. C.) and to the Hynson, Westcott and Dunning Research Fund for a grant-in-aid covering a part of the cost of this research.

Summary

A study has been made of the kinetics of the reaction between tetraphenylhydrazine and nitric oxide at 75 to 100°. Although solid tetraphenylhydrazine undergoes rapid decomposition at 100°, solutions in *o*-dichlorobenzene absorb nitric oxide quantitatively and irreversibly to give N-nitrosodiphenylamine. For nitric oxide pressures above 0.2 atm. the rate-controlling step is independent of the nitric oxide pressure and is undoubtedly the dissociation of tetraphenylhydrazine into free diphenylnitrogen radicals. The half-life of tetraphenylhydrazine at 100° is 3.1 minutes and the energy of activation for the dissociation is 30 ± 1.5 kcal. This activation energy is 10 kcal. greater than the energy of dissociation of hydrazine calculated from recent thermochemical measurements.

BALTIMORE, MD. RECEIVED FEBRUARY 17, 1940

(12) Hughes, Corruccini and Gilbert, THIS JOURNAL, **61**, 2639 (1939).

(13) The data for the bond strengths in ammonia and for the heats of dissociation of hydrogen and nitrogen were taken from Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, 1939, and Bichowsky and Rossini, "The Thermochemistry of the Chemical Substances," Reinhold Publishing Corp., New York, N. Y., 1936.

(14) This N–N bond strength is 4 kcal. less than that calculated by Pauling who used the average value for the heat of combustion of hydrazine cited in Bichowsky and Rossini (*loc. cit.*). It should be noted that the assumption of the equality of the N–H bond strengths in ammonia and in hydrazine has not received the empirical support which is available for other bonds such as C–H and O–H. We do know that the successive removal of hydrogen atoms from ammonia requires widely different energies. Thus the heat of dissociation of NH, 102.2 kcal., which is accurately known from spectroscopic data is much greater than the average strength of the N–H bonds in ammonia.

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT OF EMORY UNIVERSITY]

The Mechanism of the Esterification of Strong Organic Acids. The Esterification of Neopentyl Alcohol with the Chloroacetic Acids[1,2]

BY OSBORNE R. QUAYLE AND HARRY M. NORTON[3]

The origin of the hydrogen and hydroxyl groups which form water in esterification has been the subject of much investigation. Since the work of Reid[4,5] with the sulfur analogs of both alcohols and acids, it has been conceded that in the case of weak organic acids the hydrogen only is from the alcohol. This has been confirmed by the esterification of methyl alcohol containing a high percentage of heavy oxygen.[6] The question has remained as to whether the course of the reaction with strong organic acids is the same or whether these acids provide only the hydrogen, acting similarly to the strong mineral acids such as hydrochloric.

Neopentyl alcohol was esterified with a series of carboxylic acids varying widely in strength.

TABLE I

EXPERIMENTAL DATA

Neopentyl ester	Yield after purif., %	Ci anal., % Calcd.	Found	$n^{20}D$	d^{20}_4	d^{30}_4	d^{40}_4	B. p. at 760 mm., °C.
Acetate	55			1.3893	0.8544	0.8444	0.8346	127
Chloroacetate	52	21.56	21.47	1.4211	1.0286	1.0177	1.0076	180
Dichloroacetate	50	35.63	35.71	1.4324	1.1311	1.1203	1.1107	194
Trichloroacetate	43	45.56	45.34	1.4373	1.2142	1.2024	1.1909	202

	M. p., °C.
p-Nitrobenzoate	54.0–54.5
3,5-Dinitrobenzoate	90.0–90.5

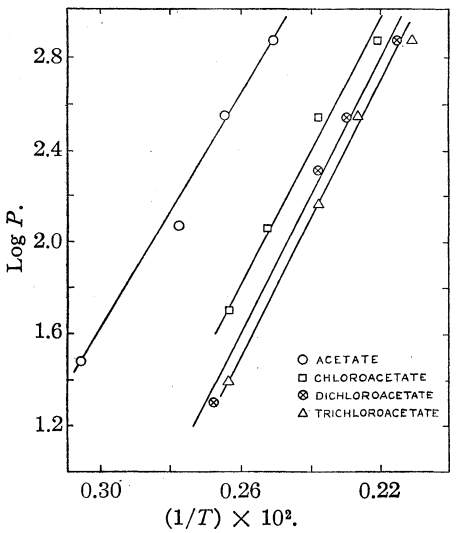


Fig. 1.—Vapor pressure of neopentyl esters.

This alcohol was chosen because of its unique property of rearranging if the electronic structure

$$CH_3:\ddot{C}:\ddot{C}:H$$
$$\quad\ddot{C}H_3\ddot{H}$$

is destroyed.[7,8,9,10] The removal of the hydroxyl group would break this structure; the removal of only hydrogen would not. Rearrangement of the neopentyl system yields *t*-amyl derivatives and is accompanied by the formation of unsaturated derivatives.

The neopentyl esters were made of chloroacetic, dichloroacetic and trichloroacetic acids, in addition to that of acetic acid previously discussed by Whitmore.[7] These esters when treated with bromine in a quantitative manner showed no evidence of the unsaturation which accompanies rearrangement.

Small portions of each ester (10 g.) were saponified and the resulting alcohol was identified in each case as neopentyl alcohol. Identification was established by mixed melting point determinations on the original alcohol with the alcohol obtained on saponification and on the *p*-nitrobenzoate derivatives. Since neopentyl alcohol was obtained from each ester, the neopentyl con-

(1) The authors acknowledge with grateful thanks the advice and assistance of Dr. E. Emmet Reid, research consultant to the Department.

(2) Abstracted from the thesis presented by Harry M. Norton to the Graduate School of Emory University in partial fulfilment of the requirements for the degree of Master of Science.

(3) Present address, University of Buffalo.

(4) E. E. Reid, *Am. Chem. J.*, **43**, 489 (1910).

(5) L. S. Pratt and E. E. Reid, THIS JOURNAL, **37**, 1939 (1915).

(6) I. Roberts and H. C. Urey, *ibid.*, **60**, 2391 (1938).

(7) F. C. Whitmore, "Organic Chemistry," D. Van Nostrand, Inc., New York City, 1937, p. 128.

(8) G. Edgar, G. Calingaert and R. E. Marker, THIS JOURNAL, **51**, 1487 (1929).

(9) F. C. Whitmore and H. S. Rothrock, *ibid.*, **54**, 3431 (1932).

(10) F. C. Whitmore, *ibid.*, **54**, 3279 (1932).

figuration had been maintained throughout all esterifications and saponifications. The linkage between the oxygen and carbon of the alcohol had been maintained at all times and the mechanism of the reaction is the same regardless of the strength of the acid.

Experimental

The neopentyl alcohol was prepared by the Grignard reaction from *t*-butyl chloride and formaldehyde gas. The latter was prepared by heating paraformaldehyde dried *in vacuo* over concentrated sulfuric acid for five days. Satisfactory yields of the acetates were obtained by standard methods.

The esters were hydrolyzed by 25% potassium hydroxide. The alcohol produced in each case was dried and the *p*-nitrobenzoate and the 3,5-dinitrobenzoate were made. No depressions in mixed melting point determinations were found, indicating that the alcohol obtained upon saponification was in each case neopentyl alcohol.

Table I and Fig. 1 summarize the experimental data obtained.

Summary

Neopentyl acetate, chloroacetate, dichloroacetate and trichloroacetate have been prepared, hydrolyzed and the resulting alcohol identified as neopentyl alcohol. No evidence of any rearrangement of the neopentyl group was obtained.

The refractive index, specific gravity at three temperatures, and boiling points at four pressures have been determined for each of the esters prepared.

The melting points of the 3,5-dinitrobenzoate and the *p*-nitrobenzoate of neopentyl alcohol are reported.

The conclusions are drawn (1) that in the esterification of alcohols by carboxylic acids varying in strength from that of glacial acetic to that of trichloroacetic, the water removed is composed of the hydrogen from the alcohol and the hydroxyl from the acid; (2) that in the hydrolysis of these esters the rupture of the carbon–oxygen linkage occurs between the oxygen of the alcohol residue and the carbon of the acid group.

EMORY UNIVERSITY, GEORGIA

RECEIVED DECEMBER 16, 1939

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF DUKE UNIVERSITY]

The Action of Elementary Fluorine Upon Organic Compounds. VIII. The Influence of Dilution on the Vapor Phase Fluorination of Ethane[1]

BY DEWALT S. YOUNG, NOBUKAZU FUKUHARA AND LUCIUS A. BIGELOW

In a previous paper of this series[2] we have described the vapor phase fluorination of ethane, using the pure gases in progressively varying proportions. The chief products were carbon tetrafluoride and hexafluoroethane, together with some higher boiling, partially fluorinated material, the liquid volume of which never exceeded 30% of the total condensate. This paper presents the results obtained when the fluorine was diluted progressively with nitrogen. They showed that the yield of the desired fluoroethanes could be raised to 90% of the total condensate under appropriate conditions.

The fluorinations were run in a metal apparatus, over copper gauze, as described before,[2] except that nitrogen, measured by a flowmeter, was introduced into the fluorine line. Two reaction chambers were used in series at the three highest dilutions, and adequate precautions taken throughout to avoid back pressure. The products were subsequently rectified in a Booth–Podbielniak low temperature fractionating unit,[2] and the higher boiling constituents divided into a number of empirically chosen cuts, from which pentafluoroethane CF_3CHF_2, *sym*-tetrafluoroethane CHF_2CHF_2, and 1,1,2-trifluoroethane CHF_2CH_2F were later isolated. However, no mono- or difluoroethanes were found, even when the fluorine was highly diluted.

Since it is known that alkyl monofluorides such as ethyl fluoride tend to be unstable, and also that ethylene fluoride decomposes spontaneously at 0°,[3] it seemed possible that these compounds, if formed at all, might have been decomposed immediately over the catalyst at the temperature of the reaction zone. Granting this, the fluorination

(1) This paper has been constructed in part from portions of Mr. Young's Doctorate Thesis, presented to the Graduate School of Duke University in October, 1939.

(2) Calfee, Fukuhara and Bigelow, THIS JOURNAL, **61**, 3552 (1939).

(3) Henne and Midgley, *ibid.*, **58**, 882, 884 (1936).

TABLE I

THE PRODUCTS OBTAINED BY RECTIFYING THE FLUORINATED ETHANE

Liquid volume % of material boiling	Gas volume ratio of fluorine to ethane to nitrogen											
	2.3:1:0[a]	2:1:2	2:1:4	2:1:6	2:1:8	4:1:0[a]	4:1:4	4:1:8	4:1:12	4:1:16	4:1:40	4:1:80
All $<-105°$ (mostly CF_4)	10	5	5	5	0	20	Trace	5	5	Trace	0	0
$-104°$ (Azeotrope A[2])	15	0	0	0	0	20	0	0	0	0	0	0
$-96°$ (Azeotrope B[2])	50	40	25	15	15	15	5	0	0	0	0	0
$-89°$ (Ethane)	0	25	25	50	50	0	0	0	0	0	0	0
$-78°$ (Hexafluoroethane)	5	0	0	0	0	30	25	30	0	0	0	0
-50 to $-40°$	..	5	10	5	10	..	20	20	25	30	30	30
-40 to $-35°$	..	5	5	10	5	..	Trace	0	0	0	0	0
-35 to $-28°$	..	Trace	5	5	30	..	Trace	5	0	0	0	0
-28 to $-19°$	..	10	10	10		..	15	15	40	40	35	20
All $>-19°$	..	10	15	15		..	20	15	25	20	25	30
All $>-78°$	15	30	45	45	45	15	55	55	90	90	90	80
Total vol. of condensate for 10 hr. in ml.	20	23	23	22	22	14	14	14	12	9[b]	8[b]	10

[a] From ref. 2 for comparison. [b] After the removal of SiF_4.

of ethane may perhaps be represented simply as follows.

$$C_2H_6 \xrightarrow{F_2} CH_3CH_2F \xrightarrow{-HF} CH_2{=}CH_2 \xrightarrow{F_2}$$
$$CH_2F{-}CH_2F \xrightarrow{-HF} CHF{=}CH_2 \xrightarrow{F_2}$$
$$CHF_2{-}CH_2F \xrightarrow{F_2} CHF_2{-}CHF_2 \xrightarrow{F_2}$$
$$CF_3CHF_2 \xrightarrow{F_2} C_2F_6$$

This formulation, naturally, is to be regarded as subject to further experimental confirmation, but it is supported to some extent by the observations of Hass, McBee and Weber, working with vapor-phase chlorination.[4] They noted that such thermal decompositions took place to a greater extent in the presence of free chlorine than when the corresponding alkyl halides were heated alone. This was in accord with their free radical, chain mechanism for chlorination, which would seem to apply equally well to fluorination. They also state that in vapor phase chlorinations, there is a tendency against the formation of dihalides with two chlorine atoms attached to the same carbon atom. Correspondingly, the suggested scheme does not predict the formation of the compound CH_3CHF_2, or even of CH_3CF_3, and actually neither of these was found.

Table I shows the quantities of the original fractions produced, expressed in liquid volume per cent. of the total condensate in the same run, as compared with the gas volume ratios of the reactants. In order to make the recorded values really significant, the figures have been rounded off to the nearest 5%, but naturally this increased considerably the deviation of the total from one hundred in some cases.

Two series of runs were made, in which the volume ratios of fluorine to ethane were 2:1 and 4:1, respectively. In the first case, the proportion of the product boiling higher than hexafluoroethane ($-78°$) rose progressively to 45% when the ratio of fluorine to nitrogen was 1:2; after which further dilution had but little effect, and much of the ethane was being recovered unchanged. When the figures were recalculated on the basis of the ethane actually fluorinated, this value continued to rise to 95%, when the fluorine to nitrogen ratio was 1:4. In the second series, it should be noted that when the dilution ratio exceeded 1:3, essentially no organic product boiling below $-50°$ was obtained. However, due to the incomplete absorption of hydrogen fluoride under these conditions, the material contained a considerable amount of silicon tetrafluoride. This compound has no liquid range at atmospheric pressure, sublimes at $-90°$, and was difficult to handle in the still. In this series, in which most of the ethane reacted, the proportion boiling above $-78°$ rose to 90% when the dilution ratio was 1:3, after which there was little further change even when the ratio was increased to 1:20. From these results it was clear that the higher boiling, partially fluorinated ethanes readily could be formed in excellent yield by diluting the fluorine appropriately with nitrogen. It will be seen also that as the dilution was increased, distinct accumulations of material, amounting under favorable conditions to 30–40% of the total condensate were formed in the boiling ranges of -50 to $-40°$, -28 to $-19°$, and above $-19°$; while less and less of the product boiled below $-50°$, as would be expected. The sudden disappearance of hexafluoroethane, and the corresponding increase in the fraction boiling from -28 to $-19°$ when the dilution ratio was increased above 1:2, are worthy of note. Also, in considering the results it should be recognized that in these experiments no attempt has been made to control either

(4) Hass, McBee and Weber, *Ind. Eng. Chem.*, **28**, 333 (1936).

the temperature of the reaction zone or the time required for the gases to pass through it. We hope to make a study of the influence of these important factors later on.

Although a constant boiling fraction (b. p. about −48°) had been observed from the first,[5] repeated distillation of the product boiling from −50 to −40° at atmospheric pressure failed to separate it into pure components. However, on redistillation at elevated pressure, a pure compound was isolated, boiling at −38° at 1200 mm., and −48.5° at atmospheric pressure. It froze sharply at −103°, and had a molecular weight of 119. This was the hitherto unknown pentafluoroethane, CF_3CHF_2 (mol. wt. 120).

Anal. Calcd. for C_2HF_5: F, 79.2. Found: F, 79.0, 79.1.

When the material boiling in the range from −28 to −19° was distilled at reduced pressure, a fraction was isolated, boiling at −46 to −50° at 200 mm., which on redistillation at atmospheric pressure yielded another pure compound boiling from −23.5 to −22.5° with a molecular weight of 101–102. This was *sym*-tetrafluoroethane (b. p. −23°,[6] mol. wt. 102).

Anal. Calcd. for $C_2H_2F_4$: F, 74.5. Found: F, 74.5, 74.2.

Most of the product boiling above −19° consisted of a third pure compound, boiling at 3°, and freezing at −84°, with a constant molecular weight of 84. This was undoubtedly 1,1,2-trifluoroethane (b. p. 5°,[6] mol. wt. 84).

Anal. Calcd. for $C_2H_3F_3$: F, 67.8. Found: F, 67.8, 67.9.

(5) Calfee and Bigelow, THIS JOURNAL, **59**, 2072 (1937).
(6) Henne and Renoll, *ibid.*, **58**, 887, 889 (1936).

In addition to these compounds, a small amount of material was isolated boiling at −56 to −55°, and freezing at −132°, with a molecular weight of 103, but the quantity obtained was insufficient for analysis. Also, a constant boiling mixture, b. p. −19°, mol. wt. 92–98, was obtained, at times in considerable amounts, as well as small quantities of other materials, but these were not separated. No trace of ethyl fluoride (b. p. −38°) was found, even in a special run in which the ratio of fluorine to ethane was 2:6, although in this case over a quarter of the product boiled in the vicinity of 26° with a molecular weight of 70–75.

The writers are glad to express here their appreciation to Mr. Elbert H. Hadley for valuable assistance, and to the Duke University Research Council for a grant.

Summary

A study has been made of the influence of nitrogen dilution on the vapor-phase fluorination of ethane, and it has been found that a mixture of partially fluorinated ethanes can be obtained in excellent yield under suitable conditions.

Pentafluoroethane CF_3CHF_2, *sym*-tetrafluoroethane CHF_2CHF_2 and 1,1,2-trifluoroethane CHF_2CH_2F have been isolated from the reaction products boiling above −78°. The first of these is a new compound, and the others have not been prepared previously by direct fluorination.

DURHAM, NORTH CAROLINA RECEIVED JANUARY 19, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY]

The Synthesis of Some New Pyrimidines and Uric Acids fom Cystamine[1]

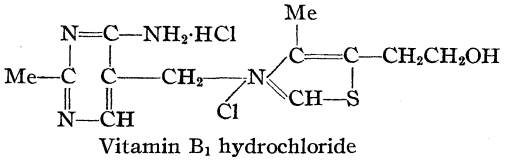
BY EDWARD JAMES MILLS, JR.,[2] AND MARSTON TAYLOR BOGERT

Attention recently has been directed increasingly to the important role played by various organic sulfur compounds concerned with vital physiological processes, and the present paper is a contribution in a field whose exploration seems to hold promise of interesting and perhaps useful results.

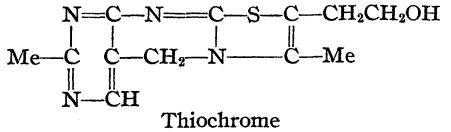
The great therapeutic value of Vitamin B_1, and its structural relationship to thiochrome, suggests the possibility of discovering other remedial drugs containing both the pyrimidine and thiazole nuclei, perhaps even when these two cycles have coalesced to a single bicyclic system with two atoms common to each of its constituent rings.

(1) Presented before the Organic Division at the Cincinnati Meeting of the American Chemical Society, April 8, 1940.
(2) E. R. Squibb & Sons Research Fellow at Columbia University, 1937–1939; present address, Department of Anatomy, College of Physicians and Surgeons, Columbia University, New York.

Fusion of the pyrimidine and thiazole, or of the purine and thiazole, cycles obviously will result in different structures depending upon the points of attachment of the two rings.

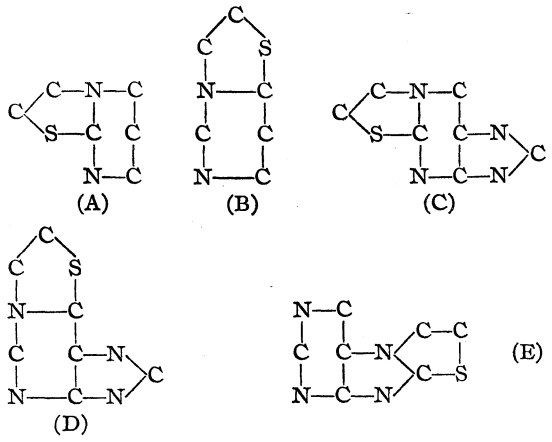


Vitamin B_1 hydrochloride



Thiochrome

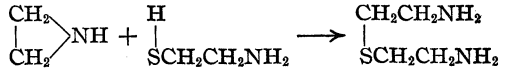
The polycyclic systems with which this communication deals are represented by skeletons (A), (B), (C) and (D):



For the synthesis of derivatives of (A), (B), (C) or (D), a convenient initial material is *beta*-mercaptoethylamine, and the Flow Sheets beyond show the progress made by utilizing that compound.

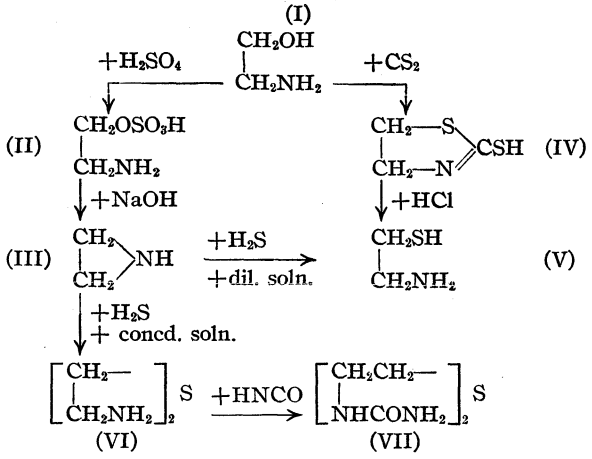
In 1936, Ochiai,[3] and Ochiai and Kitagawa,[4] prepared compounds containing the skeleton (E), but gave no information concerning their pharmacological properties.

The *beta*-mercaptoethylamine (V) required for our experiments was prepared by the hydrolysis of 2-mercaptothiazoline (IV), and also by the action of hydrogen sulfide upon a dilute solution of ethyleneimine (III). Of the two processes, the latter was the more satisfactory. The reaction in this case, as shown on Flow Sheet A, is a simple one, whether the cyclic (III), or the acyclic formula (CH_2=$CHNH_2$), be assigned to the imine. It was attempted by Gabriel and Eschenbach[5] many years ago, by passing hydrogen sulfide through ethyleneimine cooled to 0°, but their product was the sulfide (VI) and not the mercaptan (V) or its oxidation product the disulfide (VIII). It seems likely that this was due to a secondary reaction between the mercaptan first formed and the remaining unaltered imine.



A study of this problem and some preliminary experiments, convinced us that the conditions for optimum yields of the mercaptan (V) desired, or of the disulfide (VIII), would be (1) high concentration of hydrogen sulfide, (2) low concentration of the imine (III), and (3) low local concentration of the mercaptan (V) formed, to avoid the production of the monosulfide (VI). As described in detail beyond, the application of these conclusions resulted in yields of the mercaptoethylamine amounting to 85–95% of that calculated.

FLOW SHEET A



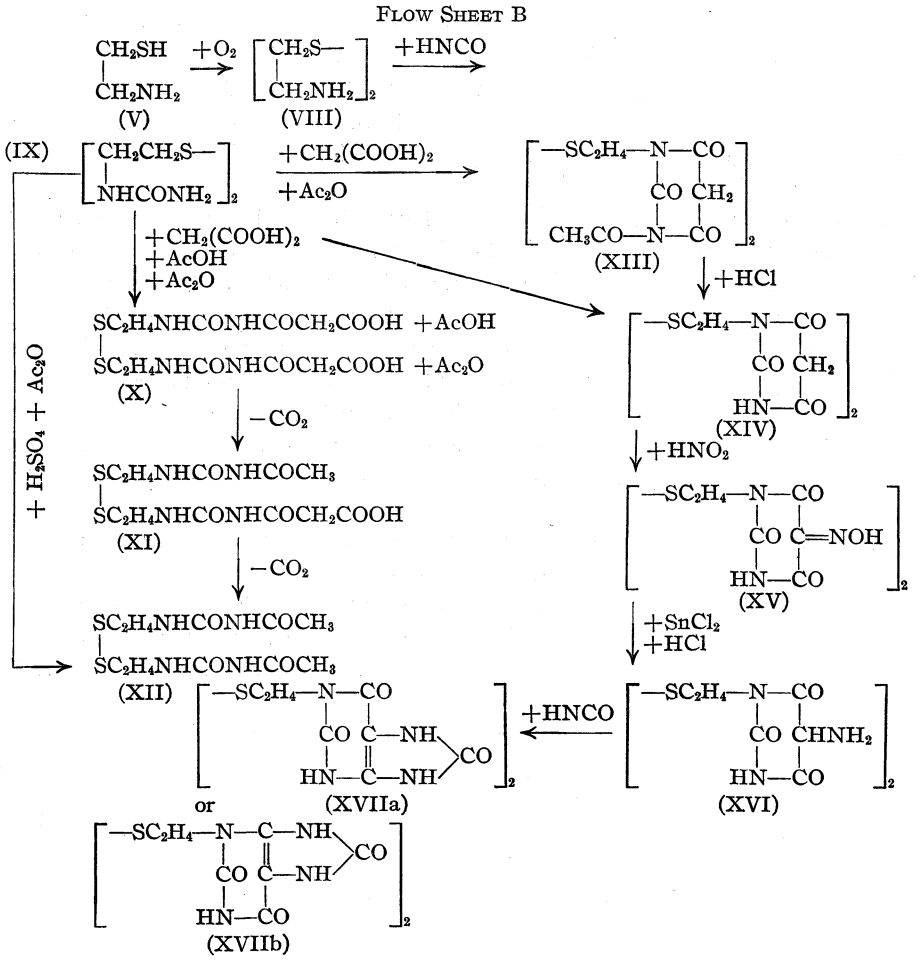
By oxidation, the mercaptan was easily converted into the disulfide (VIII) (cystamine or decarboxycystine), whose urea derivative (IX) may prove of interest if it should be found to possess hypoglycemic properties resembling those reported by Ackerman and Heinsen[6] for the analogously constituted diguanidino-diethyldisulfide. It is hoped that it also can be examined, together with its disulfoxide, to determine the effect, if any, upon the regulation of growth by cell proliferation, that phenomenon of natural chemical control of growth by sulfhydryl-disulfide–disulfoxide systems which has been studied so extensively and so ably by Hammett and his co-workers.[7]

The disulfide uric acid (XVII) also may merit attention in connection with cell proliferation studies, since it is structurally a uric acid with an alkyl disulfide side chain, or a cystamine in which the terminal nitrogen atoms form a part of two purine nuclei.

As will be observed, all of these compounds, as shown on Flow Sheet B, were retained in the stable disulfide form, to simplify purification and to avoid complications which would arise were a free mercapto group present. The reduction of the disulfide to the mercaptan was postponed purposely until it became necessary to reduce the disulfide uric acid (XVII) for the preparation of the *beta*-mercaptoethyl derivative and its cyclization product the thiazolidinouric acid.

(3) Ochiai, *Ber.*, **69B**, 1650 (1936).
(4) Ochiai and Kitagawa, *J. Pharm. Soc. Japan*, **56**, 979 (1936).
(5) Gabriel and Eschenbach, *Ber.*, **30**, 2497 (1897).
(6) Ackerman and Heinsen, *Z. physiol. Chem.*, **235**, 115 (1935).
(7) Hammett, *et al.*, *Protoplasma*, 1929–1933, numerous articles.

FLOW SHEET B



It has been learned that pyrimidines of type XIV, carrying either a *beta*-mercaptoethyl or an alkyldisulfide side chain in position 1, are very sensitive to alkaline solutions, the cycle tending to break open between positions 1 and 6, with formation of malonuric acids of the structure $RNHCONHCOCH_2COOH$. For this reason, the use of sodium ethylate as a condensing agent[8] in the preparation of these barbituric acids was not satisfactory.

This is in line with the findings of Aspelund and Skoglund,[9] who reported that 5,5,-1-trisubstituted barbituric acids were split by alkalies into both $RNHCONHCOCR_2COOH$ and $H_2NCONRCOCR_2COOH$, the former being produced in the larger quantity.

On the other hand, such pyrimidines are quite stable to acid solutions. The 3-acetyl derivative (XIII), for example, could be hydrolyzed readily to the unacetylated compound (XIV) by the action of hot 30% hydrochloric or sulfuric acid, without any apparent rupture of the pyrimidine cycle.

From the cystamine urea (IX), by condensation with malonic acid, in the presence of acetic acid and acetic anhydride, according to the method of Biltz and Wittek,[10] and Hepner and Frenkenberg,[11] the barbituric acid (XIV) was obtained, together with its acetyl derivative (XIII) and the dimalonuric acid (X). The latter (X) yielded the barbituric acid (XIV) when digested in glacial acetic acid solution with acetic anhydride; and the same product resulted when the acetyl derivative (XIII) of the barbituric acid was hydrolyzed by mineral acid.

Treatment of a mixture of the cystamine urea and malonic acid (IX) with acetic anhydride at 85–90°, also gave the acetylated barbituric acid (XIII).

The dimalonuric acid (X), when heated alone or with weakly acid solutions, lost first one and then a second mole of carbon dioxide, yielding successively the acetyl malonuric acid (XI) and then the diacetyl derivative (XII). The latter was also formed when the diureido disulfide (IX) was dissolved in acetic anhydride, a few drops of concentrated sulfuric acid added, and the mixture heated for three hours at 100°.

Grimaux[12] reported that when a mixture of urea and malonic acid was treated with phosphorus oxychloride, there resulted barbituric acid and an unidentified by-product, which latter was also formed when pure barbituric acid was

(8) Fischer, *Ann.*, **335**, 338 (1904).

(9) Aspelund and Skoglund, *Acta Acad. Aboensis, Math. et Phys.*, **10**, No. 10, 22 pp. (1937); *C. A.*, **31**, 6634 (1937).

(10) Biltz and Wittek, *Ber.*, **54**, 1035, 1046 (1921).

(11) Hepner and Frenkenberg, *ibid.*, **65**, 123 (1932).

(12) Grimaux, *Compt. rend.*, **88**, 85 (1879).

subjected to the action of phosphorus oxychloride. Conrad and Guthzeit,[13] repeating this work, concluded that this by-product was probably the 5-acetylbarbituric acid, arising from the decomposition of the malonic acid into carbon dioxide and acetic acid.

Sembritzky[14] has described a 1,3-diethyl-5-acetylbarbituric acid, produced by heating a mixture of diethylurea, malonic acid and phosphorus oxychloride in sealed tubes at 100°. Biltz and Wittek,[10] in developing their method of preparing N-alkylated barbituric acids from substituted ureas, malonic acid, and acetic anhydride, found that an excess of the latter led to the formation of acetylated barbituric acids. Using monomethylurea, malonic acid, acetic anhydride and sulfuric acid, they obtained what they believed to be the 1-methyl-5-acetylbarbituric acid, and prepared therefrom an oxime, a hydrazone and a phenylhydrazone. Further, acid hydrolysis of this acetyl derivative yielded no 1-methylbarbituric acid. These experimental observations led them to assign position 5 to the acetyl group. While such proof would be acceptable in the case of a 1,3-dialkylbarbituric acid, it is not so convincing for a monoalkylated acid, since the remaining NH group is easily acetylated and the resulting acetyl derivative is fairly resistant to de-acetylation by acids.

The acetyl derivative (XIII) obtained by us, when refluxed for six to eight hours with concentrated hydrochloric acid, gave the expected disulfide barbituric acid (XIV), while its sodium violurate was deep red. Based upon these experiments, and upon the analytical results for both (XIII) and (XIV), we believe that compound (XIII) carries its acetyl group in position 3 and not 5.

From the barbituric acid (XIV), the violuric acid (XV) was secured either by the action of sodium nitrite or, better, by treatment with isoamyl nitrite in acid solution.

For the reduction of violuric acids to uramils, such reagents as hydriodic acid,[10,15] hydrogen sulfide,[15] ammonium sulfide,[16,17] and sodium hydrosulfite,[18] have been used. Inasmuch as the uramil derivative was to be treated with cyanic acid, for conversion into the corresponding uric acid, the reducing agent employed had to be one which would attack only the isonitroso group and not the disulfide linkage. Such a selective reduction was accomplished by using stannous chloride and hydrochloric acid, with yields of the uramil about 50% of that calculated.

The experiments of Fruton and Clarke[19] have shown that, in solutions of *p*H 7, the reaction $RSSR \rightleftarrows 2RSH$ is a thermodynamically reversible system, the oxidation–reduction potential being a function thereof, independent of the substituents and equal to −0.23 volt for the reaction as written. Since the normal oxidation–reduction potential for the $Sn^{++++} \rightleftarrows Sn^{++}$ system equals +0.13 volt,[20] and since oximes and isonitroso compounds are irreversibly reduced to the amines by stannous chloride in hydrochloric acid solution,[21] it was concluded that no considerable reduction of the disulfide linkage would occur unless this reagent were used in large excess.

From this uramil (XVI), the uric acid derivative (XVII) was produced by the action of nitrourea, as a white crystalline solid, which remained unmelted at 350°. No intermediate pseudouric acid was detected. Apparently the urea group in position 5 of the pyrimidine cycle closed to the glyoxaline ring as soon as formed.

Manifestly, the method of synthesis does not enable us to decide whether the correct structure for the final product should be represented by (XVIIa) or (XVIIb). The synthesis of one or the other of these by a method which will resolve this uncertainty is now under way and the results will be reported later.

Preliminary experiments for the reduction of the disulfide uric acid (XVII) to the corresponding *beta*-mercaptoethyl derivative have been disappointing and, as it will be sometime before an additional supply of the disulfide can be synthesized, it has seemed to us desirable to record the results of our work to date. It remains to be ascertained also whether the *beta*-mercaptoethyl derivative so formed will close up spontaneously to a thiazolidinouric acid of (C) or (D) structure, or can be so cyclized by appropriate treatment.

Acknowledgments.—We are indebted to Drs. A. Wilbur Duryee and J. Nybor, of the New York Post Graduate Medical School, for the physiological tests with ethyleneimine reported in this

(13) Conrad and Guthzeit, *Ber.*, **15** 2845 (1882).
(14) Sembritzky, *ibid.*, **30**, 1816 (1897).
(15) Bayer, *Ann.*, **127**, 223 (1863).
(16) Traube, *Ber.*, **33**, 3040 (1900).
(17) Traube, *Ann.*, **331**, 74 (1904).
(18) Hepner and Fajersztejn, *Bull. soc. chim.*, [5] **4**, 854 (1937).
(19) Fruton and Clarke, *J. Biol. Chem.*, **106**, 667 (1934).
(20) Getman and Daniels, "Outlines of Theoretical Chemistry." John Wiley & Sons, Inc., New York, N. Y., 6th ed., 1937, p. 440.
(21) Gabriel, *Ber.*, **43**, 2494 (1910).

paper; and to Mr. Saul Gottlieb of our own Organic Laboratories, for the microanalyses which appear in the Experimental Part.

Experimental

beta-**Mercaptoethylamine** (V) was prepared from commercial ethanolamine (I) by two different routes: (a) *via* 2-mercaptothiazoline (IV), and (b) *via* ethyleneimine (III).

(a). **2-Mercaptothiazoline** was obtained from ethanolamine and carbon disulfide essentially as described by Knorr and Rössler,[22] and this in turn hydrolyzed to the mercaptoethylamine by the action of concentrated hydrochloric acid, as recorded by Gabriel and Leupold.[23] This gave a yield of hydrochloride practically equal to that calculated; white crystals, m. p. 70.2–70.7° (cor.); m. p. in the literature,[24] 70–72°. The free base, sublimed *in vacuo*, melted at 97–98.5°. Gabriel and Colman[25] gave the m. p. as 99–100°. It was further identified by oxidation in aqueous solution, with 30% hydrogen dioxide, to taurine.

Ethyleneimine (III) was prepared from commercial ethanolamine (I), by the process of Wenker.[26] The total yield of the intermediate *beta*-aminoethylsulfuric acid (II) was 85.9%; of the ethyleneimine from this, 25–30%, b. p. 54–56°. Wenker gives the b. p. as 55–56.5°.

This imine is strongly caustic and burns the skin. Inhalation of the vapors causes acute inflammation of the eyes, nose and throat, with symptoms resembling those of bronchitis. After two to three days, the irritation subsides and the tissues return to normal, without suffering any apparent permanent injury. Danehy and Pflaum[27] also have called attention to the toxicity of this compound.

Through the courtesy of Drs. A. Wilbur Duryee and J. Nybor, of the New York Post Graduate Medical School, some physiological experiments were carried out on a white rabbit, weighing 5.4 lb., to ascertain the effect of ethyleneimine upon the heart, since one of the authors (Mills) suffered some cardiac disorders while working with this substance.

The rabbit was subjected to an abdominal injection of 1 cc. of a $M/6$ solution of the imine in water (0.89 cc./100 cc. water). Electrocardiographic studies of this animal showed no marked cardiac changes.

After ten days, an intra-peritoneal injection of 2 cc. of a solution of 1.8 cc. of the imine in 100 cc. of water (*ca.* $M/3$) was given, and still no marked heart damage was detected. But within three days the rabbit died, and the post-mortem examination disclosed a gross hemorrhage of the lungs, congested and swollen kidneys, a flabby heart and a severe peritonitis.

A cooled solution of 91.1 g. (2.1 mols) of ethyleneimine in 819 cc. of absolute ethanol was added dropwise (three to four hours) to 200 cc. of chilled absolute ethanol surrounded by an ice pack, while a current of hydrogen sulfide was passed through the well stirred mixture. The solution was concentrated under reduced pressure to 50–75 cc., in the absence of air, to avoid oxidation of the mercaptan, and the concentrate well cooled. The mercapto amine separated as a white solid, which was air-dried, washed with petroleum ether and dried again, when it melted at 97–98.5° (cor.); yield, 139 g., or 85.5%. The free base had a disagreeable odor, and oxidized to the disulfide on standing in the air.

beta,beta'-**Diamino-ethylsulfide (Thioethylamine)** (**VI**).—When a 25% (or stronger) solution of ethyleneimine in 95% ethanol was treated with a stream of hydrogen sulfide, without either cooling or stirring, and the mixture was then concentrated under diminished pressure, the *beta, beta'*-diamino-ethylsulfide separated as a yellowish oil. It has been described by Gabriel and his collaborators.[28] Our product was identified by conversion into the corresponding compound, VII.

beta,beta'-**Diureido-ethylsulfide** (**VII**).—The crude thioethylamine (VI), in aqueous solution, was subjected to the action of nitrourea in excess.[29,30,31] After heating the solution at 100°, it was evaporated to dryness under reduced pressure, and the diureide (VII) crystallized from water. It formed white crystals, m. p. 221–222° (cor.).

Anal. Calcd. for $C_6H_{14}O_2N_4S$: C, 34.9; H, 6.8; N, 27.2. Found: C, 34.6; H, 6.5; N, 27.7.

Cystamine (*beta,beta'*-**Diamino-ethyldisulfide, Dithioethylamine**) (**VIII**).—The mercaptoethylamine was dissolved in slightly more than sufficient water, or 95% ethanol, to effect solution, and a current of oxygen was bubbled through until the solution no longer reduced a solution of iodine in potassium iodide, by which time the characteristic unpleasant odor of the mercaptan had disappeared. Concentration of this solution under reduced pressure yielded a thick oil. This was dehydrated by repeated addition of absolute ethanol and evaporated *in vacuo*, since the oil could not be distilled without decomposition.

Dihydrochloride.—An aqueous or alcoholic solution of the disulfide was mixed with an excess of alcoholic hydrochloric acid and the mixture evaporated to a small volume of viscous material under diminished pressure. Addition of a small amount of methanol, or ethanol (95% or absolute), precipitated the dihydrochloride as a white solid, which was removed and washed with a little chilled alcohol. More of the salt was recovered from the filtrate by similar treatment. The yield from the mercaptan was practically that calculated from the original imine, about 65%.

Anal. Calcd. for $C_4H_{14}N_2S_2Cl_2$: C, 21.3; H, 6.3; N, 12.4. Found: C, 21.6; H, 6.3; N, 12.2.

This salt when heated began to shrink at about 206° (cor.), and melted at 212–212.5° (cor.). Coblentz and Gabriel,[32] and Coblentz,[33] reported its m. p. as 203°, whereas Fruton and Clarke[19] found 214°.

beta,beta'-**Diureido-ethyldisulfide** (**IX**).—To one mol of the cystamine (VIII), in aqueous or alcoholic solution, 2.2 mols of nitrourea was added slowly, while heating care-

(22) Knorr and Rössler, *Ber.*, **36**, 1281 (1903).
(23) Gabriel and Leupold, *ibid.*, **31**, 2837 (1898).
(24) Gabriel, *ibid.*, **22**, 1139 (1889).
(25) Gabriel and Colman, *ibid.*, **45**, 1643 (1912).
(26) Wenker, THIS JOURNAL, **57**, 2328 (1935).
(27) Danehy and Pflaum, *Ind. Eng. Chem.*, **30**, 778 (1938).
(28) Gabriel, *Ber.*, **24**, 1114, 3100 (1891).
(29) Thiele and Lachmann, *Ann.*, **288**, 281 (1895).
(30) Davis and Blanchard, THIS JOURNAL, **51**, 1790 (1929).
(31) Carlton and Day, *J. Org. Chem.*, **1**, 552 (1936).
(32) Coblentz and Gabriel, *Ber.*, **24**, 1123 (1891).
(33) Coblentz, *ibid.*, **24**, 2132 (1891).

fully to control the reaction. After about an hour at 100°, the gas evolution ceased, and the solution was evaporated to dryness *in vacuo*. The residual solid was crystallized repeatedly from water or alcohol, in both of which it was quite soluble hot and very difficultly soluble cold. The pure compound formed white crystals, m. p. 166–167° (cor.).

Anal. Calcd. for $C_6H_{14}O_2N_4S_2$: C, 30.2; H, 5.9; N, 23.5. Found: C, 30.3; H, 5.8; N, 23.6.

Ethyldisulfide-*beta,beta'*-dimalonuric Acid (X).—By the usual sodium ethylate condensation of the diureido disulfide (IX) with malonic ester, in absolute ethanol solution at 105–110°, this dimalonuric acid was obtained, with small amounts (2–3%) of the dibarbituryl disulfide (XIV). A better method of preparing the dimalonuric acid follows.

A mixture of 4.7 g. of the diureido disulfide and 4.2 g. of malonic acid was dissolved in 25 cc. of glacial acetic acid at 50° and to this mixture, stirred under a reflux and protected from ingress of moisture, there was added slowly (thirty to sixty minutes) 9.2 g. of acetic anhydride, while the mixture was heated to 65–70°. This was followed by four hours of heating at 70–80°, and three hours at 80–90°, after which the mixture was permitted to cool. The yellowish precipitate of the dibarbituryl disulfide (XIV) (3%), m. p. 208.5–212.5° (cor.), was filtered out, and the filtrate concentrated *in vacuo* to a reddish oil. Treatment of this oil with hot absolute ethanol precipitated more of (XIV), but extracted the dimalonuric acid (X). The alcohol extract was concentrated *in vacuo* and the residual red oil crystallized repeatedly from hot water. A white crystalline solid was thus obtained, in a yield of 25–30%.

Anal. Calcd. for $C_{12}H_{18}O_8N_4S_2$: C, 35.1; H, 4.4. Found: C, 35.4; H, 4.6.

The behavior of this product on heating was significant. At 141–142° (cor.), it melted with evolution of carbon dioxide, recongealed, remelted at 150–151° (cor.), with evolution of a second mole of carbon dioxide, congealed again and finally melted with decomposition at 197.5–199° (cor.). With sodium nitrite, the compound gave a red salt.

***beta*-Acetylureido-ethyldisulfide-*beta'*-malonuric Acid (XI).**—When the dimalonuric acid (X) was warmed for a short time in slightly acidulated water, a white crystalline solid was obtained which, after recrystallization from warm water, melted at 150–151° (cor.), with evolution of gas, recongealed and then melted with decomposition at 197.5–199° (cor.). With sodium nitrite, it formed a red salt.

Anal. (of XI). Calcd. for $C_{11}H_{18}O_6N_4S_2$: C, 36.0; H, 4.9. Found: C, 35.5; H, 4.9.

***beta,beta'*-Diacetylureido-ethyldisulfide (XII).**—When an aqueous solution of (XI) was boiled, carbon dioxide was split out and a white solid obtained, which was repeatedly crystallized from boiling water, in which it was very difficultly soluble. The product began to shrink at 206° (cor.) and melted at 209–210° (cor.).

Another method of preparing the same compound consisted in dissolving the diureido disulfide (IX) in excess of acetic anhydride, adding a few drops of concentrated sulfuric acid, and heating the mixture for three hours at 100°, followed by removal of acetic acid and excess of acetic anhydride by concentration *in vacuo*. After repeated crystallization from water, the white powder began to shrink at 206° (cor.) and melted at 209–210° (cor.).

Anal. Calcd. for $C_{10}H_{18}O_4N_4S_2$: C, 37.2; H, 5.6; N, 17.4. Found: C, 37.8; H, 5.4; N, 17.0.

With sodium nitrite, the compound gave no color reaction, thus indicating the absence of a reactive malonic methylene group.

***beta,beta'*-Di-(1-barbituryl)-ethyldisulfide (XIV)** was prepared by three different methods.

(1) To a solution of 23.8 g. of the diureido disulfide (IX) and 20.9 g. of malonic acid in 100 cc. of glacial acetic acid at 50°, there was added dropwise, under a reflux, 40.8 g. of acetic anhydride, in the course of an hour, while the mixture was well stirred and protected from moisture. After eight hours of heating at 80–90°, the solution was concentrated *in vacuo* to a thick red oil, which was extracted with 200 cc. of boiling absolute ethanol. As the extract cooled, the dibarbituryl disulfide (XIV) separated as a pale yellow crystalline solid. It was filtered out, washed with chilled absolute ethanol, dried in a vacuum desiccator, and crystallized from water; yield, 9.8 g., or 26.2%; m. p. 216.8–218.8° (cor.).

Anal. Calcd. for $C_{12}H_{14}O_6N_4S_2$: C, 38.5; H, 3.8; N, 15.0. Found: C, 38.6; H, 4.0; N, 14.9.

Concentration *in vacuo* of the alcoholic filtrate from (XIV), yielded a large quantity of the dimalonuric acid (X), which was used in the preparation of (XIV) by the third method as noted beyond. Another by-product was the acetylated barbituric acid (XIII) described in the following pages.

The above process is based upon that of Biltz and Wittek[10] for the preparation of N-alkylated barbituric acids from substituted ureas, malonic acid, and acetic anhydride.

(2) A mixture of 1.9 g. of *beta,beta'*-di-(1-[3-acetylbarbituryl])-ethyldisulfide (XIII) with 25 cc. of concentrated hydrochloric acid was refluxed for two and one-half hours. The insoluble material was removed and refluxed for another two and one-half hours with a fresh 25-cc. lot of concentrated hydrochloric acid. The combined hydrochloric acid extracts were evaporated *in vacuo* to a pale yellow powder. This was crystallized four times from water, using Norit as a decolorizing agent, and then melted at 215.5–216.5° (uncor.); yield, 0.3 g., equivalent to 33%, after deducting the 0.9 g. of initial material (XIII) unaltered by the hydrochloric acid.

(3) To a solution of 1.9 g. of the dimalonuric acid (X), recovered from Method (1) above, in 25 cc. of glacial acetic acid, there was added slowly, with protection against absorption of moisture, 1.5 g. of acetic anhydride, while the mixture was heated under a reflux. After three hours of further heating at 80°, the warm solution was diluted with two volumes of water, which gave a solution sufficiently acid to precipitate the barbituric acid (XIV) desired, but not the initial dimalonuric acid (X). After standing for eighteen to twenty-four hours, the white precipitate was collected, washed free from acid, and crystallized twice from water, m. p. 211.5–214.5° (cor.). The mixed m. p. with an authentic sample of the barbituric acid (XIV), m. p. 216.8–218.8° (cor.), was 213–216.5°

(cor.); mixed m. p. with an authentic sample of the diacetylureido compound (XII), m. p. 209–210° (cor.), was 188–193° (uncor.); yield, 1 g., or 78.4%, after deducting 0.5 g. of unchanged initial material isolated from the acetic acid solution by evaporation *in vacuo*.

***beta,beta'*-Di-(1-[3-acetylbarbituryl])-ethyldisulfide (XIII).**—The diureidodisulfide (IX) was mixed with slightly more than the calculated amount of malonic acid, a small excess of acetic anhydride was added, and the mixture was heated at 70° for four hours. Acetic acid and excess of acetic anhydride were distilled off *in vacuo*, the residue treated with half the original quantity of acetic anhydride, the mixture heated for an hour at 70°, and acetic acid and acetic anhydride distilled off *in vacuo*. The oily residue was dissolved in 10% sodium hydroxide, and 10% hydrochloric acid added until the solution was acid to Congo-red. The orange-red precipitate was collected and purified by further precipitation from sodium carbonate and sodium bicarbonate solutions with 10% hydrochloric acid. A pale yellow product was thus obtained, in 80% yield, which was very slightly soluble in the usual neutral organic solvents. By reprecipitation with 10% hydrochloric acid from sodium bicarbonate solutions, and drying at 111° *in vacuo* for two and one-half hours, a pure compound was secured, which shrank at 214–217° (cor.) and melted at 219–223° (cor.).

Anal. Calcd. for $C_{16}H_{18}O_8N_4S_2$: C, 41.9; H, 4.0; N, 12.2. Found: C, 41.7; H, 4.3; N, 12.2.

***beta,beta'*-Di-(1-(violuryl)-ethyldisulfide (XV).**—A suspension of 1.1 g. of the barbituryl disulfide (XIV) in 20 cc. of water was treated slowly with 0.5 g. of sodium nitrite, with vigorous stirring. Upon completion of the addition, the pinkish solution was heated at 100° for thirty minutes, which changed its color to a purple, then cooled to room temperature, 1 cc. of concentrated sulfuric acid added, the mixture heated for an hour at 100° and then over a free flame until the red color was discharged. As the solution cooled, a yellow precipitate separated, which was filtered out, washed with cold water until acid-free, and dried *in vacuo* for twenty-four hours. There was thus obtained 1.1 g. (91% yield) of a yellow powder, which turned red at about 200°, and melted at 218.5–219.5° (cor.) with decomposition to a deep red liquid.

Difficulty was experienced in getting an analytically pure sample by this method, since inorganic salts or the sodium salt of the violurate, were carried down with the precipitate. Repeated crystallization from water, however, gave a practically pure product.

Anal. Calcd. for $C_{12}H_{12}O_8N_6S_2$: C, 33.3; H, 2.8. Found: C, 33.1; H, 3.0.

When the red solution of the sodium violurate stood for two to four days, the pyrimidine ring apparently broke open between positions 1 and 6, and no violuric acid (XV) could be recovered.

This violuric derivative (XV) was prepared also by the following process. A suspension of 2.4 g. of the barbituryl disulfide (XIV) in 50 cc. of 95% ethanol was cooled in an ice-bath, and 15 g. of isomamyl nitrite stirred in. After the careful addition of 0.5 cc. of concentrated hydrochloric acid, the mixture was stirred for fifteen to thirty minutes at 0°, one hour while warming up to room temperature, and thirty minutes at 40°. The solution was concentrated *in vacuo* to a small volume, cooled, the precipitate filtered out, washed twice with chilled 95% ethanol, and dried to a pale yellow powder, identical in m. p., and other respects, with the product of the first process; yield, 2.4 g., or 89%, and more was recovered from the filtrates. With sodium hydroxide or potassium hydroxide, it formed a purple isonitroso salt.

***beta,beta'*-Di-(1-uramilyl)-ethyldisulfide (XVI).**—To a solution of 1.1 g. of the violuric acid (XV) in 25 cc. of concentrated hydrochloric acid, there was added 1.9 g. of stannous chloride, and the mixture was heated at 100° for five hours. When the solution no longer reduced an iodine–potassium iodide solution, it was either evaporated to dryness at 100°, extracted with 60% ethanol, and precipitated by the addition of absolute ethanol; or absolute ethanol was added directly to the reduced solution. Cooling of either of these solutions gave a precipitate, which was filtered out and crystallized by dissolving it in a small amount of concentrated hydrochloric acid, reprecipitating with absolute ethanol and cooling to 0°. This precipitate was collected, washed with chilled absolute ethanol and dried *in vacuo* at 75° over phosphorus pentoxide for two hours. The pale yellow product shrank at 145°, turned reddish-brown at 155–160°, sintered at 170–171.5° and finally turned red and decomposed without showing any definite m. p.; yield, 55–60%.

Anal. Calcd. for $C_{12}H_{16}O_6N_6S_2$: C, 35.6; H, 4.0. Found: C, 35.2; H, 4.1.

With potassium hydroxide or sodium hydroxide, no color indicative of an isonitroso salt was obtained. The compound gave a positive murexide reaction.

1 (or 3)-(*beta*-Ethyldisulfide)-uric Acid (XVII).—A suspension of 0.4 g. of the above uramil (XVI) in 20 cc. of water was made faintly alkaline to litmus by the addition of dilute (10%) potassium hydroxide. To this there was added 0.25 g. of nitrourea, and the mixture was heated at 100° until the evolution of gas ceased. The nitrourea used contained sufficient sulfuric acid to change the reaction of the solution to the acid side, so it was filtered hot and cooled. The solid which precipitated was removed and crystallized from water. A white crystalline compound resulted, which was not melted, but only slightly charred, at 350°. Ignited on platinum foil, it left no ash. It dissolved in 5% sodium bicarbonate solution, was reprecipitated by hydrochloric acid, and gave a positive murexide reaction. For analysis, it was crystallized thrice from water and dried over phosphorus pentoxide *in vacuo* for two hours at 76°.

Anal. Calcd. for $C_{14}H_{14}O_6N_8S_2$: C, 37.0; H, 3.1; N, 24.7. Found: C, 36.9; H, 3.2; N, 24.9.

Summary

1. *beta*-Mercaptoethylamine is prepared most conveniently by passing hydrogen sulfide through an alcoholic solution of ethyleneimine. Some physiological tests on the toxicity of ethyleneimine are reported.

2. This mercaptan is easily oxidized to the corresponding disulfide (cystamine) by the action of air or oxygen upon its aqueous or alcoholic solution.

3. Cystamine is converted into the diurea by treatment with nitrourea.

4. This diurea when condensed with malonic acid, in the presence of acetic anhydride, yields the corresponding barbituric acid, as well as malonuric acid derivatives of cystamine and acetylation products.

5. From the disulfide barbituric acid, there have been obtained the corresponding violuric acid, uramil, and uric acid.

6. The latter is to be used as initial material for the preparation of *beta*-mercaptoethyl and thiazolidino uric acids.

NEW YORK, N. Y. RECEIVED FEBRUARY 24, 1940

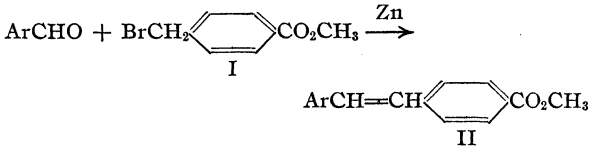
[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

The Synthesis of Certain Carbalkoxystilbenes

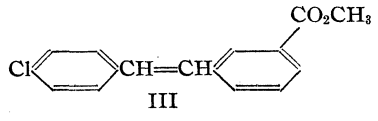
BY REYNOLD C. FUSON AND H. G. COOKE, JR.

Carbalkoxystilbenes of the type $ArCH{=}CHC_6H_4CO_2R$, needed for certain studies on the reversibility of the Friedel–Crafts condensation, could not be found in the literature. It was necessary, therefore, to devise ways for synthesizing them. The present paper reports three such methods.

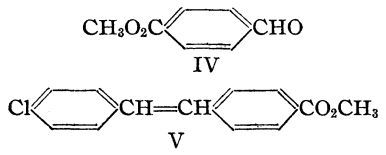
The first to be studied was the condensation of aromatic aldehydes with methyl α-bromo-*p*-toluate (I) by an adaptation of the Reformatsky reaction. This method was suggested by the vinylogous relationship between the α-bromo-*p*-toluates and bromoacetic esters. Experiments showed that the method could be used. Benzaldehyde, *p*-chlorobenzaldehyde and *p*-bromobenzaldehyde were condensed with methyl α-bromo-*p*-toluate to give the corresponding *p*-carbomethoxystilbenes (II).



The activation of the bromine atom by the carbomethoxy group proved, however, not to be essential. Similar results were obtained with the *meta* isomer of the bromotoluate. *p*-Chlorobenzaldehyde condensed with methyl α-bromo-*m*-toluate to give 4-chloro-3′-carbomethoxystilbene (III).



This type of condensation was found to take place also with simple benzyl halides. Thus *p*-chlorobenzyl bromide condensed with methyl terephthalaldehydate (IV) to give 4-chloro-4′-carbomethoxystilbene, the product (V) being identical with that from methyl α-bromo-*p*-toluate and *p*-chlorobenzaldehyde. These two



methods give about the same yields: approximately 20% of the theoretical. The former is preferable because the starting materials are less difficult to obtain.

The preparation of the α-bromotoluates[1] was accomplished by the method of Davis and Perkin.[2] The terephthalaldehydate was much more difficult to prepare. It was found that Mayer and Sieglitz's method[3] for α-naphthaldehyde could be applied successfully to methyl α-bromo-*p*-toluate to give methyl terephthalaldehydate.

After this work was completed Meerwein, Büchner and Emster[4] reported a new method for making substituted stilbenes from cinnamic acids and primary aromatic amines. For certain carbalkoxystilbenes this procedure proved to be superior to the methods already worked out. Applied to cinnamic acid and *p*-aminobenzoic esters it gave yields of 36 to 52%. The method gives low yields when applied to chlorocinnamic acids and consequently is not very helpful in making the halogen substituted stilbenes required in this work.

Experimental

Methyl α-Bromo-*p*-toluate.—Eighty-three grams of bromine was added slowly, with stirring, to 80 g. of *p*-

(1) Zal'kind, *J. Russ. Phys.-Chem. Soc.*, **46**, 508 (1914).
(2) Davis and Perkin, *J. Chem. Soc.*, **121**, 2202 (1922).
(3) Mayer and Sieglitz, *Ber.*, **55**, 1835 (1922).
(4) Meerwein, Büchner and Emster, *J. prakt. Chem.*, **152**, 237 (1939).

toluyl chloride heated to approximately 180°.[2] The bromination mixture was allowed to cool and 50 cc. of methanol was added dropwise. Distillation of this reaction mixture under reduced pressure gave 72 g. of methyl α-bromo-*p*-toluate; b. p. 115–117 (3 mm.). After crystallization from methanol or low-boiling petroleum ether the ester melted at 54–55°. This melting point agrees with that reported by Zal'kind,[1] who made the ester by direct esterification of α-bromo-*p*-toluic acid.

Methyl α-Iodo-*p*-toluate.—To a solution of 50 g. of methyl α-bromo-*p*-toluate in 100 cc. of acetone was added a solution of 33 g. of sodium iodide in 150 cc. of acetone, and the mixture was refluxed for fifteen minutes. The sodium bromide was removed by filtration, the acetone was distilled and the residue was taken up in ether. The ether solution was washed with 1% sodium thiosulfate solution and dried over anhydrous magnesium sulfate. The ether was distilled, and the iodo ester was crystallized from methanol; m. p. 76–77°, yield 51 g.

Anal. Calcd. for $C_9H_9O_2I$: C, 39.13; H, 3.29. Found: C, 39.12; H, 3.35.

Methyl α-Bromo-*m*-toluate.—The method of synthesis was similar to that outlined for the para isomer. Distillation of the reaction mixture under reduced pressure gave 68 g. of the methyl α-bromo-*m*-toluate; b. p. 112–114° (3 mm.). After recrystallization from methanol or low-boiling petroleum ether the ester melted at 46–47°.

Anal. Calcd. for $C_9H_9O_2Br$: C, 47.16; H, 3.93; Br, 35.02. Found: C, 47.37; H, 4.09; Br, 35.08.

Methyl α-Iodo-*m*-toluate.—The conversion of the bromo ester to the corresponding iodo ester was found to proceed in the manner described for the para isomer. The iodo ester was recrystallized from methanol and low-boiling petroleum ether; m. p. 52–53°; yield 78%.

Anal. Calcd. for $C_9H_9O_2I$: C, 39.13; H, 3.29. Found: C, 39.38; H, 3.44.

The Condensation of Methyl α-Bromo-*p*-toluate with *p*-Chlorobenzaldehyde.—Twenty-five grams of methyl α-bromo-*p*-toluate in 100 cc. of dry benzene was added dropwise to a refluxing mixture of 21 g. of *p*-chlorobenzaldehyde, 50 cc. of dry benzene and 8 g. of zinc dust. The mixture was refluxed with stirring for eighteen hours, then decomposed with 100 cc. of dilute hydrochloric acid. The solid was removed by filtration, and the benzene layer was separated, washed with a 5% solution of sodium carbonate, and dried over anhydrous magnesium sulfate. The dry benzene solution was refluxed for two hours with 15 cc. of acetic anhydride. The solution was then concentrated under reduced pressure to a thick sirup. The 4-chloro-4′-carbomethoxystilbene solidified on cooling and was recrystallized from methanol.

Numerous attempts were made to increase the yield by using such solvents as toluene, ethyl ether and butyl ether in place of benzene. The iodo ester was used in place of the bromo ester and magnesium was substituted for zinc, but the above conditions were the most successful.

4-Chloro-4′-carbomethoxystilbene Bromide.—An excess of a 5% solution of bromine in carbon tetrachloride was added to a solution of 1 g. of 4-chloro-4′-carbomethoxystilbene in 25 cc. of carbon tetrachloride. The reaction mixture was heated to a temperature of 70° for twenty minutes. The carbon tetrachloride was removed by distillation and the 4-chloro-4′-carbomethoxystilbene bromide was recrystallized from methanol.

Debromination of 4-Chloro-4′-carbomethoxystilbene Bromide.—A solution of 1 g. of sodium iodide in 30 cc. of acetone was added to a solution of 1 g. of 4-chloro-4′-carbomethoxystilbene bromide in 30 cc. of acetone. This mixture was refluxed for fifteen minutes, the precipitate of sodium bromide removed by filtration and the acetone distilled. The residue was dissolved in ether and washed with a 1% solution of sodium thiosulfate. After the ether solution had been dried over anhydrous calcium chloride, the ether was distilled, and the 4-chloro-4′-carbomethoxystilbene crystallized from methanol; m. p. 161–162°, yield 95%. There was no depression of melting point when this product was mixed with the parent stilbene.

The condensation of other aromatic aldehydes and benzyl halides was carried out in the manner given for the synthesis of 4-chloro-4′-carbomethoxystilbene. The stilbene in each case was transformed into the corresponding dibromide which in turn was reconverted to the parent stilbene by treatment with sodium iodide in acetone. The results of these syntheses are collected in Table I. The yields in the debromination reactions varied from 86 to 92%. Purification of the stilbenes and their bromides was carried out in each case by recrystallization from methanol.

Attempted Condensation of Methyl α-Iodotoluates with Acetone.—When the meta and para α-iodotoluates were treated with zinc and acetone the only products were the corresponding methyl toluates and the bibenzyls produced by coupling. The 4,4′-dicarbomethoxybibenzyl melted at 118–119°.[5] The 3,3′-dicarbomethoxybibenzyl was a new compound. It was recrystallized from methanol, m. p. 84–85°.

Anal. Calcd. for $C_{18}H_{18}O_4$: C, 72.51; H, 6.05. Found: C, 72.79; H, 5.86.

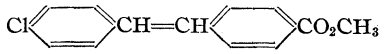
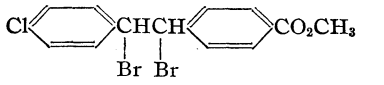
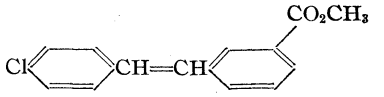
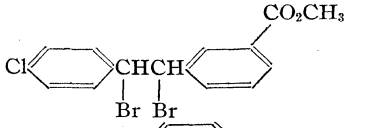
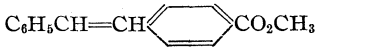
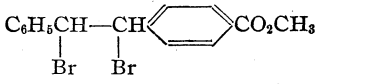
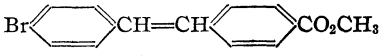
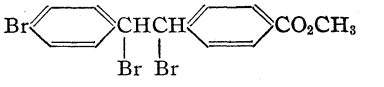
The Condensation of Benzyl Chloride with Benzaldehyde.—A solution of 45 g. of benzyl chloride in 200 cc. of dry benzene was added dropwise to a refluxing mixture of 38 g. of benzaldehyde, 100 cc. of dry benzene and 25 g. of zinc dust. The mixture was refluxed for twenty-four hours and decomposed with dilute hydrochloric acid. The solid was removed by filtration and the benzene layer was separated, washed and dried. The dry benzene solution was fractionally distilled to give 12 g. of diphenylmethane, b. p. 260–265°, and 16 g. of stilbene, b. p. 300–310°. Diphenylmethane is known to form when benzyl chloride is heated in the presence of zinc[6]; the structure of this hydrocarbon was proved by its oxidation to benzophenone. By the method of mixed melting points the high-boiling compound was shown to be *trans*-stilbene, m. p. 123–124° (from methanol); yield, 24%.

Preparation of Methyl Terephthalaldehyde.—This aldehyde was prepared by the same method that Mayer and Sieglitz[3] used for the preparation of α-naphthaldehyde. A solution of 28 g. of hexamethylenetetramine in 300 cc. of water was added to 44 g. of methyl α-bromo-*p*-toluate dissolved in 500 cc. of methanol. The solution was refluxed for seven hours, and the methanol was distilled.

(5) Fischer and Wolfenstein, *Ber.*, **37**, 3215 (1904).

(6) Zincke, *Ann.*, **159**, 367 (1871).

TABLE I

	M. p., °C.	Yield, %	Formula and calcd. for	Analyses, % C	H
	161–162	22	$C_{16}H_{13}O_2Cl$	70.46	4.81
			Found	70.62	4.79
	202–203 (dec.)	90	$C_{16}H_{13}O_2ClBr_2$	44.41	3.01
			Found	44.52	3.29
	110–111	18	$C_{16}H_{13}O_2Cl$	70.46	4.81
			Found	70.42	4.71
	175–176	90	$C_{16}H_{13}O_2ClBr_2$	44.41	3.01
			Found	44.03	3.22
	158–159	21	$C_{16}H_{14}O_2$	80.67	5.93
			Found	80.63	6.16
	192–193	91	$C_{16}H_{14}O_2Br_2$	48.24	3.55
			Found	48.31	3.71
	179–180	20	$C_{16}H_{13}O_2Br$	60.57	4.13
			Found	60.64	4.34
	211–213	87	$C_{16}H_{13}O_2Br_3$	40.27	2.75
			Found	40.78	2.95

The aqueous residue was extracted with 1000 cc. of ether, and the ether solution was washed with a dilute solution of sodium bicarbonate and dried over anhydrous calcium chloride. The ether was removed by distillation and the residue distilled under diminished pressure in an atmosphere of nitrogen. Eighteen grams of methyl terephthalaldehydate was obtained, b. p. 95–97° (2 mm.), m. p. 61–62° (from low-boiling petroleum ether). This melting point agrees with that observed by Simonis,[7] who prepared the ester by direct esterification of terephthalaldehydic acid.

The Condensation of *p*-Chlorobenzyl Bromide with Methyl Terephthalaldehydate.—A solution of 14 g. of *p*-chlorobenzyl bromide in 75 cc. of dry benzene was added dropwise to a refluxing mixture of 10 g. of methyl terephthalaldehydate, 50 cc. of dry benzene and 6 g. of zinc dust. The mixture was refluxed for ten hours and decomposed with dilute hydrochloric acid. The solid was removed by filtration, and the benzene layer was washed and dried over anhydrous magnesium sulfate. The dry benzene solution was refluxed for two hours with 15 cc. of acetic anhydride. The solution was concentrated to a thick sirup under reduced pressure, and the residue was allowed to cool. The partially solidified residue was washed with methanol, and the solid was crystallized from methanol to give 3.2 g. of 4-chloro-4′-carbomethoxystilbene melting at 158–160°. By the method of mixed melting points this compound was shown to be identical with the stilbene obtained from methyl α-bromo-*p*-toluate and *p*-chlorobenzaldehyde. A bromide was prepared from this product which was shown by the method of mixed melting points to be identical with the 4-chloro-4′-carbomethoxystilbene bromide which had been previously prepared.

(7) Simonis, *Ber.*, **45**, 1585 (1912).

Distillation of the oil gave a compound which distilled at 160–170° (2 mm.) and melted at 100° (from methanol). Its composition corresponded to that of *p,p′*-dichlorobibenzyl.

Anal. Calcd. for $C_{14}H_{12}Cl_2$: C, 66.91; H, 4.82. Found: C, 66.71; H, 5.01.

Preparation of 4-Carbomethoxystilbene from Cinnamic Acid and Methyl *p*-Aminobenzoate.—The general directions used by Meerwein[4] for the preparation of substituted stilbenes were used in this synthesis of 4-carbomethoxystilbene. The diazonium salt of methyl *p*-aminobenzoate was made by adding a solution of 9 g. of sodium nitrite in 15 cc. of water to a mixture of 50 cc. of 25% hydrochloric acid, 19 g. of methyl *p*-aminobenzoate and 50 g. of ice. Throughout this experiment the reaction mixture was well stirred. An ice-bath was placed around the reaction flask and 27.5 g. of sodium acetate was added. A solution of 18.5 g. of cinnamic acid in 150 cc. of acetone was added and the ice-bath was removed. Five minutes later a solution of 5.3 g. of cupric chloride in 15 cc. of water was added and the mixture was stirred for one hour at room temperature. The 4-carbomethoxystilbene was removed, washed with methanol and crystallized from methanol, m. p. 158–159°; yield, 52%.

By the method of mixed melting points this compound was shown to be identical with the stilbene prepared from methyl α-bromo-*p*-toluate and benzaldehyde. The bromide prepared from this stilbene was shown to be identical with the previously prepared 4-carbomethoxystilbene bromide.

4-Carbethoxystilbene.—By use of the foregoing procedure a 36% yield of 4-carbethoxystilbene was obtained from ethyl *p*-aminobenzoate. It was crystallized from ethanol, m. p. 105–106°.

Anal. Calcd. for $C_{17}H_{16}O_2$: C, 80.92; H, 6.38. Found: C, 80.77; H, 6.43.

The **bromide** was recrystallized from absolute ethanol, m. p. 180–181°; yield 90%.

Anal. Calcd. for $C_{17}H_{16}O_2Br_2$: C, 49.51; H, 3.91. Found: C, 49.89; H, 4.07.

Treatment of the bromide with sodium iodide in acetone gave an 85% yield of the parent stilbene.

Summary

Carbomethoxystilbenes of the type $ArCH{=}CHC_6H_4CO_2CH_3$ have been prepared from aromatic aldehydes and the appropriate methyl α-bromotoluates by the action of zinc.

Similar results have been obtained by condensing benzyl halides with methyl terephthalaldehydate.

For the unsubstituted carbalkoxystilbenes the method of Meerwein, Büchner and Emster was found to be excellent.

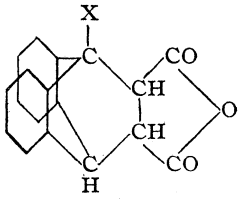
URBANA, ILLINOIS RECEIVED FEBRUARY 23, 1940

[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

Bicyclic Structures Prohibiting the Walden Inversion. Some Bicyclo[2,2,2]octane Derivatives with Substituents at the Bridge-Head[1]

BY PAUL D. BARTLETT AND SAUL G. COHEN

It has been shown in the laboratories of Barnett[2] and of Bachmann[3] that maleic anhydride readily undergoes addition to 9-substitution products of anthracene, yielding dibenzobicyclooctadiene derivatives such as I with substituents at the bridge-head position. These are among the few compounds known which are structurally incapable of replacement reactions with Walden inversion. In connection with our study of such compounds in the apocamphane series[4] the substances I, II and III, in which X is Br, NH_2 and OH are of special interest.



I	X = Br
Ia	X = H
II	X = NH_2
III	X = OH
IV	X = $OOCCH_3$
V	X = NO_2
VI	X = $NHCOCH_3$
VII	X = $NHCOOC_2H_5$

These compounds have three principal features not found in the apocamphanes. The bridge-head carbon atom is directly bound to two phenyl groups, which in the acyclic analogs means an enhanced reactivity of the group X. The presence of two potential acid groups provides water-solubility in the salts, making these compounds quite different in manipulation from the apocamphanes. Finally, the dibasic acids show geometrical isomerism.

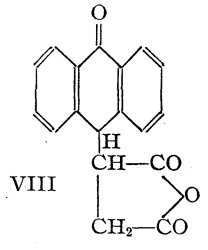
(1) Presented before the Organic Division of the American Chemical Society at its Boston meeting, September, 1939.

(2) Barnett, Goodway, Higgins and Lawrence, *J. Chem. Soc.*, 1224 (1934).

(3) Bachmann and Kloetzel, *J. Org. Chem.*, **3**, 55 (1938).

(4) Bartlett and Knox, THIS JOURNAL, **61**, 3184 (1939).

Barnett and his co-workers[2] observed that the addition product from 9-bromoanthracene (I) withstood treatment with alcoholic alkali for forty minutes without any replacement of the bromine. They also obtained only decomposition products from attempts to hydrolyze the corresponding acetate (IV). The direct reaction of maleic anhydride with anthranol or anthrone occurred only in the sense of a Michael condensation with the latter, yielding an uncyclized addition product (VIII).

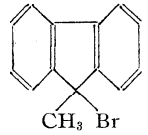


VIII

From these results Barnett concluded that the compound III must be incapable of existence.

Where our experiments have duplicated those of Barnett and his co-workers, there is complete agreement. We subjected the bromo compound, I, in different experiments, to treatment for fifteen to eighteen hours with boiling 15 to 30% potassium hydroxide, with no other effect than to open the anhydride ring and isomerize the *cis*- into the *trans*-dibasic acid. The aqueous extract of the product, after acidification and shaking with ether, gave no precipitate with silver nitrate. As the nearest analogous compound without the bridged ring structure we

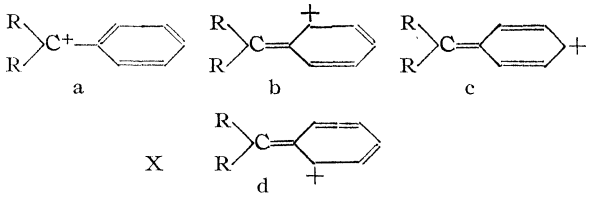
selected 9-methyl-9-bromofluorene (IX) for comparison. This compound, dissolved in ethyl alcohol at 25°, formed bromide ion at a unimolecular rate with a half-period of about five minutes. Although there is a possibility of elimination of hydrogen bromide from this compound, the isolation of impure 9-methyl-9-ethoxyfluorene in 52% yield shows that replacement of the bromine also was occurring. The corresponding half-period of the bridgehead bromine compound (I) at 83° is surely more than 1200 hours, since otherwise an easily detectable quantity of bromide ion would have been present in our experiments. Assuming a temperature coefficient of two for a ten degree rise in temperature, we find that at the same temperature there is at least a million-fold difference in reactivity between the bromine of I and that of IX. The difference is surely much greater than this, since the 50% aqueous medium in which the bicyclic compound was tested is much more favorable to bromine replacement reactions than the pure alcohol used for IX.[5]



IX

This inertness of the bromine in I is subject to interpretation along the same lines as indicated by Bartlett and Knox,[4] but the special structural features of this bromo compound make possible a new perspective on the problem. There is little opposition to the view that true and comparatively stable carbonium ions can be formed by the dissociation in appropriate solvents of diaryl and triarylmethyl bromides. The work of Walden[6] has shown this by conductivity methods, and indeed Ziegler and Wollschitt[7] have found that triphenylmethyl bromide is a completely strong electrolyte in liquid sulfur dioxide. Therefore even those who are unwilling to consider the ionization mechanism for the solvolysis of purely aliphatic tertiary halides must take it into account for highly arylated methyl bromides.

The source of the stabilization which facilitates such ionization in the arylated methyl halides is now well recognized in the contribution of the various bond structures Xa-d to the total (resonance) structure of the carbonium ion. It will be noted that three of these structures have double bonds to the central carbon atom and hence cannot be expected to contribute significantly to the resonance unless the geometry of the ion as a whole can be made compatible with such structures. This means that the central carbon atom, the three atoms directly connected to it, and in fact all the atoms of the phenyl group, must lie in the



X

same plane. This is obviously impossible in any carbonium ion that might be formed by the removal of Br^- from the compound I.

We thus derive, for carbonium ions stabilized by aromatic resonance, the generalization that the ion must approach a planar structure to be stable, and that any stereochemical conditions prohibiting a planar structure will markedly raise the energy barrier to the formation of the ion. Bartlett and Knox proposed that this might be the case for all carbonium ions, even those without aromatic resonance, taking the planar structure of trimethylborane (which, like the *t*-butyl cation, has a central atom with only six electrons) as an analogy.

With respect to reaction with metallic sodium, the bromine at the bridge-head is not wholly inert. In the reduction of 0.1 g. of I with a total of 4 g. of sodium in the presence of alcohol, 0.01 g. of the *trans*-reduction product was isolated and identified by mixed melting point with a synthetic sample prepared by boiling the addition product of maleic anhydride and anthracene with alkali. This seems to indicate that the hindrance to the momentary formation of a free radical at the bridge-head position is not as great as the hindrance to the formation of a carbonium ion. It is not purely the difference between a reagent which attacks the carbon and one which attacks the halogen, for the silver ion, which also must attack the bromine atom directly, fails to produce any silver bromide from this compound. Silver powder likewise gave no detectable reaction.

Experience in the apocamphane series suggested attempting the preparation of the hydroxy compound III or its *cis*- or *trans*-dibasic acid from the corresponding amino compound. Two

(5) Hughes, *J. Chem. Soc.*, 255 (1935).

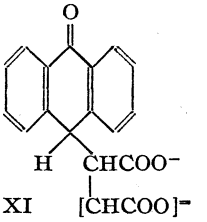
(6) Walden, "Chemie der freien Radikale," S. Hirzel, Leipzig, 1924.

(7) Ziegler and Wollschitt, *Ann.*, **479**, 90 (1930).

possible sources of this amino compound, the corresponding nitro and acetamino compounds (V and VI), were prepared with ease by the addition of maleic anhydride to 9-nitro- and 9-acetaminoanthracene, respectively. In neither case was the conversion into the amino compound achieved. The addition of maleic anhydride to ethyl N-9-anthrylcarbamate gave a bridge-head urethan (VII) which, as in the apocamphane series, was much more amenable to hydrolysis than the corresponding amide (VI). Sixteen hours of boiling with 35% alkali only converted the latter into the still acetylated *trans*-acid (in 80% yield), while the urethan was hydrolyzed in about an hour by 20% sodium hydroxide. Purification through the copper salt gave an amino-acid, m. p. 260–262°, of unknown configuration with respect to the two carboxyl groups.

When an acidified solution of this amino-acid was treated with sodium nitrite under controlled conditions, a variable yield of a white solid melting at 174–175° was obtained. Its analysis was correct for the dibasic acid from III, and although stable to heat its behavior in the presence of alkali was that to be expected from Barnett's results. In the presence of 10% sodium hydroxide it immediately acquired a deep orange color, and after thirty minutes of boiling, acidification and ether extraction, there resulted a mixture melting over a wide range above 130°. The results in preparing this compound were not reproducible and several other compounds were encountered in isolated runs but not satisfactorily identified.

The instability of the hydroxy compound to alkali probably is not uniquely related to the bicyclic ring structure. It is seen readily from the formula that III is a beta-hydroxy-anhydride, and its acid is an internal ketol condensation product of the acid of Barnett's compound, VIII. In the presence of a base this ketol condensation should be mobilized, and the equilibrium undoubtedly would be in favor of the uncyclized product. This is because the salt related to VIII can be enolized and converted into the alkali derivative of the corresponding anthranol. Actually, the compound VIII was never obtained from our hydroxy compound nor from Barnett's acetoxy compound (IV) with the bicyclic ring system. The only identifiable compounds which we obtained from the treatment of III with alkali were anthraquinone (obtained in the presence of oxygen) and dihydrodianthrone[8] obtained from a reaction in the absence of air. Both these products were identified by mixed melting points. The compound VIII does not yield these products on similar treatment, and hence is not intermediate in their formation from III. The mechanism of the deketolization of the cyclic compound may be such as to yield an ionic modification of VIII especially well adapted to the Michael retrogression to anthrone and maleate or fumarate ion. The molecular species XI would be of this kind.



XI

Experimental

Anthracene was brominated according to the directions of Barnett and Cook.[9] The crude product was distilled *in vacuo* as was done by Bachmann and Kloetzel[3] and crystallized several times from ligroin (b. p. 90–120°) and then from alcohol. The product was obtained as fine yellow needles melting at 101–103°.

9-Bromo-anthracene-9,10-endo-α,β-succinic Anhydride. (I).—The addition of maleic anhydride to 9-bromo-anthracene was carried out by refluxing equivalent quantities of the two reactants in dry xylene (5 cc. per gram of bromo-anthracene) for two and one-half hours. The product crystallized from the cooled solution in 94% yield, as white prisms, melting at 253–254°.[2]

Treatment of I with Alkali.—One-half gram of I was dissolved in 14 cc. of 21% aqueous potassium hydroxide and the solution was boiled for eighteen hours. The solution was acidified with chloride-free nitric acid, filtered and extracted with ether. Addition of a solution of silver nitrate to the water layer gave no precipitate or opalescence. Similar results were obtained when 50% aqueous alcohol was used as the solvent in this alkali treatment.

From this experiment a solid was recovered from the ether extract weighing 0.4 g., sintering at 210° and melting at 231°. Recrystallization from ether–petroleum ether gave white prisms melting at 238–240°; melting point, mixed with starting material, 224°. This product, not identical with either the starting material or the acid obtained from it by gentle treatment with alkali and acidification, is evidently the *trans*-dibasic acid.

Anal.[10] Calcd. for $C_{18}H_{13}O_4Br$: C, 57.94; H, 3.51. Found: C, 58.20; H, 3.70.

Solution in acetic anhydride and seeding with the anhydride starting material produced a small quantity

(8) Houben, "Das Anthracen und die Anthrachinone," Verlag Georg Thieme, Leipzig, 1929, p. 179.

(9) Barnett and Cook, *J. Chem. Soc.*, **125**, 1086 (1924).

(10) Analysis was performed by H. S. Wight.

of this anhydride, which may have been produced by a slow isomerization to the *cis*-form followed by dehydration, or it may have been present as an impurity in the *trans*-acid.

In an attempt to carry the alkali treatment still farther, we boiled 0.2659 g. of the anhydride with 10 cc. of 50% aqueous potassium hydroxide in a copper vessel. On the ninth day a hole had been eaten through the vessel and the material ran out. From an extract of the bench-top we recovered 35% of the bromine-containing *trans*-acid.

The *cis*-acid from I was obtained in practically quantitative yield when 0.1 g. of the anhydride was dissolved in 10 cc. of 10% potassium hydroxide by boiling and the solution cooled and acidified. This acid melted at 106°, re-solidified and melted again at 253–254°, both alone and when mixed with the original anhydride. When this *cis*-acid was dissolved in warm acetic anhydride, the original anhydride immediately crystallized quantitatively.

***cis–trans*-Isomerism of the Acid from Ia.**—The anhydride Ia, m. p. 258–260°, prepared according to Clar,[11] when boiled four hours with 2% potassium hydroxide, yielded a product which, after drying *in vacuo*, melted at 258–260° alone, and when mixed with the starting material. However, on boiling for sixteen hours with 3 g. of potassium hydroxide in 14 cc. of water, a product was obtained melting at 241°, which depressed the melting point of the original anhydride to 223°. Diels and Alder[12] prepared the *trans*-acid, m. p. 241–242°, by boiling 5 g. of the *cis*-dimethyl ester for twenty minutes in a solution of 0.5 g. of sodium in 100 cc. of alcohol. Treatment with the concentrated alkali for intermediate lengths of time gave mixtures of the *cis*- and *trans*-acids.

Treatment of I with Silver Nitrate.—A solution of 1.0226 g. of the anhydride and 1 g. of silver nitrate in 70 cc. of alcohol was heated to boiling for two and one-half hours on the steam-bath and allowed to stand for three days. There was a precipitate weighing 0.0248 g. Of this, 0.0118 g. was ignited in a porcelain crucible, leaving a residue of 0.0044 g. of silver which, after a second ignition, weighed 0.0042 g. These figures correspond to 37.3 and 35.5% of silver, respectively. Solution in nitric acid and precipitation gave 0.0054 g. of silver chloride. On the basis of 35.5% of silver the equivalent weight of the silver-containing precipitate was 304; calculated for $C_{18}H_{11}O_4BrAg_2$, 293.5. The precipitate is therefore accounted for as the silver salt of the bromine-containing dibasic acid, and not as silver bromide.

Treatment of the Bromo Compound I with Silver Powder.—Four-tenths gram of silver powder was added to a solution of 0.1779 g. of the compound I in 25 cc. of acetone. The solution was kept at room temperature for two days, and was boiled for sixteen days. The mixture was filtered and the solvent was removed. The residue weighed 0.16 g. and was identical with the starting material. When this procedure was carried out in boiling xylene, again only starting material was recovered.

Reduction of I with Sodium.—The bromo-anhydride (0.1 g.) was dissolved in about 20 cc. of alcohol containing a little sodium ethoxide, and 1 g. of sodium was added. When this had dissolved, the solution was acidified, diluted with water and extracted with ether. The ether was evaporated and the residue again dissolved in alcohol and treated with sodium. After four such treatments with a gram of sodium each time, 0.01 g. of *trans*-reduction product was recovered, m. p. 234–235°. Mixed with synthetic material of melting point 241°, the melting point was 234–237°, while a large depression was obtained on mixture with the *trans*-bromo-acid. In a number of such reduction runs, silver bromide was precipitated from the aqueous extract of the product, the maximum amount obtained being 95.4% of the theoretical, from a run in which the reaction mixture was boiled during the reduction. The reduction in most of the runs was less than 50%, and the organic product consisted of difficultly separable mixtures.

9-Methylfluorenol was made in 94% yield of crude product by the method of Ullmann and von Wurstemberger[13] and melted at 172° after crystallization from benzene.

9-Methyl-9-bromofluorene.—0.87 g. of 9-methylfluorenol was dissolved in 20 cc. of anhydrous ether. At 0°, hydrogen bromide was passed into this solution until it was fuming strongly, with anhydrous magnesium sulfate present to remove the water formed. After two hours at 0°, a yellow color had developed. The solution was then filtered and the ether was removed under reduced pressure in a stream of dry nitrogen. The oil residue was extracted with 10 cc. of petroleum–ether at room temperature, and a small quantity of red oil which did not dissolve readily was discarded. The solution was cooled in dry-ice and nearly colorless crystals were deposited, 0.92 g., 80% yield, melting at 48.5–49.5°. The recrystallized product melted at 50°. It has been reported previously by Keizo Nakamura.[14] It was kept in dry-ice until used, since on standing at room temperature in the light, it was converted into a red oil with loss of hydrogen bromide.

Reaction of 9-Methyl-9-bromofluorene with Alcohol.—0.92 g. of 9-bromo-9-methylfluorene was dissolved in 10 cc. of absolute alcohol. After eleven hours at room temperature, the solution was poured into twice its volume of water. The mixture was cooled in an ice-bath, and the solid which formed was filtered off, 0.65 g., melting nearly completely at 75°, but with a small quantity of solid persisting until a much higher temperature. The solid was taken up in 25 cc. of ether, giving a yellow solution and a white insoluble solid, 0.10 g., which turned yellow on exposure to air, and decomposed over a wide range to about 250°. Evaporation of the ether gave a solid, 0.55 g., melting poorly to 77°. This was dissolved in petroleum ether (35–60°) and the solution was filtered from a small quantity of insoluble material, 0.02 g., decomposing over a range to 110°. Concentration of the petroleum ether gave 0.3 g. of solid melting 75–80°, and 0.11 g. melting 72–79°. Recrystallization from dilute alcohol gave fine white needles, melting at 82–83°.

Anal. Calcd. for $C_{16}H_{16}O$: C, 85.68; H, 7.20. Found: C, 85.63; H, 7.29.

Reaction of 9-methyl-9-bromofluorene with alcohol was followed kinetically by titrating aliquot portions of the

(11) Clar, *Ber.*, **64**, 2194 (1931).

(12) Diels and Alder, *Ann.*, **486**, 191 (1931).

(13) Ullmann and von Wurstemberger, *Ber.*, **38**, 4107 (1905).

(14) Keizo Nakamura, *Sci. Papers Inst. Phys. Chem. Research Tokyo*, **14**, 184 (1930).

reaction mixture against standard base: 0.6949 g. of 9-methyl-9-bromofluorene was dissolved in 50 cc. of absolute ethyl alcohol at 25.0° and 5-cc. portions were withdrawn at intervals. Each portion was pipetted into a 125-cc. glass-stoppered Erlenmeyer flask containing 50 cc. of water and 5 cc. of chloroform. By quick shaking the solution was cleared and the acid was then neutralized with 0.5525 *N* sodium hydroxide. The end-points were sharp.

TABLE I

Time in minutes	Cc. of base
4.5	2.29
22.08	3.73
33.33	4.21
51.17	4.56
∞	4.90

When the logarithms of the concentrations of bromo compound were plotted against time, the slope of the line gave a rate constant of 0.0442 min.$^{-1}$.

9-Nitroanthracene was made by the nitration of anthracene according to the directions of Dimroth.[15] From 50 g. of anthracene was obtained 35 g. of 9-nitroanthracene, a 56% yield, orange needles, melting at 145–146°.

The nitrobicyclo compound V was obtained when a solution of 1.5 g. of 9-nitroanthracene and 1 g. of maleic anhydride in 5 cc. of xylene was boiled for two hours. The product, twice crystallized from xylene, weighed 1.2 g. (56% yield) and melted at 244–245°.

Anal. Calcd. for $C_{18}H_{11}NO_5$: C, 67.30; H, 3.45. Found: C, 67.54; H, 3.84.

Attempts to reduce this to the amino compound (II) by stannous chloride did not lead to the desired product.

9-Aminoanthracene was made by the reduction of 9-nitroanthracene with stannous chloride, the method of Meisenheimer and Connerade.[16] We obtained, in 91% yield, a yellow product which rapidly became brown on exposure to air. It melted unsharply at 135–140°, after softening at 120°. The highest reported melting point is 145–150° after softening at 135°[16] and it has also been reported as decomposing upward from 115°.[17] On long standing in a desiccator it was converted to a compound melting at 216–217°. A solution of 9-aminoanthracene in benzene, on standing for several months, also deposited crystals of this high melting compound. We did not characterize it further.

The reactions of maleic anhydride with 9-aminoanthracene, and with 9-aminoanthracene hydrochloride, did not lead to the desired product.

N-9-Anthrylacetamide was made by the action of acetic anhydride on 9-aminoanthracene at room temperature, the method of Goldmann.[17] The product is obtained, in practically quantitative yield, as slightly colored needles, melting at 272–274°.

The addition of maleic anhydride to N-9-anthryl acetamide was carried out by boiling a solution of 2.7 g. of the former and 4 g. of the latter in 20 cc. of xylene for four and one-half hours. The product (VI) was deposited from the cooled reaction solution in 91% yield, as white prisms, melting unsharply at 268°, after sintering from 257°.

(15) Dimroth, *Ber.*, **34**, 221 (1901).
(16) Meisenheimer and Connerade, *Ann.*, **330**, 165 (1904).
(17) Goldmann, *Ber.*, **23**, 2522 (1890).

Anal.[10] Calcd. for $C_{20}H_{15}O_4N$: C, 72.05; H, 4.54. Found: C, 71.95; H, 4.51.

The bridge-head amide (VI) proved resistant to acid or base hydrolysis, and the bridge-head amine could not be prepared from it.

One-half gram of the amide was dissolved in a solution of 5 g. of sodium hydroxide in 14 cc. of water, and boiled for sixteen hours. Acidification of the black reaction solution gave 0.4 g., 76% yield, of a white solid, sintering at 250°, and melting at 253°, and depressed to 242° on mixture with the starting material. Analysis indicated that it was the dibasic acid, and the melting point depression that it was the *trans*-isomer.

Anal.[10] Calcd. for $C_{20}H_{17}O_4N$: C, 68.38; H, 4.88. Found: C, 68.10, 68.39; H, 4.91, 4.87.

A solution of 0.2 g. of the amide VI in 10 cc. of concentrated sulfuric acid was allowed to stand at room temperature for one hour. Water was added until a slight turbidity formed, and the solution was warmed for one-half hour on the steam-bath. Color began to develop, so the heating was stopped. The solution was poured into water, and the product was extracted with benzene. We obtained 0.17 g., 85% yield, of starting material, sintering at 250° and melting at 263°. Its melting point was elevated on mixture with the starting material. Little or no hydrolysis had taken place.

Ethyl 9-Anthrylcarbamate.—Twenty-one grams of 9-nitroanthracene was reduced with stannous chloride as directed by Meisenheimer and Connerade.[16] The tin double salt was decomposed with dilute ammonia, and the amine was extracted with ether. The amine was not isolated, but this ether solution was dried over magnesium sulfate, and treated with 20 cc. of ethyl chloroformate. The reaction was allowed to run for thirty-six hours at room temperature, and a precipitate of the urethan and the amine hydrochloride formed. This solid was filtered off, and evaporation of the filtrate gave a small quantity of the urethan. The solid was boiled for a few minutes in 500 cc. of xylene and filtered, and from the cooled filtrate the urethan crystallized. Combined with that obtained from the mother liquor, the yield was 9.4 g., 75%. The solid filtered from the boiling xylene was suspended in dilute alkali and extracted with ether. The ether extract was treated with ethyl chloroformate and more of the urethan was made. The urethan was crystallized twice from xylene, and was obtained as fine, light yellow needles, melting at 224–225°.

Anal.[10] Calcd. for $C_{17}H_{15}O_2N$: C, 76.96; H, 5.70. Found: C, 77.15; H, 5.77.

The addition compound VII was obtained in 95% yield when 15 g. of maleic anhydride and 4.2 g. of ethyl 9-anthrylcarbamate were boiled in 60 cc. of dry xylene for 2.75 hours. There was a rapid development of an orange-red color, which slowly faded during the progress of the reaction. The product crystallized from the cooled reaction medium in colorless prisms, melting at 252–254°, with decomposition. It was washed with benzene and hexane, dried *in vacuo* and analyzed.

Anal.[10] Calcd. for $C_{21}H_{17}O_5N$: C, 69.38; H, 4.72. Found: C, 69.38; H, 4.49.

Bridge-head Amine (II) Hydrolysis of the Urethan VII.—In one of a series of preparations, 0.3 g. of the bridge-

head urethan was boiled for 1.25 hours in 20 cc. of 20% sodium hydroxide. A yellow color developed. The solution was filtered, acidified and warmed until the carbon dioxide was removed. The solution was made neutral, the silica which formed was filtered off, and a solution of 1 g. of cupric acetate in a little water was added. The mixture was warmed for a few minutes, and the precipitated copper salt was filtered off. The calcium and mercuric salts were soluble, whereas the copper salt precipitated from even a weakly acidic solution. When the reaction is run on a larger scale, the copper salt is rather to be centrifuged than filtered. The copper salt was suspended in a little water and dissolved by addition of a few drops of concentrated hydrochloric acid. Hydrochloric acid was added, so that the solution was about 6 normal. The solution was cooled in ice and the product slowly crystallized. The product also crystallizes out if the copper salt is merely dissolved in concentrated hydrochloric acid. We obtained 0.15 g. of crude product, 51% yield. It was purified by solution in water and precipitation by addition of hydrochloric acid. It melted at 260–262° with decomposition.

Anal.[10] Calcd. for $C_{18}H_{16}NClO_4$: C, 62.53; H, 4.66; N, 4.05. Found: C, 62.28; H, 4.74; N, 3.94.

Treatment of the Amine II with Nitrous Acid.—To a solution of 0.62 g. of the amine II in 40 cc. of 20% hydrochloric acid, a solution of 0.7 g. of sodium nitrite was added and the mixture allowed to stand at room temperature for several hours. A white turbidity appeared immediately. The mixture was extracted with ether, the ether dried and concentrated and petroleum ether added. There was obtained 0.37 g. (65% yield) of a product giving the correct analysis for the hydroxy compound III, m. p. 174–175°.

Anal.[10] Calcd. for $C_{18}H_{14}O_5$: C, 69.68; H, 4.55. Found: C, 69.54; H, 4.83.

This product was later obtained without prior isolation of the amine II. A solution of 0.3 g. of the bridge-head urethan VII in 20 cc. of 20% sodium hydroxide was boiled for thirty minutes. The solution was acidified, and to the clear acidic solution 0.5 g. of sodium nitrite was added. After standing one-half hour at 0° and at room temperature for sixteen hours, the mixture was saturated with hydrogen chloride gas and extracted with ether. The ether was dried and concentrated, and on addition of petroleum ether this product was obtained in 62% yield.

Measurement of the Nitrogen Evolved in the Nitrous Acid Reaction.—One-half gram of the bridge-head urethan VII was hydrolyzed by boiling for one hour in 25 cc. of 20% sodium hydroxide. The solution was neutralized and 3 cc. excess of concentrated hydrochloric acid was added. The flask was immersed in an ice-bath, and a solution of 0.5 g. of sodium nitrite was admitted. The nitrogen, carried on a stream of carbon dioxide, was passed through alkaline permanganate and collected over 50% potassium hydroxide. The reaction was complete in a few hours at 0°.

TABLE II

Time, hours	Vol. N_2 (unlevelled), cc. t = 30°
2	28
3.5	35
4	36
4.5	36.3, levelled vol. 34 cc.

Corrected for temperature, 30.6 cc.
Calculated, 31 cc.

The gas gave no test for oxides of nitrogen with starch-iodide paper and it did not support combustion.

While the reaction was proceeding at 0°, a white solid precipitated. However, it turned to a yellow oil when it was filtered off, or when the solution was allowed to warm up to room temperature. In one instance, we filtered off the solid which formed, but could isolate from it only an impure compound (1.5%) melting 160–200°. From the filtrate, worked up as usual, we obtained, in 4% yield, an impure product, melting 175–200°, and, in 19% yield, the compound melting at 174–175°, and an oil residue.

The results of this nitrous acid reaction were not strictly reproducible, the yields varying over a wide range. Several other compounds, none of them identical with any prepared by Barnett and his co-workers,[2] were found in different runs, usually in small yields, but they have not yet been satisfactorily identified.

Behavior of the Product of the Nitrous Acid Reaction.—Thirteen milligrams was boiled in 0.8 cc. of xylene for fifteen minutes. The compound was slightly soluble and stable, and was recovered both from the undissolved residue and from the filtrate.

Treatment with Alkali.—(a) The orange solution of 0.2 g. of the hydroxy compound in 20 cc. of 10% sodium hydroxide was boiled for one-half hour. A red color developed and the solution became turbid. Acidification discharged most of the color, and precipitated 0.1 g. of a yellow solid which melted at 258–269°. After crystallization from acetic acid and from xylene it darkened at 270° and melted at 277–280°, and on mixture with anthraquinone it melted at 279°. The product was apparently anthraquinone, obtained in 75% yield.

(b) The solution of 0.1 g. of the hydroxy compound in 10 cc. of 10% sodium hydroxide was boiled for thirty minutes in a stream of nitrogen. The orange solution was cooled and acidified. The color was discharged and a yellow solid formed, weighing 0.06 g. This sintered at 130°, melted to a large extent at 160°, and completely at 198°. After standing in ether solution for several weeks, it was converted to a compound melting at 240–250°.

These same compounds were obtained from anthrone. One-fourth gram of anthrone was boiled for thirty minutes in 50 cc. of 10% sodium hydroxide. On acidification a yellow compound, sintering at 145°, melting to a large extent at 155° and fully molten at 198°, was obtained. This melting range was not affected on mixture with the compound obtained above. Oxidation of this by ferric chloride in acetic acid solution, the method of Dimroth,[18] yielded dihydrodianthrone, melting at 245–257°, and at 242–257° on mixture with the compound obtained above.

Summary

The addition product (I) of maleic anhydride to 9-bromoanthracene, which is structurally incapable of a Walden inversion in the replacement of the bromine, shows no replacement of this bromine on boiling for eighteen hours with 30%

(18) Dimroth, *Ber.*, **34**, 222 (1901).

potassium hydroxide in 50% aqueous ethyl alcohol. This extends the observations of Barnett and his co-workers to more drastic conditions.

Two interpretations of this and similar facts are considered, that a Walden inversion must attend such a replacement reaction, or that a carbonium ion must be formed in which the central carbon atom and the three atoms directly combined with it lie in a common plane. The latter concept, advocated previously by Bartlett and Knox by analogy to boron compounds, is here correlated with the resonance normally present in an arylated carbonium ion. This interpretation is favored but not conclusively proved.

The bromine can be replaced by hydrogen by means of reduction with sodium and alcohol.

Maleic anhydride has been added to ethyl N-9-anthrylcarbamate to yield a bridged-ring urethan (VII) which is readily hydrolyzed to the aminodibasic acid related to II. Nitrous acid converts this into a compound which is probably the dibasic acid with hydroxyl on the bridge-head. As expected by Barnett, this compound is very unstable to alkali. Its decomposition is interpreted as ketol cleavage.

CAMBRIDGE, MASSACHUSETTS RECEIVED MARCH 2, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE CREIGHTON UNIVERSITY]

The Partial Pressure of Hydrogen Chloride from its Solutions in *o*-Nitrotoluene, *m*-Nitrotoluene and *n*-Hexane at 25°

BY S. JAMES O'BRIEN AND CHRISTOPHER L. KENNY

In an earlier paper[1] the partial pressure of hydrogen chloride from its solutions in various solvents was interpreted in terms of an acid–solvent reaction. The results so obtained may be taken as a measure of the relative basicities of the solvents used. It also has been pointed out[2,3,4] that the problem of solvent basicity can be attacked by means of infrared absorption studies. In work of this type the position of a certain absorption band, which is attributed to the formation of a hydrogen bond and which shifts to longer wave lengths in the more basic solvents, is considered a measure of the basicity of the solvent. It seemed of interest to determine to what extent the conclusions concerning the basicities of solvents obtained from such infrared absorption data parallel those obtained from partial pressure experiments. It was decided, then, to measure the partial pressure of hydrogen chloride from its solutions at 25° in the ortho and meta isomers of nitrotoluene in order to compare these and other similar available data with those obtained from infrared absorption investigations.[5]

Also, a few measurements of the partial pressure of hydrogen chloride from *n*-hexane solutions at the same temperature were made in order to determine whether the deviation of hydrogen chloride from the law of Raoult in this solvent is positive, as might be anticipated from the results obtained with haloforms in hydrocarbon solutions,[6] and from the fact that the rate of addition of hydrogen chloride to ethylenes is so very much greater in aliphatic than in aromatic hydrocarbons.[7]

Experimental

Apparatus and Method.—The apparatus and method were in general the same as those employed in the previous work.[1,8] The time allowed for the establishment of the solution–vapor equilibria ranged from two to five days. In the analysis of the solutions of the nitrotoluenes it was found to be advantageous to add a drop or two of capryl alcohol to the solutions before titration with sodium hydroxide. The constant temperature bath was regulated at 25.00 ± 0.02°.

Materials.—The liquids used were Eastman Kodak Company products. The *m*-nitrotoluene and *n*-hexane were not further purified. Since the *o*-nitrotoluene had a slightly pink color which turned to a deep purple on the

(1) S. J. O'Brien, C. L. Kenny and R. A. Zuercher, THIS JOURNAL, **61**, 2504 (1939).

(2) W. Gordy and P. C. Martin, *J. Chem. Phys.*, **7**, 99 (1939).

(3) W. Gordy, *ibid.*, **7**, 93 (1939).

(4) W. H. Rodebush and A. M. Buswell, *J. Phys. Chem.*, **43**, 219 (1939).

(5) Since this paper was written, an article by W. Gordy and S. C. Stanford, *J. Chem. Physics*, **8**, 170 (1940), has appeared in which a study of this kind has been made. Gordy and Stanford relate the basicities of solvents as derived from shifts of the OD vibrational band of CH_3OD in these solvents, to those derived from measurements of the solubilities of monofluorodichloromethane. This comparison seems to be in accord with the opinion, stated later in this paper, concerning the discrepancies between the basicities of solvents as intimated by infrared absorption and solubility studies.

(6) G. F. Zellhoefer, M. J. Copley and C. S. Marvel, THIS JOURNAL, **60**, 1337 (1938).

(7) S. F. O'Connor, L. H. Baldinger, R. R. Vogt and G. F. Hennion, *ibid.*, **61**, 1454 (1939).

(8) J. Saylor, *ibid.*, **59**, 1712 (1937).

addition of hydrogen chloride, it was purified by allowing it to stand over calcium oxide and distilling it from phosphorus pentoxide. The liquid obtained was yellow in color and maintained this color when hydrogen chloride was added. Results obtained using the unpurified *o*-nitrotoluene were, however, not significantly different from those obtained using the purified material as is shown in Table I. The physical constants of the liquids, taken as an index of purity, are as follows: *n*-hexane, $n^{20}D$ 1.3741; *o*-nitrotoluene, $n^{20}D$ 1.5476; *m*-nitrotoluene, $n^{20}D$ 1.5479; m. p. 15.35°.

The hydrogen chloride was generated and introduced into the liquids as in the previous work.[1]

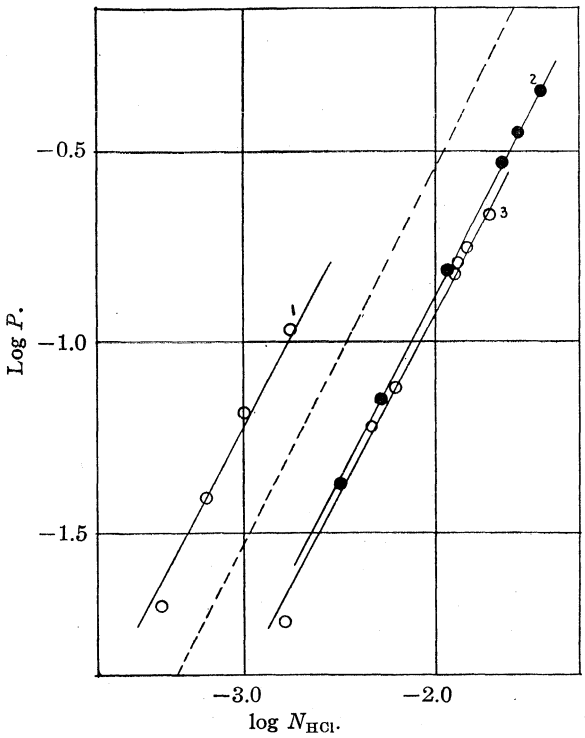


Fig. 1.—The partial pressure of hydrogen chloride from solutions in (1) *n*-hexane, (2) *o*-nitrotoluene and (3) *m*-nitrotoluene. The broken line represents Raoult's law.

Results

The results obtained are given in Tables I, II and III, in which the first column gives the molal concentration of hydrogen chloride in the solutions, the second gives the partial pressure of hydrogen chloride from the solutions in mm. of mercury, and the third column gives the Henry law constant, $k = p/m$, in atmospheres per mole per 1000 g. of solvent.

TABLE I

THE PARTIAL PRESSURE OF HYDROGEN CHLORIDE FROM ITS SOLUTIONS IN *o*-NITROTOLUENE AT 25°

m	*p*, mm.	*k*
0.259	340	1.72[a]
.202	269	1.75
.164	224	1.79
.0839	113	1.78
.0821	112	1.79
.0382	53.1	1.82
.0233	31.9	1.80
		Mean 1.77 ± 0.03

[a] Unpurified solvent was used.

TABLE II

THE PARTIAL PRESSURE OF HYDROGEN CHLORIDE FROM ITS SOLUTIONS IN *m*-NITROTOLUENE AT 25°

m	*p*, mm.	*k*
0.1385	167	1.54
.1037	132	1.68
.0939	122	1.71
.0918	116	1.67
.0438	56.7	1.70
.0343	44.3	1.69
.0116	13.9	1.58
		Mean 1.65 ± 0.05

TABLE III

THE PARTIAL PRESSURE OF HYDROGEN CHLORIDE FROM ITS SOLUTIONS IN *n*-HEXANE AT 25°

m	*p*, mm.	*k*
0.020	81.5	5.4
.0111	49.2	5.8
.0073	28.3	5.1
.0042	15.7	4.9
		Mean 5.3 ± 0.3

The mean value of the Henry law constant was taken as the slope of the best straight line, intersecting the origin, that could be drawn through a plot of pressure against molality. The deviation indicated is the average deviation from this mean.

The data listed in the tables are also shown graphically in Fig. 1, where the logarithm of the pressure is plotted against the logarithm of the mole fraction of the solutions. The theoretical curve was obtained using the value of 30.3 atm., calculated in the previous paper[1] for the fugacity of hydrogen chloride from the pure liquid at 25°.

Discussion

In Table IV, the reciprocals of the Henry law constants (molal solubility at 1 atm.) for hydrogen chloride in benzene, nitrobenzene, the nitrotoluenes, ethyl acetate and diethyl ether are compared with the positions in these solutions of the hydrogen chloride infrared absorption band which occurs at 3.46 μ in the pure hydrogen chloride. From this it will be seen that with the exception of the two nitrotoluenes the order of basicities as suggested by the two types of measurement is, in general, the same. The greater solubility of hydrogen chloride in the meta compound is, however, in accord with the assumption of a greater tend-

TABLE IV

Solvent	Position of band (microns)	$1/k$
Benzene	3.48[a,b]	0.491[d]
Nitrobenzene	3.69[a,c]	.505[d]
m-Nitrotoluene	3.75[a]	.607
o-Nitrotoluene	3.78[c]	.565
Ethyl acetate	3.88[c]	5.7[e]
Diethyl ether	4.08[c]	6.0[e]

[a] D. Williams, *Phys. Rev.*, **50**, 719 (1939). [b] E. K. Plyler and D. Williams, *ibid.*, **49**, 215 (1939). [c] Ref. 2. [d] Ref. 1. [e] These are simply molal solubilities calculated from the data of D. R. Chesterman, *J. Chem. Soc.*, 906 (1935).

ency for chelation in the ortho compound,[9] since chelation has been shown to result in a reduction of solubility if that property depends on the formation of a hydrogen bond.[10] That a chelate bond of this type should be stable in the presence of hydrogen chloride seems, however, contrary to the interpretation of the results obtained in the preceding paper[1] (p. 2507).[11] There, the high solubility of hydrogen chloride in ethylene glycol in comparison with that of monofluorodichloromethane in this solvent was explained in terms of a reduction of the association of the glycol molecules by the presence of hydrogen chloride.[12] This point is being further investigated, by similar partial pressure studies in progress in this Laboratory. If the solubility of hydrogen chloride can be taken as an index of the basic character of the solvent, it seems that the intensity, as well as the position of the absorption band must be taken into consideration when this property is to be interpreted not only in terms of the occurrence but also the extent of the solvent–solute reaction.[13]

Since hydrogen chloride solutions in the nitrotoluenes correspond with the law of Henry, and since the deviations from the law of Raoult are negative, the data may be interpreted in terms of the reaction between the solute and solvent represented by the equation

$$S + HCl = S \longrightarrow H—Cl$$

where S represents the solvent and S ⟶ H—Cl a compound formed by means of a hydrogen bond, some atom in the solvent acting as the electron donor. The equilibrium constant for this reaction is given by the equation[1]

$$K_a = f_0 - km_s/km_s \qquad (1)$$

where f_0 is the fugacity of liquid hydrogen chloride (30.3 atm. at 25°), k the Henry law constant and m_s the number of moles of solvent in 1000 g. Values of K_a calculated from the above data are 1.35 and 1.53 for ortho- and meta-nitrotoluene, respectively. As a measure of the basicity of the solvent, K_a should be more suitable than the molal solubility used in Table IV. This equilibrium constant was not used in the table, however, due to the inclusion of ethyl acetate and ether solutions, for which the existing data are not sufficient to show whether equation (1) is applicable.

While the value being used for the fugacity of liquid hydrogen chloride is far from satisfactory, there can be little doubt that the data obtained for the *n*-hexane solutions demonstrate a positive deviation from the law of Raoult, since the vapor pressure of hydrogen chloride from the solutions is greater than that required by the law even if the fugacity of liquid hydrogen chloride were equal to its vapor pressure (46.8 atm. at 25°). Treatment of these results in terms of association of the solvent seems to be out of the question for a liquid like hexane. Solutions which show a positive deviation from the law of Raoult can, no doubt, be better interpreted through a consideration of the internal pressures of the liquids involved.[14] However, it seems best to postpone further discussion along these lines until additional data can be presented.

Summary

1. Measurements are reported of the partial pressure of hydrogen chloride at 25° from its solutions in *o*-nitrotoluene, *m*-nitrotoluene and *n*-hexane over the concentration ranges 0.023–0.259, 0.012–0.139 and 0.004–0.02 molal, respectively.

2. The conclusions concerning the basicity of liquids derived from these measurements are compared with those obtained from the infrared absorption spectra of hydrogen chloride in various solvents. The comparison seems to show that

(9) N. V. Sidgwick and R. K. Callow, *J. Chem. Soc.*, **125**, 527 (1924).

(10) M. J. Copley, G. F. Zellhoefer and C. S. Marvel, THIS JOURNAL, **60**, 2672 (1938).

(11) It should be pointed out that J. J. Fox and A. E. Martin, *Proc. Roy Soc.* (London), **A162**, 437 (1937), suggested a similar interpretation of the infrared absorption of phenol in chloroform solutions as compared with its absorption in carbon tetrachloride solutions. The high "concentration" of the solvent, chloroform, would favor a phenol–chloroform reaction in such solutions, although this is a reaction which may not occur when the haloform is the solute, as intimated by solubility measurements[9] (pp. 2667–2668).

(12) See, however, J. Errera and H. Sack, *Trans. Faraday Soc.*, **34**, 740–741 (1938).

(13) Fox and Martin, *loc. cit.*; J. Errera, R. Gaspart and H. Sack, *J. Chem. Physics*, **8**, 63 (1940).

(14) J. H. Hildebrand, "Solubility of Non-electrolytes," second edition, Reinhold Publishing Co., Inc., New York, N. Y., 1936, especially pp. 107–122.

intensities as well as position of infrared absorption bands are required for an accurate estimate of the basicity of solvents.

3. In the nitrotoluene solutions, hydrogen chloride corresponds with the law of Henry and shows negative deviations from the law of Raoult. The data in these solutions are interpreted in terms of a reaction between solute and solvent. In the hexane solutions hydrogen chloride also corresponds with the law of Henry, but the deviation from the law of Raoult is positive.

OMAHA, NEBRASKA RECEIVED FEBRUARY 17, 1940

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF INORGANIC CHEMISTRY AT THE MASSACHUSETTS INSTITUTE OF TECHNOLOGY, NO. 76]

Preparation of Cobalt Carbonyl, Cobalt Nitrosyl Carbonyl and Cobalt Carbonyl Hydride by the Cyanide Method

BY ARTHUR A. BLANCHARD AND PAUL GILMONT

Brockway and Anderson[1] have prepared cobalt nitrosyl carbonyl for the purpose of electron diffraction studies by the method of Blanchard, Rafter and Adams,[2] saturating an alkaline suspension of cobaltous cyanide with carbon monoxide, but they state that on passing nitric oxide into the still alkaline solution no nitrosyl carbonyl is formed. They obtain this product only after acidification. This is contrary to the findings of Blanchard, Rafter and Adams, who found that cobalt nitrosyl carbonyl vapor could be swept from the still alkaline solution. The present studies confirm the latter statement. Furthermore, the product obtained by treating the alkaline solution with nitric oxide is undoubtedly purer than that obtained from the acidified solution.

Ewens and Lister[3] prepared cobalt carbonyl hydride, also for electron diffraction studies, by a modification of the method of Coleman and Blanchard[4] by saturating an alkaline suspension of cobaltous cyanide with carbon monoxide, then acidifying and sweeping the volatile hydride from the solution. The fact that the volatile hydride $HCo(CO)_4$ is obtained when cyanide is used as a carrier makes it seem probable that the fundamental reaction of oxidation and reduction is the same as when cysteine is the carrier, namely: $2CoCl_2 + 11CO + 12KOH \rightarrow 3K_2CO_3 + 2KCo(CO)_4 + 4KCl$. In absence of the carrier, no absorption of carbon monoxide takes place. The carrier, whether cysteine or cyanide, forms an intermediate complex containing carbon monoxide and cobalt; the latter reacts further to yield the salt of $HCo(CO)_4$ and the carrier is regenerated. Schubert[5] has very beautifully identified the intermediate complexes in the case of cysteine. Acidification liberates the volatile acid $HCo(CO)_4$ from its salt. Treatment with NO produces the volatile nitrosyl carbonyl, probably according to the reaction: $KCo(CO)_4 + NO + H_2O \rightarrow CO(CO)_3NO + CO + KOH + {}^1/_2 H_2$.

(1) Brockway and Anderson, *Trans. Faraday Soc.*, **33**, 1233 (1937).
(2) Blanchard, Rafter and Adams, THIS JOURNAL, **56**, 16 (1934).
(3) Ewens and Lister, *Trans. Faraday Soc.*, **35**, 681 (1939).
(4) Coleman and Blanchard, THIS JOURNAL, **58**, 2160 (1936).

Experimental

A large number of runs with varying proportions of cyanide and alkali were carried out and the proportions given in the following statements were found to produce the best results in the shortest time.

A shaking apparatus capable of keeping the liquid in the condition of a fine spray and yet allowing the passage of gases during the shaking is provided. It is swept out with carbon monoxide and approximately 50 ml. of a solution about 0.5 formal in cobalt nitrate, 0.5 formal in potassium cyanide and 4.0 formal in potassium hydroxide is introduced as follows: 7.3 g. of $Co(NO_3)_2 \cdot 6H_2O$ in 15 ml. of water is allowed to enter through a side arm, then 5 cc. of water to wash the arm, then 11.2 g. of potassium hydroxide in 11 ml. of water, then 5 cc. of water, then 1.6 g. of potassium cyanide in 3 ml. of water and lastly, 5 cc. of water.

The exit stopcock is closed and the solution shaken. A total absorption of 2200 to 2600 cc. of carbon monoxide takes place in about seven hours, 2 liters in the first two to three hours, the rate falling during the next three to five hours. During this absorption the solution changes from a blue suspension, through a pink suspension, to a yellow solution almost free of suspended matter.

Cobalt Nitrosyl Carbonyl.—The yellow liquid is a solution of the potassium salt of cobalt carbonyl hydride. The carbon monoxide is displaced from the shaker by nitric oxide and the shaker is started. Soon the solution turns red and after a while a deep yellow gas begins to show in

(5) Schubert, *ibid.*, **55**, 1877 (1933).

the shaker. This is the cobalt nitrosyl carbonyl and it is swept from the shaker by a very slow stream of nitric oxide, dried by passing through calcium chloride and phosphorus pentoxide, and frozen in a trap cooled with solid carbon dioxide and alcohol. Sweeping with nitric oxide at the rate of 2 liters per hour until no further product is obtained takes about five hours. A yield of 2.5 g. of $Co(NO)(CO)_3$ can be obtained or 58%.

Cobalt Carbonyl Hydride.—A solution of the potassium salt of cobalt carbonyl hydride is prepared as in the foregoing directions. A 500-ml. distilling flask fitted with an inlet tube reaching to the bottom and another short inlet tube and a drying train and trap leading from the side arm is provided. The long inlet tube is attached to the shaker and the apparatus is filled with carbon monoxide. The shaker is tilted and the solution is run into the flask. The flask is cooled with ice water and 30 ml. of 12 *N* hydrochloric acid is added slowly with hand shaking through the short tube. The surplus of hydrochloric acid after the surplus potassium hydroxide, potassium carbonate, potassium cyanide and $KCo(CO)_4$ have reacted gives a concentration of approximately 2.3 *N*. With a slow stream of carbon monoxide passing, the flask is allowed to come to room temperature, but care must be taken that the evolution of gas (carbon dioxide and $Co(CO)_4H$) does not carry the foam into the drying train. A slow stream of carbon monoxide is continued for ten hours to sweep the hydride from the solution. Sweeping at a lower temperature (10–15°) takes a longer time but produces a better yield of a cleaner product.

The cobalt carbonyl hydride condenses in the trap at −79° to a nearly white to light yellow solid. It melts at −33° to a light yellow liquid and begins to decompose above that temperature into cobalt tetracarbonyl and hydrogen. If it is sealed in a tube and brought to room temperature a high pressure results which will burst an ordinary tube. It is true that the presence of hydrogen tends to reverse the reaction.[6] The cobalt carbonyl hydride vapor in the tube has a deep yellow color. A yield of 2.2 g. of $Co(CO)_4H$[7,8] can be obtained or 44%.

Cobalt Tetracarbonyl $[Co(CO)_4]_2$.—The trap in which the hydride is collected should be connected through a tube of perhaps 100-ml. capacity with a sample tube and the system evacuated. Cooling the sample tube to −79° and removing the trap from the carbon dioxide ice, the hydride is distilled into the sample tube. The latter is allowed to come to room temperature and the hydride to decompose. The trap is again cooled to −79°, the hydrogen is pumped out and the remaining yellow cobalt carbonyl hydride vapor is condensed in the trap. The hydride is again distilled back into the sample tube and this process is repeated until, when no more yellow vapors appear after several days of standing, the sample tube is sealed off.

Summary

Carbon monoxide is absorbed almost quantitatively by an alkaline suspension of a cobalt salt to form $KCo(CO)_4$, but only when a carrier such as a small amount of a cyanide is present.

Nitric oxide displaces the volatile cobalt nitrosyl carbonyl $Co(NO)(CO)_3$ from the resulting solution even when the solution is distinctly alkaline.

Acids displace the volatile cobalt carbonyl hydride, $HCo(CO)_4$.

Cobalt tetracarbonyl $[Co(CO)_4]_2$ is obtained by allowing the hydride to decompose spontaneously at room temperature.

CAMBRIDGE, MASSACHUSETTS RECEIVED JANUARY 25, 1940

(6) Hieber, Schulten and Marin, *Z. anorg. allgem. Chem.*, **240**, 261 (1939).

(7) It is noteworthy that cobalt carbonyl hydride vapor mixed with a large amount of carbon monoxide at room temperature can be carried through long connections and a drying train without showing any sign of decomposition.

(8) The odor of cobalt carbonyl hydride is so intolerable that the danger from inhaling it is much less than from nickel carbonyl. It is, however, probably equally poisonous and since there is no antidote and the injury resulting from inhaling it is permanent, the utmost caution should be used to keep it from escaping into the laboratory.

[CONTRIBUTION FROM THE LABORATORY OF PHYSICAL CHEMISTRY, UNIVERSITY OF WISCONSIN]

The Physical Chemical Investigation of Certain Nucleoproteins. I. Preparation and General Properties

BY R. OWEN CARTER[1,2] AND JAMES L. HALL[1,3]

Nucleoproteins are present in all cells, occurring in highest concentration in the nucleoplasm. Since no systematic investigation of the physicochemical properties of this class of proteins has been made, it has been selected by us as the first class of tissue proteins to be studied. This report describes the preparation and some properties of two members of this group, the nucleohistone of the calf thymus, and the nucleoprotein of the hog thyroid. For the first of these are given the phosphorus and nitrogen contents, the apparent specific volume, and the refractive index increment, along with viscosity studies of its solutions and a titration curve.

Calf Thymus Nucleohistone

Preparation.—The calf thymus nucleohistone was prepared by a modification of the method of Huiskamp.[4] The glands, obtained directly from the animal carcasses, were reduced to a pulp, suspended in two to three times their volume of pure water, and extracted at 5° for twenty-four to thirty-six hours. The extract was filtered and clarified and the nucleohistone precipitated as the corresponding salt by addition of an equal volume of either 2% sodium chloride solution, or 0.2% calcium chloride solution. All work was done near the freezing temperature.

The sodium salt is a dense gel-like material which dissolves either in pure water or 5% sodium chloride solution. The calcium salt is insoluble in pure water but dissolves easily in solutions of 2% calcium chloride or 5% sodium chloride, though in the last case it is converted to the sodium salt.

Phosphorus Content of Sodium Nucleohistone.—Sodium nucleohistone which had been dialyzed against distilled water until the dialyzate gave no chloride test was frozen and dried to constant weight in a vacuum over phosphorus pentoxide. Samples of this dried protein were completely ashed with alcoholic magnesium nitrate and phosphate determinations were made colorimetrically with a small Duboscq calorimeter following the method of Fiske and Subbarow.[5] These colored solutions do not absorb light as required by Beer's law. The corrections for this deviation given by Bodansky[6] were found to apply and were used in the calculations.

TABLE I

PHOSPHORUS CONTENT OF CALF THYMUS NUCLEOHISTONE

Sample, g.	Color. reading,[a] mm.	Vol. of solution, cc.	Wt. P, g.	Per cent. P
0.0309	15.3	250	0.00137	4.43
.0510	9.3	250	.00238	4.67
.0241	18.6	250	.00109	4.52
.0174	10.8	100	.00081	4.66
			Average	4.6 ± 0.1

[a] The standard containing 0.02 mg. P in 5 cc. was set at 20 mm.

Nitrogen Content of Sodium Nucleohistone.—This value was determined by the micro-Kjeldahl method of Pregl. Because of the deliquescence of the dried protein, these determinations were performed on aliquots of solutions.

TABLE II

NITROGEN CONTENT OF CALF THYMUS NUCLEOHISTONE

Mg. N/g. soln.		Mg. protein/g. soln.		N, %
3.105, 3.040, 3.063	3.069	18.39, 18.37	18.38	16.70
2.984, 2.984	2.984	17.81, 17.84	17.83	16.74
1.363, 1.368	1.366	8.15		16.76
				Average 16.73 ± 0.02

Apparent Specific Volume of Sodium Nucleohistone.—For this determination a double bulb pycnometer of the Ostwald type was used. All measurements were made at 25 ± 0.005°. The protein solution was sterilized with merthiolate and completely dialyzed against distilled water. In two determinations made at a protein concentration of 1.7805%, the result was $V = 0.6575 \pm 0.003$. This is in contrast to the usual protein value of 0.73 to 0.75. Such a low value is reasonable, however, since nucleic acid, which makes up a large part of the nucleohistone molecule, has a density of about 2.15 g. per cc.[7] as compared to the usual protein density of 1.33 g. per cc.

Refractive Index Increment.—The refractive index of solutions of nucleohistone is a linear function of the protein concentration, permitting the use of refractive index methods for following concentration. As determined by use of a Bausch and Lomb immersion refractometer at 25.0°, the difference between the refractive indices of the protein solution and solvent, divided by the concentration of the protein, was found to be $(1.76 \pm 0.02) \times 10^{-3}$ per g. per 100 cc.

Viscosity of Sodium Nucleohistone Solutions.—Three series of viscosity measurements were made with the sodium nucleohistone solutions, (a) in dilute buffer,

(1) This work is taken in part from portions of the theses submitted in June, 1939, to the Faculty of the University of Wisconsin by R. Owen Carter and James L. Hall in partial fulfilment of the requirements for the degree of Doctor of Philosophy.

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(4) W. Huiskamp, *Z. physiol. Chem.*, **32**, 145 (1901).

(5) C. H. Fiske and Y. Subbarow, *J. Biol. Chem.*, **66**, 375 (1925).

(6) M. Bodansky, *ibid.*, **99**, 197 (1932).

(7) G. Schmidt, E. G. Pickels and P. A. Levine, *ibid.*, **127**, 257 (1939).

0.005 *M* in KH_2PO_4 and 0.005 *M* Na_2HPO_4, at 25°; (b) in the same buffer at 0.7°; and (c) in the same buffer plus 5% sodium chloride at 25°. A Washburn–Williams viscometer was used. The densities were determined pycnometrically. The data of Table III show that the presence of 5% sodium chloride causes a great increase in the viscosities of these solutions. The concentration of protein, *c*, is given in g. per 100 cc. of solution; time of outflow, *t*, is in seconds; η/η_{H_2O} is the viscosity relative to water; and η/η_0 is the viscosity relative to solvent.

TABLE III

VISCOSITIES OF SODIUM NUCLEOHISTONE SOLUTIONS

Concn. of protein, %	Density	Time, sec.	η/η_{H_2O}	η/η_0
(a) In dilute phosphate buffer at 25°				
Water		168.0		
Solvent	0.9986	168.2	1.0027	
0.815	1.0013	247.8	1.4812	1.4772
.611	1.0006	220.2	1.3153	1.3118
.407	0.9999	204.1	1.2183	1.2150
.196	.9992	185.6	1.1071	1.1041
.098	.9988	177.6	1.0590	1.0561
(b) In dilute phosphate buffer at 0.7°				
Water		324.0		
Solvent	1.0007	327.4	1.0113	
0.815	1.0037	495.6	1.5354	1.5182
.611	1.0030	436.0	1.3498	1.3347
.407	1.0022	400.2	1.2380	1.2242
.196	1.0014	363.0	1.1220	1.1095
.098	1.0011	345.6	1.0679	1.0560
(c) In phosphate buffer containing 5% of NaCl at 25°				
Solvent	1.0326	176.3	1.087	
0.846	1.0355	937.5	5.796	5.332
.315	1.0338	387.5	2.392	2.201
.158	1.0333	288.1	1.777	1.635
.079	1.0329	220.9	1.362	1.253
.039	1.0327	197.5	1.220	1.122

Titration Curve for Sodium Nucleohistone.—A titration curve was obtained by using nucleohistone which had been twice precipitated with sodium chloride and then dissolved in and dialyzed against distilled water until the dialyzate was chloride free. The initial *p*H of this dialyzed solution was about 5.4. Either 0.1 *N* sodium hydroxide or hydrochloric acid was continuously titrated into a 4% protein solution. The *p*H was measured at intervals by means of a glass electrode. The results, calculated on the basis of moles of acid or base bound per gram of protein are shown in Fig. 1.

The curve is completely reproducible although the characteristics of the glass electrode make the *p*H values beyond *p*H 9.5 very doubtful. The apparent break in the curve just below *p*H 2 is possibly genuine, since the nucleohistone hydrolyzes in acid solution and releases the comparatively strong nucleic acid. The entire acid combining capacity may be accounted for on the basis of the phosphorus present in the protein molecule. Because of the insolubility of the protein over part of the range, and because it was not possible to determine an exact isoelectric point, no attempt is made to estimate individual amino acids from the curve.

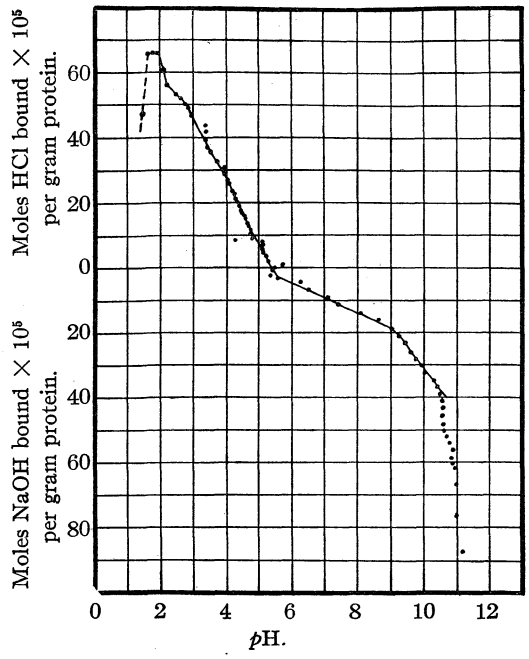

Fig. 1.—Titration curve of thymus nucleohistone: acid and base combining capacity.

Nucleoprotein from the Hog Thyroid

The nucleoprotein of the hog thyroid gland was prepared after the method of Heidelberger and Palmer.[8] It was found quite impossible to separate the thyroglobulin from the nucleoprotein by salting out at various concentrations of ammonium or sodium sulfates, thus completely confirming the work of Heidelberger and Palmer in this respect. Accordingly the nucleoprotein was precipitated and purified by precipitation at *p*H 4.9 with either 0.1 *N* hydrochloric or acetic acid. In the purification of the nucleoprotein a negative iodine test was used as a criterion of the absence of thyroglobulin.

Free diffusion and sedimentation velocity experiments indicate that the protein so prepared is more or less polydisperse, but electrophoretic studies indicate that the amount of nucleic acid present is independent of the preparational method. When the diffusion curves are analyzed by a statistical method, an average diffusion constant can be calculated. This value depends upon the previous treatment of the protein. Material prepared with acetic acid gives a much lower diffusion constant than that prepared with hydrochloric acid. Precipitation of purified nucleoprotein with ammonium sulfate also gives a material having a low diffusion constant.

The sedimentation, diffusion, and electrophoretic studies of these substances will be reported in later papers of this series.

Acknowledgments.—The writers wish to express their gratitude for the helpful advice of J. W. Williams throughout the course of their work and to acknowledge the suggestions of Dr. H. P. Lundgren in connection with the prepa-

(8) M. Heidelberger and W. W. Palmer, *J. Biol. Chem.*, **101**, 433 (1933).

ration of the nucleoprotein of the hog thyroid. One of us (R. O. C.) wishes to acknowledge financial assistance received from the Wisconsin Alumni Research Foundation.

Summary

1. Certain striking physical and chemical properties of the calf thymus nucleohistone protein have been presented. The phosphorus and nitrogen contents were accurately determined. The specific volume, refractive index increment, and viscosity of this protein in solution, as well as a titration curve are given.

2. The effect of certain preparational methods on the centrifugal and diffusion properties of the hog thyroid nucleoprotein has been briefly discussed.

RECEIVED FEBRUARY 17, 1940

[CONTRIBUTION FROM THE NEW YORK STATE AGRICULTURAL EXPERIMENT STATION]

The Calculation of Weight Average Molecular Weights during the Course of Decomposition of Homogeneous Linear Polymers

BY WALTER H. DURFEE[1] AND Z. I. KERTESZ[2]

For materials that occur naturally and that are composed of large molecules (in whatever sense the word molecule may be understood), some degree of heterogeneity as regards size of the individual molecules must be assumed. This natural heterogeneity is further increased upon progressing degradation until the lower polymers become dominant and, finally, by complete depolymerization, homogeneity is attained.

Such heterogeneity is obvious in any pectin isolated from plant material.[3] Its heterogeneity is increased by the chemical manipulations necessary for its isolation. On the other hand, there is ample evidence to show[4] that by extracting the crude pectic materials with 50% ethanol the lower polymers originally present (or formed during preparation) are removed, together with some other materials, usually accompanying pectins in nature. It is obvious, however, that even material prepared by this latter method contains a certain range of the various polymers and is not entirely homogeneous.

For several years one of us (Z. I. K.) has been engaged in research on the chemical and physical structure of the pectin molecule. One method of approach to this problem is through a study of the changes which take place in the chemical and physical structure of pectin upon enzymic hydrolysis. It is hoped that by such a study information can be gained concerning the naturally occurring pectic materials.

It has been reported recently[5] that when the decomposition of pectin is followed by various methods, the conclusions drawn concerning the average degree of polymerization are not in agreement. This led to an investigation of the number and weight averages[6] (M_n, M_w) for the "molecular weight" during the course of decomposition. During this work a formula was developed for the calculation of the M_w for any stage of progressive decomposition of a homogeneous linear polymer which, the authors feel, may also be useful to other workers dealing with such materials.

Several articles dealing with similar calculations already have appeared in the literature. W. Kuhn[7] made a study of the kinetics of the decomposition of chain-like polymers and calculated the proportions of various fission products occurring during the course of the hydrolysis. Dostal and Mark[8] investigated the heterogeneity of materials composed of macromolecules and proposed a method for the determination of the distribution of the proportion of fractions having various molecular weights in the mixture. More recently Lassatre[9] considered the degree of polymerization of cellulose during hydrolysis. All these authors approached the problem from the kinetical point of view and we feel that there is need to consider the basic relation between

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(2) Department of Chemistry, New York State Agricultural Experiment Station. Approved by the Director for publication as Journal Paper No. 369, January 30, 1940.

(3) Pectin is considered as a polymer of galacturonic anhydride residues in which the carboxyl groups are mostly changed to the methyl ester.

(4) Schneider, *et al.*, *Ber.*, **69**, 309, 2530, also 2537 (1936); **70**, 1611, also 1617 (1937); **71**, 1553 (1938), etc.

(5) Kertesz, THIS JOURNAL, **61**, 2544 (1939).

(6) Kraemer and Lansing, *J. Phys. Chem.*, **39**, 153 (1935).

(7) W. Kuhn, *Ber.*, **63**, 1503 (1930).

(8) Dostal and Mark, *Trans. Faraday Soc.*, **33**, 350 (1937).

(9) Lassatre, not yet published.

M_n and M_w in a more general manner, without considering the rate at which the progressive decomposition proceeds. In the present work it has been assumed that the number of broken linkages can be chemically determined (as is mostly the case) and thus the progress of the decomposition may be followed in that manner. The purpose of the calculations was to determine the M_w (and M_n) corresponding to any definite extent of hydrolysis as measured by the number of linkages broken irrespective of the velocity of the reaction.

Methods Used and Results Obtained.—Some assumptions have been made in order to increase the general validity of the results as well as for the purpose of defining their limitations. The question whether these assumptions hold in the case of pectins is not the subject of this paper and will be dealt with elsewhere. The molecules have been assumed to be composed of n identical units coupled by $n-1$ linkages to form a chain-like compound. The original material (composed of n units each of the molecular weight m, so that $M = mn$) has been assumed to be homogeneous in its molecular weight. It has been assumed that fission occurs as easily in a linkage of two units as in a long chain and furthermore that each step in the fission occurs simultaneously in all pieces of all chains, thus ignoring the impossibility of fission occurring in single units.

The calculation of the M_n at any degree of hydrolysis is obvious and simple. It will always equal M (original)$/p = mn/p$, where p is the number of groups or pieces into which the original chain of n units has split. The number of linkages opened is always $p-1$.

In the calculation of the M_w the size of each of the p groups, as well as all of the various possible ways in which the original chain of n units may be split into p groups, must be considered. In order to take all possibilities into consideration, it is necessary to assume the presence of a large number of molecules. While it is true that if a chain is split progressively in such a way that all the resulting groups are composed of the same number of units, the values of M_n and M_w will be equal, these values will differ considerably from each other when an average of all possible splittings is calculated, as can be done by formula (4).

We denote by $K(n,p)$ the number of ways that the n units of a chain may be split into p groups, each containing one or more units. (Obviously, $1 \leqq p \leqq n$). There being $n-1$ linkages and $p-1$ partitions between groups, $K(n,p)$ is the number of ways that the $p-1$ partitions may be distributed among the $n-1$ linkages

$$K(n,p) = {}_{n-1}C_{p-1} = \frac{(n-1)!}{(n-p)!\,(p-1)!} = \frac{(n-1)(n-2)\ldots(n-p+1)}{1\cdot 2\ldots(p-1)} \qquad (1)$$

Now $M_w = \sum_i f_i M_i$, where f_i is "the fractional weight of the constituent of molecular weight M_i," and the summation extends over all "constituents."[6] A "constituent" is one of the p groups: if it contains n_i units its f_i is n_i/n, and its $M_i = mn_i$. Thus $f_i = M_i/mn$, and for a single chain we have

$$M_w = \sum_{i=1}^{p} f_i M_i = \sum_{i=1}^{p} \frac{M_i^2}{mn} = \frac{1}{mn}\sum_{i=1}^{p} M_i^2 \qquad (2)$$

This must be averaged over all $K(n,p)$ possible arrangements of n units in p groups. To do this, suppose $K(n,p)$ chains arranged one below another. There being p groups in each chain, there will be p columns, and in each column a group of r units will occur as many times as the number of ways in which the remaining $n-r$ units can be split into $p-1$ groups, namely

$$K(n-r, p-1) = {}_{n-r-2}C_{p-2}$$

Hence, considering all p columns, a group of r units, each with $f_i = r/n$, $M_i = mr$, occurs $p\cdot{}_{n-r-1}C_{p-2}$ times, contributing to the total $f_i M_i$ the amount $\frac{mpr^2}{n}\cdot{}_{n-r-1}C_{p-2}$. Summing this for all values of r from 1 to $n-p+1$, and dividing by $K(n,p)$ for the average, we have

$$M_w = \sum_{r=1}^{n-p+1} \frac{mpr^2}{n}\cdot{}_{n-r-1}C_{p-2}/{}_{n-1}C_{p-1} \qquad (3)$$

This expression reduces without difficulty to

$$M_w = \frac{2n-p+1}{p+1}\,m \qquad (4)$$

The ratio of M_n to M_w is, therefore

$$\frac{M_n}{M_w} = \frac{n(p+1)}{p(2n-p+1)} \qquad (5)$$

which is less than unity for $1 < n < p$.

This ratio has a minimum value for $p = \sqrt{2n+2} - 1$, namely, $n/(\sqrt{2n+2}-1)^2$.

Consider, as an example, a chain of ten units split into seven groups. We may assume $m = 1$. We may analyze this situation as follows

(a) 6 groups of 1 unit each, 1 group of 4 units

Units	1	1	1	1	1	1	4	
f_i	.1	.1	.1	.1	.1	.1	.4	
M_i	1	1	1	1	1	1	4	
f_iM_i	.1	.1	.1	.1	.1	.1	1.6	$\Sigma f_iM_i = 2.2$

There are seven such arrangements, corresponding to the seven places in which the 4-group may fall; hence, we have a total $\Sigma f_iM_i = 7 \times 2.2 = 15.4$.

(b) 5 groups of 1 unit each, 1 group of 2 units and 1 of 3 units

Units	1	1	1	1	1	2	3	
f_i	.1	.1	.1	.1	.1	.2	.3	
M_i	1	1	1	1	1	2	3	
f_iM_i	.1	.1	.1	.1	.1	.4	.9	$\Sigma f_iM_i = 1.8$

There are 42 such arrangements obtainable by placing the 2-group and 3-group in all possible positions, giving a total $\Sigma f_iM_i = 42 \times 1.8 = 75.6$.

(c) 4 groups of 1 unit each, 3 groups of 2 units each

Units	1	1	1	1	2	2	2	
f_i	.1	.1	.1	.1	.2	.2	.2	
M_i	1	1	1	1	2	2	2	
f_iM_i	.1	.1	.1	.1	.4	.4	.4	$\Sigma f_iM_i = 1.6$

There are 35 such arrangements obtainable by placing the three 2-groups in all possible positions, giving a total $\Sigma f_iM_i = 35 \times 1.6 = 56.0$.

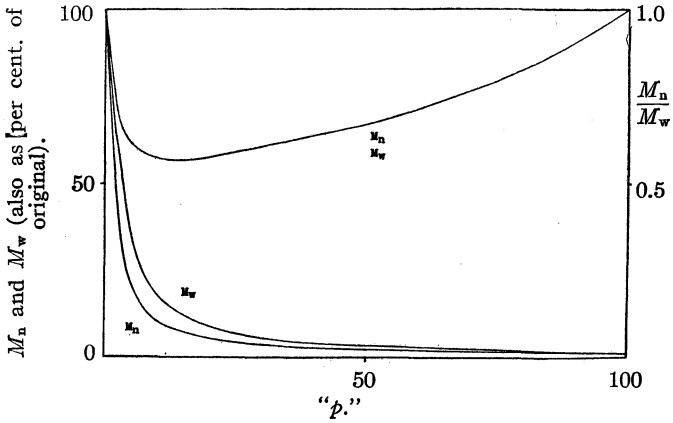


Fig. 1.—The weight average molecular weight (M_w), number average molecular weight (M_n) and the ratio M_n/M_w in case of progressive splitting of a 100 unit chain ($n = 100$, $m = 1$).

Adding these results we have $\Sigma f_iM_i = 147.0$, obtained by using a total of 84 arrangements. The average is 147.0/84 = 1.75, which is the value of M_w.

This method of analysis quickly becomes impracticable as the value of n increases. The results may be obtained directly, however, from formulas (1) and (4). In the example considered, $n = 10$ and $p = 7$, hence

$$K(10,7) = {}_9C_6 = 84; \quad M_w = \frac{20 - 7 + 1}{7 + 1} = \frac{14}{8} = 1.75$$

Figure 1 shows the values of M_n and M_w, again assuming $m = 1$, for a chain originally of 100 units progressively hydrolyzed, that is, for values of p from 1 to 100. In addition, the values of the ratio M_n/M_w are plotted. This ratio is a minimum for $p = 13$. At this point, we have $M_n = 7.7$, $M_w = 13.4$, and $M_n/M_w = 0.57$. To the right of this point, the curves slowly converge again, meeting at the point ($p = 100$), indicating complete hydrolysis.

It is realized that in order to have a sufficient number of the various early split-products present the number of molecules required from the starting material is very high; but assuming a *random* distribution in the size of those chains available for the various steps in the fission, the values obtained for the M_w will not be influenced.

Summary

A formula has been developed for the calculation of the weight average molecular weight of a linear polymer undergoing progressive splitting. An example is given to show the validity of the formula obtained. By the use of the formula the trend of average number and weight molecular weights for a polymer containing 100 units was calculated and is shown in Fig. 1. At the point representing 13% of complete hydrolysis the ratio between the two averages reaches a minimum, 0.57.

GENEVA, NEW YORK RECEIVED FEBRUARY 7, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BRYN MAWR COLLEGE]

Substituted Vinyl Barbituric Acids. IV. Derivatives Containing a Primary 1-Alkenyl Group

BY ARTHUR C. COPE, WALTER H. HARTUNG,[1,2] EVELYN M. HANCOCK AND FRANK S. CROSSLEY[2]

Previous papers in this series have described the preparation and properties of barbituric acids substituted in the 5-position by (1-alkylvinyl) groups, RCH=C(R')—. This paper concerns barbituric acids containing "primary 1-alkenyl" groups, RCH=CH—, or R_2C=CH, in the 5-position.

The 5-(primary 1-alkenyl)-5-alkylbarbituric acids were prepared by condensing (primary 1-alkenyl)-alkylmalonic esters[3] with urea in the presence of alcoholic sodium ethoxide. Appreciable quantities of the substituted malonic esters underwent cleavage during the condensation, producing monocarboxylic esters and amides derived from them.[4] The yields of purified barbituric acid derivatives, which are recorded in Table I, were low in several cases, due partly to the occurrence of cleavage as a side reaction during the condensations, and partly to difficulties encountered in purification of the products. Most of the substituted barbituric acids did not crystallize readily, and in several cases a number of recrystallizations were required. Only one of the two possible geometric isomers was isolated in each case.

The structures of the barbituric acid derivatives must be those indicated in Table I, since there is no other position in the alkenyl groups which the double bond can take, unless the extremely improbable assumption is made that the double bond can migrate farther into the carbon chain. In the case of the first three compounds listed in Table I, which are 5-propenyl-5-alkyl-barbituric acids, such a migration would produce the corresponding 5-allyl-5-alkyl-barbituric acids, which are known.[5]

The three 5-propenyl-5-alkyl-barbituric acids (Table I) were proved to be different from the corresponding 5-allyl-5-alkyl derivatives by direct comparison in two cases, and by a divergence of physical properties in the third. Moreover, the position of the double bond in 5-propenyl-5-butyl-barbituric acid was definitely established by ozonization, which produced acetaldehyde.

The purity of two of the (primary 1-alkenyl)-alkyl-barbituric acids was established by quantitative reduction. One of the compounds reduced was 5-(1-butenyl)-5-ethyl-barbituric acid, and the reduction product was proved to be 5-butyl-5-ethyl-barbituric acid by direct comparison with a commercial sample of the latter (Neonal).

Experimental Part

The barbituric acid condensations were carried out in the manner previously described.[4a] The properties of the products and the yields of material purified by recrystallization to constant melting point are recorded in Table I.

In each preparation the neutral by-products were separated by ether extraction of the aqueous alkaline solutions containing the substituted barbituric acids, before acidification (as in ref. 4a). In all but two cases, distillation of these extracts gave a mixture of the original substituted malonic ester, the monocarboxylic ester formed by cleavage of a carbethoxy group from the dicarboxylic ester (see ref. 4a), and a small quantity of a solid amide. The quantity of this mixture varied from 10 to 30% of the weight of the original substituted malonic ester.

The amide formed as a by-product in the preparation of 5-isopropyl-5-(1-butenyl)-barbituric acid was present in sufficient quantity to permit isolation and purification, by washing free from ester with hexane and recrystallization from ether and hexane; m. p. 123–124°. Analysis indicated that this amide was 2-isopropyl-2-hexenamide, as expected by analogy with similar cases (ref. 4; the position of the double bond is assumed by analogy).

Anal. Calcd. for $C_9H_{17}ON$: N, 9.03. Found: N, 8.92.

Approximately 40% of the substituted malonic esters, free from cleavage products, were recovered from the condensations which produced 5-(1-isobutenyl)-5-ethyl-barbituric acid and 5-propenyl-5-isopropyl-barbituric acid, respectively.

Structure of 5-(Primary 1-alkenyl)-5-alkyl-barbituric Acids. Quantitative Reductions.—5-(1-Butenyl)-5-ethyl-barbituric acid (3.00 g.) was dissolved in 25 cc. of alcohol and shaken with hydrogen in the presence of 1 g. of palladinized charcoal catalyst. Reduction was complete in thirty minutes, and 98.5% of the theoretical quantity of hydrogen was required (within experimental error of one molar equivalent). The reduction product was isolated by filtering the catalyst and crystallizing from dilute alcohol; yield 2.6 g. (87%); m. p. 122–123°. It was proved to be

(1) Present address: University of Maryland, School of Pharmacy, Baltimore, Md.

(2) Technical Division, Sharp and Dohme, Inc.

(3) Cope, Hartung, Hancock and Crossley, THIS JOURNAL, **62**, 314 (1940).

(4) Analogous to the cleavage (or alcoholysis) previously observed in similar cases: (a) Cope and Hancock, *ibid.*, **61**, 96 (1939); (b) Cope and McElvain, *ibid.*, **54**, 4311 (1932).

(5) Their melting points are recorded by Volwiler, *ibid.*, **47**, 2236 (1925).

TABLE I

5-(PRIMARY 1-ALKENYL)-5-ALKYL-BARBITURIC ACIDS

5-(Primary 1-alkenyl) group	5-Alkyl group	M. p., °C. (uncor.)	Yield, %	Formula	Nitrogen, % Calcd.	Found[k]
Propenyl $CH_3CH{=}CH-$	Propyl	150.5–151[a]	40[i]	$C_{10}H_{14}O_3N_2$	13.33	13.38
	Isopropyl	140–141[a]	40[i]	$C_{10}H_{14}O_3N_2$	13.33	13.45
	Butyl	127.5–128.5[b]	50[i]	$C_{11}H_{16}O_3N_2$	12.50	12.49
1-Butenyl $CH_3CH_2CH{=}CH-$	Ethyl	109–110[b]	30[j]	$C_{10}H_{14}O_3N_2$	13.33	13.39
	Propyl	83–84[c]	20	$C_{11}H_{16}O_3N_2$	12.50	12.42
	Isopropyl	107–108[b]	70	$C_{11}H_{16}O_3N_2$	12.50	12.55
	Isopropyl-N-methyl	Liquid[e]	33[i]	$C_{12}H_{18}O_3N_2$	11.76	12.01
	Isopropyl-2-thio	109–110[b]	30	$C_{11}H_{16}O_2N_2S$	11.66	11.68
	Butyl	111–112[b]	12	$C_{12}H_{18}O_3N_2$	11.76	11.71
1-Isobutenyl $(CH_3)_2C{=}CH-$	Ethyl[f]	161.5–162[d]	22[j]	$C_{10}H_{14}O_3N_2$	13.33	13.33
1-Pentenyl $CH_3CH_2CH_2CH{=}CH-$	Ethyl	96.5–98[d]	18	$C_{11}H_{16}O_3N_2$	12.50	12.66
	Isopropyl	94–95[b]	28	$C_{12}H_{18}O_3N_2$	11.76	11.82
1-Isopentenyl $(CH_3)_2CHCH{=}CH-$	Ethyl	126.5–127[a]	30	$C_{11}H_{16}O_3N_2$	12.50	12.36
	Propyl	101–102[d]	12	$C_{12}H_{18}O_3N_2$	11.76	11.72
	Isopropyl	121.5–122[a]	70	$C_{12}H_{18}O_3N_2$	11.76	11.72
1-Methyl-1-butenyl[g] $CH_3CH_2CH{=}C(CH_3)-$	Ethyl-2-thio	150–152[a]	43[i]	$C_{11}H_{16}O_2N_2S$	11.67	11.59
	Propyl-N-methyl	50.5–52.5[h]	18[i]	$C_{13}H_{20}O_3N_2$	11.10	11.11

[a] Recrystallized from dilute alcohol. [b] Recrystallized from benzene and pentane. [c] Distilled in vacuum; b. p. 185–190 (1.5 mm.); then crystallized from benzene and pentane. [d] Recrystallized from ether and pentane. [e] Distilled in vacuum; b. p. 138–142 (1.5 mm.) [f] Geometric isomerism is not possible for this compound. [g] These two compounds are 5-(secondary 1-alkenyl)-5-alkyl-barbituric acids, related in structure to a series previously described in THIS JOURNAL, **61**, 776 (1939). They were prepared by the method used for their homologs, from esters described in THIS JOURNAL, **60**, 2903 (1938). [h] Distilled in vacuum, b. p. 154–158 (1 mm.), then crystallized from ether and pentane. [i] Using two equivalents of sodium ethoxide in a procedure otherwise similar to that described in ref. 4a. [j] Using one equivalent of sodium ethoxide. [k] We are indebted to Mr. C. S. Miller for semi-micro Kjeldahl analyses.

5-butyl-5-ethyl-barbituric acid by determining the mixed m. p. with a commercial sample of Neonal, which gave no depression.

A similar reduction of 3.00 g. of 5-(1-butenyl)-5-isopropyl-barbituric acid required 99.0% of one molar equivalent of hydrogen, and 2.8 g. (93%) of 5-butyl-5-isopropyl-barbituric acid, m. p. 154–155°, was isolated as the reduction product in the same manner.

Anal. Calcd. for $C_{11}H_{18}O_3N_2$: N, 12.39. Found: N, 12.37.

The identity of this sample of 5-butyl-5-isopropyl-barbituric acid was established by the fact that it did not depress the m. p. of a known sample (m. p. also 154–155°) prepared by the reduction of 5-butyl-5-isopropenyl barbituric acid.[4a] Another known sample prepared by the condensation of ethyl butyl-isopropylmalonate with urea had the same m. p.[6]

Comparison of Propenyl and Allyl Alkyl-barbituric Acids.—A mixed m. p. of 5-propenyl-5-isopropyl-barbituric acid (m. p. 140–141°) and 5-allyl-5-isopropyl-barbituric acid (m. p. 136–137°) was 121–127°. A mixture of 5-propenyl-5-butyl-barbituric acid (m. p. 127.5–128.5°) and 5-allyl-5-butyl-barbituric acid (m. p. 126–127°) had m. p. 106–120°.

Ozonization.—The ozonization of 5-propenyl-5-butyl-barbituric acid[7] produced acetaldehyde, m. p. of the 2,4-dinitrophenylhydrazone and mixed m. p. with a known sample 166–168° (cor.).[8]

Pharmacological Data

The results of pharmacological tests of the 5-(primary 1-alkenyl)-5-alkyl-barbituric acids are recorded in Table II. The 1-butenyl and 1-isopentenyl derivatives, particularly those in which the total number of carbon atoms in the groups attached to the barbituric acid nucleus is seven or eight, are the most effective hypnotics with the highest therapeutic ratios of the series. The compounds in which isopropyl is the alkyl group substituted in the 5-position are particularly effective.

The most noteworthy fact about the pharmacological action of these barbiturates is the very short duration of narcosis produced by several of them, particularly the 5-(1-butenyl)-5-isopropyl and 5-(1-isopentenyl)-5-isopropyl derivatives. These substances are short acting even at relatively high dose levels. We have observed similar durations of action heretofore only with N-substituted barbituric acids.

(6) The m. p. of 209–210° recorded by Shonle and Moment, THIS JOURNAL, **45**, 248 (1923), for 5-butyl-5-isopropyl-barbituric acid must be in error.

(7) By a procedure described by Cope and Hancock, *ibid.*, **61**, 358 (1939).

(8) Campbell, *Analyst*, **61**, 392 (1936).

TABLE II

5-(PRIMARY 1-ALKENYL)-5-ALKYL-BARBITURIC ACIDS—RESULTS OF PHARMACOLOGICAL TESTS IN WHITE MICE[a,b]

5-(Primary 1-alkenyl) group	5-Alkyl group	Administration	AD 50 mg./kg.	AD 100 mg./kg.	LD 50 mg./kg.	Ratio, LD 50/AD 50	Duration at AD 100 Induction, minutes	Duration at AD 100 Anesthesia, hours
Propenyl	Propyl	I.p.	160	180	420	2.6	8	1.0
$CH_3CH{=}CH-$	Propyl	Oral	215	240	550	2.6	22	1.5
	Isopropyl	I.p.	110	120	425	3.9	7	0.6
	Isopropyl	Oral	140	160	520	3.7	10	.5
	Butyl	I.p.	110	120	320	2.9	8	.2
	Butyl	Oral	200	260	480	2.4	9	3.0
1-Butenyl	Ethyl	I.p.	90	110	225	2.5	9	0.3
$CH_3CH_2CH{=}CH-$	Ethyl	Oral	130	150	320	2.5	16	>3.0
	Propyl	I.p.	110	125	340	3.1	6	0.3
	Isopropyl	I.p.	60	75	250	4.2	3	.6
	Isopropyl	Oral	100	120	300	3.0	3	.3
	Isopropyl-N-methyl	I.p.	75	80	350	4.7	3	.1
	Isopropyl-2-thio	I.p.	45	60	180	4.0	3	.3
	Isopropyl-2-thio	Oral	55	80	180	3.3	1	>3.0
	Butyl	I.p.	65	80	225	3.5	6	0.3
	Butyl	Oral	160	180	450	2.8	9	.8
Isobutenyl $(CH_3)_2C{=}CH-$	Ethyl	I.p.	575	800	1100	1.9	20	>4.0
1-Pentenyl	Ethyl	I.p.	80	100	210	2.6	4	1.6
$CH_3CH_2CH_2CH{=}CH-$	Ethyl	Oral	120	140	290	2.4	6	2.0
	Isopropyl	I.p.	75	100	225	3.0	3	0.3
	Isopropyl	Oral	150	160	380	2.5	2	1.0
1-Isopentenyl	Ethyl	I.p.	70	80	260	3.7	7	0.2
$(CH_3)_2CHCH{=}CH-$	Ethyl	Oral	100	120	360	3.6	4	1.0
	Propyl	I.p.	115	140	310	2.7	6	0.3
	Isopropyl	I.p.	50	70	200	4.0	5	.2
	Isopropyl	Oral	70	80	280	4.0	4	.2
1-Methyl-1-butenyl[c]	Ethyl-2-thio	I.p.	45	50	170	3.8	6	.3
$CH_3CH_2CH{=}C(CH_3)-$	Propyl-N-methyl	I.p.	80	90	300	3.8	3	.2

[a] We are indebted to Mr. Harry J. Pratt for technical assistance in making these determinations. [b] The method of testing and the meaning of terms and symbols are described in the first paper of this series (ref. 4a) [c] See footnote "g," Table I.

Summary

A series of fifteen substituted vinyl alkyl barbituric acids has been prepared in which the substituted vinyl groups are of the type RCH=CH— or $R_2C{=}CH-$. The chemical and pharmacological properties of the compounds are recorded.

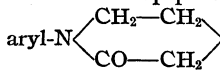
BRYN MAWR, PENNA. RECEIVED FEBRUARY 19, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF SWARTHMORE COLLEGE]

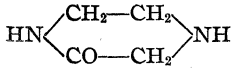
A Synthesis of Monoketopiperazines

BY SAMUEL R. ASPINALL

Monoketopiperazines of the type

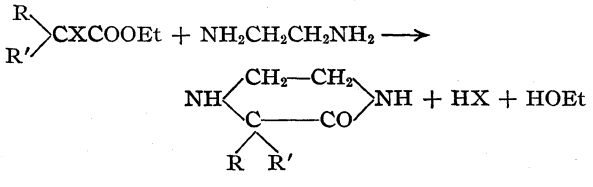


were prepared by Bischoff and Nastvogel in 1889[1] by condensing N,N′-diarylethylenediamines with chloroacetic acid in the presence of sodium acetate; and in 1892 Bischoff and Trapesonzjanz[2] prepared the same compounds by reducing 1,4-diaryl-2,3-diketopiperazines[3] using various metal–acid combinations. The 2,3-diketopiperazines had been obtained by heating N,N′-diarylethylenediamines with oxalic acid. No significant information in regard to yields is given in any of this work. No further synthetic work on monoketopiperazines has been carried out and the non-arylated type

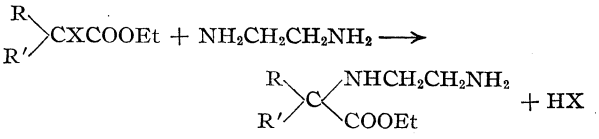


never has been reported.

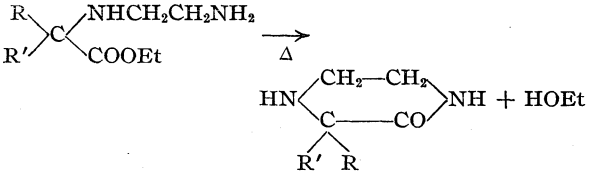
In connection with a more extended study of the interaction of ethylenediamine and various organic esters,[4] it has now been found that α-halogen esters react with ethylenediamine to give satisfactory yields of the non-arylated type of monoketopiperazines according to the following equation, where R and R′ may be alkyl or hydrogen.



That the first phase of the reaction is alkylation of the ethylenediamine is evidenced by the fact that when the two reactants are mixed there is a violent reaction with evolution of heat and the simultaneous liberation of ionic halogen. This is consistent with the usual behavior of aliphatic amines with α-halogen compounds; furthermore, it is generally true that an amidation at room temperature by means of an ester is not a fast, violent reaction. It is then obvious that the reaction should be carried out under conditions favorable to the formation of a monoalkylethylenediamine, as follows



This requires slow addition of the halogen ester to an excess of ethylenediamine diluted as much as feasible with some inert solvent. The liberated halogen acid, which is absorbed by the reaction mixture, is destroyed by sodium ethylate, the sodium halide so produced is filtered off and the solvent and excess ethylenediamine are removed by distillation at the water pump. When the residual monoalkylethylenediamine is heated at 200° under high vacuum, cyclization occurs and the monoketopiperazine distils over as a pale yellow oil. After solidification, it is obtained as a pure white, well-defined solid by recrystallization.



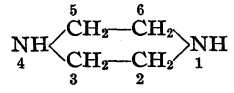
Experimental

The following description of the synthesis of 2-ketopiperazine is typical also of its 3-alkyl and 3,3,-dialkyl derivatives.

2-Ketopiperazine.—One-sixth of a mole (20.4 g.) of ethyl chloroacetate dissolved in 100 cc. of absolute alcohol is slowly added at room temperature to a well-stirred solution of one mole (60 g.) of anhydrous ethylenediamine in 300 cc. of absolute alcohol. The addition requires about three hours and the mixture is allowed to stand for an additional two hours. One-sixth of a mole (11.3 g.) of sodium ethylate in alcohol solution is added, the precipitated sodium chloride filtered off and the alcohol and excess ethylenediamine removed by distillation at the water pump. Upon heating the residual reaction mass at 200° under 5 mm. pressure, 2-ketopiperazine is formed and distils at about 165° (uncor.) as a pale yellow oil. After solidification, it is obtained as well-defined white crystals melting at 136° (cor.) by recrystallization from acetone–petroleum ether. The yield is 45% of the theoretical.

The effects of using other reaction temperatures, other concentrations of reactants and replacement

(1) Bischoff and Nastvogel, *Ber.*, **22**, 1783 (1889).
(2) Bischoff and Trapesonzjanz, *ibid.*, **25**, 2931 (1892).
(3) The piperazine ring is numbered as shown



(4) Arthur J. Hill and Samuel R. Aspinall, THIS JOURNAL, **61**, 822 (1939); Samuel R. Aspinall, *ibid.*, **61**, 3195 (1939).

TABLE I

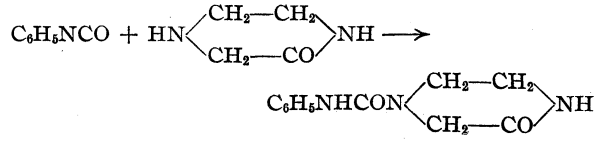
MONOKETOPIPERAZINES AND THEIR BENZENE SULFONAMIDES

Reacting ethyl ester	Product	M. p., °C. cor.	Yield, %	Recryst. solvent[a]	N, % Calcd.	N, % Kjeld.[b]	Benzenesulfonamide M. p., °C. cor.	Benzenesulfonamide N, % Calcd.	Benzenesulfonamide N, % Kjeld.[b]
α-Chloroacetate	$C_4H_8ON_2$	136	45	Acetone	28.00	28.15	188	11.67	11.69
α-Bromo-*n*-butyrate	$C_2H_5C_4H_7ON_2$	60	60	EtOAc	21.88	21.97	148	10.45	10.50
α-Bromo-isobutyrate	$(CH_3)_2C_4H_6ON_2$	134	40	EtOAc	21.88	21.89	206	10.45	10.54

[a] Precipitation of the ketopiperazines is more complete if petroleum ether is added to the solvent. [b] Reported analytical results are the averages of two determinations, neither of which differs from the calculated by more than 0.15% absolute error.

of chloroacetic ester by bromoacetic ester were studied. 1. Syntheses carried out at −15°, 0° and +80° gave the same yields as those at room temperature. 2. The extent to which ethylenediamine is present in excess profoundly affects the yield of end-product, because a large excess of ethylenediamine favors the monoalkylation essential to the eventual formation of monoketopiperazine. When one mole of ethylenediamine is treated with one mole of ethyl chloroacetate under the conditions described above, there is a quantitative precipitation of one-half mole of ethylenediamine dihydrochloride which is insoluble in the absolute alcohol medium. The remaining one-half mole of ethylenediamine was necessarily dialkylated and it is found that no monoketopiperazine is obtained. When one mole of ethylenediamine is treated with one-third mole of ethyl chloroacetate, there is no precipitation of ethylenediamine dihydrochloride (which is soluble in the alcohol–ethylenediamine medium) and the yield of monoketopiperazine is 25% of the theoretical. It is probable that the yield of monoketopiperazine could be increased to any desired amount if a sufficient excess of ethylenediamine were used. 3. The replacement of the chloroester by the bromoester has no effect on the yield, but has the disadvantage that the sodium bromide formed by the addition of sodium ethylate is soluble in the reaction mixture and special steps must be taken for its removal before a smooth distillation is possible. The method adopted was as follows. After addition of the bromoester in the usual way, the alcohol and most of the ethylenediamine were removed by distillation at the water pump and a dilute benzene solution of one equivalent of sodium ethylate was added. The sodium bromide, which is insoluble in benzene, was filtered off, the benzene and remaining ethylenediamine removed and the product distilled as before. 3-Ethyl-2-ketopiperazine and 3,3-dimethyl-2-ketopiperazine were prepared by this procedure from ethyl α-bromo-*n*-butyrate and ethyl α-bromo-isobutyrate, respectively.[5]

The ketopiperazines, which are extremely soluble in cold water and alcohol and insoluble in ether and petroleum ether, are best recrystallized from ethyl acetate or acetone, with or without the addition of petroleum ether. The compounds react strongly basic in water solution and give the usual diagnostic reactions of amines. For purposes of further characterization the ketopiperazines were converted to crystalline benzene sulfonamides by shaking an aqueous solution of 2.5 equivalents of the base with benzenesulfonyl chloride. The sulfonamides precipitated immediately with evolution of heat, and were recrystallized from water. Monoketopiperazine itself was more thoroughly characterized by preparing and analyzing the following derivatives. (1) The picrate was made in alcohol and recrystallized from water. (2) The hydrochloride was prepared by passing dry hydrogen chloride into an absolute alcohol solution of the base, and recrystallizing from absolute alcohol. It is extremely soluble in water. (3) The phenyl ureido derivative, which precipitated immediately with evolution of heat when an acetone solution of the base was treated with one equivalent of phenyl isocyanate, was recrystallized from absolute alcohol.



The phenyl thioureido derivative, similarly prepared from phenyl isothiocyanate, was recrystallized from 95% alcohol. Further investigation of this synthesis is in progress.

(5) The low solubility reported for potassium bromide in alcohol and alcohol–water mixtures indicates that potassium ethylate or even potassium hydroxide could be advantageously used to precipitate hydrogen bromide from the original reaction mixture without the use of benzene.

TABLE II
DERIVATIVES OF 2-KETOPIPERAZINE

	M. p., °C. cor.	N, % Calcd.	Kjeld.[a]
Picrate	180	21.28	21.19
Hydrochloride	208	20.51	20.65
Phenylurea	171	19.18	19.18
Phenylthiourea	199	17.87	17.85

[a] Reported analytical results are the averages of two determinations, neither of which differs from the calculated by more than 0.15% absolute error.

Summary

1. A practical synthesis for the hitherto unknown 2-ketopiperazine and its 3-alkyl and 3,3-dialkyl derivatives has been developed.

2. A study of the reaction between ethylenediamine and α-halogen esters under different conditions has been carried out.

3. The piperazines prepared in this study have been fully characterized by reaction with such typical amine reagents as benzenesulfonyl chloride, picric acid, hydrogen chloride, phenyl isocyanate and phenyl isothiocyanate.

SWARTHMORE, PA. RECEIVED FEBRUARY 29, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING, THE UNIVERSITY OF TEXAS]

The Relationship of Inositol, Thiamin, Biotin, Pantothenic Acid and Vitamin B_6 to the Growth of Yeasts

BY ROGER J. WILLIAMS, ROBERT E. EAKIN AND ESMOND E. SNELL

The specific chemical substances found to be effective constituents of culture media for promoting the growth of yeasts are of general biological interest. Inositol, found to be a growth factor for yeast in the laboratory of W. Lash Miller,[1] is of widespread occurrence in the tissues of plants and animals. Thiamin (vitamin B_1), first found to be effective for yeast in the author's laboratory,[2] was a recognized vitamin long before and has since proved to be of widespread significance in cellular physiology, functioning as the organic moiety of co-carboxylase (and perhaps in other ways). Biotin, discovered in the laboratories of F. Kögl,[3] is widely distributed and is physiologically effective for a number of organisms.[4,5,6] Pantothenic acid, discovered and concentrated in the author's laboratory,[7,8] is now recognized as identical to the filtrate factor or the chick antidermatitis vitamin,[9,10] and probably stimulates the growth of rats.[11] It is of ubiquitous occurrence and has been found essential for the growth of many bacteria[12,13] and to stimulate the growth of green plants[14] and the respiration of widely different tissues. It appears to be an essential constituent of some important enzyme systems.[15] β-Alanine is a component part of pantothenic acid[16] and may itself serve as a precursor of pantothenic acid both for yeasts and for certain bacteria.[13,16,17] Vitamin B_6 (adermin), recently found to be a growth factor for yeast,[18,19] bacteria,[20] and higher plants,[21] has for some time been recognized as a vitamin essential for rats.

Through the kindness of Professor Kögl, who has placed a sample of biotin at our disposal, we are now in a position to study the interaction of all of the factors enumerated above in promoting the growth of yeasts. The results of such studies may prove of great interest both from the standpoint of yeast physiology and because of the light which they may throw on the interplay of these

(1) E. V. Eastcott, *J. Phys. Chem.*, **32**, 1094 (1928).
(2) R. J. Williams and R. R. Roehm, *J. Biol. Chem.*, **87**, 581 (1930).
(3) F. Kögl and B. Tönnis, *Z. physiol. Chem.*, **242**, 43 (1936).
(4) F. Kögl and van Hasselt, *ibid.*, **243**, 189 (1936).
(5) F. Kögl and N. Fries, *ibid.*, **249**, 93 (1937).
(6) E. E. Snell and R. J. Williams, THIS JOURNAL, **61**, 3594 (1939).
(7) R. J. Williams, *et al.*, *ibid.*, **55**, 2912 (1933).
(8) R. J. Williams, *et al.*, *ibid.*, **60**, 2719 (1938).
(9) T. H. Jukes, *ibid.*, **61**, 975 (1939).
(10) D. W. Woolley, H. A. Waisman and C. A. Elvehjem, *ibid.*, **61**, 977 (1939).
(11) Y. Subbarow and G. H. Hitchings, *ibid.*, **61**, 1615 (1939).
(12) E. E. Snell, F. M. Strong and W. H. Peterson, *ibid.*, **60**, 2825 (1938).
(13) J. H. Mueller and A. W. Klotz, *ibid.*, **60**, 3086 (1938).
(14) R. J. Williams and E. Rohrmann, *Plant Physiol.*, **10**, 559 (1935).
(15) E. F. Pratt and R. J. Williams, *J. Gen. Physiol.*, **22**, 637 (1939).
(16) H. Weinstock, *et al.*, THIS JOURNAL, **61**, 1421 (1939).
(17) R. J. Williams, W. A. Mosher and E. Rohrmann, *Biochem. J.*, **30**, 2036 (1936).
(18) R. E. Eakin and R. J. Williams, THIS JOURNAL, **61**, 1932 (1939).
(19) A. S. Schultz, L. Atkin and C. N. Frey, *ibid.*, **61**, 1931 (1939).
(20) E. F. Möller, *Z. physiol. Chem.*, **254**, 285 (1938).
(21) W. J. Robbins and M. B. Schmidt, *Proc. Natl. Acad. Sci.*, **25**, 1 (1939).

physiological principles in biological phenomena in general.

While aspartic acid[22] (placed in our basal medium), leucine,[23] ethanolamine, riboflavin, nicotinamide, carotene and doubtless other recognized compounds may under suitable conditions increase growth or respiration of yeast, the effects are relatively small and these effects are not included in the present study.

The "optimal" concentration of any specific substance in a nutrient medium depends upon the strain of yeast, the cultural conditions, and particularly upon the other constituents of the medium. For practical reasons, however, we have fixed the concentration of each nutrilite at a level somewhat above that required to produce a "maximum" response when tested alone and have studied the growth curves of three distinct (and highly different) strains of "*Saccharomyces cerevisiae*" under the influence of the five more significant substances mentioned above.

The basal medium used throughout was similar to that used in other studies from the author's laboratory[16,24] and contained as the source of organic nitrogen 0.1 g. of *l*-aspartic acid per liter. This has the general effect of increasing yeast crops, though experiments have shown that it can be omitted (in some cases at least) without changing the general trend of the results in any major way.

Experimental

The carefully sterilized media (50 ml. batches in 250 ml. Erlenmeyer flasks) were each seeded with 0.2 mg. of the yeast under investigation and allowed to grow for one hundred to one hundred and sixty hours at 30°. At intervals the cultures were shaken and samples aseptically withdrawn and their yeast content determined with a thermocouple turbidimeter.[25,26]

The media used were composed as indicated below. An addendum when used was always in the same concentration, as follows: inositol 5 γ per ml. of the final medium; thiamin 0.04 γ per ml.; biotin 0.0001 γ per ml.; pantothenic acid 0.006 γ per ml.; β-alanine 1 γ per ml.; vitamin B_6 0.04 γ per ml. Since previous experiments had shown that β-alanine could serve as a precursor of pantothenic acid, this substance was substituted for pantothenic acid in some of the media as indicated. The amount of β-alanine used is much more than equivalent on a stoichiometric basis to the pantothenic acid addendum.

(1) Basal alone.
(2) Basal + pantothenic acid (p. a.).
(3) Basal + β-alanine.
(4) Basal + biotin.
(5) Basal + inositol, thiamin, biotin and B_6 (no p. a.).
(6) Basal + inositol, thiamin, biotin and β-alanine (no B_6).
(7) Basal + inositol, biotin, β-alanine and B_6 (no thiamin).
(8) Basal + thiamin, biotin, β-alanine, and B_6 (no inositol).
(9) Basal + inositol, thiamin, β-alanine and B_6 (no biotin).
(10) Basal + inositol, thiamin, biotin, p. a. and B_6 (complete p. a.).
(11) Basal + inositol, thiamin, biotin, β-alanine and B_6 (complete β-alanine).
(12) Same as 11 above + 0.2 mg./ml. crude liver extract.

The strains of yeast used were (1) Gebrüder Mayer (G. M.), (2) "Old Process" (O. P.), and (3) yeast isolated (repeatedly) from Fleischmann baker's yeast (pound goods) (F. B.).[27]

The results of the tests are presented in Figs. 1, 2 and 3.

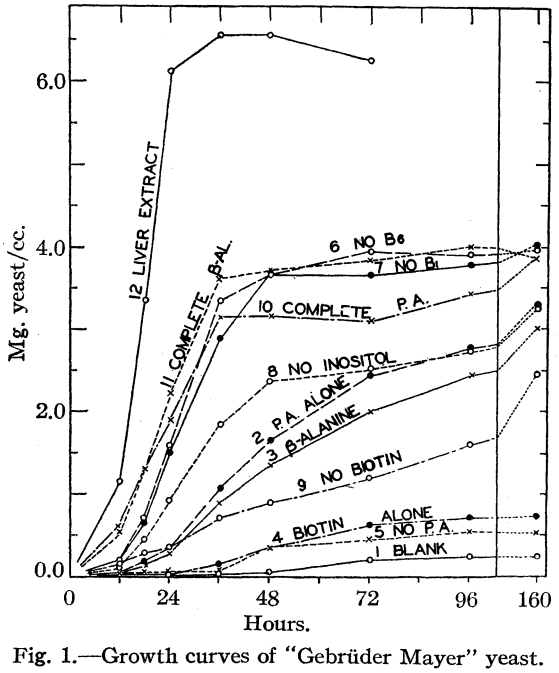


Fig. 1.—Growth curves of "Gebrüder Mayer" yeast.

Discussion of Results

In order to conserve space, separate curves are not given showing in more detail the growth during the first twenty-four hours. From many standpoints this is the most interesting period, since in the practical utilization of yeasts in the fermentation industries, the immediate response to the medium is often of much greater importance than what may happen after a long time interval. The great majority of studies of yeast growth have

(22) R. J. Williams and E. Rohrmann, THIS JOURNAL, **58**, 695 (1936).
(23) W. Lash Miller, *Trans. Roy. Soc. Can.*, **30**, 99 (1936).
(24) R. J. Williams and D. H. Saunders, *Biochem. J.*, **28**, 1887 (1934).
(25) Williams, McAlister and Roehm, *J. Biol. Chem.*, **83**, 315 (1929).
(26) Snell, Eakin and Williams, THIS JOURNAL, **62**, 175 (1940).
(27) Cultures of these yeasts, all of which are or have been grown commercially for baking purposes, are being sent to the American Type Culture Collection, Georgetown Univ. Med. School, Washington, D. C., where duplicates may be obtained.

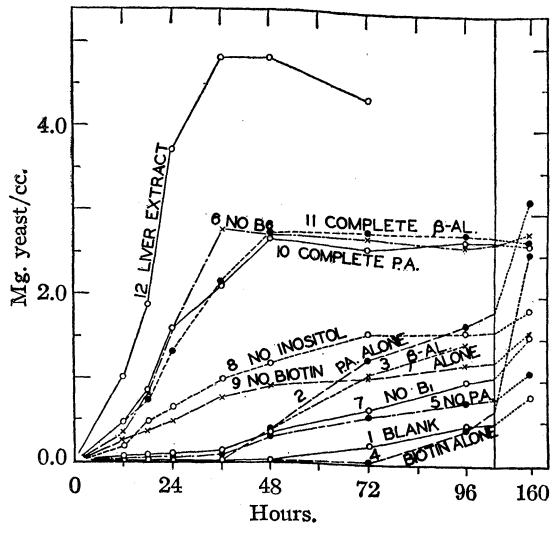


Fig. 2.—Growth curves of "Old Process" yeast.

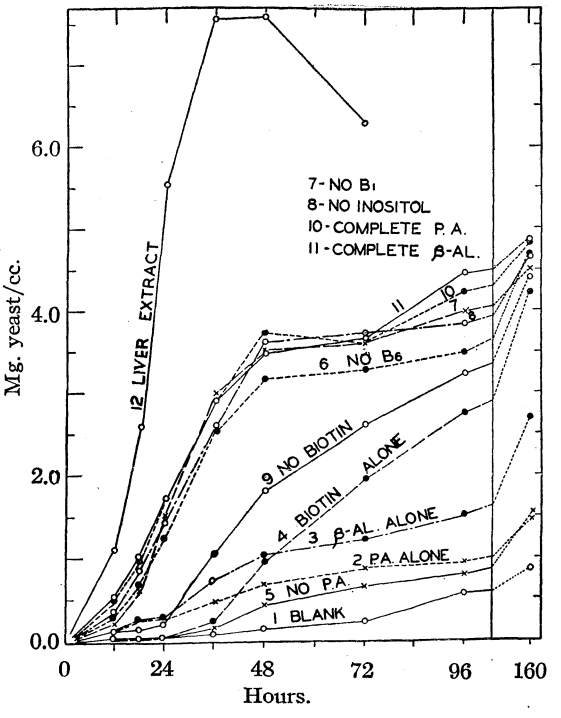


Fig. 3.—Growth curves of Fleischmann baker's yeast.

also involved a comparatively short period of incubation. The problem of whether and to what extent yeast is able to grow in a medium after many days of incubation is of scientific and academic, rather than practical interest.

It is obvious that when continued growth takes place in a medium devoid of a particular substance the substance is either dispensable or can be synthesized by the yeast from other constituents of the medium. On the basis of available evidence we shall assume tentatively in such cases that synthesis is taking place.

Inositol.—F. B. yeast grows at only a slightly diminished rate, and up to high levels in the absence of inositol. G. M. yeast is more dependent upon an exogenous source of inositol, and O. P. yeast most dependent. There is a question in view of the fact that the growth curve of the O. P. yeast flattens after seventy-two hours, whether it is capable of indefinite growth in the absence of inositol.

Thiamin.—Both F. B. and G. M. yeasts are able to grow to high levels in the absence of thiamin, but O. P. yeast is dependent on an external source for rapid growth. It appears that O. P. yeast may develop an ability to synthesize thiamin, because after thirty-six hours the growth curve rises more rapidly; growth continued throughout the period of observation.

Biotin.—In no case does biotin alone induce an appreciable increase in growth during the first twenty-four hours (under our conditions, light seeding etc.). F. B. yeast is markedly affected by biotin (alone) after this period; other yeasts are less affected. When biotin is left out and the other nutrilites are put in, each yeast grows less than the maximum (with all five nutrilites), but F. B. yeast curiously yields most nearly maximum growth.

Pantothenic Acid (and β-Alanine).—The close correspondence between curves 2 and 3, Figs. 1, 2 and 3, and curves 10 and 11, Figs. 1, 2, and 3, in which pantothenic acid and β-alanine are interchanged, shows that for the purpose of these experiments pantothenic acid and β-alanine are practically equivalent physiologically. This is in line with the known fact that β-alanine is a precursor of pantothenic acid.[16]

None of the yeasts grow, except very slowly, during the first twenty-four hours in the absence of an exogenous source of pantothenic acid. Each yeast appears to be able to grow continuously in the synthetic medium when pantothenic acid or β-alanine is present. When the other four nutrilites are present and pantothenic acid is absent, growth continues at a low rate with F. B. and O. P. yeast, but with G. M. yeast growth ceases after a few days. This is in line with the previous observation that this yeast is apparently unable to bring about the synthesis of pantothenic acid.[17]

Vitamin B_6.—This vitamin appears dispensable for all three yeasts, yet its physiological effects

are noticeable in each case. Its absence from the medium is most noticeable in the case of G. M. yeast at the end of a twelve-hour growth period. In this case the "complete" medium yielded about three times the amount of yeast as the same medium lacking B_6.

Unknown Factors.—That unknown factors play an important part in stimulating the rapid growth of yeasts is evidenced by the fact that each yeast is strikingly stimulated when a liver extract is added to the medium containing all five of the nutrilites. Extracts of yeast also contain these additional stimulatory substances, which cannot be replaced by a higher concentration of the five nutrilites under consideration. For some yeasts at least biotic acid[28] is an important nutrilite.

Growth over Long Periods.—Although biotin and pantothenic acid are unlike chemically and are tested for under entirely different conditions, it does appear that when growth over a long period is concerned, they are in a measure interchangeable. Thus in the case of the F. B. and O. P. yeasts either biotin alone or pantothenic acid (or β-alanine) alone causes a substantial increase (100% or more) over the blank. For G. M. yeast biotin alone was relatively ineffective even after one hundred and sixty hours (*cf.* curves 1–4, Figs. 1, 2, 3). The same apparent replaceability of one nutrilite by others is observed in some cases where only one nutrilite is omitted from the medium. Similar phenomena have been observed in the senior author's laboratory when the mold *Trichophyton interdigitale* failed to grow on an amino acid medium but did grow appreciably when *any one* of three nutrilites (inositol, thiamin or pantothenic acid) was furnished.[29]

These results suggest that when one nutrilite alone is furnished it leads to the more ready synthesis of those which are lacking in the medium. It may be that the one nutrilite by furnishing the means of completing one of several enzyme systems enables the organism to derive energy for metabolic and synthetic activity.

Ability to Grow in a Synthetic Medium.—From the growth curves it appears that F. B. and O. P. yeasts are eventually able to grow continuously, though very slowly, in a medium containing none of the nutrilites. The growth of G. M. yeast, however, ceases after about three days, at which time about a 60-fold increase has taken place. The original yeast seeding of course has in it all of the requisites for growth. The extent to which growth can take place in a synthetic medium seems to depend on how far these original substances can be "diluted" by passage to the daughter cells and to what extent the yeast is able to synthesize the substances. G. M. yeast seems to be limited in its ability to grow in a synthetic medium by the fact that synthesis of pantothenic acid cannot take place. Whether G. M. yeast can through long "training" be induced to synthesize pantothenic acid is, again, unknown.

This work has been generously supported by grants from the Rockefeller Foundation and from Standard Brands, Inc., of New York.

(28) Eakin and Williams, *J. Biol. Chem.*, **128**, xxiii (1939).
(29) Mosher, *et al.*, *Plant Physiol.*, **11**, 795 (1936).

Summary

The growth curves of three distinct (and highly different) strains of "*Saccharomyces cerevisiae*" were studied in media containing different combinations of inositol, thiamin, biotin, pantothenic acid (or β-alanine) and vitamin B_6. Among the conclusions drawn are the following. At least two of the yeasts can grow continuously without inositol. Thiamin is especially important for one yeast only. Biotin alone will not immediately stimulate the yeast growth from small seedings but in proper combination its effect is striking and evident at very minute doses. Pantothenic acid (or its precursor β-alanine) is highly essential for the immediate growth of all of the yeasts and when added alone is able to induce continued growth of all the yeasts tested. B_6 is relatively unimportant as a constituent of the culture media. Substances of unknown nature present in liver and yeast extracts play an important role in promoting rapid growth. Yeasts during a long incubation period show considerable ability to grow in the absence of various nutrilites, and under such conditions one nutrilite alone may serve whereas for rapid growth several are required.

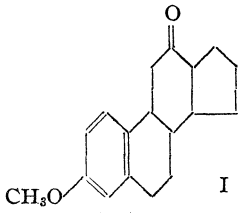
AUSTIN, TEXAS RECEIVED JANUARY 18, 1940

[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

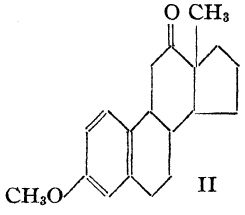
The Direct Introduction of the Angular-Methyl Group

BY ROBERT BURNS WOODWARD*

As a result of the great interest in the chemistry of the sterols and related substances, considerable effort has been expended in the past six years to elaborate methods for the synthesis of substances containing methyl groups at the bridgeheads of bicyclo-(0,3,4)-nonanes and bicyclo-(0,4,4)-decanes, the so-called angular-methyl groups. Several elegant methods have been evolved, notably those of Linstead[1a] and Robinson.[1b] With one exception, these procedures are in essence syntheses of the bicyclic systems involved from simpler compounds containing appositely substituted methyl groups. Only Robinson has in a few isolated instances introduced with difficulty an angular-methyl group in a compound already containing the bicyclic system. For example, 7-methoxy-3-keto-1,2,3,4,9,10,11,12-octahydro-1,2-cyclopentenophenanthrene[2] (I) on vigorous



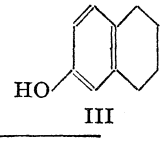
I



II

treatment with potassium *t*-butylate, followed by methyl iodide, is transformed into a methyl derivative in which the substituted group is presumed to be in the angular position (II).

In this communication is described a method for the direct production of substances having the carbon skeleton of 9-methyl-bicyclo-(0,4,4)-decane (IV) from 6-hydroxy-1,2,3,4-tetrahydronaphthalene (III). It is at once apparent that the relationship of compounds having the skeleton (IV) to the tetralol (III) is also that which androsterone (VI) and the other male hormones bear to oestrone (V), and that these experiments may be



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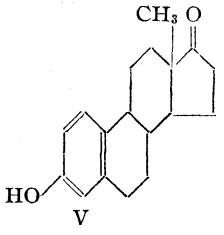
IV



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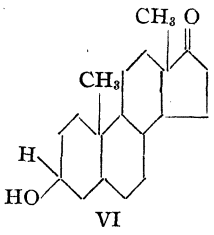
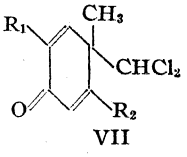


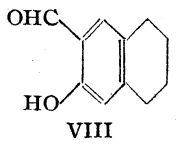
VI

considered as models for the conversion of oestrone into one or more of the androgenic hormones.

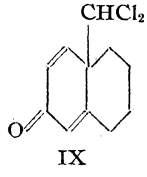
It has been shown by von Auwers[3a,b,c] and collaborators in a brilliant series of investigations that *o*- and *p*-alkyl substituted phenols, on treatment with chloroform and alkali under the conditions of the Reimer–Tiemann synthesis, are converted only in part into the expected aldehydes, the remainder being used in the formation of cyclohexadienones, the ratio of normal to abnormal products varying strikingly with the structure of the phenol. From *p*-cresol, for example, 2-hydroxy-5-methylbenzaldehyde is formed almost to the exclusion of 4-methyl-4-dichloromethyl-$\Delta^{2,5}$-cyclohexadienone-1 (VII, $R_1 = R_2 = H$), while ψ-cumenol, on the other hand, gives over 80% of the abnormal product, 2,4,5-trimethyl-4-dichloro-



VII



VIII



IX

methyl-$\Delta^{2,5}$-cyclohexadienone-1 (VII, $R_1 = R_2 = CH_3$). We were led by these results to undertake the investigation of the Reimer–Tiemann reaction with 6-hydroxy-1,2,3,4-tetrahydronaphthalene (III).

The latter, on treatment with chloroform and 10% aqueous sodium hydroxide, was mainly converted into two products. The first, representing about 50% of the tetralol consumed in the reaction, was an aldehyde, m. p. 82°, which was found to be identical with the aldehyde obtained from the same phenol by Thom and Kross[4] through the Gattermann synthesis. Previous work[4,5] on

* Member of the Society of Fellows, Harvard University.

(1) (a) Hibbet, Linstead and Millidge, *J. Chem. Soc.*, 476 (1936); (b) DuFeu, McQuillin and Robinson, *ibid.*, 53 (1937).

(2) Peak and Robinson, *ibid.*, 1581 (1937).

(3) (a) Von Auwers and v. Erggelet, *Ber.*, **32**, 3598 (1899); (b) v. Auwers and Winternitz, *ibid.*, **35**, 465 (1902); (c) v. Auwers and Keil, *ibid.*, **35**, 4207 (1902).

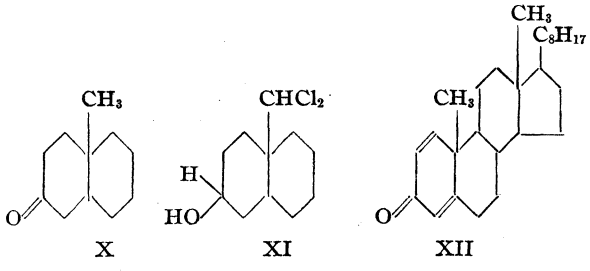
(4) Thom and Kross, *Arch. Pharm.*, **265**, 336 (1927).

(5) Schroeter, *Ann.*, **426**, 30, *et seq.* (1922); *cf.* Robinson and Walker, *J. Chem. Soc.*, 1531 (1935).

the orientation of (*ar*)-2-tetralol makes it highly probable that this aldehyde is 6-hydroxy-1,2,3,4-tetrahydronaphthalene-7-aldehyde (VIII). In our work the substance was characterized through its semicarbazone. This compound on heating undergoes an interesting change for which analogy is found in the behavior of the semicarbazone of salicylic aldehyde,[6] in that above the melting point it resolidifies in beautiful long yellow needles of the corresponding azine.

The second product of the reaction was a beautifully crystalline, non-acidic substance, m. p. 167.5–168.5°, having the formula $C_{11}H_{12}OCl_2$. While the analogy with the work of von Auwers lends strong presumptive support to the formulation of this compound as 10-dichloromethyl-2-keto-$\Delta^{1,9;\ 3,4}$-hexahydronaphthalene (IX), our work proves unambiguously that this formulation is correct.

On hydrogenation in methyl alcohol with Adams catalyst, the substance smoothly adds three moles of hydrogen with the formation of an alcohol, $C_{11}H_{18}OCl_2$, m. p. 92.5–93°, characterized by an α-naphthylurethan, m. p. 152.5–153°. Under the above conditions, it was not possible either to stop the reaction at the tetrahydro stage, or to remove the halogen atoms to an appreciable extent. However, under more drastic conditions, *viz.*, hydrogenation of the dichloro-alcohol in 10% alcoholic potassium hydroxide over palladinized barium sulfate, it was possible to remove both halogen atoms with the formation of a methyldecalol which on oxidation with chromate mixture was transformed into 10-methyl-decalone-2 (X), identical with an authentic sample prepared by the method of Robinson.[1b]



X XI XII

These transformations indicate clearly that the alcohol $C_{11}H_{18}OCl_2$ must be formulated as 10-dichloromethyl - 2 - hydroxydecahydronaphthalene (XI), and that the abnormal Reimer–Tiemann product from which it was obtained is 10-dichloromethyl-1-keto-$\Delta^{1,9;3,4}$-hexahydronaphthalene (IX).

(6) Borsche, *Ber.*, **34**, 4299 (1901).

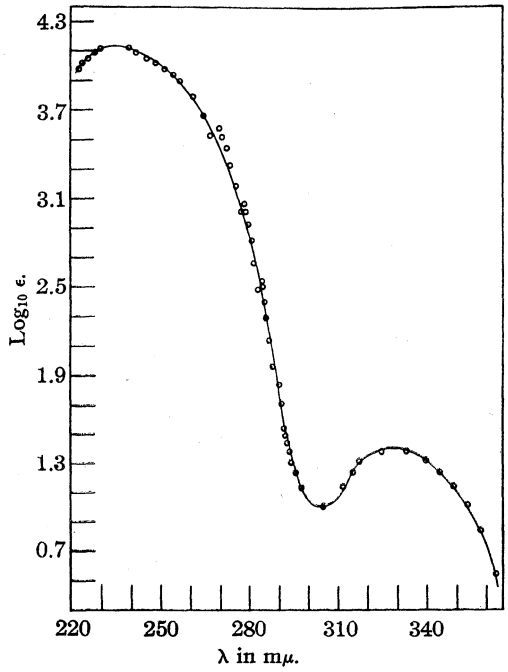


Fig. 1.—Ultraviolet absorption spectrum of 10-dichloromethyl-2-keto-$\Delta^{1,9;\ 3,4}$-hexahydronaphthalene in alcohol.

The ultraviolet absorption spectrum[7] (Fig. 1) of the latter substance gives confirmatory evidence of its structure. The maximum at 235 mμ (log ϵ = 4.14) is clearly a consequence of the conjugation of carbonyl and ethylenic double bonds, while the less intense maximum at 329 mμ (log ϵ = 1.38) must be ascribed to the carbonyl group. In this connection, it is instructive to note that cholestadiene-1,4-one-3 (XII), the only other cyclohexadienone for which ultraviolet absorption data are known, is reported by Inhoffen and Huang-Minlon[8] to have an intense band at 235 mμ (log ϵ = 4.1). It is a striking fact that both these compounds exhibit strong absorption in the same region as do those substances containing but one ethylenic bond in conjugation with the carbonyl group, as will be apparent from an inspection of Table I.

On the other hand phorone,[9] which likewise contains a cross-conjugated system, shows the expected shift of the intense band toward the red. This observation might well lead one to question the validity of the assumption of cross-conjugated systems in Inhoffen's compound and in ours. Inhoffen's degradative work,[10] however, as well as

(7) We are indebted to Mr. D. M. Bowen of this Laboratory for the absorption measurements.

(8) Inhoffen and Huang-Minlon, *Ber.*, **71**, 1720 (1938).

(9) Bielecki and Henri, *ibid.*, **47**, 1715 (1914).

(10) Inhoffen and Huang-Minlon, *ibid.*, **72**, 1686 (1939).

TABLE I

Ketone	λ max.	Log ε max.
Mesityl oxide	235	4.14[a]
Δ^4-Cholestenone	240	4.21[b]
Δ^1-Cholestenone	*ca.* 230	..[c]
Eremophilone	243	3.90[d]
Pulegone	252	3.91[b]
α-Cyperone	251	4.28[d]
$\Delta^{1,4}$-Cholestadienone	235	4.1[e]
10-Dichloromethyl-2-keto-$\Delta^{1,9;3,4}$-hexahydronaphthalene	235	4.14[e]

[a] Morton, *J. Chem. Soc.*, 719 (1926). [b] Menschick, *et al.*, *loc. cit.* [c] Inhoffen, *loc. cit.* [d] Gillam, *J. Chem. Soc.*, 676 (1936). [e] This paper.

the hydrogenation of his substance to compounds of the coprostane, rather than the cholestane, series, proves beyond doubt that his material has in fact the structure (XII).

These considerations lead us to suggest that the rule of Menschick, Page and Bossert,[11] *viz.*, that substances exhibiting strong absorption (log ε = 4.0–5.0) in the vicinity of 235–250 mμ contain an α,β-unsaturated carbonyl system, be extended to include the possibility that such absorption is a consequence of cross-conjugation of two ethylenic bonds with a carbonyl group.

Experimental

6-Hydroxy-1,2,3,4-tetrahydronaphthalene-7-aldehyde (VIII) and 10-Dichloromethyl-2-keto-$\Delta^{1,9;3,4}$-hexahydronaphthalene (IX).—3.5 grams of 6-hydroxy-1,2,3,4-tetrahydronaphthalene was dissolved in 80 cc. of 10% aqueous sodium hydroxide in a flask equipped with an efficient reflux condenser and a dropping funnel. After the reaction mixture had been immersed in a water-bath at 75°, pure chloroform was dropped in slowly from the funnel. With the addition of the first few drops of chloroform, the solution turned yellow; as more was added the color gradually deepened to orange. In the course of three hours, 13.0 g. of chloroform was added. The reaction was then allowed to continue for one-half to three-quarters of an hour, when the water-bath was removed and the reaction mixture allowed to cool. More chloroform was now added, the mixture was well shaken, and the two layers separated, the neutral aqueous layer being discarded. The chloroform was evaporated on the steam-bath and the residual red oil, which crystallized partially on cooling, distilled *in vacuo* from a 10-cc. Claisen flask, b. p. 4–5 mm., *ca.* 130–150°. The distillate, a clear yellow, very sirupy liquid which deposited crystals on scratching, was triturated with 5% aqueous sodium hydroxide, the resulting solid was filtered at the pump, and washed with water until the sparingly soluble sodium salt of the hydroxy-aldehyde had been completely dissolved. The bright yellow filtrate was made neutral with dilute hydrochloric acid, the precipitated oil taken up in ether and recovered in the usual way. The oil thus obtained weighed 1.8 g., and crystallized slowly on standing as octagonal prisms, m. p. 80–82°; mixed with an authentic sample of 6-hydroxy-1,2,3,4-tetrahydronaphthalene-7-aldehyde,[4] m. p. 80–82°.

The solid remaining on the funnel after the removal of the sodium salt by washing was dissolved in methanol, the reddish solution was filtered from a small amount of amorphous material, and evaporated to a very small volume. The crystals which separated were recrystallized from cyclohexane, 0.8 g. of colorless stout hexagonal prisms, m. p. 167.5–168.5°, being obtained. (Occasionally long needles of the same m. p. were obtained on crystallization from methyl alcohol, but the above form is more common from either solvent.) Further recrystallization failed to change the melting point.

Anal. Calcd. for $C_{11}H_{12}OCl_2$: C, 57.2; H, 5.2; Cl, 30.5. Found: C, 57.15; H, 4.91; Cl, 30.3.

10-Dichloromethyl-2-hydroxydecahydronaphthalene (XI).—150 mg. of 10-dichloromethyl-2-keto-$\Delta^{1,9;3,4}$-hexahydronaphthalene was dissolved in 20 cc. of absolute methanol, a small amount of platinum oxide catalyst added, and the reaction mixture shaken with hydrogen at 30.5° and 755 mm. In five minutes 57 cc. (3.5 mols) of hydrogen had been taken up, and there was no further absorption. The clear solution was filtered to remove catalyst, evaporated to a small volume on the hot-plate, and then to "dryness" in a current of warm air. A clear, viscous oil of camphoraceous odor remained. Since it could not be crystallized on trituration with cyclohexane or petroleum ether, it was allowed to stand overnight, when it crystallized partially in waxy prisms, sintering at 67°, melting at 73–76°. The oil was then dissolved in a small amount of methanol, and the solution was allowed to stand for a few hours after enough water had been added to cause strong turbidity. At the end of this time the material had crystallized in beautiful rosets of needles. This process was repeated five times, the period necessary for crystallization becoming shorter with each repetition. 10-Dichloromethyl-2-hydroxydecahydronaphthalene finally was obtained as beautiful silky needles, m. p. 92.5–93°, extremely soluble in methanol, and giving a strong Beilstein test. The material sublimed easily in colorless rosets in high vacuum at 64°.

Anal. Calcd. for $C_{11}H_{18}OCl_2$: C, 55.70; H, 7.66. Found: C, 55.90; H, 7.73.

α-Naphthylurethan of 10-Dichloromethyl-2-hydroxydecahydronaphthalene.—The clear colorless oil obtained on hydrogenation of 130 mg. of 10-dichloromethyl-2-keto-$\Delta^{1,9;3,4}$-hexahydronaphthalene in the manner described above was allowed to stand overnight over phosphorus pentoxide in the vacuum desiccator. An approximately equivalent amount of freshly distilled α-naphthylisocyanate was added, the two substances were mixed completely, and the reaction mixture placed in the vacuum desiccator over phosphorus pentoxide. After six days, the flask contained a mass of prisms, and a small amount of oil. The reaction mixture was dissolved in 6–8 cc. of hot middle-boiling ligroin, and the solution filtered from a small amount of insoluble tarry material. After concentrating to 2–3 cc. on the hot-plate, the solution was allowed to stand overnight. The stout hard prisms which had separated were filtered, washed with a small amount of petroleum ether, and recrystallized twice from hot ligroin.

(11) Menschick, Page and Bossert, *Ann.*, **495**, 233 (1932).

Hard, compact glistening aggregates of plates, m. p. 152.5–153°, were formed.

Anal. Calcd. for $C_{22}H_{25}O_2NCl_2$: C, 65.0; H, 6.21. Found: C, 64.99; H, 6.42.

10-Methyl-decalone-2 (X).—220 mg. of 10-dichloromethyl-2-hydroxy-decahydronaphthalene was dissolved in 20 cc. of 10% methanolic potassium hydroxide, 0.5 g. of palladinized barium sulfate added, and the reaction mixture shaken with hydrogen for six hours at 29° and 759 mm. At the end of this time 42 cc. (1.9 mols) of hydrogen had been taken up. The reaction mixture was then poured into 60 cc. of water and extracted exhaustively with ether (6 hand extractions). The combined ethereal extracts were dried over sodium sulfate, the ether was removed, and the residual colorless viscous oil allowed to stand in the vacuum desiccator over phosphorus pentoxide. Since it did not crystallize on standing overnight, it was dissolved in 5 cc. of glacial acetic acid and oxidized directly by dropping in slowly a solution of 100 mg. of chromic oxide in 4 cc. of glacial acetic acid and 1 cc. of water. After stirring for four hours, the reaction mixture was poured into water, extracted exhaustively with ether, and the combined ethereal extracts dried over anhydrous sodium sulfate. The residual oil obtained on evaporating the ether was converted into the 2,4-dinitrophenylhydrazone in the usual manner, pale yellow needles from methyl alcohol, m. p. 151–152°, mixed with an authentic sample prepared by Robinson's method, m. p. 151–152°. On hydrolyzing this derivative with 5% sulfuric acid and working up in the usual manner, 100 mg. of a colorless oil of camphoraceous odor was obtained which solidified on standing, m. p. 46°, mixed with Robinson's ketone, m. p. 45–46°.

Summary

A novel method for the direct introduction of the angular-methyl group is described. These experiments may be considered as models for the transformation of oestrone or oestradiol into substances of the testosterone–androsterone group.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASSACHUSETTS

RECEIVED MARCH 7, 1940

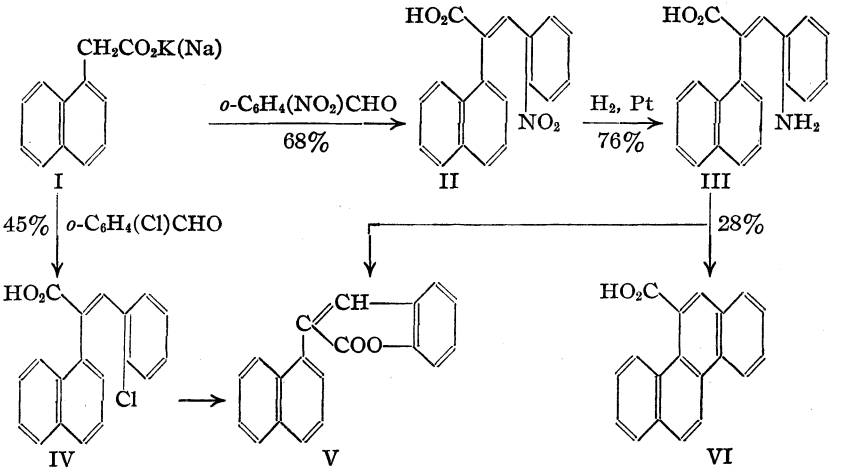
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

5-Methylchrysene

BY LOUIS F. FIESER AND LLOYD M. JOSHEL[1]

In a previous attempt to synthesize 5-methylchrysene a rearrangement was encountered in a final dehydrogenation step and the product, isolated in small yield, proved to be the 6-methyl isomer.[2] Another route not requiring a dehydrogenation now has been investigated, the plan being to obtain the 5-methyl compound from the corresponding carboxylic acid.

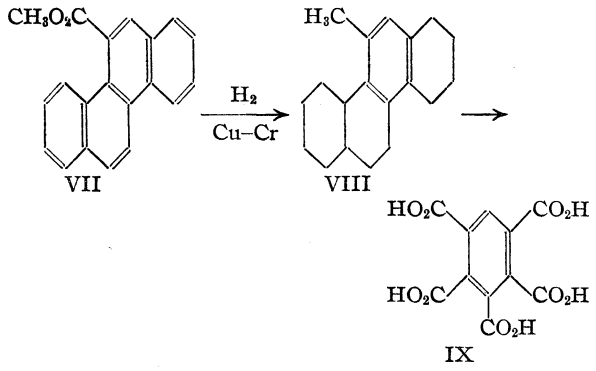
One scheme for obtaining the desired intermediate consisted in the condensation of α-naphthylacetic acid with *o*-chlorobenzaldehyde and fusion of the product IV with potassium hydroxide, following the synthetic method employed by Hewett.[3] The only crystalline product isolated proved to be the lactone of α-(1-naphthyl)-*o*-hydroxycinnamic acid, V. We then turned to the Pschorr synthesis, which already has been carried to the stage of the 5-acid VI by Weitzenböck and Lieb.[4] The condensation product II was obtained in improved yield and was conveniently reduced to the amine III by catalytic hydrogenation. Weitzenböck and Lieb state that the Pschorr ring closure afforded in about 20% yield a crude product which was purified with difficulty. A number of variations were tried in the present work and the best result was a 28% yield of pure chrysene-5-carboxylic acid by a procedure



(1) Fellow of the Finney-Howell Research Foundation.
(2) Fieser, Joshel and Seligman, THIS JOURNAL, 61, 2134 (1939).
(3) Hewett, *J. Chem. Soc.*, 1286 (1938).
(4) Weitzenböck and Lieb, *Monatsh.*, 33, 549 (1912).

using copper bronze and sodium hypophosphite.[5] A neutral by-product of the reaction had the composition of the lactone V.

On attempting to obtain either the 5-methyl or 5-hydroxymethyl compound by the direct reduction of the 5-carbomethoxy derivative VII it became apparent that the nucleus is reduced about as easily as the ester group. Reduction with sodium and ethanol gave a non-crystalline product having approximately eight hydrogen atoms more than the expected carbinol. The only crystalline reaction product isolated in various attempted hydrogenations over copper chromite catalyst was obtained on conducting the reaction at 250° for seventeen hours and proved to be 5-methyl-1,2,3,4,7,8,9,10,11,12,13,14-dodecahydrochrysene (VIII), for it gave benzene-pentacarboxylic acid (IX) on oxidation with dilute nitric acid.



With a shorter reaction period the product was a glass having approximately the composition of an octahydride. On attempting to prevent over-hydrogenation at 250° by using a nitrogen–hydrogen mixture containing just the required amount of the latter gas[6] we recovered the ester unchanged. Hydrogenation in the usual way at 160° gave a glassy mixture having the composition of a dihydro derivative of the ester VII.

The preparation of the desired 5-methyl derivative was accomplished satisfactorily by converting the acid VI by the Sonn and Müller reaction to the aldehyde, which was isolated as the semicarbazone, and reducing this by the Wolff–Kishner method. The hydrocarbon, m. p. 116.8–117.6°, proved identical with the 5-methylchrysene synthesized by Dr. M. S. Newman by a different method.[7]

(5) Ruggli and Staub, *Helv. Chim. Acta*, **20**, 37 (1937).

(6) Durland and Adkins, THIS JOURNAL, **60**, 1501 (1938); Stutsman and Adkins, *ibid.*, **61**, 3303 (1939).

(7) Private communication, and *ibid.*, **62**, 870 (1940).

Experimental Part[8]

α-(1-Naphthyl)-o-chlorocinnamic Acid (IV).—A mixture of 6.4 g. of the sodium salt of α-naphthylacetic acid, 4.5 g. of freshly distilled *o*-chlorobenzaldehyde, and 50 cc. of acetic anhydride was heated in a bath at 135° for twenty-five hours and poured into water. After standing overnight the orange-yellow resin was separated by decantation and extracted with boiling aqueous potassium carbonate. After clarification with Norit and cooling the potassium salt of IV separated as colorless plates (washed with potassium carbonate solution). From the filtrate, by acidification and crystallization of the precipitate from benzene, there was obtained 1 g. of *o*-chlorocinnamic acid, m. p. 209–211°. The acid liberated from the potassium salt on crystallization from benzene–ligroin was obtained as colorless prisms which partially melted at 160°, solidified, and remelted at 171–172.5°; yield 4.3 g. (45%). The behavior on melting was not altered by recrystallization as such or as the potassium salt.

Anal.[9] Calcd. for $C_{19}H_{13}O_2Cl$: Cl, 11.48. Found: Cl, 11.29.

In a typical attempted cyclization 4.5 g. of the chloro acid IV was fused with 25 g. of potassium hydroxide at 200–235° for five minutes and the temperature was raised to 245° in ten minutes. The crude acidic material was refluxed overnight with alcoholic hydrogen chloride and the neutral fraction separated and distilled in vacuum. The glassy distillate yielded no crystalline trinitrobenzene derivative, but after saponification and acidification a crystalline product was obtained from benzene–ligroin. This formed needles, m. p. 241–243°, dec., amounting to 0.15 g. (4%). On recrystallization the substance formed light buff needles, m. p. 244–245°, and did not depress the m. p. of the sample of the lactone V obtained as a by-product in the Pschorr synthesis.

α-(1-Naphthyl)-o-nitrocinnamic Acid (II).—The potassium salt of α-naphthylacetic acid was prepared by exactly neutralizing the acid in methanol with methyl alcoholic potassium hydroxide and evaporating to dryness. A solution of 25 g. of the salt and 20 g. of *o*-nitrobenzaldehyde in 200 cc. of acetic anhydride was heated in a bath at 125–130° for one hour and poured into excess dilute hydrochloric acid. After standing overnight the aqueous layer was decanted and the residue extracted with boiling potassium carbonate solution. The clarified filtrate when treated with more potassium carbonate and cooled deposited the salt of II in glistening plates. The alkaline mother liquor afforded 2.5 g. of *o*-nitrocinnamic acid, m. p. 245–247° (from acetone). The acid liberated from the salt crystallized from benzene–ligroin as yellow prisms, m. p. 181–182°; yield 24.2 g. (68%). A recrystallized sample melted at 181.8–182.8°.

Weitzenböck and Lieb[4] obtained a product, m. p. 173–174°, in 40% yield after a reaction period of eight to nine hours. In the present work it was found advantageous to shorten the period of heating and to separate the two acidic products through the salts rather than by crystallization as such.

(8) All melting points are corrected. Microanalyses by Lyon Southworth except as noted.

(9) Analysis by Herbert S. Wight.

α-(1-Naphthyl)-o-aminocinnamic Acid (III).—While the nitro compound II can be reduced in good yield on a small scale with ferrous sulfate,[4] hydrogenation seemed more satisfactory with larger amounts. With 32 g. of acid in 250 cc. of absolute ethanol and 0.2 g. of Adams catalyst, 90% of the theoretical amount of hydrogen was absorbed in two hours and the reaction then stopped. On two crystallizations from dilute alcohol the amino acid formed silvery white plates, m. p. 175–176°; yield 22 g. (76%).

Chrysene-5-carboxylic Acid (VI).—A solution of 4.5 g. of the amino acid III in 175 cc. of alcohol was treated with 1.8 cc. of concentrated sulfuric acid, followed by 3.6 cc. of amyl nitrite. After being stirred at room temperature for one-half hour the deep orange solution was added from a dropping funnel during forty-five minutes to a stirred suspension of 0.2 g. of copper bronze in 15 cc. of water and 15 g. of sodium hypophosphite at 45–50°. A test for diazonium salt with β-naphthol was negative within five minutes after the addition. The mixture was poured into excess potassium carbonate solution, the alcohol was distilled, and the hot solution was clarified with Norit and acidified. The light brown, granular precipitate was dried and allowed to stand in solution in 100 cc. of 3–5% methyl alcoholic hydrogen chloride for twelve hours. The solution was diluted with water, extracted with ether, and the acid VI, which is not esterified under these conditions, was extracted with aqueous sodium carbonate solution. The carbonate extract was clarified with Norit and the liberated acid crystallized twice from acetone–benzene, furnishing 1.2 g. (28%) of satisfactory product as buff needles, m. p. 225–226°, dec.

The neutral fraction was distilled in vacuum and crystallized three times from acetone–benzene, yielding 0.1–0.2 g. of yellow needles, m. p. 244.5–245.5°, dec., having the composition of the **lactone of α-(1-naphthyl)-o-hydroxycinnamic acid (V).**

Anal. Calcd. for $C_{19}H_{12}O_2$: C, 83.80; H, 4.44. Found: C, 83.59; H, 4.42.

As solvent in the Pschorr reaction dioxane[10] or acetic acid proved less satisfactory.

Methyl 5-chrysene carboxylate was prepared from 2.5 g. of the acid in 50 cc. of acetone, treated with an ethereal solution of diazomethane from 5 cc. of nitrosomethylurethan. On distillation in vacuum and crystallization from benzene the ester formed colorless prisms, m. p. 159–160° (90% yield).

Anal. Calcd. for $C_{20}H_{14}O_2$: C, 83.89; H, 4.93. Found: C, 83.85; H, 5.04.

Bouveault Reduction.—After treatment in benzene with the calculated amount of ethanol and sodium, the ester was largely recovered unchanged. In another experiment 0.4 g. of powdered sodium was added in two portions to 0.3 g. of the ester in 5 cc. of benzene and 20 cc. of absolute ethanol and the mixture was refluxed for a few minutes, when all the sodium had reacted. After dilution, acidification and removal of the solvents with steam, the product was distilled in vacuum. A small amount (10 mg.) of the starting ester crystallized from the distillate and the main product was a light yellow glass probably consisting mainly of 5-hydroxymethyloctahydrochrysene (calcd. for $C_{19}H_{22}O$: C, 85.67; H, 8.33. Found: C, 84.99; H, 7.77).

5 - Methyl - 1,2,3,4,7,8,9,10,11,12,13,14 - dodecahydrochrysene (VIII).—Hydrogenation of 1 g. of the ester in 8 cc. of dioxane with 0.1 g. of copper-chromite catalyst 37KAF was conducted at 250° and 2100 lb. (140 atm.) pressure for seventeen hours. Distillation in vacuum and crystallization from benzene–alcohol furnished 0.52 g. (58.5%) of colorless needles, m. p. 95–99°. On recrystallization the hydrocarbon melted at 98.8–99.8° (0.35 g.).

Anal. Calcd. for $C_{19}H_{26}$: C, 89.70; H, 10.30. Found: C, 89.90; H, 10.56.

For oxidation 0.3 g. of the hydrocarbon was heated with 1.5 cc. of concentrated nitric acid and 3 cc. of water at 195–200° for twenty-two hours. The clear yellow solution was taken to dryness and the residue allowed to stand for several hours with diazomethane solution. After sublimation of the ester at 2 mm. pressure, crystallization from ether–ligroin gave 0.05 g. of prisms and after recrystallization the sample of **pentacarbomethoxybenzene** melted at 146–149.5°.

Anal. Calcd. for $C_{16}H_{16}O_{10}$: C, 52.18; H, 4.38. Found: C, 52.28; H, 4.73.

Pentacarbomethoxybenzene is described as melting at 150.5° with previous sintering.[11] The ester of prehnitic acid (1,2,3,4), which would be the expected product if the alternate non-terminal ring were aromatic, melts at 131–133°.

Other Hydrogenations.—On hydrogenation of the ester as above but for only four hours there was obtained a small amount of the crystalline dodecahydride and a colorless glass of composition corresponding approximately to an octahydride (calcd. for $C_{19}H_{22}$: C, 91.15; H, 8.85. Found: C, 90.50; H, 8.35). On conducting the reaction at 160° for four hours the non-crystalline product corresponded most closely to a dihydro ester (calcd. for $C_{20}H_{16}O_2$: C, 83.31; H, 5.59. Found: C, 83.10; H, 5.83.

Chrysene-5-aldehyde Semicarbazone.—A mixture of 0.56 g. of chrysene-5-carboxylic acid, 0.5 cc. of phosphorus pentachloride, and 10 cc. of benzene was refluxed for ten minutes and the resulting solution was evaporated to dryness at reduced pressure. The residue was taken into 15 cc. of dry acetone and treated with 2 cc. of aniline, and after boiling for a few minutes the anilide which separated was collected, washed with benzene, and heated with 0.5 g. of phosphorus pentachloride in 5 cc. of benzene for one-half hour. Evaporation in vacuum left the chloroanilide as a bright red oil. This was dissolved in 5 cc. of ethylene chloride and added to a solution prepared by passing hydrogen chloride into 1.5 g. of anhydrous stannous chloride suspended in 15 cc. of dry ether. After sixteen hours at 0°, 15 cc. of water was added and the mixture refluxed for two hours and steam distilled. The residue was extracted with benzene, the solvent was replaced by absolute alcohol, 5 cc. of pyridine and 0.3 g. of semicarbazide hydrochloride were added and the solution was refluxed for one hour and diluted with water. The semicarbazone crystallized as light yellow microprisms, m. p. 260–263°, dec.; yield 0.34 g. (53%). Recrystallized from acetic acid, the substance melted at 266–268°, dec.

(10) Cassaday and Bogert, THIS JOURNAL, **61**, 2461, 3055, 3058 (1939).

(11) Späth, Wessely and Kornfeld, *Ber.*, **65**, 1549 (1932).

Anal. Calcd. for $C_{20}H_{15}ON_3$: N, 13.41. Found: N, 13.21.

5-Methylchrysene.—The semicarbazone (0.23 g.) was heated with a solution from 0.3 g. of sodium and 10 cc. of absolute alcohol in a sealed tube at 200° for nine hours. After dilution and acidification the product was extracted with benzene and the washed and dried solution was passed through a tower of alumina. After vacuum distillation the product was fractionally crystallized from alcohol to remove a small amount of chrysene. The 5-methyl compound then crystallized from alcohol in colorless needles, m. p. 116.8–117.6°; yield 0.03 g. (17%).

Anal. Calcd. for $C_{19}H_{14}$: C, 94.18; H, 5.82. Found: C. 94.35; H, 5.61.

The hydrocarbon shows strong blue-violet fluorescence in ultraviolet light. The substance did not depress the m. p. of a sample kindly supplied by Dr. M. S. Newman. The **picrate** formed red needles, m. p. 141.6–142.4°, from alcohol.

Anal. Calcd. for $C_{25}H_{17}O_7N_3$: N, 8.91. Found: N, 8.80.

Summary

Chrysene-5-carboxylic acid, obtained by the Pschorr synthesis, has been converted through the aldehyde (Sonn–Müller reaction) to the 5-methyl compound. In attempts to reduce the ester with sodium and ethanol or by high pressure hydrogenation, the aromatic nucleus was invariably attacked.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASSACHUSETTS RECEIVED MARCH 12, 1940

[CONTRIBUTION NO. 220 FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Oxidation Products of Sulfanilamide

BY MARGARET K. SEIKEL[1]

Sulfanilamide (I) oxidizes with ordinary oxidizing agents either to azobenzene-4,4′-disulfonamide (II) or to azoxybenzene-4,4′-disulfonamide (III). Both II and III can be reduced to I and to hydrazobenzene-4,4′-disulfonamide (IV).[2] Oxidation of sulfanilamide with cold alkaline ferricyanide produced a 20% yield of the azo compound II.[3] A better method for preparing II, with the over-all yield of brighter colored product as high as 46%, comprises the series of reactions I→III→IV→II. II could be converted into III by heating for several hours with hydrogen peroxide in glacial acetic acid.[4]

When I was oxidized in glacial acetic acid with 30% hydrogen peroxide, the azoxy compound III was obtained in 70% yields after only half an hour's heating. The speed with which III was obtained from I in comparison with the slow conversion of II to III indicated that II is probably not an intermediate in the former reaction; likewise IV yielded mainly II by the same treatment.[5] However, with this reagent *p*-toluidine is oxidized first to the corresponding azo compound so undoubtedly the sulfonamido group affects the course of the reaction.

If I was oxidized by hydrogen peroxide in dilute sulfuric acid, the product was a mixture of II and III. If hydrochloric acid was employed as the acidifying agent, partial chlorination yielded mixtures of products. Oxidations by hydrogen peroxide in neutral or basic solutions were too slow to be practical.

Reductions of II, III or material believed to be a mixture of the two by stannous chloride in hydrochloric acid regenerated sulfanilamide in 35–50% yields.[3a] Reductions with hydrosulfite in alkaline solution produced quantitative yields of IV.

Reoxidation of IV to II occurred very readily with various oxidizing agents, but 1 *N* ferric chloride was preferable because it yielded instantaneous and quantitative results.

Sulfanilamide may be chlorinated in the cold by treatment with a great excess of hydrochloric acid and only a moderate excess of hydrogen peroxide, the previously unreported 3,5-dichloro-4-amino-benzenesulfonamide (V) separating in fair yields. The reaction undoubtedly occurs through an intermediate chloramide.

Experimental

All melting points are uncorrected and were taken by the method described in Mulliken's "Identification of

(1) Research Associate.

(2) For biological tests on II, III and IV see *Compt. rend.*, **205**, 181 (1937).

(3) (a) Laar, *Ber.*, **14**, 1928–1934 (1881); (b) Limpricht, *ibid.*, 1356–1359; (c) Scudi, THIS JOURNAL, **59**, 1480–1483 (1937). No melting point is recorded.

(4) Compare Angeli, *Chem. Zentr.*, **81**, II, 731 (1910).

(5) Compare D'Ans and Kneip, *Ber.*, **48**, 1145 (1915).

Pure Organic Compounds," Vol. I, page 218, on a 360° thermometer immersed in a mixture of sulfuric acid and potassium acid sulfate to the 0° point. Analytical values represent averages of closely agreeing duplicate determinations.

Oxidation Procedures: Ferricyanide.—Sulfanilamide (0.85 g., 0.005 mole) dissolved in 5 ml. of water containing 1.4 g. (0.025 mole) of potassium hydroxide was treated at room temperature with an aqueous solution of 6.58 g. (0.02 mole) of potassium ferricyanide. The precipitated potassium derivative of II was filtered off after ten to thirty minutes and converted to the free amide. The 17–25% yield of tan product was most readily purified by several recrystallizations from 30–40% pyridine (its solubility in alcohol is low) from which it separated in fronds of dull apricot hair-like needles, m. p. 312° dec. after sintering above 300°.

Anal. Calcd. for $C_{12}H_{12}N_4O_4S_2$: C, 42.3; H, 3.55; N, 16.5. Found: C, 42.2; H, 3.63; N, 16.6.

It forms a vivid yellow solution in concentrated sulfuric acid and dissolves fairly readily in dilute alkali.

Hydrogen Peroxide–Acetic Acid.—A solution of 5 g. of sulfanilamide in 30 ml. of 30% hydrogen peroxide and 120 ml. of glacial acetic acid was heated for one-half hour at 100°. A 58% yield (3.0 g.) of the 6-mm. shining orange needles of III was filtered from the hot solution, and on cooling the mother liquor deposited an additional 14% yield. The same reaction occurs slowly at room temperature, a 64% yield being obtained in one day. III was easily purified by one or two recrystallizations from 30% pyridine from which it separated as yellow-orange plate-needles, m. p. 289–290° with violent evolution of gas.

Anal. Calcd. for $C_{12}H_{12}N_4O_6S_2$: C, 40.4; H, 3.39; N, 15.7. Found: C, 40.4; H, 3.49; N, 15.3.

The compound gave an orange-yellow solution in concentrated sulfuric acid. It did not free iodine from potassium iodide in acetic acid.

Hydrogen Peroxide–Sulfuric Acid.—When sulfanilamide was oxidized by 30% hydrogen peroxide in the presence of 6 *N* sulfuric acid, slower precipitation of a product occurred. After recrystallization, the vivid orange needles representing a mixture of II and III generally melted around 296° with violent evolution of gas.

Anal. Calcd. for $C_{12}H_{12}N_4O_4S_2$: C, 42.3; H, 3.55; N, 16.5. Calcd. for $C_{12}H_{12}N_4O_5S_2$: C, 40.4; H, 3.39; N, 15.7. Found: C, 41.2; H, 3.31; N, 16.0.

The mixture gave a yellow-orange solution in concentrated sulfuric acid.

Reduction Procedures: Stannous Chloride.—II, III and the mixture of the two were reduced by heating 0.25 g. of material with 1.0 g. of stannous chloride and 4 ml. of 10 *N* hydrochloric acid for ten minutes at 100°. After being made basic with bicarbonate, the reaction mixtures were evaporated to dryness by air and extracted twice with acetone. The residues obtained by evaporating the acetone were either recrystallized from or extracted with boiling water depending on the amount of high melting insoluble impurity present. From the aqueous solutions 35–50% yields of sulfanilamide melting around 160° were isolated. After further purification, material from any of the initial sources did not lower the melting point of an authentic sample.

Hydrosulfite.—Solutions of 0.10 g. of II, III and the mixture of the two in 5 ml. of 0.2 *N* sodium hydroxide were heated to boiling and treated with solid practical sodium hydrosulfite until decolorization was complete, the separation of an intermediate precipitate being disregarded. The amounts of hydrosulfite used were as follows: for II, 0.08, 0.08 g. or 0.27 g. per millimole; for III, 0.15, 0.15, 0.15 g. or 0.54 g. per millimole; for the mixture, 0.13, 0.13, 0.13 g. After boiling five minutes and cooling, the solutions deposited 100% yields of IV, m. p. 224–224.5° to a red melt which resolidified. Recrystallization from water containing a trace of hydrosulfite to prevent reoxidation produced white fronds with the melting point unchanged. Samples from the various initial materials did not lower each other's melting points.

Anal. Calcd. for $C_{12}H_{14}N_4O_4S_2$: C, 42.1; H, 4.12. Found: from II, C, 42.1; H, 4.17; from III, C, 42.1; H, 4.10; from mixture, C, 42.1; H, 3.91.

Oxidation of Hydrazo Compound IV.—When an aqueous solution of IV was heated on the steam-bath, it soon assumed a yellow tinge and in two hours the rust colored needles of II separated, m. p. 308° dec. If IV was heated with enough 30% hydrogen peroxide to dissolve it, a 70% yield of II, m. p. 311° dec., could be obtained in an hour. When hydrogen peroxide and acetic acid were used in the proportions employed in the preparation of III, a 95% yield of II, m. p. 307° dec., was obtained after five minutes of heating. The speediest reoxidation resulted when a hot aqueous solution of IV (0.10 g. in 5–7 ml.) was treated with 1.0 ml. of 1 *N* ferric chloride; 90–100% yields of II separated instantaneously.[6]

After two recrystallizations from 30% pyridine, II was obtained as pure orange opaque flat needles, m. p. 314° dec., and it did not lower the melting point of II obtained by ferricyanide oxidation of I.

Anal. Calcd. for $C_{12}H_{12}N_4O_4S_2$: C, 42.3; H, 3.55. Found: C, 42.2; H, 3.41.

Oxidation of II to III.—When II was dissolved in hot 30% hydrogen peroxide and glacial acetic acid in the proportions used for the oxidation of I, the product isolated after at least three hours of heating melted at 291° with violent evolution of gas; it did not lower the melting point of III but did lower that of II.

Chlorination.—Sulfanilamide (0.43 g., 0.0025 mole) was dissolved in 15 ml. of 6 *N* hydrochloric acid (0.08 mole) and treated with 2 ml. of 30% hydrogen peroxide (0.02 mole) at room temperature. It was found most advantageous to filter off the precipitate when the mixture first assumed a yellow tinge (thirty to forty-five minutes); the product would then be practically colorless. The 60–80% yield of V was recrystallized twice from large volumes of water (200–300 ml. per gram) producing shining colorless needles, m. p. 205–205.5°.

Anal. Calcd. for $C_6H_6Cl_2N_2O_2S$: Cl, 29.7. Found: Cl, 29.5.

The proportions of acid and peroxide suggested were

(6) The high yields and speed of the reduction and reoxidation steps allows II to be prepared quickly and in good yields by way of III and IV. Experimentally a 46% yield, m. p. 308–309° dec., was obtained when the intermediate products were not purified.

determined empirically to be the best for a speedy reaction and a pure product.

Proof of Structure of V.—When V was desulfamidated by 75% sulfuric acid in the manner described for the analogous dibromo compound,[7] a 51% yield of 2,6-dichloroaniline, m. p. 38–39° (recorded 39°), could be steam distilled from the reaction mixture. This was acetylated with acetic acid and acetyl chloride,[8] m. p. 178.5–179°, recorded 175°, after recrystallization from 25% acetic acid.

(7) Fuchs, *Monatsh.*, **36**, 125 (1915).

(8) Beilstein and Kurbatow, *Ann.*, **196**, 215, 219–220 (1879).

Summary

1. On oxidation sulfanilamide yields the corresponding azo- and azoxy-benzenes which may be reduced to the hydrazo compound.

2. It can be chlorinated readily by a mixture of hydrogen peroxide and hydrochloric acid.

CAMBRIDGE, MASS. RECEIVED FEBRUARY 13, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF BIOCHEMISTRY, COLLEGE OF AGRICULTURE, UNIVERSITY OF WISCONSIN]

The Mutarotation and Rotatory Dispersion of Derivatives of Aldehydo-*d*-galacturonic Acid[1]

BY ROBERT J. DIMLER AND KARL PAUL LINK

Aldehydo tetraacetyl methyl-*d*-galacturonate and one of its ethyl hemiacetals were prepared by Link and Campbell[2] as the first derivatives of the aldehydo form of a hexuronic acid. Prior to this work on *d*-galacturonic acid Wolfrom and Morgan[3] had prepared the corresponding derivatives of the parent sugar *d*-galactose. They also reported[4,5] on the optical properties of aldehydo-*d*-galactose pentaacetate and its hemiacetals. In this communication we have extended the mutarotation and rotatory dispersion study to the aldehydo derivatives of *d*-galacturonic acid.

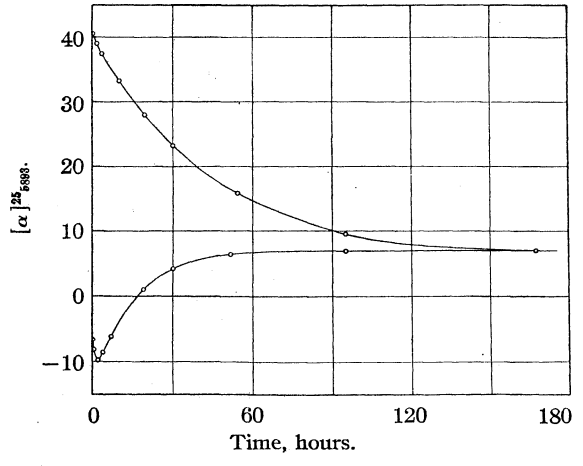
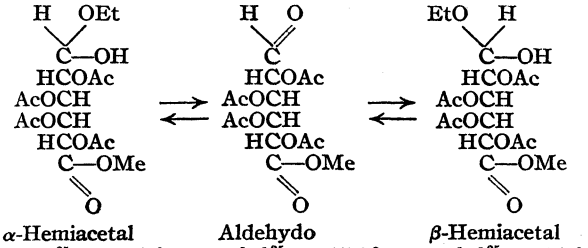


Fig. 1.—Mutarotation of α- and β-ethyl hemiacetal tetraacetyl methyl *d*-galacturonate in alcohol-free chloroform.

The isomeric α- and β-ethyl hemiacetals of tetraacetyl methyl-*d*-galacturonate have been obtained by variation of the method of preparation and fractional crystallization. This is the first member of the hemiacetal series for which both of the predictable forms have been realized. The designation of the isomers as α- and β- is based on the usage proposed by Hudson,[6] in which that derivative in the *d*-series having the more positive rotation is assigned the prefix α. The β-ethyl hemiacetal exhibits a mutarotation (Fig. 1) similar to that of the compounds of galactose studied by Wolfrom.[5] The α-ethyl hemiacetal shows a regular mutarotation without a minimum as seen in Fig. 1.

The mutarotation of the α- and β-ethyl hemiacetals involves the establishing of an equilibrium among the three compounds.



α-Hemiacetal $[\alpha]^{25}_{5893}$ +40.7° Aldehydo $[\alpha]^{25}_{5893}$ −15.6° β-Hemiacetal $[\alpha]^{25}_{5893}$ −6.7°

The minimum in the mutarotation curve for the β-ethyl hemiacetal is attributed to the primary rapid formation of the free aldehydo compound. The resulting aldehyde and alcohol recombine

(1) Published with the approval of the Director of the Wisconsin Agricultural Experiment Station.

This study is part of a thesis to be submitted to the Graduate Faculty of the University of Wisconsin in partial fulfilment of the requirements for the degree of Doctor of Philosophy. R. J. Dimler is indebted to the Wisconsin Alumni Research Foundation for a fellowship in 1936–37 and to the Graduate Research Fund for an assistantship in 1937–40.

(2) Campbell and Link, *J. Biol. Chem.*, **120**, 471 (1937).

(3) Wolfrom and Morgan, THIS JOURNAL, **52**, 2464 (1930).

(4) Wolfrom, *ibid.*, **53**, 2275 (1931).

(5) Wolfrom and Morgan, *ibid.*, **54**, 3390 (1932).

(6) Hudson, *ibid.*, **31**, 66 (1909).

in a second order reaction to form either of the isomeric hemiacetals. Since the concentration of the reactants in this reaction is low, the ratio of the aldehydo form will be high, as shown by the rotation of the equilibrium mixture. While differences in the *rate* of mutarotation for independent determinations can be noted, the curves obtained are of reproducible form. These variations are probably due to catalysts arising in the chloroform on standing. The nature of the compounds involved has not been investigated.[7]

The ethyl ester of ethyl hemiacetal tetraacetyl *d*-galacturonic acid, prepared in order that a compound might be used in which both alkyl groups were the same, was obtained only in the form of the β-isomer. The mutarotation, as shown in Fig. 2, is typical of the β-hemiacetals.

The rotatory dispersion of aldehydo pentaacetyl *d*-galactose was shown by Hudson, Wolfrom and Lowry[8] to be attributable to the induced dissymmetry of the aldehyde group, with only a small contribution from the other asymmetric centers of the molecule. The galacturonic acid structure contains another possible source of induced activity, namely, the carboxyl group (as the ester).

TABLE I

ROTATORY DISPERSION OF ALDEHYDO TETRAACETYL METHYL *d*-GALACTURONATE

$$[\alpha]^{25}\lambda = -\frac{13.81}{\lambda^2 - 0.090} + \frac{11.12}{\lambda^2 - 0.055};\ (c, 4;\ CHCl_3)$$

λ, Å.	$[\alpha]^{25}\lambda$	O − C[a]
4358	−54.4	+1.4
4679	−39.2	±
4800	−34.9	+0.2
4861	−33.0	+0.2
5086	−27.1	+0.1
5209	−24.7	+0.1
5350	−22.3	±
5461	−20.6	+0.1
5780	−16.8	±
5893	−15.6	±
6104	−13.9	−0.1
6362	−12.0	±
6438	−11.6	±
6563	−11.0	−0.1
6708	−10.2	±

[a] O − C is the difference between the observed specific rotation and the rotation calculated from the Drude equation.

(7) Wolfrom[4] has suggested that hydrogen chloride is the responsible agent. We have observed that dry or moist hydrogen chloride or absolute alcohol in chloroform has no effect on the rate. However, alcoholic hydrogen chloride produces immediate equilibrium.

(8) Hudson, Wolfrom and Lowry, *J. Chem. Soc.*, 1179 (1933).

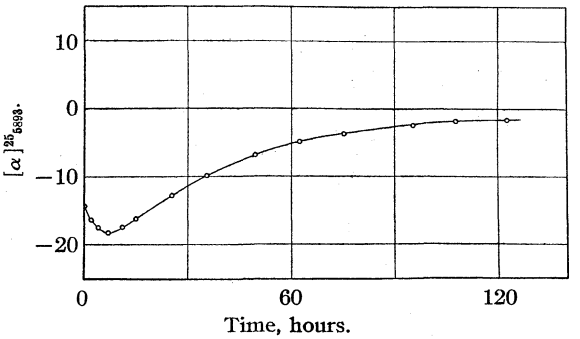


Fig. 2.—Mutarotation of β-ethyl hemiacetal tetraacetyl ethyl *d*-galacturonate in alcohol-free chloroform.

The methyl and ethyl esters of aldehydo tetraacetyl *d*-galacturonic acid were shown to have a complex rotatory dispersion by a preliminary plotting of the reciprocal of the specific rotation against the square of the wave length, the points lying on a curve instead of a straight line. Two-term Drude equations were then determined for the dispersions. These equations, with the difference between the observed rotations and those calculated from the equations, are given in Tables I and II. Since the observations were made only in the visible region of the spectrum the significance of the Drude equations is more qualitative than quantitative.

TABLE II

ROTATORY DISPERSION OF ALDEHYDO TETRAACETYL ETHYL *d*-GALACTURONATE

$$[\alpha]^{25}\lambda = -\frac{12.42}{\lambda^2 - 0.090} + \frac{7.07}{\lambda^2 - 0.055};\ (c, 4;\ CHCl_3)$$

λ, Å.	$[\alpha]^{25}\lambda$	O − C[a]
4358	−71.0	+0.8
4678	−53.1	±
4800	−48.1	+0.1
4861	−45.8	+0.1
5086	−38.8	±
5209	−35.8	+0.1
5350	−32.8	−0.1
5461	−30.7	−0.1
5780	−25.5	+0.1
5893	−24.0	+0.1
6104	−21.6	±
6362	−19.2	±
6438	−18.6	±
6563	−17.5	+0.1
6708	−16.5	+0.1

[a] O − C is the difference between the observed specific rotation and the rotation calculated from the Drude equation.

The rotatory dispersion of the methyl and ethyl esters of aldehydo tetraacetyl *d*-galacturonic acid is complex but normal. The rotation is

dominated by the activity due to the induced dissymmetry of the aldehyde group, with an active band at about 2900 Å. A comparison of rotation constants of the two different esters and also the galactose derivative studied by Hudson, *et al.*,[8] shows that the groups on the terminal carbon remote from the aldehyde group have little influence on the magnitude of the activity induced in the carbonyl group. This is in accord with the present conception of induced dissymmetry.

The remaining active groups contribute a rotation of opposite sign and smaller magnitude. The dispersion constant may be assigned to the induced dissymmetry of the carboxyl group, with an active absorption band in the region of 2300 Å. While the carboxyl group often shows another active band at about 1700 Å., the limited range of dispersion studied in this case does not permit consideration of the possibility of such a contribution. Similarly, the small contribution of the other asymmetric centers, demonstrated for galactose, cannot be detected in this study. It may be concluded that the dispersion is probably more complex than is implied by a two-term Drude equation. The equations obtained indicate only the dominant sources of optical activity.

Experimental

Standardization of the Polarimeter.—The rotatory dispersions were studied with the use of a Franz Schmidt and Haensch polarimeter No. 52B with a monochromator attachment. The instrument was standardized by a modification of the method of Bencowitz.[9] A spectroscope was set with a sodium light and checked against a mercury arc. This spectroscope was then used to determine the wave length of the light transmitted by the monochromator. The settings were thus determined for the monochromator which would give the desired wave lengths. The results were checked by determining the rotatory dispersion of a 26% solution of Bureau of Standards sucrose, for which the dispersion formula is known.

Ethylmercaptal Methyl-*d*-galacturonate.—The method used by Campbell and Link[2] was modified to permit simultaneous mercaptalation and esterification. To a solution of 10 g. of *d*-galacturonic acid in 60 cc. of approximately 1 *N* hydrogen chloride–methanol (dry), was added 15 cc. of ethyl mercaptan. After standing at room temperature for one and one-half hours, the solution was refluxed gently for one-half hour. Concentration of the solution under reduced pressure gave a mass of crystals which was removed by filtration and washed with cold methanol. The mother liquors were concentrated to obtain another crop of crystals. In this way about four crops of crystals were obtained; yield of the crude product was 9.2 g. (57%). For acetylation it is sufficient to dry the crude preparation in a vacuum desiccator. If the product is to be kept for any length of time it should be recrystallized since the hydrogen chloride adhering to the crystals may cause decomposition.

Ethylmercaptal Tetraacetyl Methyl-*d*-galacturonate.—The method used was that described by Campbell and Link.[2] From the 9.2 g. of ethylmercaptal methyl-*d*-galacturonate prepared as above about 11.5 g. (71%) of the acetate (recrystallized once, m. p. 109–110°) was obtained.

Aldehydo Tetraacetyl Methyl-*d*-galacturonate.—This compound was prepared by the method of Wolfrom and Morgan.[3] The crude product was recrystallized several times to obtain the pure aldehydo tetraacetyl methyl-*d*-galacturonate; m. p. 135–136°; $[\alpha]^{25}_{5893}$ −15.6° (*c*, 4; $CHCl_3$).

The rotatory dispersion in alcohol-free chloroform was determined in a 4-dm. semi-micro jacketed tube at 25°. The rotations obtained with a comparison to the values calculated from the two-term Drude equation, are given in Table I.

Anal. Calcd. for $C_{15}H_{20}O_{11}$: $-OCH_3$, 8.25. Found: $-OCH_3$, 8.29.

β-Ethylhemiacetal Tetraacetyl Methyl-*d*-galacturonate.—Without fractionation the first time, 2.5 g. of the crude aldehydo compound was crystallized from 8 cc. of boiling absolute ethanol. The resulting 1.8 g. of crude ethyl hemiacetal was recrystallized with fractionation from 8 cc. of boiling ethanol. The first crop obtained from quiescent crystallization was 0.8 g.; initial $[\alpha]^{25}_{5893}$ −5.9°. The second crop, obtained by vigorous stirring of the mother liquor, was 0.2 g.; initial $[\alpha]^{25}_{5893}$ +3.0°. Repeated fractional crystallizations of the first fractions yielded the apparently pure β-isomer; m. p. 127–130° (on the Kofler microscope stage[10] with crossed nicols one observes the loss of ethyl alcohol at about 127° and the sharp melting of the remaining aldehydo compound at 135–136°); $[\alpha]^{25}_{5893}$ −6.7° initial, with equilibrium value of +7.1° (*c*, 4; $CHCl_3$).

The mutarotation of the ethyl hemiacetal in alcohol-free chloroform is shown by the curve in Fig. 1. Independent determinations showed differences in the length of time required to reach equilibrium, but the form of the curve was the same for all. The differences in rate probably are due to catalysts formed in the chloroform on standing.

Anal. Calcd. for $C_{17}H_{26}O_{12}$: alkoxyl, 18.06. Found: alkoxyl, 18.2.

α-Ethyl Hemiacetal Tetraacetyl Methyl-*d*-galacturonate.—The ethyl hemiacetal was prepared directly from the mercaptal by the method of Campbell and Link.[2] The 5.3 g. of crude product was recrystallized first without fractionation from absolute alcohol. On fractional crystallization of the 3.7 g. from 10 cc. of boiling absolute alcohol, as above, the first crop was 0.5 g., initial $[\alpha]^{25}_{5893}$ −2.2°; the second crop was 2.1 g., initial $[\alpha]^{25}_{5893}$ +15.8°. Further fractionation of second crops yielded the apparently pure α-isomer; m. p. 105–107° (on the Kofler microscope stage loss of ethyl alcohol is observed at about 105° and melting of the aldehydo compound at 135–

(9) Bencowitz, *J. Phys. Chem.*, **32**, 1163 (1928).

(10) Pregl–Roth, "Die quantitative organische Mikroanalyse," Berlin, 1935.

136°); $[\alpha]^{25}_{5893}$ +40.7° initial, changing to a final value of +7.1° (*c*, 4; $CHCl_3$).

The mutarotation, observed in alcohol-free chloroform, is shown by the curve in Fig. 1.

Anal. Calcd. for $C_{17}H_{26}O_{12}$: alkoxyl, 18.06. Found: alkoxyl, 18.1.

Ethylmercaptal Ethyl-*d*-galacturonate.—This compound was prepared from *d*-galacturonic acid in the same manner as the methyl ester. A dry hydrogen chloride–ethanol solution (approx. 1 *N*) was used as the solvent. The ethyl ester did not crystallize as readily as the methyl ester. By the repeated addition of absolute ethanol and removal under reduced pressure crystallization was induced. The concentrate was placed in a refrigerator for twenty-four hours to permit more complete crystallization.

From 10 g. of *d*-galacturonic acid, the yield was 9.6 g. (57%). Recrystallization from absolute ethanol gave a pure product; m. p. 128–129°; $[\alpha]^{25}_{5893}$ +15.7° (*c*, 2; EtOH).

Anal. Calcd. for $C_{12}H_{24}O_6S_2$: S, 19.53. Found: S, 19.62.

Ethylmercaptal Tetraacetyl Ethyl-*d*-galacturonate.—This acetyl derivative was prepared by the same method used for the corresponding methyl ester. From 9.6 g. of crude ethyl mercaptal ethyl ester the yield after one recrystallization was 11.5 g. (79%); m. p. 80–81°; $[\alpha]^{25}_{5893}$ +11.0° (*c*, 4; $CHCl_3$).

Anal. Calcd. for $C_{20}H_{32}O_{10}S_2$: S, 12.92. Found: S, 12.93.

Aldehydo Tetraacetyl Ethyl-*d*-galacturonate.—The preparation is similar to that of the corresponding methyl ester. The compound is quite soluble in toluene; m. p. 95–97°; $[\alpha]^{25}_{5893}$ −24.0° (*c*, 4; $CHCl_3$).

The rotations obtained in the study of the rotatory dispersion with a comparison to the values calculated from the two-term Drude equation, are given in Table II.

Anal. Calcd. for $C_{16}H_{22}O_{11}$: —OEt, 11.54. Found: —OEt, 11.7.

β-Ethylhemiacetal Tetraacetyl Ethyl-*d*-galacturonate.—The hemiacetal was prepared by both of the methods which were used for the methyl ester. The resulting compounds were apparently identical and could not be fractionated; m. p. 105–106°; $[\alpha]^{25}_{5893}$ −14.4° initial, reaching equilibrium at −1.6° (*c*, 4; $CHCl_3$). The course of the mutarotation, observed in alcohol-free chloroform, is shown by the curve in Fig. 2.

Anal. Calcd. for $C_{18}H_{28}O_{12}$: —OEt, 20.70. Found: —OEt, 20.8.

Summary

1. The α- and β-ethyl hemiacetals of aldehydo tetraacetyl methyl-*d*-galacturonate have been prepared. The mutarotation of the two compounds in chloroform indicates an interconversion over the aldehydo form.

2. The ethyl ester of ethyl mercaptal, ethyl mercaptal tetraacetyl, aldehydo tetraacetyl and ethyl hemiacetal tetraacetyl *d*-galacturonic acid have been prepared. Through mutarotation studies the ethyl hemiacetal tetraacetyl ethyl-*d*-galacturonate obtained is characterized as a β-hemiacetal.

3. The rotatory dispersions of the aldehydo tetraacetyl methyl- and ethyl-*d*-galacturonate have been shown to be complex but normal. Two-term Drude equations have been calculated for the dispersions to obtain a qualitative interpretation of the results.

MADISON, WISCONSIN RECEIVED MARCH 1, 1940

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

The Dipole Moments and Structures of Certain Compounds of Sulfur, Selenium and Phosphorus

BY C. P. SMYTH, G. L. LEWIS, A. J. GROSSMAN AND F. B. JENNINGS, III

The dipole moments of hydrogen disulfide and sulfur and selenium monochlorides have been measured with a view to obtaining evidence as to the two possible structures, the Y-shaped or irregular tetrahedral such as S—SCl_2 and the more extended structures such as Cl—S—S—Cl, as well as getting some information bearing on the magnitudes of the bond moments. Selenium oxychloride and phosphoryl and thiophosphoryl chlorides have been investigated for the sake of the bond moments involved. Indeed, bond moment values obtained from the measurements on the two latter compounds already have been published,[1] and electron diffraction measurements have been made upon the more volatile of these several substances. The moments were obtained with the apparatus and methods previously described,[2,3] the dielectric constants and densities of solutions of the substances in benzene or heptane being determined.

Preparation of Materials.—Benzene and heptane were purified as in previous work.[4]

Hydrogen Disulfide.—The material was prepared from sodium polysulfide and purified in the manner described

(1) Smyth, THIS JOURNAL, **60**, 183 (1938).
(2) Lewis and Smyth, *J. Chem. Phys.*, **7**, 1085 (1939).
(3) Lewis and Smyth, THIS JOURNAL, **61**, 3063 (1939).
(4) Smyth and Walls, *ibid.*, **54**, 1854 (1932).

by Butler and Maass[5]; d^{25}_4 1.3279, $n^{25}D$ 1.62635, $n^{22}D$ 1.63237.

Sulfur Monochloride.—Material previously prepared in this Laboratory was fractionally distilled at 10 mm. over sulfur; b. p. (10 mm.) 39°.

Selenium Monochloride.—The material was prepared from selenium and purified by methods described in the literature.[6,7] In spite of all precautions, it could not be regarded as very pure.

Selenium Oxychloride.—Material from the Eastman Kodak Company was vacuum distilled seven times in a glass apparatus which had been acidified with dry hydrogen chloride and completely sealed except for the outlet to the pump. It was then recrystallized and the third recrystallization crop was quickly filtered through a sintered glass crucible. After another vacuum distillation, this material was used for the measurements; $n^{20}D$ 1.65159.

Phosphoryl Chloride.—Material from the Baker and Adamson General Chemical Company was fractionally distilled twice; b. p. 107.0–107.1°, $n^{25}D$ 1.45816, d^{25}_4 1.6659. As this fractionation did not alter the boiling point and raised the refractive index by only 0.0001, a second sample of refractive index 1.45797 was used without purification for a second series of measurements, which agreed well with the first.

Thiophosphoryl Chloride.—Material from the Eastman Kodak Company was dried with calcium chloride and fractionally distilled twice; b. p. 125.0°, $n^{25}D$ 1.5432, d^{25}_4 1.6271.

Experimental Results.—The dielectric constants ϵ and the densities d of benzene or heptane solutions containing mole fraction c_2 of solute are given in Table I, the polarizations P_2 being listed in the last column. The polarization of the pure solvent is given as P_1. The measurements were carried out at 25° with the exception of those on a second set of solutions of phosphoryl chloride in benzene at 10, 40 and 60°, which agreed well with the results on the first set measured at 25°. Table II lists in the second column the values of MR_D, the molar refraction for the D sodium line, calculated for the colored sulfur monochloride and selenium monochloride as the sums of the atomic refractions given in the literature,[8] and for the other substances from the data in the present paper, the density of selenium oxychloride being taken from the literature.[9] A value obtained from the data of Lenher and Kao[7] for selenium monochloride is practically identical with that calculated for the corresponding sulfur compound and is, therefore, to be regarded as too

(5) Butler and Maass, THIS JOURNAL, **52**, 2184 (1930).

(6) Blanchard, Phelan and Davis, "Synthetic Inorganic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1936, p. 335.

(7) Lenher and Kao, THIS JOURNAL, **47**, 772 (1925); **48**, 1550 (1926).

(8) Eisenlohr, "Spektrochemie organischer Verbindungen," F. Enke, Stuttgart, 1912.

(9) Henby and Sugden, *J. Chem. Soc.*, 1058 (1929).

TABLE I

DIELECTRIC CONSTANTS, DENSITIES AND POLARIZATIONS

c_2	ϵ	d	P_2
Benzene–Hydrogen Disulfide (25°)			
0.00000	2.276	0.87344	(26.667 = P_1)
.04962	2.380	.88572	44.5
.10021	2.485	.89825	43.3
.14604	2.581	.90959	42.3
.19871	2.691	.92263	41.3
Benzene–Sulfur Monochloride (25°)			
.0580	2.509	.9218	76.6
.1097	2.711	.9624	73.6
.2415	3.256	1.0666	69.3
.3392	3.559	1.1382	64.2
Benzene–Selenium Monochloride (25°)			
.0760	2.838	1.0188	115
.1711	3.543	1.2060	102
.2596	4.251	1.3840	93.7
.3783	5.280	1.6218	85.8
Benzene–Selenium Oxychloride (25°)			
.00743	2.349	0.88158	165
.01265	2.400	.88730	163
.02013	2.474	.89550	160.8
.03467	2.616	.91144	156.0
.04380	2.706	.92145	153.5
Benzene–Thiophosphoryl Chloride (25°)			
.01815	2.324	.8888	73.1
.03091	2.362	.8998	73.3
.05691	2.432	.9219	71.6
.07938	2.499	.9418	70.9
.1175	2.603	.9741	69.9
.1698	2.749	1.0178	69.0
Heptane–Thiophosphoryl Chloride (25°)			
.00000	1.922	0.67944	(34.64 = P_1)
.02445	1.958	.6960	72.9
.04330	1.990	.7089	72.1
.07316	2.043	.7296	71.2
.1012	2.089	.7496	70.1
.1468	2.174	.7826	69.6
.1675	2.215	.7979	69.5
Benzene–Phosphoryl Chloride (25°)			
.00000	2.278	.87339	(26.693 = P_1)
.01937	2.433	.8893	140.9
.03925	2.599	.9056	139.0
.09528	3.087	.9514	132.3
.19205	3.994	1.0294	121.5

c_2.....	0	0.01950	0.03930	0.07046	0.09712	0.1961
t, °C.	ϵ					
10	2.309	2.473	2.655	2.941	3.198	4.201
40	2.242	2.390	2.545	2.794	3.012	3.877
60	2.199	2.330	2.470	2.698	2.890	3.669
	d					
10	0.88880	0.9044	0.9216	0.9475	0.9696	1.0511
40	.85693	.8728	.8888	.9138	.9352	1.0142
60	.83520	.8508	.8665	.8912	.9123	.9900
	P_1	P_2				
10	26.678	143.4	143.0	138.6	135.3	123.1
40	26.669	138.3	136.4	132.6	129.3	119.1
60	26.680	131.0	130.2	127.8	124.4	115.7

TABLE II

MOLAR REFRACTIONS, POLARIZATIONS AND DIPOLE MOMENTS

Substance	MR_D	P_∞	$\mu \times 10^{18}$
H_2S_2	17.64	45.8(25°)	1.17
S_2Cl_2	28	80.9(25°)	1.60
Se_2Cl_2	36	126(25°)	2.1
$SeOCl_2$	25.0	168(25°)	2.62
$POCl_3$	25.13	147.0(10°)	2.36
		143.4(25°)	2.39
		140.0(40°)	2.41
		133.4(60°)	2.42
		Mean value =	2.40
$PSCl_3$	32.8	74.3(25°)	1.41 (in benzene)
		74.4(25°)	1.41 (in heptane)

low. The difference of 7.9 in the two values makes a difference of only 0.09 in the moment values. The last two columns of Table II give the polarization P_∞ obtained by extrapolation to $c_2 = 0$ of the values of P_2 in Table I and the dipole moments.

Discussion of Results

The moment of diphenyl disulfide,[10] which is apparently an extended structure C_6H_5—S—S—C_6H_5, is 1.81. The C–S bond moment was calculated[1] on the reasonable assumption of an 112° C–S–C angle. If it is assumed that the greater separation of the attached groups in the disulfide prevents widening of the C–S–S angle by repulsion, this may be taken as 90°. Complete freedom of rotation around the S–S bond would then give a calculated moment[11] = 1.414 × 1.3 = 1.84 in excellent agreement with the observed 1.81. If the C–S–C angle used in calculating the bond moment were really less than 112° or if the C–S–S angle were much widened by repulsion, the calculated moment would be lower than the observed. It would appear, however, that the observed moment is consistent with the extended structure with all positions of rotation around the S–S bond equally probable. A 90° azimuthal angle as suggested in the case of hydrogen peroxide[12] would lead to the same calculated value.

An analogous extended structure, H–S–S–H, for hydrogen disulfide, which is indicated by the electron diffraction measurements made in this Laboratory,[13] leads to a calculated moment value 1.41 × the H–S bond moment 0.68, if the H–S–S valence angle is 90°, as seems highly probable, and if all positions of rotation around the S–S bond are equally probable or if the azimuthal angle is 90°. The value thus calculated 0.96 is 0.21 lower than the observed value 1.17, which cannot be more than 0.05 high because of neglect of atomic polarization. The discrepancy might arise from differences in the inductive effects in this molecule from those in the hydrogen sulfide molecule, from the moment of which the H–S bond moment is calculated. It would, however, be accounted for if the hydrogen disulfide contained a small proportion of Y-shaped molecules $H_2S^+ - S^-$, in which the large moment of the semipolar bond between the sulfur atoms could easily raise the mean moment to the observed value. It appears highly probable, however, that the largely predominant structure is H–S–S–H.

The problem of the structures of sulfur and selenium monochlorides is analogous to that of the disulfides. Raman spectra investigations have led Matossi and Aderhold[14] to ascribe a Y-shaped structure $SSCl_2$ to sulfur monochloride, while Morino and Mizushima[15] have concluded the structure to be Cl–S–S–Cl. Palmer's[16] electron diffraction measurements are interpreted as indicating an extended Cl–S–S–Cl structure. The dipole moment 1.0 found by Morino and Mizushima[15] for sulfur monochloride in heptane solution is much lower than the value 1.60 found here in benzene solution. If the bond moment value 0.5 calculated[1] from a somewhat doubtful moment value for SCl_2 but consistent with the sulfur and chlorine electronegativities is correct, the two chlorines would have to be on the same side of the extended structure of the molecule with a 90° Cl–S–S angle and a zero azimuthal angle to account for the moment value observed by Morino and Mizushima. Even this structure would fail to account for the much higher moment found in benzene solution. If the molecule had the bent Y-shaped or tetrahedral structure $^-S—^+SCl_2$, the large moment of the semipolar bond between the sulfurs should exceed the small opposing S–Cl moments by an amount sufficient to give a resultant moment, at least, as large as 1.6. The moment 1.6 found for thionyl chloride,[17] which has been shown by electron

(10) Bergmann and Tschudnowsky, *Z. physik. Chem.*, **17B**, 107 (1932).

(11) Smyth, Dornte and Wilson, THIS JOURNAL, **53**, 4242 (1931).

(12) Penney and Sutherland, *Trans. Faraday Soc.*, **30**, 898 (1934).

(13) Stevenson and Beach, THIS JOURNAL, **60**, 2872 (1938).

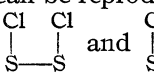
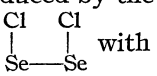
(14) Matossi and Aderhold, *Z. Physik*, **68**, 683 (1931).

(15) Morino and Mizushima, *Sci. Papers Inst. Phys. Chem. Research, Tokyo*, **32**, 220 (1937).

(16) Palmer, THIS JOURNAL, **60**, 2360 (1938).

(17) Smith, *Proc. Roy. Soc.*, London, **138**, 154 (1932).

diffraction[16] to have a similar bent Y-shaped or irregular tetrahedral structure is identical with that here found for S_2Cl_2, although the more accurate vapor value 1.44 found by Coop and Sutton[18] is slightly lower.

The moment of selenium monochloride is 0.5 higher than that of the corresponding sulfur compound and the moment of selenium oxychloride is 1.0 higher than that reported for thionyl chloride. An increase in moment is to be expected from the more positive character of selenium as compared to sulfur, but, as in the cases of other bonds involving atoms of considerable size,[19] the increase is greater than would be anticipated from the difference 0.1 in the electronegativities of the two elements.[1,20] If moments 1.1 and 1.55 are assigned to the S—Cl and Se—Cl bonds, respectively, the moments of the two monochlorides can be reproduced by the unbranched structures  and  with 90° sulfur or selenium valence angles and freedom of rotation around the S–S or Se–Se bond when the molecules are surrounded by benzene but with much reduced freedom when the molecules are in heptane, somewhat as observed in the case of the ethylene halides.[11,21] However, this necessitates the assumption of the incorrectness of the SCl_2 moment value from which the S–Cl moment was previously calculated and gives a value higher than those of the P–Cl and I–Cl bonds, than which it should be lower. Also, the Se–Cl value is closer to that of As–Cl, 1.6, than the electronegativity difference 0.4 between Se and As would lead one to expect. If the Cl–S–S angle in S_2Cl_2 were 103° as reported by Palmer[16] instead of 90° as roughly assumed here, a still higher value would have to be assigned to the S–Cl moment. The moments of the monochlorides can be accounted for without the assumption of these seemingly too high bond moments if the molecules have the branched structures with semipolar bonds or if the substances, under the conditions of measurement, contained a considerable proportion of the branched molecules. The coexistence of the extended and the branched structures would thus be consistent with the moments observed for hydrogen disulfide as well as for the two monochlorides. If this is the correct explanation of the moments, a moment of about 0.8 is to be assigned to the Se–Cl bond.

Coop and Sutton[18] have used the moments of thionyl chloride 1.44 and sulfuryl chloride 1.795 together with the assumption of tetrahedral structures to calculate approximate moment values, 0.61 for the S–Cl bond and 2.16 for the S–O bond. Use of the bond moment 0.5 for S–Cl together with the valence angles of the somewhat distorted tetrahedral structures reported by Palmer[16] for these two molecules gives an S–O value 1.64 in thionyl chloride and 2.36 in sulfuryl chloride. All of these values are lower than the value 2.5 for S–O calculated by Coop and Sutton from the moments of dimethylsulfone and dimethyl sulfide, but are not far from the S–O bond values calculated previously by one of the writers[1] from earlier values of the moments of these compounds. In this previous work the moment of the semipolar $S^+—O^-$ bond was concluded to be about 3.0, of the magnitude usually found for semipolar bonds. While the discrepancies in the values calculated above arise in part from uncertainties in the valence angles used, it appears fairly certain that the S—O bond moment in thionyl chloride is lower than the usual semipolar $S^+—O^-$ moment. Palmer attributes the abnormally short S–O bond distance found in these compounds to contributions from triply-bonded structures. The contributions from such structures as $^-S\equiv{}^+O$ would, of course, oppose the normal bond moment and reduce the value observed for it. Lister and Sutton[22] regard the bond as predominantly double in character, which would involve a moment lower than that of a semipolar bond. In either case, a moment lower than that of the usual hybridized semipolar bond is to be expected.

If it is assumed that the valence angles in selenium oxychloride are identical with those in thionyl chloride and the Se–Cl moment is taken as 0.8, the Se–O moment obtained is 2.95. Raising of the Se–Cl value to 1.5 would increase the Se–O value obtained only to 3.04. The Se–O bond value 3.0 thus obtained is typical of the somewhat hybridized semipolar bond. The more positive character of the selenium evidently reduces the contributions from the doubly-bonded and the much less probable triply-bonded structures.

(18) Coop and Sutton, *Trans. Faraday Soc.*, **35**, 505 (1939).

(19) Smyth, Grossman and Ginsburg, THIS JOURNAL **62**, 192 (1940).

(20) Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1939, p. 64.

(21) Stearn and Smyth, THIS JOURNAL, **56**, 1667 (1934).

(22) Lister and Sutton, *Trans. Faraday Soc.*, **35**, 495 (1939).

The data on phosphoryl chloride and thiophosphoryl chloride have already been used[1] to calculate the moments of the semipolar $P^+—O^-$ and $P^+—S^-$ bonds. As each of these bonds lies in the axis of symmetry of its molecule[23,24] with its moment acting in the opposite direction to the resultant of the three P–Cl bond moments, the semipolar bond moment was calculated by adding the moment of the PCl_3 molecule 1.1 to the moment observed for the whole molecule. A slight revision of the data on thiophosphoryl chloride raises the $P^+—S^-$ moment value from 2.4 to 2.5, the $P^+—O^-$ value 3.5 remaining unchanged. It was recognized that, as usual in the case of such bonds, neither of these was a pure semipolar bond as other resonating forms, particularly double-bonded structures, contributed to the structures of the molecules. The difference 1.0 between the $P^+—S^-$ and $P^+—O^-$ bonds appears surprisingly large, especially in view of the fact that the C=S bond moment is greater by 0.3 than the C=O moment.[1] Coop and Sutton[18] suggest that their low value for thiophosgene 0.28 as compared to 1.18 for phosgene[25] may be due to the inductive effects of the two C–Cl moments upon the very polarizable sulfur. In $PSCl_3$, the three P–Cl dipoles are farther from the S than are the two C–Cl dipoles in $CSCl_2$, but there are three of them instead of two. It appears quite reasonable, therefore, to attribute the lower moment value obtained for the $P^+—S^-$ bond as compared to the $P^+—O^-$ bond less to any inherent structural difference or even to the lower electronegativity of sulfur as compared to oxygen, than to the greater opposing moments induced by the P–Cl dipoles in the sulfur atom, which is much more polarizable than the oxygen.[26] The inherent moment of the $P^+—S^-$ bond is presumably not appreciably different from that of the $P^+—O^-$, the two lying in the neighborhood of 3.5, where most of the more or less hybrid semipolar bonds seem to lie.

(23) Brockway and Beach, THIS JOURNAL, **60**, 1836 (1938).
(24) Beach and Stevenson, *J. Chem. Phys.*, **6**, 75 (1938).
(25) Smyth and McAlpine, THIS JOURNAL, **56**, 1697 (1934).

Summary

The dielectric constants and densities of solutions of hydrogen disulfide, sulfur monochloride, selenium monochloride, selenium oxychloride, phosphoryl chloride and thiophosphoryl chloride in benzene or heptane have been measured and used to calculate the dipole moments of the molecules of the solutes.

The hydrogen disulfide moment may be explained by an extended structure H–S–S–H, but may be best explained if the substance contains also a small proportion of branched molecules H_2S–S. The sulfur monochloride and selenium monochloride moments may be explained with difficulty by extended structures, Cl–S–S–Cl and Cl–Se–Se–Cl, but correspond better to branched structures, S–SCl_2 and Se–$SeCl_2$, in the form of an irregular tetrahedron like that of $SOCl_2$ and $SeOCl_2$, or to a mixture of the extended and the branched structures.

The value 3.0 is calculated for the moment of the Se–O bond in selenium oxychloride which has more polar character than the S–O bond in thionyl chloride. The moments of phosphoryl chloride and thiophosphoryl chloride have been used to calculate the values 3.5 and 2.5 for the moments of the semipolar bonds $P^+—O^-$ and $P^+—S^-$, the latter of which is lowered more than the former by induction.

PRINCETON, NEW JERSEY RECEIVED MARCH 7, 1940

(26) Smyth, *Phil. Mag.*, **50**, 361 (1925).

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

The Thermodynamics of *n*-Heptane and 2,2,4-Trimethylpentane, Including Heat Capacities, Heats of Fusion and Vaporization and Entropies

BY KENNETH S. PITZER

Thermodynamic functions for the saturated hydrocarbons through the butanes and tetramethylmethane were given by the writer in 1937.[1] More recent experimental work[2] has confirmed the general scheme used at that time, and the numerical values there listed within their respective limits of error. This paper represents the beginning of an attempt to extend this work through the octanes. The researches of Parks and co-workers[3] have included most of the hydrocarbons in this range; however, their entropies are based on long extrapolations of the heat capacity curve from 90°K. Thus, while accurate enough for their original purpose, these data are of doubtful value for the more precise work now at hand. It would be nice if lower temperature measurements on a few compounds should confirm the accuracy of Parks' extrapolations. The results presented below tend to support this hope for the normal paraffins but indicate that the branched chain compounds may deviate by large amounts.

Apparatus.—The calorimeter used for the condensed phases already has been described.[4] A calorimeter, somewhat similar to the one described by Bennewitz and Rossner[5] was used to measure the heats of vaporization. Data also were obtained on the heat capacity of the vapors. However, since work is continuing on certain aspects of the design and operation of the heat capacity calorimeter, a detailed description seems hardly worthwhile at present.

The parts used for heat of vaporization measurements may be described briefly as comprising a dewar with electrical heater inside in which the liquid is vaporized, and a condenser system in which the amount vaporized in a given time can be measured accurately. The dewar is rather tall and narrow (40 cm. long by 4.2 cm. diameter) with the heater near the bottom. During measurements a considerable height of liquid is present above the heater, tending to bring the vapor temperature to equilibrium and to prevent heat loss through the lead-in wires. The heater has a resistance of about 30 ohms and the lead wires are of no. 18 copper. A White potentiometer is used for measuring the heating energy, readings being taken across a 0.01-ohm standard resistance for the current, and across a suitable volt box for the potential. The error of these measurements is much less than 0.1%. The batteries supplying the heating current are steady within about 0.1% for the period of a measurement, which ranges from ten minutes to nearly an hour. The vaporizer dewar is jacketed with a bath of boiling liquid so as to maintain a temperature a few tenths of a degree higher outside than inside. The heat leak through the dewar is usually insignificant under these conditions, which further assure that no reflux can occur in the tube carrying vapor from the dewar. This tube of course passes through the jacket.

After leaving the vaporizer the gas passes through the specific heat calorimeter and then goes to the condensers. These comprise first a permanent condenser and reservoir and second a removable sample bulb. The latter is immersed in cold water, and the gas is condensed in a small tube before entering the bottom of the bulb. A second connection equalizes the pressure between the sample bulb and the reservoir so that practically no disturbance occurs when a change is made from one to the other. The sample bulb is connected with ground glass joints and has stopcocks on both openings.

A heat of vaporization measurement involves the following operations: 1. The jacket around the vaporizing dewar is adjusted to the proper temperature. 2. The current in the vaporizing heater is started and adjusted. 3. When a steady state has been attained, the flow is turned into the sample bulb for an accurately timed interval. 4. During this interval numerous precise readings are taken on the heater current and potential.

As a check on the accuracy of this calorimeter the heat of vaporization of water was measured. Three runs at different rates of heating gave 9730, 9740 and 9720 cal. per mole. In a recent paper Osborne, Stimson and Ginnings[6] report 9723 cal. per mole at the boiling point. The agreement is thus perfect, considering the experimental error of the present work.

Materials.—The 2,2,4-trimethylpentane had been recovered from other experiments in this University. The boiling point was remarkably constant and the heat capacity immediately below the melting point indicated less than 0.01% of solid insoluble, liquid soluble impurity. The *n*-heptane was obtained from the Eastman Kodak Co. After two fractionations its premelting heat capacity indicated 0.15% impurity. This impurity cannot have any large effect on the results reported below, and very probably is of no consequence at all. The melting point and heat of fusion were appropriately corrected assuming Raoult's law.

(1) Pitzer, *J. Chem. Phys.*, **5**, 473, 752 (1937).

(2) Kemp and Egan, THIS JOURNAL, **60**, 1521 (1938); Kistiakowsky and Nazmi, *J. Chem. Phys.*, **6**, 18 (1938); Kistiakowsky, Lacher and Ransom, *ibid.*, **6**, 900 (1938); Kistiakowsky and Rice, *ibid.*, **7**, 281 (1939); Kistiakowsky, Lacher and Stitt, *ibid.*, **7**, 289 (1939).

(3) Parks, Huffman and Thomas, THIS JOURNAL, **52**, 1032, 3241 (1930); Parks and Huffman, *ibid.*, **52**, 4381 (1930); Parks, Huffman and Barmore, *ibid.*, **53**, 3876 (1931).

(4) Latimer and Greensfelder, *ibid.*, **50**, 2202 (1928); Pitzer and Coulter, *ibid.*, **60**, 1310 (1938).

(5) Bennewitz and Rossner, *Z. physik. Chem.*, **B39**, 126 (1938).

(6) Osborne, Stimson and Ginnings, *J. Research Natl. Bur. Standards*, **23**, 197 (1939).

Melting and Boiling Points.—Since precise measurements of these physical constants have been reported by several workers, no attempt was made to obtain exact values in the course of this work. Approximate values were observed which are in agreement within 0.1° or less in each case. We shall adopt the results obtained by Smith and Matheson[7] and by Brooks,[8] which are for *n*-heptane, m. p. 182.52° and b. p. 371.51°, and for 2,2,4-trimethylpentane, m. p. 165.79° and b. p. 372.33°K. (273.10°K. = 0°C.).

TABLE I

THE MOLAL HEAT CAPACITY OF *n*-HEPTANE

$CH_3(CH_2)_5CH_3$ mol. wt. 100.19

T, °K.	C_p, cal./deg.	*T*, °K.	C_p, cal./deg.
15.14	1.500	79.18	18.53
17.52	2.110	86.56	19.83
19.74	2.730	96.20	21.58
21.80	3.403	106.25	23.22
24.00	4.122	118.55	25.09
26.68	4.935	134.28	27.15
30.44	6.078	151.11	29.54
34.34	7.370	167.38	31.96
38.43	8.731	Melting point	
42.96	10.02	194.60	48.07
47.87	11.36	218.73	48.49
53.18	12.80	243.25	49.77
58.96	14.27	268.40	51.71
65.25	15.69	296.51	53.68
71.86	17.04	317.65	55.72

TABLE II

THE MOLAL HEAT CAPACITY OF 2,2,4-TRIMETHYLPENTANE

(Iso-octane) $(CH_3)_3CCH_2CH(CH_3)_2$ mol. wt. 114.22

T, °K.	C_p, cal./deg.	*T*, °K.	C_p, cal./deg.
14.37	1.967	89.75	20.99
15.70	2.421	100.66	23.37
17.24	2.968	109.68	25.30
19.51	3.806	119.54	27.42
22.09	4.870	130.00	29.58
24.95	5.916	141.42	31.91
28.35	7.002	152.94	34.19
32.28	8.171	160.69	35.92
36.23	9.418	Melting point	
40.19	10.44	171.15	44.58
44.34	11.36	182.89	45.43
49.42	12.49	203.80	47.15
55.01	13.68	233.44	50.06
60.77	14.94	256.60	52.50
66.87	16.09	279.95	54.97
74.05	17.56	301.93	57.60
81.81	19.24	317.34	59.40

Solid and Liquid Heat Capacities.—The heat capacities were measured by the usual methods and are reported in Tables I and II. The unit is the defined calorie, equal to 4.1833 Int. joules, which is used throughout this paper. Above 90°K. the heat capacities of both substances were measured by Parks, Huffman and Thomas.[3] The agreement is reasonably satisfactory, and is better at the lower temperatures than near room temperature. The largest differences are about 1%, the values of Parks being lower in these cases. Over considerable regions the agreement is within 0.2%, which is approximately the accuracy claimed for the present investigation. The points at the highest and lowest temperatures are somewhat more uncertain than the others.

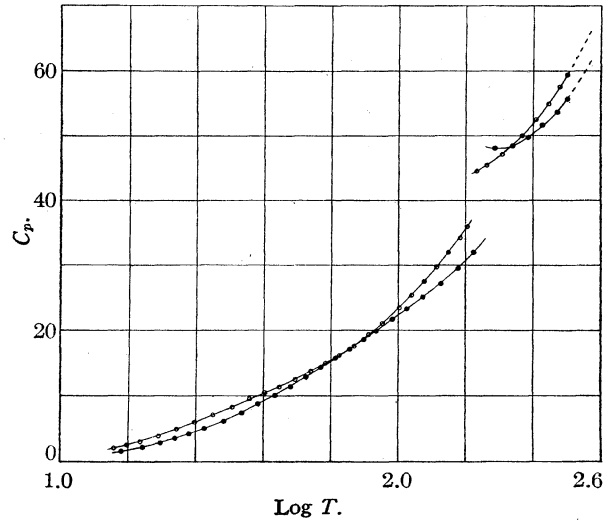


Fig. 1.—The molal heat capacity of solid and liquid *n*-heptane (solid circles) and 2,2,4-trimethylpentane (open circles) in cal. per degree.

Figure 1 shows the two heat capacity curves graphically. Although the two substances never differ very greatly, the curves are by no means parallel. In particular, at 90°K. (log T = 1.95) where Parks began measurements, the heat capacities are almost equal and the 2,2,4-trimethylpentane has the greater slope. Thus almost any reasonable extrapolation would have the curves cross, and give the heptane the larger entropy at 90°K. However, this is not correct, and it illustrates the danger of heat capacity extrapolations from such a high temperature.

Heats of Fusion.—Table III presents the heat of fusion results. The agreement between the individual results is remarkable, particularly when one considers that the temperature intervals and rates of heating were varied considerably. The

(7) Smith and Matheson, *Natl. Bur. Standards J. Research*, **20**, 641 (1938).

(8) Brooks, *ibid.*, **21**, 847 (1938); for earlier work see Egloff, "Physical Constants of Hydrocarbons," Reinhold Pub. Corp., New York, N. Y., 1939.

TABLE III

THE HEATS OF FUSION OF *n*-HEPTANE AND 2,2,4-TRIMETHYLPENTANE

Temperature interval, °K.	Time of energy imput, min.	$\Delta H°_{\text{Fusion}}$, cal./mole deg.
n-Heptane, m. p. = 182.52°K.		
175.80–184.24	24	3356.0
173.95–184.61	20	3355.6
	Average	3355.8 ± 4
(Parks, Huffman and Thomas[3] 3385)		
2,2,4-Trimethylpentane, m. p. = 165.79		
163.13–168.45	22	2201.7
162.93–168.36	33	2201.4
	Average	2201.6 ± 2
(Parks, Huffman and Thomas[3] 2160)		

uncertainties given are based on estimates of the various constant errors.

It is quite possible that the heats of fusion reported by Parks, Huffman and Thomas[3] are calorimetrically in better agreement than would appear from Table III. The differences may arise from their treatment of the premelting heat for the less pure samples that they had available. The lack of any appreciable impurity precludes such an error in the 2,2,4-trimethylpentane value from this research. If Raoult's law is not even approximately followed the *n*-heptane result may be in error by somewhat more than the uncertainty listed. Any error of this nature will, however, be approximately compensated in the heat capacities just below the melting point and therefore does not appreciably affect the final entropy value.

TABLE IV

THE HEATS OF VAPORIZATION OF *n*-HEPTANE AND 2,2,4-TRIMETHYLPENTANE

Average $E \times I$ for heater, watts	Rate of flow, moles per min.	$\Delta H°$ vap. cal. per mole
n-Heptane, b. p. = 371.51°K.		
14.80	0.02776	7650
7.81	0.01458	7680
This research, weighted average		7660 ± 20
Mathews[9]		7649
Bennewitz and Rossner[5]		7850
2,2,4-Trimethylpentane, b. p. = 372.33°K.		
15.01	0.02899	7420
14.89	.02886	7410
9.96	.01936	7380
6.06	.01166	7450
	Weighted average	7410 ± 20

Heats of Vaporization.—The apparatus and procedure in measuring heats of vaporization were described above, where the check measurements with water were also mentioned. The results for the hydrocarbons are given in Table IV, together with those from other observers. The result for *n*-heptane reported by Mathews[9] is in excellent agreement with the value obtained in this research. Bennewitz and Rossner's result differs, however, by about 3%.

Smith and Matheson[7] have reported accurate vapor pressure–temperature curves for both of these substances. If the true molal volumes of the saturated vapors were known, good heats of vaporization could be calculated. Careful measurements of these volumes were carried out, using the Dumas method. While these results were not as accurate as the calorimetric values, they agree within the 1% uncertainty to be assigned to the former. The volumes at the boiling points for both substances are approximately 4.5% lower than would be calculated from the perfect gas law.

Gas Heat Capacities.—Measurements of the heat capacity of these hydrocarbons as gases were made in connection with the heat of vaporization work. The calorimeter was mentioned above, but, as was stated there, a complete description will be postponed until developments now in progress have been more nearly completed. The present results are to be regarded as less accurate than results to be obtained in the near future. The values obtained are for 423°K. except in the case of steam which was measured at 432°K. All are at a constant pressure of one atmosphere. The results are: for H_2O, 8.4; for CCl_4, 22.7; for *n*-heptane, 53.9; and for 2,2,4-trimethylpentane, 61.6 cal. per degree per mole.

From the work of Gordon,[10] Wilson,[11] and Keyes and co-workers,[12] one may calculate an accurate heat capacity for steam to compare with that obtained in this work. The value obtained is 8.49 cal. per degree. For carbon tetrachloride a complete calculation is not possible, but using the approximate (rigid rotator–harmonic oscillator) spectroscopic calculations of Vold[13] and assuming the Berthelot equation of state one obtains 22.5 cal. per degree. The true value would be expected to be a little larger. The agreement on the two "knowns" is thus to within about 1%. Probably the values for the hydrocarbons are not in error

(9) Mathews, THIS JOURNAL, **48**, 562 (1926).

(10) Gordon, *J. Chem. Phys.*, **2**, 65 (1934).

(11) Wilson, *ibid.*, **4**, 526 (1936).

(12) Collins and Keyes, *Proc. Am. Acad. Arts and Sci.*, **72**, 283 (1938); and earlier papers.

(13) Vold, THIS JOURNAL, **57**, 1192 (1935).

by much more than this amount. The value for *n*-heptane (45.1 cal. per degree at 410°K.) reported by Bennewitz and Rossner[5] seems definitely too low.

For thermodynamic calculations it would be desirable at least to estimate the temperature variation of the heat capacity. On the basis of statistical calculations to be published soon, the following equations are suggested. They should not err grossly in the range 300–600°K.

$$n\text{-heptane};\ C_p = -235.0 + 110 \log T$$
$$2,2,4\text{-Trimethylpentane};\ C_p = -227.3 + 110 \log T$$

It is suggested that these equations be used in preference to constant heat capacities for these gases until accurate data are available. They agree with the experiments at 423°K., of course.

TABLE V

THE MOLAL ENTROPY OF *n*-HEPTANE

0–15.14°K.	Debye extrapolation	0.535 cal./deg.
15.14–182.52	Graphical–solid	35.186
182.52	Fusion (3355.8/182.52)	18.386
182.52–298.10	Graphical–liquid	24.488
	Entropy at 298.10°K. (liquid)	78.60 ± 0.2
298.10–371.51	Graphical–liquid	12.55
371.51	Vaporization (7660/371.51)	20.62
	Entropy at 371.51°K. (gas)	111.77 ± 0.3

TABLE VI

THE MOLAL ENTROPY OF 2,2,4-TRIMETHYLPENTANE

0–14.13°K.	Debye extrapolation	0.683
14.13–165.79	Graphical–solid	35.309
165.79	Fusion (2201.6/165.79)	13.279
165.79–298.10	Graphical–liquid	29.132
	Entropy at 298.10°K. (liquid)	78.40 ± 0.2
298.10–372.33	Graphical–liquid	13.75
372.33	Vaporization (7410/372.33)	19.90
	Entropy at 372.33°K. (gas)	112.05 ± 0.3

Entropies.—The entropy calculations are summarized in Tables V and VI. The Debye extrapolations are for six degrees of freedom to include torsional as well as compressional waves in the crystal, and to obtain better agreement with the first few experimental points.[14] All the other contributions are based on experimental data of this research except for short ranges of the liquids just below their boiling points. These regions are shown dotted in Fig. 1. The uncertainty from this source can hardly be very large considering the regularity of heat capacity curves for liquid substances of this type.

(14) See Lord, Ahlberg and Andrews, *J. Chem. Phys.*, **5**, 649 (1937), for a fuller discussion of this matter.

It already has been mentioned that any reasonable extrapolation method starting from 90°K. cannot give the correct answer for both of these compounds. Thus the results of Parks, Huffman, and Thomas[3] can at best agree in only one case. Actually their *n*-heptane value agrees very well (78.9 cal. per degree at 298.1°K.) while their result for 2,2,4-trimethylpentane is too small (75.2 cal. per degree at 298.1°K.). When one considers that the crystals of all normal paraffins must be very similar it seems likely that a method of extrapolation from 90°K. may have a fair accuracy for this limited group of compounds. Since Parks' original[15] values for *n*-butane and *n*-heptane appear to be nearly correct,[16] the corresponding values for other normal paraffins can be used with some confidence. On the other hand it seems that crystals of branch chain compounds will possess no such similarity and that in consequence entropies based on long extrapolations may be considerably in error in these cases.

Statistical calculations in terms of molecular structure data will be presented elsewhere. It suffices to say here that these experimental entropies and gas heat capacities are consistent with internal rotation potential barriers of the same order of magnitude as have been found for simpler molecules.[1]

Summary

The thermal behavior of *n*-heptane and of 2,2,4-trimethylpentane has been investigated from 15 to 423°K. for which range heat capacities of the solid, liquid or gas are given. The following heats of fusion and vaporization were obtained: *n*-heptane, 3355.8 ± 4 and 7660 ± 20; 2,2,4-trimethylpentane, 2201.6 ± 2, 7410 ± 20 cal. per mole. The entropies were calculated for the liquid at 298.1°K. and for the gas at the boiling point respectively to be: *n*-heptane 78.60 ± 0.2 and 111.77 ± 0.3 and 2,2,4-trimethylpentane 78.40 ± 0.2 and 112.05 ± 0.3. A discussion of these results in terms of statistically calculated entropies will be presented elsewhere.

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(15) Those given in ref. 3 not the revised values given or suggested by Parks, Shomate, Kennedy and Crawford, *ibid.*, **5**, 359 (1937).

(16) For *n*-butane at its b. p. Parks obtained originally 72.5 but revision of his entropy of vaporization data will lower this a few tenths. Aston (personal communication) has recently obtained 72.0 cal. per degree.

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, POMONA COLLEGE]

The Configuration of Some Cupric, Nickelous and Cobaltous Complexes by Means of Magnetic Measurements

BY G. N. TYSON, JR., AND S. C. ADAMS

A large number of organo-metallic compounds, in which a transition metal is found in the quadricovalent state, have been prepared. In particular, the preparation of organic complexes of several metals was described by Zetzsche and co-workers,[1] and more recently by Pfeiffer and colleagues.[2] The compounds cupric, nickelous, and cobaltous disalicylaldehyde have been synthesized for this study, as well as the disalicylaldimine complexes of divalent copper and nickel. The magnetic susceptibilities of these complexes have been determined, and on the basis of these results alone, except in the case of the cupric compounds, the most probable configurations have been assigned to the molecules.

Experimental

Synthesis.—The cupric (I), nickelous (II), and cobaltous (III) disalicylaldehydes were prepared by treating approximately half saturated solutions of J. T. Baker Co. C. P. metal acetate salts in 50% alcohol with the stoichiometric amounts of carefully purified salicylaldehyde. The reactants were thoroughly mixed and allowed to stand at room temperature until the reactions were complete. The precipitated products were filtered, washed successively with water, alcohol and ether, and finally dried in a vacuum desiccator over concentrated sulfuric acid.

The cupric (IV) and nickelous (V) disalicylaldimines were prepared by suspending the corresponding disalicylaldehyde compounds in 10% solutions of aqueous ammonia and stirring vigorously until the reactions were completed. A definite color change indicated the completeness of the reaction in both cases. It has not been found possible to prepare the cobaltous disalicylaldimine compound by this method. The purification of the two salicylaldimine compounds was effected by the method as given above for the salicylaldehyde complexes.

Analytical Results.—Analyses for metal, carbon, hydrogen, and nitrogen, using standard electrolytic deposition methods for the metals, and standard micro and semi-micro methods for C, H, and N, gave the results listed in Table I.

All of the compounds were sparingly soluble in water, ether, and alcohol, and slightly soluble in solvents such as chloroform and carbon tetrachloride. No definite melting points were shown, but all compounds slowly decomposed when heated above 100°.

TABLE I

Cpd.	Metal, % Calcd.	Metal, % Found	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found	Color
I	20.79	20.10	55.00	55.35	3.74	3.43			Green
II[a]	17.42	17.53	49.90	49.30	4.17	4.26			Light green
III[a]	17.47	17.59	49.86	49.30	4.18	4.32			Orange
IV	20.92	21.12	55.34	55.28	3.98	3.97	9.22	9.16	Green
V	19.63	19.70	56.93	56.81	4.05	4.05	9.37	9.30	Orange

[a] Calculated percentages based on two molecules of water of crystallization.

Magnetic Measurements.—The results of magnetic measurements on the solid crystals by the Gouy method are shown in Table II. In the column listing the Bohr magnetons, the calculations have been made assuming complete quenching of the orbital contribution to the magnetic moment. In the conversion of the experimental data into Bohr magnetons, a correction has been made for the diamagnetism of the non-metal portion of the molecule.

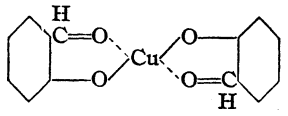
TABLE II

Cpd.	$X_s \times 10^6$	$X_m \times 10^6$	Temp., °C.	Bohr magnetons Exptl.	Bohr magnetons Calcd.	Unpaired electrons present
I	4.11	1256	22	1.9	1.73	1
II	11.43	3851	23	3.1	2.83	2
III	24.26	8180	23	4.5	3.88	3
IV	4.14	1236	20	1.9	1.73	1
V	Diamagnetic					0

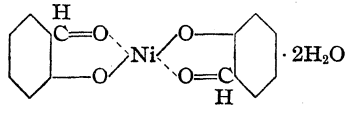
Discussion.—It is seen from Table II that the cupric disalicylaldehyde compound (I) exhibits a magnetic moment close to the theoretical value of 1.73 Bohr magnetons for one unpaired electron. However, from this datum it is not possible to decide whether the molecule is tetrahedral (sp^3 bonds) or coplanar (dsp^2 bonds) as the unpaired electron can occupy a $3d$ or $4p$ orbital. Cox and Webster,[3] in a study of analogous quadricovalent cupric complexes of β-diketones, have found a planar configuration by means of X-ray analysis. This result is in accord with the theoretical prediction of the greater strength of the planar bonds.[4] Accordingly, compound (I)

(1) Zetzsche, Silbermann and Vieli, *Helv. Chim. Acta*, **8**, 569 (1925).
(2) Pfeiffer, *et al.*, *Ann.*, **84**, 503 (1933).
(3) Cox and Webster, *J. Chem. Soc.*, 731 (1935).
(4) Pauling, "The Nature of the Chemical Bond," Cornell University Press., Ithaca, New York, 1939, p. 100.

is considered to have a planar configuration, and the formula is written as

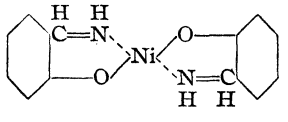


From Table II it is seen that the nickelous disalicylaldehyde compound (II) has a magnetic moment corresponding approximately to that given by two unpaired electrons. The twenty-six electrons of the nickel are in the $1s2s2p^3 3s3p^33d^3$ orbitals as completed pairs, while the two remaining $3d$ orbitals each contain an unpaired electron to account for the observed magnetic moment. The quadricovalent bonding should therefore occur in the $4s$ and three $4p$ orbitals, with the formation of the tetrahedral configuration. Thus, tetrahedral nickelous disalicylaldehyde (II) is written



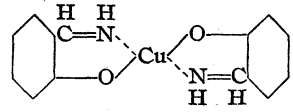
The formation of a planar configuration for this compound is also a reasonable interpretation of the data. It is possible that an unpaired electron might occupy a $4p$ in place of a $3d$ orbital, as previously noted in the copper compound. There would then be available a $3d$, $4s$, and two $4p$ orbitals for bond formation, and the planar configuration is seen to be possible.

The nickelous disalicylaldimine compound (V) is found to be diamagnetic, indicating the formation of the planar (dsp^2 bonds) configuration. It is assumed that the electrons in the two $3d$ orbitals have paired, leaving one $3d$ orbital available for bond formation together with the $4s$ and two of the $4p$ orbitals. Thus, the planar compound (V) is written

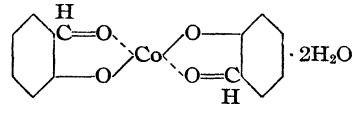


It is interesting to note that in the case of the nickelous compounds, the formation of the disalicylaldimine from the disalicylaldehyde results in the change of the probable tetrahedral configuration of the aldehyde complex to a planar structure in the aldimine compound. A marked color change also is noted, as shown in Table I.

The same reasoning is applied to cupric salicylaldimine (IV) as in the case of cupric salicylaldehyde (I). A magnetic moment corresponding to one unpaired electron is also given by (IV), so that until evidence to the contrary is obtained, the configuration of this molecule is to be considered as planar. The structural formula is



It is assumed that the twenty-five electrons in the cobalt of the cobaltous disalicylaldehyde have the electronic configuration of electron pairs in the $1s2s2p^33s3p^33d^2$ orbitals, and one unpaired electron in each of the three remaining $3d$ orbitals. The quadricovalent bonding of the cobalt would then use the $4s$ and three $4p$ orbitals, resulting in a tetrahedral configuration. Thus cobaltous disalicylaldehyde is considered to be tetrahedral, and the formula is written as



The possibility of this compound having a planar configuration must be considered as in the case of the nickel disalicylaldehyde discussed previously.

An attempt is currently being made to correlate the colors shown by these compounds, together with additional complexes of the transitional elements to be obtained, with the configuration of the molecules.[5]

Acknowledgment.—The authors desire to thank Professor Linus Pauling of the California Institute of Technology for the use of the magnetic equipment for preliminary measurements of these compounds.

Summary

From magnetic measurements made on the salicylaldehyde complexes of copper, nickel and cobalt, and the salicylaldimine complexes of copper and nickel (the synthesis and analysis of which have been given), it has been possible to assign the following configurations to the compounds: (1) cobaltous and nickelous disalicylaldehyde probably have tetrahedral configurations; (2) nickelous disalicylaldimine has a planar configuration; (3) cupric disalicylaldehyde and cupric disalicylaldimine are probably both planar in configuration.

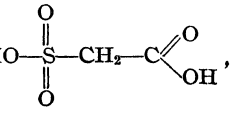
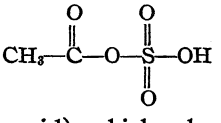
CLAREMONT, CALIF. RECEIVED FEBRUARY 13, 1940

(5) Lifschitz, *et al.*, *Z. anorg. allgem. Chem.*, **242**, Part 2, 97 (1939).

[COMMUNICATION NO. 682 FROM THE KODAK RESEARCH LABORATORIES]

The Rates of Formation of Sulfoaliphatic Acids*

BY T. F. MURRAY, JR., AND W. O. KENYON

Anhydrides of aliphatic acids are in common use as acylating agents, often in conjunction with sulfuric acid as the catalyst. Little attention apparently has been given to the fate of sulfuric acid when employed as an acylation catalyst, though Franchimont[1] as early as 1881 showed that sulfoacetic acid,  , forms when acetic anhydride and sulfuric acid react. He suggested that the reaction mechanism involved the primary formation of a mixed anhydride of sulfuric and acetic acids, 

(sometimes called acetyl sulfuric acid), which subsequently rearranges to the sulfo-acid. Anhydrides of aliphatic acids of three or more carbon atoms produce α-sulfo-acids by this method,[1] which have been resolved into their optical isomers.[2]

alpha-Sulfoaliphatic acids have been produced by other methods including the action of sulfur trioxide[3] or chlorosulfonic acid[4] on aliphatic acids, the oxidation of isethionic acid with chromic acid,[5] the action of alkali sulfites on the α-halogen acids,[6] the reaction of acetyl chloride with silver sulfate,[7] and the reaction of potassium or ammonium bisulfite with crotonic acid to form α-sulfobutyric acid.[8]

Russell and Cameron[9] have studied the acidity of sulfuric acid in mixtures of acetic anhydride with acetic acid and conclude that acetic anhydride and sulfuric acid react to form an ultra-acidic mixed anhydride which undergoes rearrangement to form sulfoacetic acid, which does not show ultra-acidic behavior. Beer[10] has suggested the formation of a compound designated as "diacetylium sulfate" from which the mixed anhydride of acetic and sulfuric acid can be formed.

In the work of Franchimont,[1] molar ratios of sulfuric acid to acetic anhydride of one to one and one to two were employed and the resulting exothermic reactions were vigorous. In view of the common use of sulfuric acid as a catalyst, it appeared of interest to determine whether sulfuric acid also reacted with anhydrides under the general conditions of esterification reactions and, if so, to ascertain the rate. In these experiments, the reaction of sulfuric acid with acetic, propionic and *n*-butyric anhydrides at various concentrations in the corresponding acids was followed, using low sulfuric acid/anhydride ratios.

Experimental

The aliphatic anhydrides were obtained by distilling C. P. grades and utilizing the following fractions: acetic anhydride 138 to 140°, propionic anhydride 166 to 168°, *n*-butyric anhydride 76 to 78° at 11 mm. Chemically pure grades of the aliphatic acids were employed as the diluents.

Specially designed reaction flasks of the Erlenmeyer type with glass-stoppered side arms through which samples could be removed periodically were used. The flasks were closed with glass stoppers carrying glass bearings through which glass stirrers were introduced. A reaction temperature of 40 ± 0.1° was chosen in order that the reactions would run practically to completion within convenient times.

Stock solutions of sulfuric acid were prepared by diluting 12.5 cc. of 95% sulfuric acid to 250 cc. with the aliphatic acid corresponding to the anhydride to be studied. These were kept in glass-stoppered flasks in the constant temperature bath. Twenty-five cc. portions of the sulfuric acid–aliphatic acid solutions were added to mixtures of calculated amounts of the aliphatic anhydrides and the additional amounts of the aliphatic acids required to produce the desired anhydride concentrations as shown in Table I. The aliphatic acid–aliphatic anhydride mixtures were brought to a temperature of 40° before the sulfuric acid solution was added.

TABLE I

Sulfuric acid–aliphatic acid mixture, cc.	Aliphatic acid, cc.	Aliphatic anhydride, cc.	Designation % anhydride
25	0	225	90
25	37.5	187.5	75
25	100	125	50
25	162.5	62.5	25

* Presented in part before the Division of Physical and Inorganic Chemistry at the Milwaukee Meeting of the American Chemical Society, September 5–9, 1938.

(1) Franchimont, *Compt. rend.*, **92**, 1054 (1881); *Rec. Trav. Chim.*, **7**, 27 (1888).

(2) Franchimont and Backer, *Akad. Amsterdam Versl.*, **23**, I, 648 (1914); *Chem. Zentr.*, **85**, II, 1391 (1914).

(3) Melsens, *Ann.*, **52**, 276 (1844).

(4) Baumstark, *ibid.*, **140**, 81 (1866).

(5) Carl, *Ber.*, **14**, 64 (1881).

(6) Collmann, *Ann.*, **148**, 109 (1868); Hemilian, *ibid.*, **168**, 145 (1873).

(7) Kammerer and Carius, *ibid.*, **131**, 165 (1864).

(8) Beilstein and Wiegand, *Ber.*, **18**, 483 (1885).

(9) Russell and Cameron, THIS JOURNAL, **60**, 1345 (1938).

(10) Beer, Dissertation, Leipzig, 1927.

In the percentages shown, no correction is made for any change in volume due to mixing.

As soon after mixing as possible, duplicate 5-cc. samples were removed for determination of the sulfuric acid content at the start of the experiments. Additional duplicate samples were removed at the designated periods of time and analyzed to determine the amount of precipitable sulfate ion present. The 5-cc. samples were added to approximately 200 cc. of distilled water containing 4 cc. of 6 *N* hydrochloric acid. The solutions were heated to boiling and the sulfate ion precipitated with 10 cc. of 10% barium chloride solution. The barium sulfate was digested in the usual manner, isolated, ignited and weighed. The barium salts of the sulfoaliphatic acids are comparatively soluble in water and were not precipitated under the conditions employed. The mixed anhydrides of the aliphatic acids with sulfuric acid quickly decomposed in the presence of water to form the corresponding acids.

In order to determine whether sulfuric acid would react with the aliphatic acid, a solution of sulfuric acid in acetic acid was prepared of approximately the concentration used in these experiments and allowed to stand for eleven days at room temperature. Samples removed at the beginning and at the end of this period gave analytical values of 0.0417 and 0.0416 g. sulfuric acid per 5 cc., respectively, which indicated that little if any sulfoacetic acid was formed.

TABLE II

50% ANHYDRIDE–50% ACID

Time	H_2SO_4 G./5 cc.	K^1/Min.$^{-1}$
	Acetic anhydride	
2 min.	0.0416	
15 min.	.0401	0.0030
30 min.	.0399	.0015
1 hr.	.0379	.0016
3 hr.	.0304	.0018
7.5 hr.	.0184	.0018
24 hr.	.0033	.0018
32 hr.	.0015	.0017
	Av.	.0019
	Propionic anhydride	
2 min.	0.0380	
30 min.	.0354	0.0025
1 hr.	.0344	.0017
2 hr.	.0318	.0015
5 hr.	.0264	.0012
8 hr.	.0224	.0011
24 hr.	.0087	.0010
32 hr.	.0058	.00098
48 hr.	.0022	.00099
56.5 hr.	.0013	.0010
72 hr.	.0001	.0014
	Av.	.0013
	n-Butyric anhydride	
2 min.	0.0380	
1.2 hr.	.0287	0.0040
2.2 hr.	.0245	.0034
5.1 hr.	.0160	.0029
8 hr.	.0104	.0027
23 hr.	.0005	.0031
	Av.	.0032

The experimental results obtained using 50% concentrations of the three anhydrides are tabulated in Table II. In order to conserve space, the analytical data for the other anhydride concentrations are not included.

The analytical results are expressed in terms of sulfuric acid though they include the sulfate which may be present as acetyl sulfuric as well as free sulfuric acid. In these experiments we are interested in the amount of sulfuric acid which has been converted into the sulfoaliphatic acid and not in the state of the residual sulfate ion. The values given are the averages of duplicate determinations.

When the experimental data are employed in the usual equation for a first-order reaction

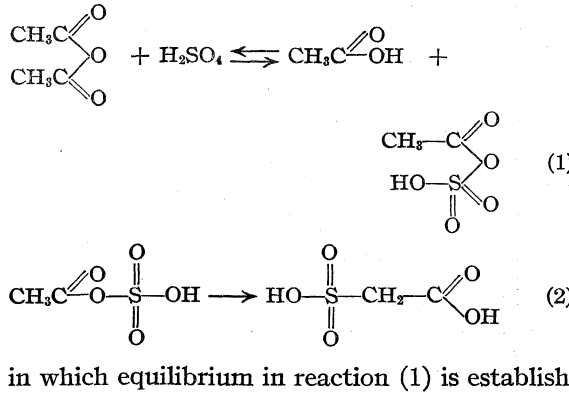
$$k^1 = \frac{1}{t} 2.303 \log \frac{a}{a - x}$$

reasonably constant values for k^1 are obtained. In these calculations, a is the amount of precipitable sulfate ion at the start of the experiment and $a - x$ is the amount of precipitable sulfate ion at time t. The average k^1 values for the various experiments are tabulated in Table III.

Discussion

Since the principal purpose of the work was to demonstrate the disappearance of sulfuric acid under conditions which simulate those prevailing in esterification reactions, the rate measurements were necessarily made over a very wide range of solvent conditions. For this reason, it is impossible to draw, in some particulars, rigorous conclusions concerning the mechanism of reaction. In spite of this fact, it is believed that a reasonably accurate formulation of the course of the reaction can be deduced in at least a semi-quantitative manner.

On the basis of independent evidence concerning the same type of reaction, Franchimont[1] and others[9] have postulated the following mechanism for the production of sulfoacetic acid



in which equilibrium in reaction (1) is established rapidly, and reaction (2) is the slow or rate-de-

TABLE III

CALCULATED FIRST-ORDER REACTION CONSTANTS

Anhydride, %	Acid, %	Acetic k^1/min.$^{-1}$ (av.)	Acetic Number of k^1 values averaged	Propionic k^1/min.$^{-1}$ (av.)	Propionic Number of k^1 values averaged	*n*-Butyric k^1/min.$^{-1}$ (av.)	*n*-Butyric Number of k^1 values averaged
90	10	0.053	3	0.021	4	0.023	5
75	25	.0115	6	.0048	6	.0082	7
50	50	.0019	7	.0013	10	.0032	5
25	75	.00049	15	.00033	12	.00085	10

termining step. By the well-known steady state treatment, the instantaneous concentration of the intermediate, acetylsulfuric acid, is given by the expression

$$\left[\mathrm{CH_3C(=O)OS(=O)(=O)OH}\right] = \frac{\left[\mathrm{(CH_3CO)_2O}\right]\left[\mathrm{H_2SO_4}\right]}{K_e\left[\mathrm{CH_3COOH}\right]} \qquad (3)$$

where K_e is the equilibrium constant in reaction (1). The differential rate expression for the over-all process is thus given as follows

$$\frac{-\,d[H_2SO_4]}{dt} = \frac{K_2}{K_e}\,\frac{\left[\mathrm{(CH_3CO)_2O}\right]\left[\mathrm{H_2SO_4}\right]}{[HAc]} \qquad (4)$$

The velocity of the over-all reaction should accordingly be proportional to the first power of the sulfuric acid concentration and to the first power of the ratio Organic anhydride/Organic acid. When the log of $\frac{a}{a-x}$ is plotted against the time, linear relationships are obtained in each experiment. Since the concentration of the anhydride and its hydrate in each case was so much greater than that of the sulfuric acid, only the latter changes appreciably in concentration throughout the course of reaction. Linearity in these relationships indicates that the sulfuric acid concentration enters to the first power as demanded by expression (4). Figure 1, in which the average apparent rate constants of the over-all reaction at various values of anhydride concentration, as tabulated in Table III, are plotted against the ratio Organic anhydride/Organic acid, shows a considerable non-random departure from linearity. The approximation is, however, about as good as can be expected, considering the change in character of the solvent in the four separate measurements. It will be observed, also, from Fig. 1, that the deviations from linearity appear to become less serious with increasing length of the chain attached to the carboxyl group, further suggesting the importance of solvent effects. It thus appears that the data obtained in this investigation are compatible with the mechanism previously proposed and, indeed, appear to afford it considerable substantiation.

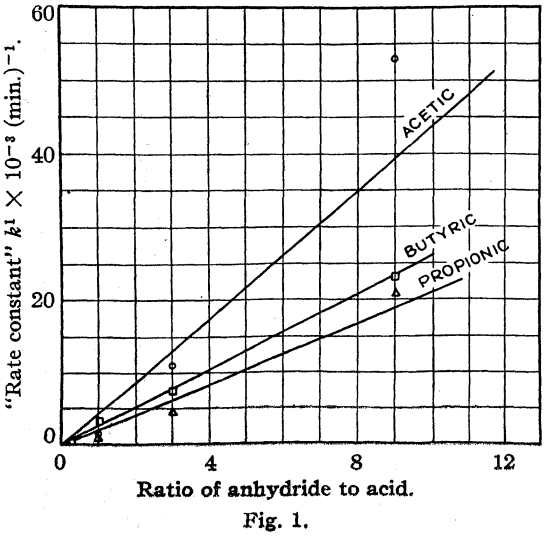
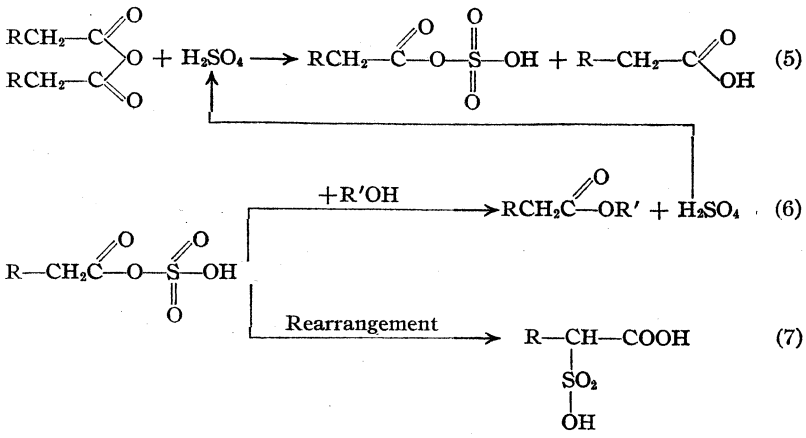


Fig. 1.

The data indicate that sulfuric acid reacts with the lower aliphatic anhydrides to form sulfoaliphatic acids even when the sulfuric acid is present in the small amounts employed to catalyze acylation reactions. In esterification processes, the reaction which produces sulfoaliphatic acids may proceed concurrently with the esterification reaction, and the rate of disappearance of the sulfate ion should depend on the original concentration of the anhydride in the reaction mixture as well as the rate at which the anhydride is withdrawn from the reaction by esterification. Since the mixed anhydride of sulfuric acid and the aliphatic acid appears to be formed quickly in esterification mixtures,[9] this compound may be the active acylating agent in many reactions as was suggested by Franchimont.[1] The possible mechanism is indicated in the following series of reactions.



The mixed anhydride of sulfuric and the aliphatic acid may react with the material to be acylated, liberating a molecule of sulfuric acid which again may react with a molecule of aliphatic anhydride, and the acylation cycle may be repeated or the mixed anhydride may rearrange to a sulfoaliphatic acid, thus removing the sulfuric acid from further participation in the acylation.

The authors wish to express their appreciation to Dr. William J. Priest of these Laboratories for his assistance in the kinetic interpretation of these data.

Summary

The rate of formation of sulfoaliphatic acids by reaction of sulfuric acid with aliphatic anhydrides at 40° has been measured, using small amounts of sulfuric acid in various concentrations of acetic, propionic and *n*-butyric anhydrides in the corresponding acids.

The rate of disappearance of sulfate ion follows the first-order reaction equation and is related to the concentration of the aliphatic anhydride. The relation between the experimental results and the mechanism of the reaction is discussed.

A mechanism of acylation in the presence of sulfuric acid catalyst is suggested.

ROCHESTER, N. Y. RECEIVED FEBRUARY 19, 1940

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

Diene Addition Products to Diaroylethylenes and their Transformation Products. II

BY ROGER ADAMS AND R. B. WEARN[1]

In a recently published article[2] it was shown that butadiene, 2,3-dimethylbutadiene and cyclopentadiene undergo an essentially quantitative addition to dibenzoylethylene with formation of dibenzoylcyclohexenes (I). Syntheses from these adducts were developed for the corresponding dibromo addition products (II), dihydroisobenzofurans (V), isobenzofurans (IV), *o*-dibenzoylbenzenes (VI), oxido-tetrahydronaphthalenes (VII) and substituted naphthalenes (VIII). A comparison of the procedures used with those previously known for the same compounds was discussed. The series of reactions is illustrated by formulas I–VIII.

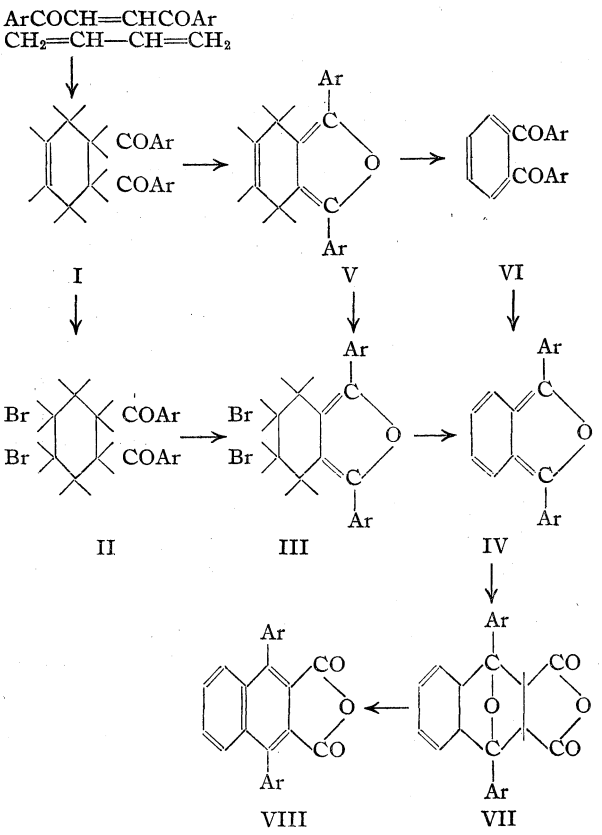
In this paper, analogous reactions between the *trans* forms of di-*p*-chlorobenzoyl, di-*p*-toluyl and dimesitoyl ethylenes and butadiene, 2,3-dimethylbutadiene and cyclopentadiene are reported in order to demonstrate the extent of applicability of these methods in preparative work Butadiene and cyclopentadiene added quantitatively to all three of the diaroyl ethylenes with formation of 4,5-diaroyl cyclohexenes (I). 2,3-Dimethylbutadiene also added to all except the dimesitoylethylene. Apparently, in this case, steric influences prevent the addition from taking place.

The cyclopentadiene addition products could in no case be converted to furans, possibly on account of the strains involved. Similarly, the dimesitoylethylene and butadiene adduct did not form a furan, due probably to steric influences.

The reactions discussed below, except for the addition of bromine to the original adducts, the 4,5-diaroyl cyclohexenes (I), apply merely to the products formed from di-*p*-chlorobenzoylethylene and di-*p*-toluylethylene with butadiene and 2,3-dimethylbutadiene.

(1) An abstract of a thesis submitted in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry.

(2) Adams and Gold, THIS JOURNAL, **62**, 56 (1940). See also Adams and Geissman, *ibid.*, **61**, 2083 (1939).



The 4,5-diaroyl cyclohexenes (I) add bromine quantitatively in chloroform solution to give 1,2-dibromo-4,5-diaroyl cyclohexanes (II).

The 4,5-diaroyl cyclohexenes (I) are converted quantitatively by means of acetic anhydride and a little phosphoric acid to 1,3-diaryl-4,7-dihydroisobenzofurans (V).

The 1,2-dibromo-4,5-diaroyl cyclohexanes (II) are unaffected by treatment with acetic anhydride and phosphoric acid but by means of acetyl chloride containing a little sulfuric acid, a reagent shown by Lutz[3] to be more effective than the former, are converted to the corresponding 1,3-diaryl-5,6-dibromo-4,5,6,7-tetrahydroisobenzofurans (III). These latter products when derived from 2,3-dimethylbutadiene derivatives are stable but when derived from butadiene derivatives partially decompose and oxidize upon attempts to recrystallize with formation of *o*-diaroyl benzenes. It is worthy of note that the dibromo compounds formed by addition of bromine to the adducts from butadiene or 2,3-dimethylbutadiene and unsubstituted dibenzoylethylene are not closed to furans by acetyl chloride and sulfuric acid.

(3) Lutz, THIS JOURNAL, **48**, 2916 (1926).

The 1,3-diaryl-5,6-dibromo-4,5,6,7-tetrahydroisobenzofurans (III) also could be prepared by direct addition of bromine to the 1,3-diaryl-4,7-dihydroisobenzofurans but the yields were poor.

o-Diaroyl benzenes (VI) are formed quantitatively from the 1,3-diaryl-4,7-dihydroisobenzofurans (V) by treatment of the latter with two moles of bromine followed immediately by sodium acetate in acetic acid and then with water.

Activated zinc and alkali convert the *o*-diaroyl benzenes (VI) to 1,3-diarylisobenzofurans (IV). The yields are usually excellent but depend upon the length of time of reduction, which varies from compound to compound. If the reduction is carried too far, the yield falls. The derivatives of butadiene in all cases reduce more rapidly than those from dimethylbutadiene.

The 1,3-diarylisobenzofurans (IV) when derived from 2,3-dimethylbutadiene also can be formed from the 1,3-diaryl-5,6-dibromo-4,5,6,7-tetrahydroisobenzofurans (III) merely by treatment with sodium acetate, acetic acid and acetic anhydride. The dibromotetrahydroisobenzofurans derived from butadiene, however, do not undergo this reaction

The addition of maleic anhydride to the 1,3-diarylisobenzofurans (IV) proceeds very smoothly to give 1,4-diaryl-1,4-oxido-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylic anhydrides (VII). The 1,3-diarylisobenzofurans containing 5,6-dimethyl groups give two isomeric oxido compounds. One is stable only in cold benzene and changes to a lower melting form when crystallized from hot benzene.

Dehydration of the 1,4-diaryl-1,4-oxido-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylic anhydrides (VII) with dry hydrogen chloride yields 1,4-diaryl-2,3-naphthalic anhydrides (VIII).

The dihydroisobenzofurans (V) and the isobenzofurans (IV) produce a blue-green fluorescence in solution.

The compounds prepared, with the methods of purification, melting points, yields and analyses are given in Tables I–IV.

Experimental

Addition of Diaroylethylenes to Dienes—General Procedure for Preparing Dibenzoyl Cyclohexenes (I).—To a solution of 40 g. (1 mole) of di-*p*-chlorobenzoylethylene in 1 liter of dry benzene was added 21.5 g. (2 moles) of crude 2,3-dimethylbutadiene (prepared by distilling pinacol from a small amount of hydrobromic acid). After refluxing overnight, the solvent was evaporated

TABLE I

4,5-DIAROYL CYCLOHEXENES

a = di-*p*-chlorobenzoylethylene[a] 1 = butadiene
b = di-*p*-toluylethylene[a] 2 = 2,3-dimethylbutadiene
c = dimesitoylethylene[a] 3 = cyclopentadiene

Reactants	4,5-Diaroyl cyclohexene	Crystalline form, white	Solvent for crystn.	M. p. (cor.), °C.	Yield, %	Formula	Analyses, % Calcd. C	Calcd. H	Found C	Found H
a, 1	4,5-Di-*p*-chlorobenzoyl-	Plates	Ethanol–acetone	125	92	$C_{20}H_{16}O_2Cl_2$	66.86	4.49	67.14	4.64
b, 1	4,5-Di-*p*-toluyl-	Needles	Ethanol–acetone	127	89	$C_{22}H_{22}O_2$	82.98	6.97	83.16	7.43
c, 1	4,5-Dimesitoyl-	Plates	Benzene	204	80	$C_{26}H_{30}O_2$	83.38	8.07	83.01	8.27
a, 2	1,2-Dimethyl-4,5-di-*p*-chlorobenzoyl-	Plates	Acetone	151	92	$C_{22}H_{20}O_2Cl_2$	68.22	5.21	68.60	5.34
b, 2	1,2-Dimethyl-4,5-di-*p*-toluyl-[b]	Prisms	Ethanol	129	90	$C_{24}H_{26}O_2$	83.20	7.57	82.18[b]	7.59
a, 3	3,6-Endomethylene-4,5-di-*p*-chlorobenzoyl-	Needles	Ligroin	139	92	$C_{21}H_{16}O_2Cl_2$	67.94	4.35	68.45	4.42
b, 3	3,6-Endomethylene-4,5-di-*p*-toluyl-	Plates	Ligroin	106	67	$C_{23}H_{22}O_2$	83.60	6.70	83.47	6.95
c, 3	3,6-Endomethylene-4,5-dimesitoyl-	Needles	Ligroin	117	80	$C_{27}H_{30}O_2$	83.90	7.80	84.23	7.93

[a] These compounds have been prepared previously by Conant and Lutz, THIS JOURNAL, 45, 1305 (1923). [b] Several additional analyses produced no better check on this compound, but the conversion to the corresponding dibromide and furan derivatives, which analyzed properly, is sufficient proof for its identity.

TABLE II

1,2-DIBROMO-4,5-DIAROYL CYCLOHEXANES, 1,3-DIARYL-4,7-DIHYDROISOBENZOFURANS, AND 1,3-DIARYL-5,6-DIBROMO-4,5,6,7-TETRAHYDROISOBENZOFURANS

a = 4,5-di-*p*-chlorobenzoylcyclohexene; b = 4,5-di-*p*-toluylcyclohexene; c = 4,5-dimesitoylcyclohexene; d = 1,2-dimethyl-4,5-di-*p*-chlorobenzoylcyclohexene; e = 1,2-dimethyl-4,5-ditoluylcyclohexene.

Reactant	1,2-Dibromo-4,5-diaroyl cyclohexane	Crystalline form, white	Solvent for crystn.	M. p. (cor.), °C.	Yield, %	Formula	Analyses, % Calcd. C	Calcd. H	Found C	Found H
a	4,5-Di-*p*-chlorobenzoyl-	Plates	Bz–lig.	181	92	$C_{22}H_{16}O_2Cl_2Br_2$	46.27	3.11	46.19	3.44
b	4,5-Di-*p*-toluyl-	Plates	Bz–lig.	177	90	$C_{22}H_{22}O_2Br_2$	55.25	4.64	55.17	4.68
c	4,5-Dimesitoyl-	Needles	Bz–lig.	202	95	$C_{26}H_{30}O_2Br_2$	58.47	5.66	58.55	5.88
d	-1,2-Dimethyl-4,5-di-*p*-chlorobenzoyl-	Hexagons	Ethanol	173	92	$C_{22}H_{20}O_2Cl_2Br_2$	48.29	3.69	48.72	3.82
e	-1,2-Dimethyl-4,5-di-*p*-toluyl-	Needles	Ligroin	184	90	$C_{22}H_{22}O_2Br_2$	56.93	5.18	56.67	5.20
	1,3-Diaryl-4,7-dihydroisobenzofuran	Needles								
a	1,3-Di-*p*-chlorophenyl-	Yellow	Bz–lig.	215	97	$C_{20}H_{14}OCl_2$	70.39	4.13	70.32	4.27
b	1,3-Di-*p*-tolyl-	Yellow	Bz–lig.	210	99	$C_{22}H_{20}O$	87.96	6.71	88.40	6.81
d	1,3-Di-*p*-chlorophenyl-5,6-dimethyl-	Green-yellow	Benzene	236	97	$C_{22}H_{18}OCl_2$	71.55	4.91	71.68	5.30
e	1,3-Di-*p*-tolyl-5,6-dimethyl-	Green-yellow	Benzene	237	95	$C_{24}H_{24}O$	87.76	7.37	87.48	7.23
	1,3-Diaryl-5,6-dibromo-4,5,6,7-tetrahydroisobenzofuran	Needles								
d	1,3-Di-*p*-chlorophenyl-	Pale green	Benzene	179	88	$C_{22}H_{18}OCl_2Br_2$	49.95	3.43	50.15	3.52
e	1,3-Di-*p*-tolyl-	Pale green	Benzene	166	81	$C_{24}H_{24}OBr_2$	59.01	4.95	59.19	5.05

TABLE III

1,2-DIAROYLBENZENES AND THE CORRESPONDING 1,3-DIARYLISOBENZOFURANS

a = 1,3-di-*p*-chlorophenyl-4,7-dihydroisobenzofuran
b = 1,3-di-*p*-tolyl-4,7-dihydroisobenzofuran
c = 1,3-di-*p*-chlorophenyl-5,6-dimethyl-4,7-dihydroisobenzofuran
d = 1,3-di-*p*-tolyl-5,6-dimethyl-4,7-dihydroisobenzofuran

Reactant	1,2-Diaroylbenzene	Crystalline form, white	Solvent for crystn.	M. p. (cor.), °C.	Yield, %	Formula	Analyses, % Calcd. C	Calcd. H	Found C	Found H
a	1,2-Di-*p*-chlorobenzoyl-[a]	Needles	EtOH–acetone	167–168	96	$C_{20}H_{12}O_2Cl_2$	...	..	...	..
b	1,2-Di-*p*-toluyl-[b]	Needles	EtOH–acetone	191	95	$C_{22}H_{18}O_2$	...	..	...	..
c	1,2-Di-*p*-chlorobenzoyl-4,5-dimethyl-	Plates	Ligroin	168–169	97	$C_{22}H_{16}O_2Cl_2$	68.94	4.21	69.07	4.35
d	1,2-Di-*p*-toluyl-4,5-dimethyl-	Plates	Ethanol	164	96	$C_{24}H_{22}O_2$	84.18	6.48	83.90	6.48
	1,3-Diarylisobenzofuran	Yellow								
a	1,3-Di-*p*-chlorophenyl-[c]	Leaflets	Ligroin	199–200	60	$C_{20}H_{12}OCl_2$	...	..	...	..
b	1,3-Di-*p*-tolyl-[d]	Leaflets	Ligroin	125	62	$C_{22}H_{18}O$	...	..	...	..
c	1,3-Di-*p*-chlorophenyl-5,6-dimethyl-	Needles	Benzene	213	70	$C_{22}H_{16}OCl_2$	71.82	4.40	72.01	4.50
d	1,3-Di-*p*-tolyl-5,6-dimethyl-	Plates	Benzene	186	75	$C_{24}H_{22}O$	88.31	6.78	88.20	7.16

[a] Reported by Blicke and Patelski, m. p. 167–168°, THIS JOURNAL, 58, 273 (1936). [b] Reported by Bauer, m. p. 190–191°, *Arch. Pharm.*, 247, 220 (1909). [c] Reported by Blicke and Patelski, m. p. 199–200°, note (*a*). [d] Reported by Guyot and Valette, m. p. 125°, *Ann. chim. Phys.*, 23, 363 (1911).

TABLE IV

1 4-DIARYL-1,4-OXIDO-1,2,3,4-TETRAHYDRONAPHTHALENE-2,3-DICARBOXYLIC ANHYDRIDES AND THE CORRESPONDING 1,4-DIARYL-2,3-NAPHTHALIC ANHYDRIDES

a = 1,3-di-*p*-chlorophenylisobenzofuran
b = 1,3-di-*p*-tolylisobenzofuran
c = 1,3-di-*p*-chlorophenyl-5,6-dimethylisobenzofuran
d = 1,3-di-*p*-tolyl-5,6-dimethylisobenzofuran

Reactant	1,4-Diaryl-1,4-oxido-1,2,3,4-tetrahydronaphthalene-2,3-dicarboxylic anhydride	Crystalline form, white	Solvent for crystn.	M. p. (cor.), °C.	Yield, %	Formula	Analyses, % Calcd. C	Calcd. H	Found C	Found H
a	1,4-Di-*p*-chlorophenyl-	Needles	Bz–lig.	264–266	94	$C_{24}H_{14}O_4Cl_2$	66.02	3.23	66.28	3.58
b	1,4-Di-*p*-tolyl-	Needles	Bz–lig.	256–258	92	$C_{26}H_{20}O_4$	78.77	5.09	78.95	5.27
c	1,4-Di-*p*-chlorophenyl-6,7-dimethyl-	Needles	Cold Bz	292–293		$C_{26}H_{18}O_4Cl_2$	67.02	3.89	67.34	4.13
			Hot Bz	270–272	95	$C_{26}H_{18}O_4Cl_2$	67.02	3.89	66.84	4.03
d	1,4-Di-*p*-tolyl-6,7-dimethyl-	Needles	Cold Bz	285–286	93	$C_{28}H_{24}O_2$	79.23	5.70	79.34	5.94
			Hot Bz	267–268						
	1,4-Diaryl-2,3-naphthalic anhydride									
a	1,4-Di-*p*-chlorophenyl-	Leaflets	Benzene	304–305[a]	61	$C_{24}H_{12}O_3Cl_2$	68.75	2.89	68.22	3.04
b	1,4-Di-*p*-tolyl-	Leaflets	Benzene	293–295[a]	55	$C_{26}H_{18}O_3$	82.52	4.80	82.18	4.99
c	1,4-Di-*p*-chlorophenyl-6,7-dimethyl-	Leaflets	Acetic acid	321–323[a]	57	$C_{26}H_{16}O_3Cl_2$	69.71	3.60	70.11	3.82
d	1,4-Di-*p*-tolyl-6,7-dimethyl-	Leaflets	Acetic acid	338–340[a]	68	$C_{28}H_{22}O_3$	82.74	5.46	82.56	5.52

[a] Bloc Maquenne.

until the resulting volume was 70 cc. On cooling the 1,2-dimethyl-4,5-di-*p*-chlorobenzoylcyclohexene crystallized.

By this procedure, di-*p*-chlorobenzoyl and di-*p*-toluyl ethylenes were added to butadiene, 2,3-dimethylbutadiene, and cyclopentadiene. Dimesitoylethylene was added to butadiene and cyclopentadiene but did not react (even under pressure in a sealed tube) with 2,3-dimethylbutadiene (see Table I).

Bromination of Dibenzoyl Cyclohexenes.—One mole of bromine was added to a saturated chloroform solution of 4,5-di-*p*-chlorobenzoylcyclohexene at 0°. The crude 1,2-dibromo-4,5-di-*p*-chlorobenzoylcyclohexane separated from a benzene–ligroin mixture.

By this procedure, the dibromo derivatives (II) of all the diaroyl cyclohexenes derived from butadiene and 2,3-dimethylbutadiene were prepared (see Table II).

Conversion of *o*-Diaroyl Cyclohexenes to the Corresponding Dihydroisobenzofurans (V).—To a suspension of 25 g. of 1,2-dimethyl-4,5-di-*p*-chlorobenzoylcyclohexene in 200 cc. of hot acetic anhydride was added 0.5 g. of sirupy phosphoric acid. The insoluble furan began to crystallize immediately, but the mixture was refluxed for five minutes. On cooling, the 1,3-di-*p*-chlorophenyl-5,6-dimethyl-4,7-dihydroisobenzofuran crystallized quantitatively.

By this method 1,3-di-*p*-tolyl-, 1,3-di-*p*-chlorophenyl-, and 1,3-di-*p*-tolyl-5,6-dimethyl dihydroisobenzofurans were also prepared. Under the same conditions, 1,3-dimesitoylcyclohexene and the 3,6-endomethylene-4,5-diaroyl cyclohexenes would not close to form furans (see Table II).

Preparation of 1,3-Diaryl-5,6-dibromo-4,5,6,7-tetrahydroisobenzofurans (III).—(a) A saturated solution of 9.2 g. of 1,2-dimethyl-1,2-dibromo-4,5-di-*p*-chlorobenzoylcyclohexane in acetyl chloride was heated to boiling. Several drops of concentrated sulfuric acid was added, and the solution was boiled for several minutes. It became dark colored, due to charring by the acid. The sides of the flask were scratched vigorously with a glass rod, and greenish needles of the 1,3-di-*p*-chlorophenyl-5,6-dibromo-5,6-dimethyl-4,5,6,7-tetrahydroisobenzofuran separated.

By this method, the corresponding di-*p*-tolyl compound also was prepared. The 1,2-dibromo-4,5-diaroylcyclohexanes (II) (without the 1,2-methyl groups) were closed to the furans under the same conditions, but pure products could not be isolated on account of their ready oxidation in solution to the *o*-dibenzoyl benzenes (VI) (see Table II).

(b) To a saturated solution of 1 g. (1 mol) of 1,3-di-*p*-chlorophenyl-4,7-dihydroisobenzofuran in chloroform at 0° was added slowly a solution of 0.49 g. (1 mol) of bromine in 2 cc. of chloroform. The product was isolated by concentrating the solvent to small volume.

By this procedure the corresponding di-*p*-tolyl compound was prepared. Due to unsatisfactory yields in both cases, this method was discarded in favor of the above (a).

Conversion of Diaryl-dihydroisobenzofurans to Corresponding *o*-Dibenzoyl Benzenes (VI).—To a suspension of 10 g. (1 mol) of 1,3-di-*p*-chlorophenyl-5,6-dimethyl-4,7-dihydroisobenzofuran in a hot solution of 20 g. of sodium acetate (anhydrous) in 400 cc. of glacial acetic acid was slowly added 8.7 g. (2 mols) of bromine. The mixture was kept boiling throughout this addition (ten minutes) and then refluxed for twenty minutes longer. Water was added until a considerable precipitate was formed in the boiling solution, and the mixture was allowed to cool. The crude 1,2-dimethyl-4,5-di-*p*-chlorobenzoylbenzene was filtered and recrystallized.

By the same method 1,2-dimethyl-4,5-di-*p*-toluyl, *o*-di-*p*-chlorobenzoyl-, and *o*-di-*p*-toluyl benzenes were prepared (see Table III).

Conversion of *o*-Diaroyl Benzenes to the Corresponding Isobenzofurans (IV).—A suspension of 5 g. (1 mol) of 1,2-dimethyl-4,5-di-*p*-chlorobenzoylbenzene in 200 cc. of absolute ethanol was heated to boiling. A solution of 5 g. of sodium hydroxide in 5 cc. of water was added to the mixture. Refluxing was continued until the solution became dark reddish-brown (from one-half to one and one-half hours). At this point, 5 g. of active zinc dust (prepared by washing with dilute hydrochloric acid followed by water) was added and refluxing continued for twenty minutes. At the end of this time, the color changed from

dark red to bright fluorescent yellow. The hot solution was then filtered, 50 cc. of acetic acid was added, and the mixture was heated to boiling. Hot water was added until crystals began to form. Boiling was continued for several minutes, and then the solution was cooled. The product was 1,3-di-*p*-chlorophenyl-5,6-dimethylisobenzofuran.

By the same method the 1,3-di-*p*-tolyl-5,6-dimethyl-, 1,3-di-*p*-tolyl-, and 1,3-di-*p*-chlorophenyl-substituted isobenzofurans were prepared. The change of color at the end of the reduction did not always take place, so the length of time for reduction, which apparently varied with the activity of the zinc, had to be estimated in each case.

Addition of Maleic Anhydride to Isobenzofurans (VII).—To a solution of 6 g. (1 mol) of 1,3-di-*p*-chlorophenyl-5,6-dimethylisobenzofuran in 200 cc. of benzene was added 1.8 g. (1.1 mols) of maleic anhydride. The reaction was complete in about five minutes in cold solution, as indicated by the sudden disappearance of fluorescence. The solvent was evaporated at room temperature under reduced pressure, and crystals of 1,4-di-*p*-chlorophenyl-1,4-oxido - 6,7 - dimethyl - 1,2,3,4 - tetrahydronaphthalene-2,3-dicarboxylic anhydride separated.

When this compound was crystallized from hot benzene solution, a lower melting isomer was obtained. This isomer was also obtained when the original addition was carried out in hot solution.

By this method the maleic anhydride adducts of 1,3-di-*p*-tolyl-5,6-dimethyl-, 1,3-di-*p*-chlorophenyl-, and 1,3-di-*p*-tolyl-substituted isobenzofurans were also prepared. These products were crystallized from hot solutions and no attempt was made to isolate the higher melting isomers except in the case of 1,3-di-*p*-tolyl-5,6-dimethylisobenzofuran (see Table IV).

Dehydration of Oxido Tetrahydro Naphthalic Anhydrides (VII) to Form the Corresponding Naphthalic Anhydrides (VIII).—A suspension of 2 g. of 1,4-di-*p*-chlorophenyl - 1,4 - oxido - 6,7 - dimethyl - 1,2,3,4 - tetrahydronaphthalene-2,3-dicarboxylic anhydride in 200 cc. of absolute methanol was saturated with dry hydrogen chloride gas. The gas was bubbled through the solution slowly to keep it saturated while it was refluxed for two hours. The mixture was then evaporated to dryness. After addition of 50 cc. of 30% aqueous potassium hydroxide and 200 cc. of ethanol, the mixture was refluxed for six hours. The solution was then cooled and acidified. The precipitate was filtered off and purified by dissolving in potassium hydroxide, followed by reprecipitation by acid. The crude 1,4-di-*p*-chlorophenyl-6,7-dimethyl-2,3-naphthalic anhydride was crystallized from hot acetic acid.

By the same method the 1,4-di-*p*-tolyl-6,7-dimethyl-, 1,4-di-*p*-chlorophenyl-, and 1,4-di-*p*-tolyl-substituted 2,3-naphthalic anhydrides were also prepared (see Table IV). Benzene was a more suitable solvent for crystallization of the last two compounds.

Summary

The new methods reported in a previous paper[2] for the preparation of dihydroisobenzofurans, isobenzofurans, *o*-dibenzoyl benzenes, and aryl- and alkyl-substituted naphthalenes from the butadiene and dimethylbutadiene adducts of dibenzoylethylene were shown to work equally well for the di-*p*-chlorobenzoyl and di-*p*-toluyl ethylenes.

Cyclopentadiene added in good yield to di-*p*-chlorobenzoyl, di-*p*-toluyl, and dimesitoyl ethylenes.

Dimesitoylethylene formed an adduct with butadiene, but did not react with 2,3-dimethylbutadiene.

The dimesitoylethylene adduct to butadiene and all of the adducts from cyclopentadiene could not be converted to furans by the usual procedures.

URBANA, ILLINOIS RECEIVED MARCH 11, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF WASHINGTON AND LEE UNIVERSITY AND HYNSON, WESTCOTT AND DUNNING, INC.]

The Halogenation of Salicylic Acid

BY LARKIN HUNDLEY FARINHOLT, A. P. STUART* AND DANIEL TWISS

The preparation of polyhalogenated salicylic acids was attempted for several reasons. In the first place, the compounds might have valuable physiological properties and, in the second place, the order in which the halogen atoms enter the available positions is interesting from a theoretical point of view.

The mono- and disubstituted halogen derivatives of salicylic acid have been prepared by previous investigators by the addition of the free halogens to a solution of salicylic acid in a suitable medium. Nothing is known, however, concerning the tri- and tetrahalogenated salicylic acids which form the subject of this investigation.

Starting with 3,5-diiodosalicylic acid prepared according to Woollett and Johnson,[1] numerous methods were applied with the object of obtaining higher iodinated derivatives, but with negative results in each case. The following methods were attempted: (I) refluxing diiodosalicylic acid

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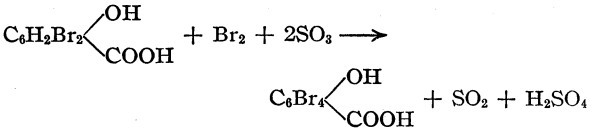
(1) "Organic Syntheses," Vol. XIV, 1934, p. 52.

with iodine in ethyl alcohol, as well as in other solvents, according to Lautemann[2]; (II) using iodine chloride, based on the method of Cofman[3]; (III) following the method of Weselsky,[4] who iodinated in the presence of mercuric oxide; (IV) by the effective method of Likhosherstov and Tzimbalist[5] using dichlorourea and potassium iodide. These methods also were tested on the acetyl derivative of 3,5-diiodosalicylic acid but with equally negative results.

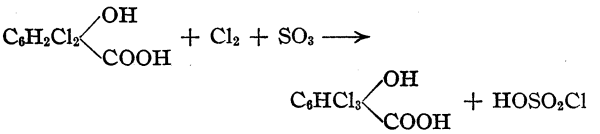
3,5-Dichloro- and 3,5-dibromosalicylic acids were prepared by the method of Earle and Jackson.[6] Attempts to substitute in these compounds more chlorine and bromine, respectively, resulted either in a replacement of the carboxyl group by halogen or no reaction at all.

Juvalta,[7] Rupp[8] and Pratt and Shupp[9] prepared polyhalogenated phthalic anhydrides by halogenating phthalic anhydride in solution in fuming sulfuric acid and Twiss and Farinholt[10] showed that *o*-sulfobenzoic anhydride may be halogenated in the same manner. The present investigation is concerned with the application of this method to salicylic acid and dihalogenosalicylic acids. The experiments with salicylic acid were not successful. The reaction yielded a water-soluble product, indicating substitution of sulfonic acid groups which, apparently, were too firmly bound to the nucleus to be replaced by halogen atoms under the conditions of the reaction. It was found necessary first to prepare the dihalogenosalicylic acids by known methods and use them as the starting materials for further halogenations. No iodine derivatives could be prepared by this method since both diiodosalicylic acid and its acetyl derivative decomposed on contact with fuming sulfuric acid, even in the cold, with liberation of iodine.

Good results were obtained with dibromo- and dichlorosalicylic acids. No attempt was made to interpret the mechanism of the process but it seems likely that the dihalogenosalicylic acids form some sort of unstable addition complex with sulfur trioxide or sulfuric acid which facilitates the substitution of the halogen atoms. According to the amount of bromine, one or two bromine atoms may be introduced into dibromosalicylic acid. The hydrogen bromide evolved in the reaction is oxidized by the sulfur trioxide and the resulting bromine made available again for further substitution. The net result of the formation of tetrabromosalicylic acid may be represented by the equation

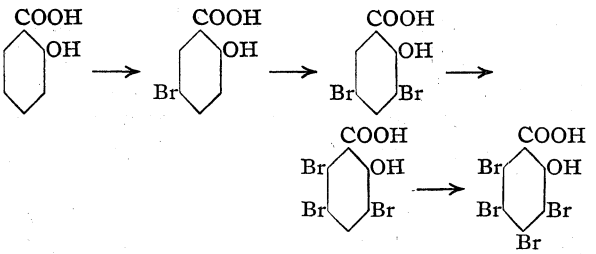


In the chlorination, the hydrogen chloride is not oxidized but combines with sulfur trioxide to form chlorosulfonic acid. It is worthy of note that the trichlorosalicylic acid cannot be chlorinated further but that a bromine atom may be substituted in the remaining free position. The formation of trichlorosalicylic acid follows the equation



The position of the third halogen in trichloro- and tribromosalicylic acids was determined by heating the acid thus formed with soda lime and identifying the resulting trihalogenophenol. It was shown that the substitution takes place in position 6, adjacent to the carboxyl group, presumably under the influence of the two halogen atoms already present. No evidence was found of the formation of isomers. The introduction of a fourth bromine atom in tribromosalicylic acid and of a bromine atom in trichlorosalicylic acid occurs without difficulty.

The order in which bromine atoms, for example, substitute in salicylic acid is represented by the scheme below. The first atom enters mainly in the position meta to the carboxyl and para to the hydroxyl group.



The replacement of the carboxyl group by a halogen atom served as a further check on the

(2) Lautemann, *Ann.*, **120**, 301 (1861).
(3) Cofman, *Gazz. chim. ital.*, **50**, II, 297 (1920).
(4) Weselsky, *Ann.*, **174**, 103 (1874).
(5) Likhosherstov and Tzimbalist, *J. Gen. Chem.* [*U. S. S. R.*], **3**, 177–182 (1933).
(6) Earle and Jackson, THIS JOURNAL, **28**, 109, 111 (1906).
(7) German Patent 50,177 (1889), *Frdl.*, **2**, 93 (1889).
(8) Rupp, *Ber.*, **29**, 1625–1634 (1896).
(9) Pratt and Shupp, THIS JOURNAL, **40**, 203, 254 (1918).
(10) Twiss and Farinholt, *ibid.*, **58**, 1561–1565 (1936).

configurations of the halogenated salicylic acids. The combined action of bromine and water on all these acids produced halogenated phenols of known constitution. In this way tetrabromosalicylic acid gave pentabromophenol, 3,5,6-tribromosalicylic acid yielded 2,3,4,6-tetrabromophenol, while 3,5,6-trichlorosalicylic acid gave 2-bromo-3,4,6-trichlorophenol and 4-bromo-3,5,6-trichlorosalicylic acid formed 2,5-dibromo-3,4,6-trichlorophenol. Similarly, 3,5,6-trichlorosalicylic acid was converted into 2,3,4,6-tetrachlorophenol by the action of chlorine in the presence of water. For complete identification, acetyl and benzoyl derivatives were prepared and the melting points compared with those given in the literature.

Experimental

Halogenation of Salicylic Acid

The preparation of the following polyhalogenated salicylic acids was carried out in a three-necked Pyrex flask, fitted with a reflux condenser and a monel metal stirrer. The flask was heated by means of an oil- or water-bath; the temperatures given refer to the bath.

3,4,5,6-Tetrabromosalicylic Acid.—In 275 ml. of 60% fuming sulfuric acid, 50 g. of 3,5-dibromosalicylic acid[11] was dissolved and 28 g. (9 ml.) of bromine slowly added through a dropping funnel under the surface of the liquid while stirring vigorously. The addition took place over a period of four hours and during this time the flask was kept in a water-bath at about 30°. Toward the latter part of the reaction a crystalline solid separated. After stirring for two more hours and standing overnight, the tetrabromosalicylic acid was filtered off on a sintered glass funnel. The filtrate gave more tetrabromosalicylic acid by pouring on ice. The yield of the crude product was nearly quantitative.

3,4,5,6-Tetrabromosalicylic acid was purified by crystallization from dilute alcohol, forming clusters of white crystals which gradually decomposed at about 235–240°.

Anal. Calcd. for $C_7H_2O_3Br_4$: Br, 70.46. Found: Br, 70.33.

Acetyl 3,4,5,6-Tetrabromosalicylic Acid.—In order to furnish a check on the results above and to prepare a suitable derivative for identification, 3,4,5,6-tetrabromosalicylic acid was acetylated by heating a small amount with acetic anhydride and several drops of concentrated sulfuric acid. The solution was then carefully diluted with water, the solid filtered off and allowed to dry spontaneously on a porous plate. The acetyl derivative of 3,4,5,6-tetrabromosalicylic acid crystallizes in needles from ligroin containing a little toluene, m. p. 162.5°.

Anal. Calcd. for $C_9H_4O_4Br_4$: Br, 64.49. Found: Br, 64.34.

3,5,6-Tribromosalicylic Acid.—After dissolving 30 g. of 3,5-dibromosalicylic acid in 200 ml. of 60% fuming sulfuric acid, 8.1 g. (2.7 ml.) of bromine was added, while stirring, over a period of one and one-half hours. After the addition of the bromine, stirring was continued for another hour. The temperature was kept at about 30° throughout the reaction. Some tribromosalicylic acid precipitated from the oleum solution and was filtered off. The filtrate was diluted by pouring on ice and more of the acid thus obtained. The yield of the crude product was nearly quantitative. 3,5,6-Tribromosalicylic acid crystallizes from toluene in rectangular plates, m. p. 210.5°.

Anal. Calcd. for $C_7H_3O_3Br_3$: Br, 63.98. Found: Br, 63.70.

Acetyl 3,5,6-Tribromosalicylic Acid.—The compound was prepared following the same procedure as for the tetrabromosalicylic acid. On dilution of the acetic anhydride solution, the acetyl derivative of 3,5,6-tribromosalicylic acid separated as an oil which, after scratching and shaking, was converted into a solid. The product crystallized from ligroin in needles, m. p. 145°.

Anal. Calcd. for $C_9H_5O_4Br_3$: Br, 57.52. Found: Br, 57.73.

3,5,6-Trichlorosalicylic Acid.—3,5-Dichlorosalicylic acid was first prepared by the method of Earle and Jackson.[6] A solution of 83 g. of this material in 200 ml. of 60% fuming sulfuric acid was heated in an oil-bath to 80–90°. While stirring vigorously, a slow stream of chlorine was passed through the solution for about fifteen hours. On cooling, crystals of trichlorosalicylic acid separated and were filtered off on a sintered glass funnel. A second crop was obtained by pouring the filtrate on ice. Based on the crude product, the yield was about 70%. 3,5,6-Trichlorosalicylic acid may be crystallized from benzene, toluene, dilute acetic acid or dilute ethyl alcohol. It forms white plates, m. p. 207°.

Anal. Calcd. for $C_7H_3O_3Cl_3$: Cl, 44.08. Found: Cl, 44.06.

Acetyl 3,5,6-Trichlorosalicylic Acid.—Prepared by the procedure described above, this compound crystallizes from ligroin in needles, m. p. 129.5°.

Anal. Calcd. for $C_9H_5O_4Cl_3$: Cl, 37.53. Found: Cl, 37.77.

Attempted Preparation of Tetrachlorosalicylic Acid.—A solution of 60 g. of 3,5-dichlorosalicylic acid in 250 ml. of 60% fuming sulfuric acid was chlorinated for six hours at 40–45°, then for six hours at 65–75° and finally for seventeen hours at 100°. The resulting compound was not the anticipated tetrachloro derivative but was 3,5,6-trichlorosalicylic acid. The addition of iodine as a catalyst did not produce different results, while an attempt to chlorinate trichlorosalicylic acid with dichlorourea, according to Likhosherstov,[5] left the starting material unaltered.

4-Bromo-3,5,6-trichlorosalicylic Acid.—To a solution of 25 g. of recrystallized 3,5,6-trichlorosalicylic acid in 175 ml. of 60% fuming sulfuric acid was added 8.1 g. [2.7 ml.] of bromine through a dropping funnel over a period of about two hours while stirring. The temperature was kept at about 30°. After the addition, the solution was stirred for another hour and then diluted by pouring over ice. The white solid which separated was obtained in nearly a quantitative yield. 4-Bromo-3,5,6-trichlorosalicylic acid crystallizes from dilute alcohol in clusters of white crystals, m. p. 213°.

(11) This compound was prepared by the method of Earle and Jackson.[6] A pure product was obtained in an 87% yield.

Anal. Calcd. amount of silver to precipitate all halogen in a 0.3181 g. sample of $C_7H_2O_3BrCl_3$: 3.971 milliequivalents. Found: 3.962.

Acetyl 4-Bromo-3,5,6-trichlorosalicylic Acid.—The acetyl derivative of 4-bromo-3,5,6-trichlorosalicylic acid was prepared in the usual manner. It separates from ligroin in white crystals, m. p. 144°.

Anal. Calcd. amount of silver to precipitate all halogen in a 0.3236 g. sample of $C_9H_4O_4BrCl_3$: 3.572 milliequivalents. Found: 3.579.

Attempted Preparation of 3,5-Dichloro-4,6-diiodosalicylic Acid.—As the instability of 3,5-diiodosalicylic acid in fuming sulfuric acid may be due to the fact that the iodine atoms are in the activated positions, ortho and para to the phenolic hydroxyl, an attempt was made to iodinate 3,5-dichlorosalicylic acid in the less reactive positions 4 and 6.

To a solution of 60 g. of 3,5-dichlorosalicylic acid in 200 ml. of 60% fuming sulfuric acid, 74.5 g. of iodine was added gradually over a period of sixteen hours. The temperature was kept at 50–60° and the mixture was stirred continuously. The procedure was marked by foaming which ceased at the end of this time. Heating was then continued at 100° with 100 ml. additional fuming sulfuric acid until the foaming subsided and the cooled reaction mixture poured on ice. A dark colored solid separated and this was shown to be free iodine. No other solid precipitated and no dichlorosalicylic acid could be recovered.

Establishment of the Positions of the Halogen Atoms by Decarboxylation

The determination of the positions of the halogen atoms in the halogenosalicylic acids was accomplished by two methods. The first consisted in decarboxylating the acid, to form the corresponding phenol, by heating in a retort with an excess of dry soda lime. The desired phenol sublimed into the neck of the retort and was removed by dissolving in alkali, then reprecipitated with acid and recrystallized from a suitable solvent. As an additional check, a functional derivative was prepared and, if already known, its melting point compared with that recorded in the literature.

2,3,4,5-Tetrabromophenol was formed by heating 2,3,4,5-tetrabromosalicylic acid with powdered soda lime in a retort at 195°. It crystallizes in white needles from dilute alcohol, m. p. 123°, and has not been reported previously in the literature.

Anal. Calcd. for $C_6H_2OBr_4$: Br, 78.03. Found: Br, 78.08.

2,3,4,5-Tetrabromophenyl acetate was prepared in the usual manner with acetic anhydride and a drop of concentrated sulfuric acid. It crystallizes from dilute acetic acid in white needles, m. p. 110.5°.

Anal. Calcd. for $C_8H_4O_2Br_4$: Br, 70.78. Found: Br, 70.93.

2,3,4,5-Tetrabromophenyl benzoate was prepared by the Schotten–Baumann reaction. It crystallizes from ethyl alcohol in clusters of white needles, m. p. 133°.

Anal. Calcd. for $C_{13}H_6O_2Br_4$: Br, 62.24. Found: Br, 62.23.

2,4,5-Tribromophenol[12] (m. p. 80°) was obtained by decarboxylating 3,5,6-tribromosalicylic acid with soda lime at 200°; benzoate, m. p. 97–98°.

2,4,5-Trichlorophenol[13] (m. p. 67.5°) was obtained by decarboxylating 3,5,6-trichlorosalicylic acid with soda lime at 185°; benzoate, m. p. 89–90°.

3-Bromo-2,4,5-trichlorophenol was obtained by heating 4-bromo-3,5,6-trichlorosalicylic acid with soda lime in a retort at 185°. This compound, which has not been prepared previously, crystallizes from ligroin in clusters of white needles, m. p. 126°.

Anal. Calcd. amount of silver to precipitate all halogen in a 0.3055 g. sample of $C_6H_2OBrCl_3$: 4.421 milliequivalents. Found: 4.399.

3-Bromo-2,4,5-trichlorophenyl benzoate was prepared by the usual method. It crystallizes from dilute alcohol in clusters of needles, m. p. 125°.

Anal. Calcd. amount of silver to precipitate all halogen in a 0.1313 g. sample of $C_{13}H_6O_2BrCl_3$: 1.381 milliequivalents. Found: 1.372.

Action of Bromine and Chlorine Water on the Halogenated Salicylic Acids

Another aid in determining the position of the halogen atoms in the halogenated salicylic acids was the replacement of the carboxyl group by bromine or chlorine, thus obtaining known halogenated phenols. For complete identification, the acetyl or benzoyl derivatives were prepared and compared with the literature.

2,3,4,5,6-Pentabromophenol.—A solution of bromine in acetic acid was added to a suspension of 2,3,4,5-tetrabromosalicylic acid in 30% acetic acid. Carbon dioxide was evolved slowly. Excess bromine solution was added, the mixture was warmed to about 60° and stirred at that temperature until no more carbon dioxide was liberated. More water was added, the mixture shaken and the solid filtered off and washed thoroughly. The yield of the phenol was nearly quantitative. 2,3,4,5,6-Pentabromophenol[14] crystallizes from dilute acetic acid in white needles, m. p. 229–230°. The acetyl derivative crystallizes from acetic acid in prisms, m. p. 198–199°.

2,3,4,6-Tetrabromophenol.—Following the same procedure as in the preparation of pentabromophenol, 3,5,6-tribromosalicylic acid in dilute acetic acid was treated with bromine to give a nearly quantitative yield of 2,3,4,6-tetrabromophenol.[15] It crystallizes from dilute alcohol in clusters of needles, m. p. 112–113°. Its acetyl derivative separates from dilute acetic acid in flat plates, m. p. 105°.

2-Bromo-3,4,6-trichlorophenol.—In the same manner as above, 3,5,6-trichlorosalicylic acid was treated with bromine water. The crude phenol thus obtained was dissolved in 5% sodium hydroxide solution, filtered from a small amount of insoluble material of unknown composition, and precipitated with hydrochloric acid. 2-Bromo-

(12) *Cf.* Kohn and Pfeifer, *Monatsh.*, **48**, 211–229 (1927).

(13) *Cf.* (a) Holleman, *Rec. trav. chim.*, **39**, 736–750 (1920); (b) Kohn and Fink, *Monatsh.*, **58**, 73–91 (1931).

(14) *Cf.* Zincke and Birschel, *Ann.*, **362**, 227 (1908); Lucas and Kemp, THIS JOURNAL, **43**, 1660 (1921).

(15) *Cf.* Hodgson, Walker and Nixon, *J. Chem. Soc.*, 1054 (1933); Zincke, *Ann.*, **363**, 262–263 (1908).

3,4,6-trichlorophenol crystallizes from dilute acetic acid in white needles, m. p. 83–84°. The melting point is several degrees higher than that given by previous investigators[13b,16] but there seems to be little doubt concerning its constitution since the benzoyl derivative is identical with that prepared by Kohn and Fink. This compound crystallizes from acetic acid in prisms, m. p. 116–117°.

2,5-Dibromo-3,4,6-trichlorophenol.—Following the same procedure, 4-bromo-3,5,6-trichlorosalicylic acid was treated with bromine water. The resulting 2,5-dibromo-3,4,6-trichlorophenol[13b] crystallizes from dilute alcohol in clusters of needles, m. p. 195°. The benzoyl derivative separates from glacial acetic acid in prisms, m. p. 177–178°.

2,3,4,6-Tetrachlorophenol.—Chlorine was passed through a suspension of 3,5,6-trichlorosalicylic acid in 30% acetic acid for several hours. A heavy oil precipitated. It was washed with water several times and treated with 5% sodium hydroxide solution, in which most of the material dissolved. The alkaline solution was filtered and then acidified with hydrochloric acid. The oil which separated soon solidified. On recrystallizing several times from ligroin, the resulting needles melted at 68–69°, the melting point of 2,3,4,6-tetrachlorophenol.[17] Its acetyl derivative[18] crystallizes from dilute alcohol, and melts at 66°.

(16) *Cf.* Fox and Turner, *J. Chem. Soc.*, 1863 (1930).

Acknowledgment.—We are indebted to David Norvell Walker for his aid in carrying out part of this investigation.

Summary

1. Tri- and tetrahalogeno substituted products of salicylic acid were prepared by halogenation in fuming sulfuric acid.

2. The positions of the halogen atoms were determined (a) by decarboxylation and identification of the resulting halogenated phenols and (b) by substitution of the carboxyl groups by bromine or chlorine and subsequent identification of the halogenated phenols.

(17) *Cf.* Tiessens, *Rec. trav. chim.*, **50**, 116 (1931); Lock and Nottes, *Monatsh.*, **67**, 320 (1936).

(18) *Cf.* Blitz and Giese, *Ber.*, **37**, 4014 (1904).

LEXINGTON, VIRGINIA
BALTIMORE, MARYLAND RECEIVED FEBRUARY 23, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES, UNIVERSITY COLLEGE, CORK]

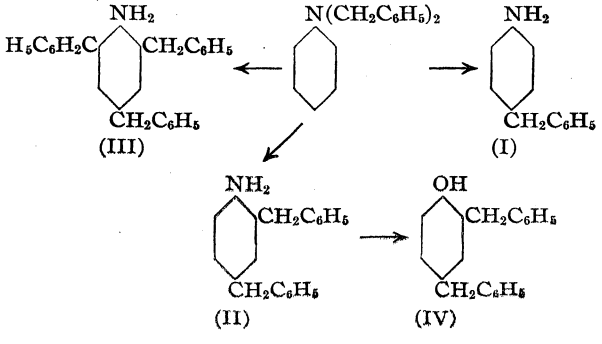
The Molecular Rearrangement of Tertiary Aryl Alkyl Anilines

BY PETER J. DRUMM, W. F. O'CONNOR AND J. REILLY

The well-known Hofmann–Martius reaction involving the rearrangement of N-substitution products of the arylamines to C-substitution compounds has, in recent years, received considerable attention. Three theories which have been put forward are that the rearrangement, which is admittedly intermolecular, consists in the migration of the alkyl group, (1) as alkyl halide, (2) as a free radical and (3) as an olefin.

It seems to the present authors, in certain cases at any rate, that another possibility may be envisaged, *viz.*, a combination of the free radical and olefin mechanisms, in which the free radical is first produced and then dissociates to give an olefin. In support of this view F. O. Rice[1] from his work on propyl radicals has concluded that all radicals higher than ethyl dissociate to give olefins. It would seem possible, therefore, in certain cases, such as in the rearrangement of isoamylaniline, where trimethylethylene has been obtained,[2] that the first step is the splitting off of the free radical isoamyl which then loses a hydrogen atom to yield the olefin trimethylethylene.

To obtain further evidence, if possible, of the mechanism involved, the authors studied the rearrangement of dibenzylaniline hydrochloride. The products isolated were *p*-aminodiphenylmethane (I), 1-amino-2,4-dibenzylbenzene (II) and an aminotribenzylbenzene which is probably 1-amino-2,4,6-tribenzylbenzene (III). The orientation of the benzyl groups in (II) was determined by its conversion into 2,4-dibenzylphenol (IV).



(1) Rice, "Annual Reports on the Progress of Chemistry," The Chemical Society, London, 1937, p. 268.

(2) Hickinbottom, *J. Chem. Soc.*, 2396 (1932).

The authors were unable to obtain evidence of the formation of dibenzyl which might be expected to occur on the basis of the "free radical" theory. An olefin mechanism is also excluded for obvious reasons. It would appear, therefore, that under the conditions employed the theory of primary dissociation into aniline and benzyl halide may be an intermediate step in the rearrangement and in support of this view it was found that on heating dibenzylaniline hydrobromide in a current of nitrogen and so removing volatile products from the sphere of reaction benzyl bromide was obtained and identified as the benzyl ester of *p*-nitrobenzoic acid. It was found that dibenzylaniline undergoes rearrangement at temperatures below 200° which is considerably lower than that necessary in the case of the alkylanilines. A similar facility of migration has been observed by Hickinbottom[3] in the case of alkylanilines with heavy groups such as the cetyl and octyl groups. A further point of interest in connection with this work is the formation of aminotribenzylbenzene. This is the first instance so far as the authors are aware where more than two groups have been introduced into the aniline ring during the molecular rearrangement of either secondary or tertiary aniline bases.

Experimental

Seventy-eight grams of dry dibenzylaniline hydrochloride was heated in a sealed tube for seven hours at 200–220°. The viscous amber-colored product was treated with dilute sodium carbonate solution, and the liberated bases extracted with ether. The ethereal solution was dried over anhydrous sodium sulfate, the ether distilled off and the residual oil fractionated. The following fractions were collected: I, 15.6 g., b. p. 180–220° at 20 mm.; II, 24.2 g., b. p. 250–285° at 20 mm.; III, 15.0 g., b. p. 290–300° at 20 mm.

p-Aminodiphenylmethane.—Fraction I was redistilled and yielded 14.1 g. of an oil boiling at 185–190° at 14 mm. This oil readily dissolved, on heating, in dilute hydrochloric acid. On cooling the hydrochloride was deposited as colorless plates melting at 219°.

Anal. Calcd. for $C_{13}H_{14}NCl$: Cl, 16.17. Found: Cl, 16.26.

On conversion of this hydrochloride into the base, the latter was obtained as a solid which separated from ligroin in the form of colorless plates which melted at 36° alone or when mixed with a specimen of pure *p*-aminodiphenylmethane.[4] Benzoyl-*p*-aminodiphenylmethane crystallizes from alcohol in long, thin, prismatic needles, m. p. 165°.

Anal. Calcd. for $C_{20}H_{17}ON$: N, 4.88. Found: N, 4.82.

Diphenylmethane-4-azo-β-naphthol forms scarlet needles from alcohol, m. p. 141°.

Anal. Calcd. for $C_{23}H_{18}ON_2$: N, 8.28. Found: N, 8.34.

Fraction II.—This fraction on redistillation gave 22.8 g. of a light-yellow colored viscous oil, b. p. 250–260° at 11 mm. On dissolving in hot aqueous alcoholic hydrochloric acid and allowing the solution to cool slowly the hydrochloride separated and was subsequently crystallized from a mixture of chloroform and light petroleum (b. p. 60–80°) from which it separated in the form of needles melting at 171°.

Anal. Calcd. for $C_{20}H_{20}NCl$: Cl, 11.47. Found: Cl, 11.69.

The free base crystallizes from light petroleum (b. p. 40–60°) in colorless needles melting at 50°.[3]

Anal. Calcd. for $C_{20}H_{19}N$: C, 87.91; H, 6.96; N, 5.12. Found: C, 87.83; H, 7.08; N, 5.13.

Identification of above Base as 1-Amino-2,4-dibenzylbenzene.—Twenty-two grams of the above base was dissolved in dilute sulfuric acid. The solution was cooled to 5° and diazotized by the addition of an aqueous solution of 5.6 g. of sodium nitrite. The whole was then heated slowly to 60° and maintained at this temperature until evolution of nitrogen was complete. The product was extracted with ether and the residue after evaporation of the latter was distilled under reduced pressure giving a pale-yellow oil, b. p. 250–255° at 10 mm. This oil which was phenolic in character was still contaminated with traces of unchanged amine which interfered with its subsequent characterization. To remove the last traces of amine the oil was boiled with tin and hydrochloric acid and the cold acid solution extracted with ether. On removal of the latter the phenol was obtained as a colorless oil, b. p. 252–254° at 10 mm. It was converted into its α-naphthyl urethan derivative by heating with α-naphthyl carbimide almost to the boiling point for a few minutes. The oily product was extracted repeatedly with hot ligroin and filtered from the di-α-naphthyl carbamide. From the filtrate the α-naphthyl urethan separated in light yellow crystals m. p. 143–144°. A mixture of this substance with the α-naphthyl urethan of 2,4-dibenzylphenol[5] melted at 143–144°, with which substance it was identical. The base melting at 50°, obtained from fraction II above, is therefore 1-amino-2,4-dibenzylbenzene.

1-Benzoylamino-2,4-dibenzylbenzene separates as long, colorless needles from alcohol, m. p. 158°.

Anal. Calcd. for $C_{27}H_{23}ON$: N, 3.71. Found: N, 3.66.

2,4-Dibenzylbenzene-1-azo-β-naphthol.—It was found advantageous to carry out the diazotization of the amine in glacial acetic acid solution. The azo-β-naphthol was obtained from alcohol–chloroform in long red needles melting at 154°.

Anal. Calcd. for $C_{30}H_{24}ON_2$: N, 6.54. Found: N, 6.73.

Fraction III.—This oil, b. p. 290–300° at 20 mm., was dissolved in warm glacial acetic acid and concentrated hydrochloric acid added. The precipitated hydrochloride

(3) Hickinbottom, *J. Chem. Soc.*, 1119 (1927).
(4) Bamler, *Ber.*, 16, 2718 (1883).
(5) Short and Stewart, *J. Chem. Soc.*, 583 (1929).

was collected and recrystallized several times from ethyl acetate from which solvent it was obtained in clusters of needles melting at 186°.

Anal. Calcd. for $C_{27}H_{26}ClN$: Cl, 8.89. Found: Cl, 8.94.

The free base from the above hydrochloride crystallizes from ligroin in colorless, prismatic plates, m. p. 61–62°.

Anal. Calcd. for $C_{27}H_{25}N$: N, 3.86. Found: N, 3.78.

This substance is a primary amine and the results of analysis of itself and its derivatives agree with its formulation as an aminotribenzylbenzene. Hofmann, in his study of the molecular rearrangement of phenyltrimethylammonium iodide, obtained mesidine.[6] By analogy it is probable that the above aminotribenzylbenzene is 1-amino-2,4,6-tribenzylbenzene.

Benzoylaminotribenzylbenzene.—This compound crystallizes from alcohol in needles, m. p. 149°. *Anal.* Calcd. for $C_{34}H_{29}ON$: N, 3.00. Found: N, 3.01.

(6) Hofmann, *Ber.*, **5**, 715 (1872).

Tribenzylbenzene-azo-β-naphthol.—Crystallizes from alcohol in scarlet prisms with copper glance, m. p. 146°. *Anal.* Calcd. for $C_{37}H_{30}ON_2$: N, 5.41. Found: N, 5.61.

Summary

The molecular rearrangement of dibenzylaniline hydrochloride has been studied. The rearrangement proceeded at a comparatively low temperature with formation of *p*-aminodiphenylmethane, 1-amino-2,4-dibenzylbenzene and a third amine which is probably 1-amino-2,4,6-tribenzylbenzene. This would appear to be the first instance where three migrating groups have been introduced into the aniline ring during the rearrangement of a secondary or tertiary aniline base.

CORK, IRELAND RECEIVED NOVEMBER 29, 1939

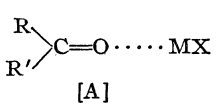
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF IOWA STATE COLLEGE]

Coördinate Compounds in the Color Test for Organometallic Compounds[1]

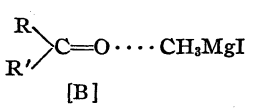
BY HENRY GILMAN AND R. G. JONES

The color test[2] is probably the most useful laboratory tool in studies on organometallic compounds. However, because Michler ketone, the essential compound in the color test, can form coördinate compounds with Grignard reagents, it is necessary to examine the possible interference effects of coördinate compounds.

The formal relationship of organometallic compounds to salts, made it a relatively short step from Werner's[3] coördination structures of the carbonyl type with salts [A], to the suggestion, which probably first was proposed by Straus,[4] for coördination compounds of ketones with the



[A]



[B]

Grignard reagent [B]. Later, v. Braun[5] and then, particularly, Meisenheimer and co-workers[6] and Hess and Rheinboldt[7] used the coördination structures as a basis for interpreting some reactions of carbonyl compounds with the Grignard reagent.[8]

There is no doubt that coördination complexes of some sort are formed with many ketones and Grignard reagents. Not only have some of the complexes been isolated and analyzed, but they have been hydrolyzed to the original ketones.[9] The most interesting and suggestive recent study is by Pfeiffer and Blank.[10] They examined the molecular compounds derived by interaction of some Grignard reagents with benzophenone, *p*-aminobenzophenone, *p*-dimethylaminobenzophenone, and, of especial interest at this time, *p,p'*-tetramethyldiaminobenzophenone or Michler ketone. In each case, the complex formed by a 1:1 ratio of ketone and Grignard reagent regenerated the ketone on hydrolysis. With benzo-

(1) This is Paper XXX in the series of "Relative reactivities of organometallic compounds; the preceding paper is: THIS JOURNAL, **62**, 980 (1940).

(2) (a) Gilman and Schulze, *ibid.*, **47**, 2002 (1925); (b) *Bull. soc. chim.*, **41**, 1479 (1927); (c) Gilman and Heck, *Rec. trav. chim.*, **48**, 193 (1929); (d) *ibid.*, **49**, 218 (1930); (e) *Ber.*, **62**, 1379 (1929); (f) Gilman, Sweeney and Heck, THIS JOURNAL, **52**, 1604 (1930); (g) Gilman and Heck, *ibid.*, **52**, 4949 (1930).

(3) Werner, *Ann.*, **322**, 296 (1902).

(4) Straus, *ibid.*, **393**, 241 (1912).

(5) Von Braun and Kirschbaum, *Ber.*, **52**, 1725 (1919).

(6) Meisenheimer and Casper, *ibid.*, **54**, 1655 (1921); Meisenheimer, *ibid.*, **61**, 708 (1928); *Ann.*, **442**, 180 (1925); **446**, 76 (1925).

(7) Hess and Rheinboldt, *Ber.*, **54**, 2043 (1921). See, also, Hess and Wustrow, *Ann.*, **437**, 256 (1924).

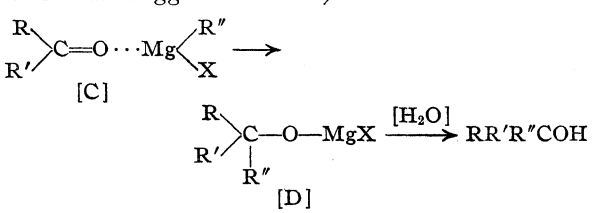
(8) Earlier adaptations of coördinate structures were proposed for the structures of Grignard reagents. Some selected references are: Baeyer and Villiger, *Ber.*, **35**, 1202 (1902); Grignard, *Compt. rend.*, **136**, 1262 (1903); Chelinzeff, *Ber.*, **38**, 3665 (1905). Modern electronic concepts of valence are discussed by Johnson in Chap. 19 of Gilman, "Organic Chemistry," John Wiley and Sons, New York, 1938. See, particularly, p. 1673, for the preliminary coördination and subsequent migrations in the reaction of ketones with Grignard reagents.

(9) Leroide, *Compt. rend.*, **148**, 1611 (1909). Fischer and Hess, *Ber.*, **45**, 912 (1912).

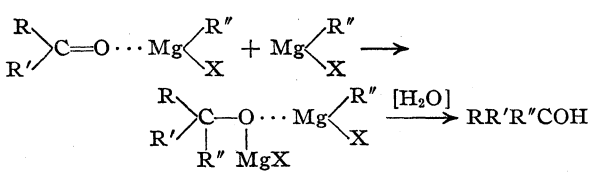
(10) Pfeiffer and Blank, *J. prakt. Chem.*, **153**, 242 (1939).

phenone a 1:2 ratio of ketone to RMgX compound produced intramolecular reaction resulting in the alcohol, triphenylcarbinol. With *p*-aminobenzophenone and *p*-dimethylaminobenzophenone it was found that a ratio of 1:3 of ketone to RMgX compound was necessary to obtain the carbinol under comparable conditions. With Michler ketone, a 1:4 ratio of ketone to RMgX compound gave *p,p'*-tetramethyldiaminodiphenylpropene, $[(CH_3)_2NC_6H_4]_2C{=}CHCH_3$, the dehydration product of the carbinol to be expected from Michler ketone and ethylmagnesium bromide.

Pfeiffer interpreted the reactions in accordance with his halochrome theory, stating that the unsaturated carbonyl carbon atom in complex [C] can become saturated in two ways. Either the R″ group wanders from the magnesium atom to the carbonyl carbon atom (as Meisenheimer[6] and Hess[7] suggested earlier)



or the R″ group of a second Grignard molecule attaches itself to the unsaturated carbon.



In accordance with the observations of Pfeiffer and Blank[10] we find that a complex is formed between Michler ketone and phenylmagnesium bromide in a 1:1 ratio in ether, and that this complex on hydrolysis yields Michler ketone. However, even though the ratio was as low as 1:1, the recovery of ketone was only 88%. Of greater significance is the fact that this mixture gave a color test. One may conclude then that the complexes from Michler ketone and Grignard reagent are not so stable but what they rearrange sufficiently to a true valence type of carbinol salt [D] to give a color test.

The stability of such complexes appears to be influenced by solvents. When the experiment with a 1:1 ratio of Michler ketone to phenylmagnesium bromide was carried out not in ether alone, but in a solution containing mostly benzene, the yield of ketone recovered was only 45%, and there was actually isolated a 42% yield of the carbinol (*p,p'*-tetramethyldiaminotriphenylcarbinol) which is the intermediate compound in the color test for phenylmetallic compounds. From the work mentioned later in this paper on the etherate of triethylgallium, one might expect that compounds like ethers would dampen the reactivity of some organometallic compounds by the formation of coördinate compounds. Fortunately, the color test is always carried out with a benzene solution of Michler ketone and this may help to give the high degree of sensitivity reported[2] for the color tests. In this connection, there is no essential difference in the sensitivity of the color tests for ethylmagnesium bromide and phenylmagnesium bromide.[2c]

Relative Reactivities of Organometallic Compounds.—There appears to be some correlation between the tendency of organometallic compounds to form coördinate compounds with ketones and the relative reactivities of organometallic compounds. We observed no stable complex with Michler ketone, in ether or in benzene, in reactions carried out with phenyllithium at room temperature with equivalent quantities of reactants. The yields of *p,p'*-tetramethyldiaminotriphenylcarbinol were 78% and 92.5%, respectively, and no Michler ketone was recovered. We reported recently[11] that a liberal excess of triphenylgallium was necessary for a color test. This is very probably due to the pronounced tendency of gallium compounds to form complexes. For example, Dennis and Patnode[12] have shown that the simple triethylgallium $[(C_2H_5)_3Ga]$ reacts violently with water; the etherate $[(C_2H_5)_3Ga{\cdot}(C_2H_5)_2O]$ vigorously; and the ammine $[(C_2H_5)_3Ga{\cdot}NH_3]$ only very slowly.

With the three arylmetallic compounds mentioned, the order of decrease in relative reactivities and increase in tendency to form coördinate compounds with ketones is: C_6H_5Li, C_6H_5MgBr, $(C_6H_5)_3Ga$.

Relative Reactivities of Functional Groups.—In a study of the relative reactivities of some functional groups with phenylmagnesium bromide, Entemann and Johnson[13] observed that benzophenone and benzoyl chloride were of about the same reactivity. It has been shown that benzoyl chloride is decidedly more reactive than benzophenone when other less reactive or-

(11) Gilman and Jones, THIS JOURNAL, **62**, 980 (1940).
(12) Dennis and Patnode, *ibid.*, **54**, 182 (1932).
(13) Entemann and Johnson, *ibid.*, **55**, 2900 (1933).

ganometallic compounds like those of mercury,[14a] thallium[14b] and gallium[11] are used. It is quite likely that all organometallic compounds which react with carbonyl containing compounds first form coördinate compounds or complexes of varying stabilities. The less reactive RM compounds may form more stable coördinate linkages with the carbonyl group in ketones than with the carbonyl group in acid halides; and the coördinate complexes with the less reactive RM compounds may stabilize themselves by the direct removal of halogen to form a metal halide rather than by prior addition of the R of the RM compound to the unsaturated carbonyl carbon atom. Varying coördination effects of solvents may influence significantly the relative reactivities of RM compounds.

Steric Hindrance.—It now appears reasonable to suggest that the absence of reaction or very slow reaction observed with some ketones and Grignard reagents may be due appreciably to the formation of coördinate compounds rather than to steric hindrance. Von Braun and coworkers[5,15] observed that $C_6H_5N(CH_3)CH_2CH_2MgX$ reacted with aldehydes but not with ketones; but did find that $C_6H_5N(CH_3)CH_2CH_2CH_2MgX$ reacted with both aldehydes and ketones. These results appear to present an excellent case for steric hindrance for not only is there less steric hindrance with aldehydes than with ketones, but the further removal of the MgX group from the nitrogen in the γ-propyl Grignard reagent should give less steric hindrance than the homologous β-ethyl Grignard reagent. However, not only do aldehydes form less stable complexes than ketones,[6,7] but Heck[2e] showed later that the β-ethyl Grignard reagent did undergo a slower than usual reaction with Michler ketone and color tests were obtained. It is possible that more stable coördination compounds are formed in such cases because of the amino groups present in both the Grignard reagent and the Michler ketone, if one may carry over the analogy from the relatively less reactive ammines of triethylgallium[12] mentioned previously. Furthermore, the experiments of Pfeiffer and Blank[10] illustrate in a striking fashion that the tendency to form coördinate complexes with the Grignard reagent increases progressively with the introduction of amino groups in the ketone: $(C_6H_5)_2CO <$ $(NH_2C_6H_4)(C_6H_5)CO$; $[(CH_3)_2NC_6H_4](C_6H_5)CO <$ $[(CH_3)_2NC_6H_4]_2CO$.

However, these authors[10] have misinterpreted the experiments of Klages[16] on the reaction of acetomesitylene with ethylmagnesium iodide. These two reactants gave a product which on hydrolysis yielded the original acetomesitylene. The product, however, was not a coördination complex stabilized in some way by steric hindrance, for reaction with the Grignard reagent was not inhibited. Actually, as Kohler and Baltzly[17] have demonstrated, Klages had in hand an iodomagnesium enolate, which on hydrolysis yields the acetomesitylene

$$(CH_3)_3C_6H_2COCH_3 \xrightarrow{[C_2H_5MgI]} (CH_3)_3C_6H_2C(OMgI)=CH_2 \xrightarrow{[H_2O]} (CH_3)_3C_6H_2COCH_3$$

Not only is there no stabilization of a complex with acetomesitylene because of steric hindrance, but an equally sterically hindered Grignard reagent (mesitylmagnesium bromide) gives a strong color test.[2e] Also, color tests are obtained with sterically hindered aliphatic Grignard reagents like the *t*-butylmagnesium halides, *t*-amylmagnesium chloride, and methyldiethylmethylmagnesium chloride.[2b]

Dimorphism with *p,p'*-Tetramethyldiaminotriphenylcarbinol.—Two forms of this carbinol were first reported[18]: a higher melting one from petroleum ether, and a lower melting one from methanol. Later,[19] only the lower melting form was isolated from several solvents including petroleum ether. In our work, we obtained both forms and showed that they could be interchanged by selection of the appropriate solvent.

Experimental Part

Phenylmagnesium Bromide and Michler Ketone.—The Grignard reagent was prepared in a nitrogen atmosphere, and its concentration was determined by the acid-titration procedure.[20]

A 0.5-cc. sample of the 1.06 molar solution of phenylmagnesium bromide was added dropwise to a rapidly stirred suspension of 1.34 g. (0.005 mole) of Michler ketone

(14) (a) Gilman and Nelson, THIS JOURNAL, **61**, 743 (1939); (b) Gilman and Jones, *ibid.*, **61**, 1513 (1939).

(15) Von Braun, Heider and Müller, *Ber.*, **50**, 1637 (1917).

(16) Klages, *ibid.*, **35**, 2635 (1902).

(17) Kohler and Baltzly, THIS JOURNAL, **54**, 4015 (1932). See subsequent papers in THIS JOURNAL, particularly by Kohler and by Fuson. It would be interesting to learn whether highly reactive organometallic compounds might add to the carbonyl group in compounds like acetomesitylene.

(18) Villiger and Kapetschni, *Ber.*, **45**, 2910 (1912).

(19) Meisenheimer and co-workers, *Ann.*, **423**, 95 (1921).

(20) Gilman, Wilkinson, Fishel and Meyers, THIS JOURNAL, **45**, 150 (1923).

in 50 cc. of dry ether. The resulting solution gave a strong positive color test when a 1-cc. sample was removed, hydrolyzed and treated with the iodine–acetic acid solution used to complete the color test.[2a] Another 4.5 cc. of the Grignard solution was then added to the Michler ketone suspension, the several operations being carried out in nitrogen, at room temperature, and with rapid stirring. A bright orange precipitate quickly formed as the phenylmagnesium bromide was added. Stirring was continued for fifteen minutes, and then the mixture was hydrolyzed by the addition of 75 cc. of dilute aqueous ammonium chloride solution. The solid which was insoluble in both the ether and water layers was filtered off, washed with ether and water, and shown by the method of mixed melting points to be Michler ketone (1.11 g.). The ether layer was separated and dried, and the ether removed by distillation. The residue was extracted with 20 cc. of hot petroleum ether (b. p. 60–68°) and the insoluble portion (0.08 g.) was shown to be Michler ketone. The total yield of ketone recovered was 1.19 g. or 88%. The experiment was repeated, again using a 1:1 ratio of phenylmagnesium bromide and Michler ketone, and the same results were obtained.

Another reaction was carried out in which 6.8 cc. of 0.73 molar phenylmagnesium bromide solution (0.005 mole of RMgX compound) was added to a stirred solution of 1.34 g. (0.005 mole) of Michler ketone in 40 cc. of dry benzene. A heavy orange precipitate formed quickly, but most of it soon went into solution. After stirring for fifteen minutes at room temperature in an atmosphere of nitrogen, the mixture was hydrolyzed with 75 cc. of dilute ammonium chloride solution. The benzene layer was separated, dried, and then the benzene removed by distillation. The residue was extracted with two 25-cc. portions of hot petroleum ether (b. p. 60–68°). The insoluble portion, after filtering and drying, weighed 0.6 g. and melted between 162 and 165°. After one crystallization from 95% ethanol, the melting point and mixed melting point with an authentic specimen of Michler ketone was 172–173°. The petroleum ether solution deposited, on cooling, 0.72 g. of granular crystals, which after crystallization from methanol melted at 106°, and were shown by the method of mixed melting points to be *p,p'*-tetramethyldiaminotriphenylcarbinol. The yield of recovered Michler ketone was 45% and the yield of carbinol was 42%. This experiment was repeated and the results were practically the same.

Color Tests with Dilute Solutions of Phenylmagnesium Bromide. [A].—A solution of phenylmagnesium bromide was diluted with dry ether and a resulting 0.238 molar solution was used in the following tests. Various quantities of this Grignard solution were added to dry test-tubes containing 2.0-cc. portions of a 0.067 molar benzene solution of Michler ketone. After about one minute, the mixtures were hydrolyzed with 1-cc. portions of water, and then 3 drops of the iodine–glacial acetic acid reagent[2a] were added. The smallest volume of the Grignard solution which would produce a positive color test was 0.07 cc. A good test was obtained when 0.1 cc. was used, and more than 0.2 cc. gave a very strong color test. The ratio of reactants in the case requiring the least quantity of Grignard reagent to give a positive test is 1.7×10^{-5} mole of phenylmagnesium bromide to 1.3×10^{-4} mole of Michler ketone in 2 cc. of solution, or a 13-fold excess of Michler ketone.

[B]. The Grignard solution was again diluted, and this time to a concentration of 0.053 molar. A 5-cc. portion of this solution was required to give a faint positive test with 1 cc. of 0.067 molar Michler ketone solution. The concentrations in this case are equivalent to 8.8×10^{-5} mole of Grignard reagent and 2.2×10^{-5} mole of Michler ketone in 2 cc. of solution, or a four-fold excess of Grignard reagent.

It will be noted that in experiment [A] the relatively high initial ratio of Grignard reagent to ketone together with the presence of much benzene combine to favor a color test. In experiment [B] the situation is reversed for not only is the initial ratio of Grignard reagent to ketone sharply decreased, but the medium is also largely ether.

Phenyllithium and Michler Ketone.—An ether solution of phenyllithium, 0.744 molar in concentration, was prepared in the usual manner from bromobenzene and lithium.[21] To a rapidly stirred suspension of 1.34 g. (0.005 mole) of Michler ketone in 50 cc. of ether was added dropwise 6.8 cc. of the 0.744 molar phenyllithium solution or 0.005 mole of phenyllithium. The suspended material quickly dissolved, and the clear brown solution was stirred at room temperature for fifteen minutes. Hydrolysis was effected by distilled water; the ether layer was separated and dried, and the ether was removed by distillation. The residue was crystallized from petroleum ether, and the white crystalline product weighed 1.35 g. and melted at 121–122°. It was then recrystallized from methanol, and found to melt at 107–107.5°. An authentic sample of *p,p'*-tetramethyldiaminotriphenylcarbinol was obtained by dissolving Merck malachite green in water, precipitating the carbinol with dilute potassium carbonate and crystallizing twice from methanol to give a product melting at 107°. A mixed melting point of the two different samples (one melting at 107–107.5° and the other at 107°) was 107–108°.

The carbinol obtained from phenyllithium (m. p. 107–107.5°) was crystallized twice from petroleum ether (b. p. 60–68°) and again melted at 120°.

No unreacted ketone was recovered, and the yield of carbinol was 78%.

The experiment with phenyllithium was repeated except that benzene was used as the solvent for the ketone. In this case the yield of carbinol melting at 105–107° (mixed melting point) was 1.6 g. or 92.5%. No Michler ketone was recovered.

Summary

A 1:1 mixture of Michler ketone and phenylmagnesium bromide in ether forms a coördination compound, which on hydrolysis gives an 88% recovery of ketone. However, the coördination compound is sufficiently unstable so that there is no interference with the color test for organometallic compounds. The stability of the complex is markedly decreased in an ether–benzene mixture, and in addition to a 45% recovery of ke-

(21) Gilman, Zoellner and Selby, THIS JOURNAL, 55, 1252 (1933).

tone there was isolated a 42% yield of *p,p'*-tetramethyldiaminotriphenylcarbinol.

A 1:1 mixture of Michler ketone and phenyllithium, in either benzene or ether, forms no stable complex and the only product isolated in excellent yields is the carbinol, which is an intermediate in the color test.

Other aspects of coördination compounds in organometallic chemistry are considered.

AMES, IOWA RECEIVED MARCH 18, 1940

[CONTRIBUTION FROM THE MENDENHALL LABORATORY OF PHYSICS, OHIO STATE UNIVERSITY]

Spectroscopic Evidence for Hydrogen Bonds: The Hexyl Alcohols. I[1]

BY SPENCER C. STANFORD[2] AND WALTER GORDY[3]

Many papers dealing with the infrared absorption spectra of the alcohols have appeared since the discovery that such spectra give direct evidence of the linkage involved in association through hydrogen bonding. The work on the alcohols through 1938 has been summarized by Freymann.[4]

Previous work, pertinent to the present discussion, may be summarized briefly as follows. In the region of the —OH fundamental vibration band, there is found, in the pure liquid at ordinary temperatures, a broad, intense band with its center at 2.95–3.00 μ. On dilution with an inert solvent such as carbon tetrachloride, or on increasing the temperature, the broad band begins to decrease in intensity. Because of this behavior the band is attributed to the presence of associated molecules. As the broad band diminishes in intensity a sharp band appears at 2.75 μ. This band increases in intensity with increased dilution or temperature and is attributed to single alcohol molecules.

Work on the overtones gives results similar to those on the fundamental. However, in the overtone regions, traces of the monomer bands are found, even in the pure liquids at ordinary temperatures, in alcohols above methyl alcohol. The increased symmetry of the potential energy curve of the proton due to hydrogen bonding causes the overtone association bands to be weak in comparison to the fundamental association band, hence the monomer band is not overlapped as much by the association band.[5]

So far as the authors know, no research has been done on a complete series of isomeric alcohols. It appeared of interest to us to study one such series to see if there are detectable differences in association due to variations in structure. Fortunately the hexyl alcohols were available to us, through the courtesy of Dr. Frank Hovorka, of Western Reserve University. The present paper reports the results of the investigation of eight of the seventeen possible hexyl alcohols.

Experimental Technique.—The preparation and purification of hexanol-1, -2, -3, 2-methylpentanol-1, -2, and -4 has been described in the literature.[6] The preparation of 3-methylpentanol-1 and 2-ethylbutanol-1 will be described in publications soon to appear. The boiling point range did not exceed $\pm 0.02°$ in any of the alcohols studied. The spectrometer and experimental method have been described in a previous paper of this series.[7]

Results and Discussion

The transmission curves for the pure liquids are given in Fig. 1. There is no trace of the monomer band at 2.75 μ. The minimum of the association band is at 2.97 μ for hexanol-1 and 3-methylpentanol-1, the other bands have their minima at 2.95 μ. This slight shift appears to be real, since we were able to reproduce the position of the minima.

There is a gradual increase in the per cent. transmission at the minimum and a decrease in the breadth of the band as one goes from hexanol-1 to hexanol-3. These and differences in intensity among the other pure liquid curves could possibly be due to error in reproducing cell thickness with such thin cells. It is probable, however, that

(1) A summary of this paper was read at the Ohio-Michigan Regional Meeting of the American Chemical Society, East Lansing, Michigan, October 28, 1939.

(2) Department of Chemistry, College of Wooster, Wooster, Ohio.

(3) Department of Physics, Mary Hardin-Baylor College, Belton, Texas.

(4) Freymann, *J. phys. radium*, **9**, 517 (1938).

(5) See, for example, Errera and Sack, *Trans. Faraday Soc.*, **34**, 728 (1938).

(6) (a) Hovorka, Lankelma and Naujoks, THIS JOURNAL, **55**, 4820 (1933); (b) Hovorka, Lankelma and Stanford, *ibid.*, **60**, 820 (1938).

(7) Gordy and Stanford, *ibid.*, **62**, 497 (1940).

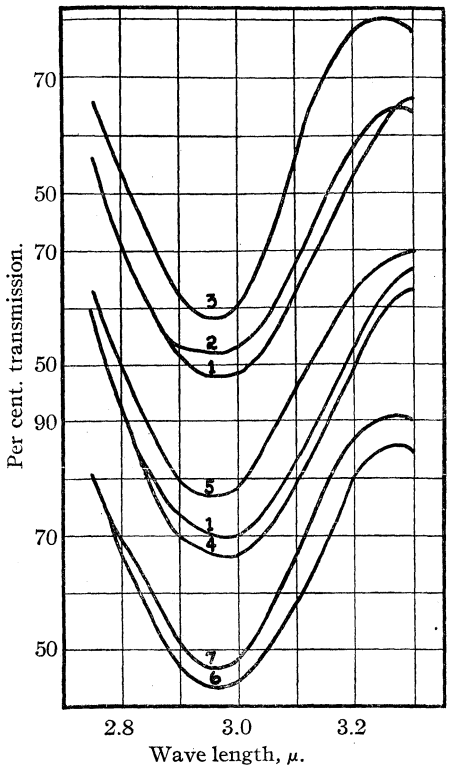


Fig. 1.—Pure liquids, cell thickness, 0.015 mm.: (1) hexanol-1; (2) hexanol-2; 2-methylpentanol-2; (3) hexanol-3; (4) 3-methylpentanol-1; (5) 2-methylpentanol-1; (6) 2-ethylbutanol-1; (7) 2-methylpentanol-4.

they are caused partly by structural differences since similar differences are noted in the solution curves where cell thicknesses are accurate.

For the solutions we have plotted molecular extinction coefficients as a function of wave length. Figure 2 shows the curves for the 0.291 molar solutions. At this concentration there is a distinct monomer band. This band is at 2.75 μ, within the limits of experimental error, for all the alcohols studied. This fact shows that there is no detectable interaction between the —OH and adjacent groups; consequently differences in the association bands may be attributed entirely to differences in association caused by variations in the structure of the alcohol molecules.

The slight differences in the bands of the pure liquids become much more pronounced in the 0.291 molar solutions. Figure 2A shows that there is a marked change in intensity and band position as the hydroxyl is moved from the 1- to the 3-position. The center of the association band for hexanol-2 is at a slightly shorter wave length (2.95 μ) than for hexanol-1 (2.97 μ). The center of the hexanol-3 band is at 2.88 μ. Figure 2B shows that the primary alcohols with side chains fall in a single group having smaller intensity and maxima at shorter wave lengths than is the case with hexanol-1. The curves for these alcohols are identical, within the limits of experimental error, so only the curve for 2-methylpentanol-1 is given. The secondary alcohol, 2-methylpentanol-4, and the tertiary alcohol, 2-methylpentanol-2, give similar curves. The maxima for these alcohols are at the same wave length (2.95 μ) as for the primary branched chain compounds but the intensity is somewhat less.

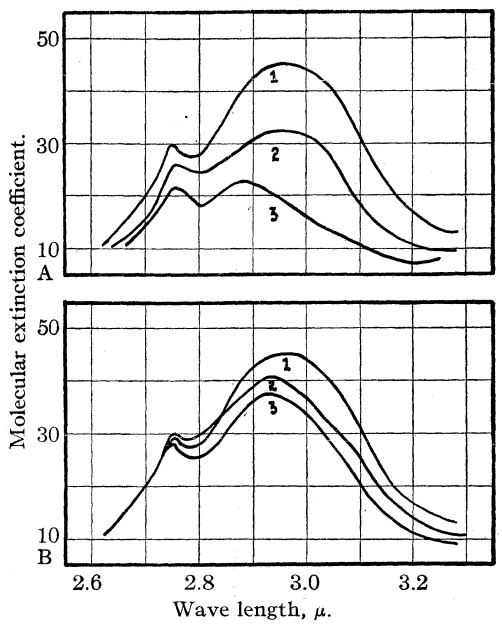


Fig. 2.—Concentration, 0.291 molar; cell thickness, 0.56 mm.: A.—(1) hexanol-1; (2) hexanol-2; (3) hexanol-3. B.—(1) hexanol-1; (2) 2-methylpentanol-1; 2-ethylbutanol-1; 3-methylpentanol-1; (3) 2-methylpentanol-4; 2-methylpentanol-2.

The curves for the 0.1 molar solutions are shown in Fig. 3. The primary alcohols, hexanol-1 and 3-methylpentanol-1 show two well defined components in the association band at 2.91 and 3.03 μ. In hexanol-2 the longer wave length component is not as pronounced and the short wave length component is at 2.89 μ. In hexanol-3 the long wave length component has completely disappeared and the short wave length component is at 2.86 μ. The remainder of the alcohols give very similar curves. The short wave length component is at 2.86 μ and the long wave length component is extremely weak and poorly defined.

The results for the 0.05 molar solutions are plotted in Fig. 4. At this concentration the long

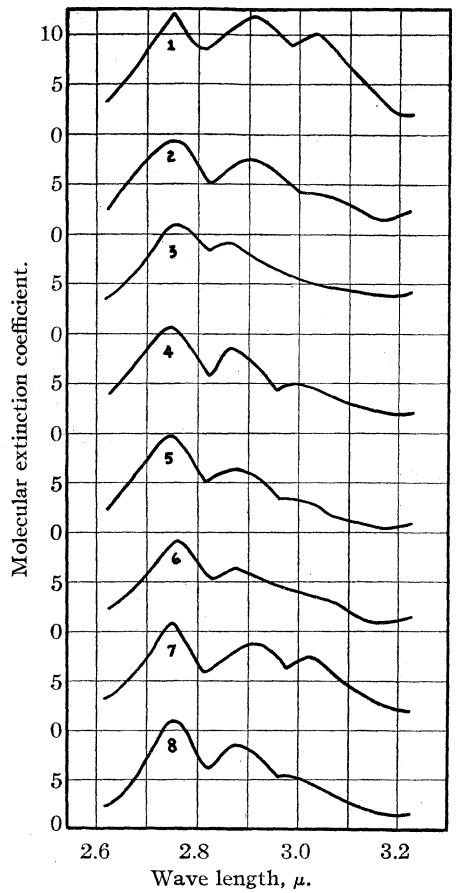


Fig. 3.—Concentration, 0.1 molar; cell thickness, 1.63 mm.: (1) hexanol-1; (2) hexanol-2; (3) hexanol-3; (4) 2-methylpentanol-1; (5) 2-methylpentanol-2; (6) 2-methylpentanol-4; (7) 3-methylpentanol-1; (8) 2-ethylbutanol-1.

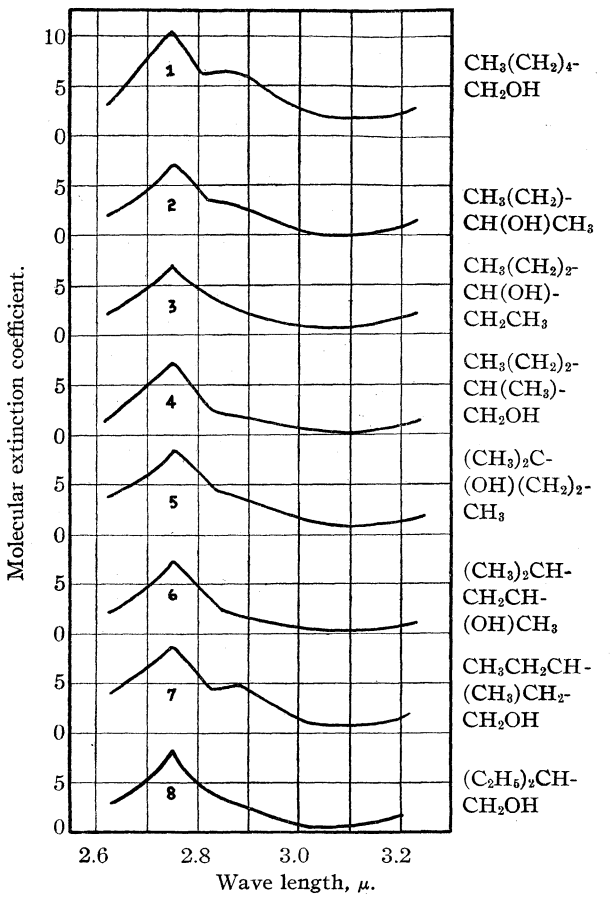
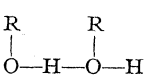


Fig. 4.—Concentration, 0.05 molar; cell thickness, 3.31 mm.: (1) hexanol-1; (2) hexanol-2; (3) hexanol-3; (4) 2-methylpentanol-1; (5) 2-methylpentanol-2; (6) 2-methylpentanol-4; (7) 3-methylpentanol-1; (8) 2-ethylbutanol-1.

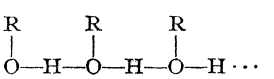
wave length component of the association band has disappeared. The curves fall into the same groups found with the 0.1 molar solutions. In hexanol-1 and 3-methylpentanol-1 there is a distinct band at about 2.86 μ. Hexanol-3 shows only the monomer band at 2.75 μ. In the remaining curves there is a slight indication of absorption in the region of the association band, showing that at this concentration these alcohols are not completely broken down into monomers.

Fox and Martin,[8] studying aliphatic alcohols in carbon tetrachloride at a concentration of 0.112 molar, resolved the association band into two components. Their results were similar to ours, in that they found the long wave length component predominant in the primary alcohols, and the short wave length component predominant in tertiary butyl alcohol. They suggested that the two components might be due to dimers and higher polymers.

In the dimer association



the energy of a single hydrogen bond is supplied by two separate —OH groups of different molecules. Here neither —OH group acts both as a proton donor and as a proton acceptor, as do the —OH groups (with the exception of the end group) of long chain polymers,



where the number of hydrogen bonds per —OH group approaches one as the chain increases in length. If the hydrogen bonds in the dimer are of the same order of strength as those in the higher

(8) Fox and Martin, *Proc. Roy. Soc.* (London), **A162**, 419 (1937).

polymer, one for the above reasons would expect the dimer association to produce less disturbance of the —OH band than the longer chain polymerization. Thus for alcohols which form long chain polymers, one would expect, as is observed, a shift to shorter wave lengths of the —OH band as the length of the chains is diminished either by dilution in an inert solvent or by an increase of temperature. When the dimer stage is reached further breaking down of the polymer would of course cause a sudden jump of the band to the position of monomeric absorption.

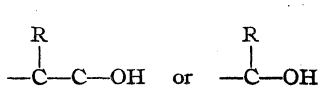
Application of this hypothesis suggests that hexanol-3 in the liquid state (Fig. 1) consists chiefly of lower polymers, possibly dimers, since the band is less intense than that for hexanol-1 and the maximum occurs at the shorter wave length. The other alcohols give curves which are more difficult of interpretation, but the results indicate that these compounds tend to form more dimers than hexanol-1.

Apparently hexanol-3, in 0.291 molar solution in carbon tetrachloride, consists almost entirely of dimers. The rest of the alcohols, at this concentration, appear to form a group intermediate between hexanol-1 and hexanol-3.

In 0.1 molar solution three well-defined groups are found. The primary alcohols, hexanol-1 and 3-methylpentanol-1, show two distinct bands with the short wave length component predominant, indicating that at this concentration more of the molecules exist as dimers than as higher polymers. Hexanol-3 is in a class by itself, with only a weak dimer band. The remainder of the alcohols form a group with very similar bands. In these alcohols there is still a trace of the higher polymer band.

In 0.05 molar solution hexanol-3 is present entirely as monomer. Hexanol-1 and 3-methylpentanol-1 still contain an appreciable amount of dimers. The rest of the alcohols show slight absorption in the region of the association band, indicating that the associated molecules are not completely broken down in these compounds.

It is evident that in all the alcohols studied, with the exception of hexanol-1 and 3-methylpentanol-1, there is something which tends to hinder the formation of polymers higher than dimers. These alcohols have the structure



hence it appears probable that the R groups tend to prevent orientations which are favorable to the production of the higher polymers.

These results are in substantial agreement with those obtained from X-ray work.[9] This seems to confirm the validity of the interpretation of the two components of the association band as being due to dimers and higher polymers.

Some time ago, Hovorka, Lankelma and Stanford[6a] measured the viscosity and density of five of the alcohols over a wide temperature range. It was found that the density and viscosity of hexanol-1 changed rather slowly with temperature. These properties varied much more rapidly in the case of hexanol-3. Hexanol-2, 2-methylpentanol-1, and -4 showed density and viscosity changes intermediate between those of the above two alcohols. The slope of the curves was nearly the same for the last three compounds. The results were interpreted as being due to different types of association and to different rates of dissociation of the associated molecules. The data of the present research are in excellent agreement with this interpretation.

The results obtained thus far indicate that the type and extent of association of a member of an isomeric series of alcohols depends chiefly on the immediate environment of the —OH group rather than on the length of the carbon chain. One would, therefore, expect to find rather similar bands in other alcohols in which the —OH group has a like environment.

In conclusion the authors wish to express their appreciation to Dr. H. H. Nielson and Dr. Alpheus W. Smith for the use of their equipment and for their constant interest in this work, and to Dr. Frank Hovorka of Western Reserve University for providing the alcohols, which made this study possible. They also wish to acknowledge a very helpful conversation with G. B. B. M. Sutherland of Cambridge University.

Summary

1. The infrared absorption spectra of hexanol-1, -2, -3, 2-methylpentanol-1, -2, -4, 3-methylpentanol-1 and 2-ethylbutanol-1 have been determined in the 3 μ region, for the pure liquids and for 0.291, 0.1 and 0.05 molar solutions in carbon tetrachloride.

2. From the behavior of the —OH band of the different liquids upon dilution in carbon tetra-

(9) Stewart, *Chem. Rev.*, **6**, 483 (1929); *Phys. Rev.*, **35**, 726 (1930); Pierce and MacMillan, THIS JOURNAL, **60**, 779 (1938).

chloride, something of the nature of association can be ascertained.

3. It was found that hexanol-3 in concentrated solutions consists chiefly of dimers and that its rate of dissociation with dilution is greater than that for the other alcohols. Hexanol-1 and 3-methylpentanol-1 show the presence of higher polymers down to and including a concentration of 0.1 molar. The rate of change of association with dilution is least for hexanol-1. The remainder of the alcohols form intermediate cases between hexanol-1 and hexanol-3, both in respect to the presence of higher polymers and rate of dissociation with dilution.

4. The difference in behavior of the hexyl alcohols has been interpreted in terms of the structural environment of the —OH group.

COLUMBUS, OHIO RECEIVED JANUARY 29, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF KENTUCKY]

The Equilibrium Constants for the Systems Alkyl Formates and Alkyl Acetates with Stearic Acid

BY CHAS. BARKENBUS, C. A. ROSWELL AND A. ELEANOR MITTS

Ester interchange with alcohols or alcoholysis has received considerable attention in the last few years. A similar type of interchange between ester and acid and called acidolysis has not been so extensively studied. Since very little work has been done from a quantitative viewpoint it was thought advisable to determine the equilibrium constants for a series of alkyl esters with stearic acid and to see how these constants varied with change of alkyl group.

The general reaction, *i. e.*

$$RCO_2R + R'CO_2H \longleftrightarrow R'CO_2R + RCO_2H$$

has been used to prepare certain esters where the conditions were favorable.[1] The first quantitative study of acidolysis was made by Reid[2] who determined the equilibrium constants for the systems benzoic acid–benzyl acetate and *p*-bromobenzoic acid–ethyl benzoate. The equilibrium mixture was analyzed by determining the density and the constants obtained checked within 5% with those calculated from the esterification constants.

Sudborough and Karve[3] obtained an equilibrium constant of unity for the two systems trichloroacetic acid–methyl acetate and trichloroacetic acid–ethyl acetate.

Gault and Chablay[4] have recently studied the system methyl palmitate–acetic acid. They determined the time needed to reach equilibrium and found that fifty hours were necessary at 100° when sulfuric acid was used as a catalyst. In their latest paper they give the equilibrium constants for methyl palmitate with acetic acid, propionic acid, *n*-butyric acid, *n*-valeric acid, and *n*-caproic acid. The analysis of equilibrium mixtures of this type is simplified by the determination of the water soluble or water insoluble acids.

Sowa[5] has determined the rate of reaction using acetic acid with various alkyl esters of propionic, benzoic and salicylic acids. He was able to show that the main reaction was one of straight interchange but that larger normal alkyl groups of esters rearrange to secondary alkyl groups when changing to the other acid. This is probably due to the intermediate formation of an olefin. It was stated that only 4% of the new ester was due to this type of reaction. To see whether this observation held for the higher fatty acids, a large scale run was made using *n*-butyl stearate and acetic acid. The butyl acetates when separated and fractionally distilled through a ten-plate Podbielniak column showed that only 2% of the esters was *s*-butyl acetate.

In this work the equilibrium was obtained by heating in a sealed glass tube at 100° about 0.02 mole of stearic acid, 0.1 mole of the ester and 0.1 g. of *p*-toluenesulfonic acid as a catalyst. The tubes were heated at various lengths of time and equilibrium was considered established when the tubes heated the longest checked with those heated next in length of time. From seventy-two to one hundred and twenty hours were usually required.

(1) Lowig, *J. prakt. Chem.*, [1] **83**, 130 (1861); Lorin, *Bull. soc. chim.*, [2] **49**, 344 (1888); Norman, *Chem. Umschau*, **30**, 250 (1924); Forneau, *Bull. soc. chim.*, **45**, 834 (1929); Pistor, *Z. angew. Chem.*, **38**, 1118 (1925); Graves, U. S. Patent 1,882,808.

(2) Reid, *Am. Chem. J.*, **45**, 479 (1911).

(3) Sudborough and Karve, *Indian Inst. Sci.*, **5**, 1 (1922).

(4) Gault and Chablay, *Compt. rend.*, **203**, 729 (1936); **207**, 293 (1938).

(5) Sowa, THIS JOURNAL, **60**, 654 (1938).

The contents were dissolved in benzene and extracted at least ten times with cold water to remove the water soluble acids. It was rather difficult to completely remove acetic acid from the benzene solution. The time consumed in the extraction caused some hydrolysis of the lower esters which made it impossible to determine the water soluble acids produced by the acidolysis. The stearate esters due to their insolubility in water were not hydrolyzed during the extraction, as was determined by running blanks.

After extraction, the benzene was evaporated and the last traces of the more volatile ester were removed under vacuum. The residue was then taken up in neutral hot alcohol and titrated. It was found that the most consistent and accurate results were obtained by titrating the insoluble acid instead of the water soluble acid. The equilibrium constants obtained never varied more than 2% and most of them checked within less than 1%.

It was found that formic acid could be more readily extracted with water and a few of the constants were determined by the quantitative oxidation of formic acid with potassium permanganate. In this case the small amount of formate esters dissolved in the water had to be removed by aeration before oxidation. This made the analysis long and great care had to be used in keeping the solutions cold to prevent hydrolysis.

The stearic acid used was a highly purified product obtained by fractional distillation of methyl stearate and by crystallization of the acid. All the esters used were fractionally distilled through a Widmer column and only those fractions having indices corresponding to those in the literature were used. The *p*-toluenesulfonic acid was prepared in the usual way except that stirring was used during the sulfonation, which gave a whiter product. The acid was not crystallized but was triturated several times with toluene and filtered. This last procedure gave a product which was completely soluble in water and, after drying in a desiccator over phosphorus pentoxide, analyzed for approximately one water of hydration.

Gault and Chablay[4] have shown for the reversible reaction $CH_3COOH + CH_3(CH_2)_{14}COOCH_3 \rightleftarrows CH_3COOCH_3 + CH_3(CH_2)_{14}COOH$ that the equilibrium can be approached from both directions. They determined the time necessary to obtain equilibrium starting from both sides and, though the time varied, the concentrations at equilibrium were the same. It was also necessary to have some comparison between the systems using palmitic acid with those using stearic acid. The equilibrium constant for methyl palmitate–acetic acid was redetermined and an average value of 1.034 for four determinations was obtained. The average value obtained by Gault and Chablay,[4] who approached the equilibrium from the other side, was 1.070. Since the above data indicate clearly that a true equilibrium is obtained in acidolysis reactions, the equilibrium constants reported in this paper were obtained by approaching the equilibrium from one direction only.

The equilibrium constants

$$K = \frac{[CH_3(CH_2)_{16}COOR][RCOOH]}{[R—COOR][CH_3(CH_2)_{16}COOH]}$$

are collected in Table I. The values all represent the mean of three independent measurements.

TABLE I

EQUILIBRIUM CONSTANT K IN THE PRESENCE OF STEARIC ACID

	Formates		Acetates	
Esters	K	Av. dev. ±%	K	Av. dev. ±%
Methyl	1.287	0.1	1.019	0.4
Ethyl	0.845	.2	0.902	.5
n-Propyl	.794	.0	.912	.6
s-Propyl	.693	.9	...	...
n-Butyl	.869	.5	.964	.5
i-Butyl	.782	.4	...	...
n-Amyl	.750	.9	.731	.6

Similar measurements were made with methyl acetate using palmitic acid instead of stearic. The corresponding value of K for this system was 1.034 ± 0.4%. This is interesting in showing that there is no significant difference between the palmitate and the stearate system.

We have also calculated similar equilibrium constants from the data of Gault and Chablay.[4] The values thus obtained were for methyl propionate, *n*-butyrate, *n*-valerate and *n*-caproate, 1.12 ± 4, 1.17 ± 10, 1.04 ± 4 and 1.02 ± 3%, respectively. These constants show a diminishing trend with increasing molecular weight of the acid, but the deviations of the individual measurements from the mean are so great as to raise some questions as to whether there was any real difference in these values of K.

It can be seen readily that the methyl group of an ester is more readily replaced by the acid hydrogen of stearic acid than are the other alkyl groups listed. The normal alkyl groups are more readily exchanged than the secondary alkyl groups or branched chain alkyl groups. Esters containing a tertiary alkyl group could not be used as they were decomposed by the acid catalyst. The extent of displacement decreases slowly with length of normal alkyl group at least as far as the normal amyl group. The only exception to this is the *n*-butyl group, which is higher.

From the data of Gault and Chablay and from Table I it can be seen that the length of the fatty acid which forms the ester does not affect the reactivity as much as does the alkyl group of the

ester. The formates are considerably more active than the acetates and from then on the decrease in activity is much smaller as the length of acid increases. In this series the exception to the above statement is methyl *n*-butyrate.

It is interesting to note that esters having a total of five carbons have higher equilibrium constants. Methyl *n*-butyrate and *n*-butyl formate have constants much higher than would be expected. *n*-Propyl acetate does not vary as much but even here the constant is the same as the preceding ester instead of decreasing. The one exception to this observation is *n*-butyl acetate, which is even higher than *n*-propyl acetate. No equilibrium constant has been run for ethyl propionate.

Hatch and Adkins[6] in their displacement series for alcoholysis observed that the values decreased until the normal amyl group was reached. A marked increase was then noticed which gradually decreased in going up the series, but all values were higher than those preceding the normal amyl group. They rationalized these anomalies by the assumption that the effect of a methyl or methylene group may be transferred directly as well as through the chain. By stereochemical considerations the methyl group of the amyl group should be close to the oxygen and act directly.

This explanation might be used for the above anomalies but it is difficult to see why *n*-amyl formate should have a smaller constant than *n*-butyl formate. If the activation is due to both ends of the ester being close together, then the observation that it occurs only in esters having five carbons would be logical. This, however, does not explain why *n*-butyl acetate should have a large constant.

(6) Hatch and Adkins, THIS JOURNAL, **59**, 1694 (1937).

Summary

The equilibrium constants for the reaction of several alkyl formates and alkyl acetates with stearic acid have been determined. Increasing the length of the alkyl group of the ester decreases the value of the constant. However, when the total number of carbons in the ester reaches five, higher values are obtained. Secondary and branched-chain alkyl esters give lower values than the normal alkyl esters.

LEXINGTON, KY. RECEIVED FEBRUARY 14, 1940

[CONTRIBUTION FROM THE PENNSYLVANIA STATE COLLEGE]

Optical Constants of Benzamide, its Homologs, and Some Aliphatic Amides[1]

BY M. L. WILLARD AND CHARLES MARESH[2]

Two homologous series of organic amides, namely, an aromatic series based on benzamide and an aliphatic series based on acetamide, were studied optically by means of the petrographic microscope and the Fedorow universal stage as modified by R. C. Emmons.

Materials.—The derivatives and reagents used in this study were obtained from the Eastman Kodak Company. **Acetamide** was recrystallized from 95% alcohol. **Propionamide** and **butyramide** were used as obtained. ***n*-Valeramide** was recrystallized from fusion giving flat plates suitable for optical study. **Isovaleramide** was prepared from isovaleryl chloride and concentrated ammonia solution and purified by sublimation.

Benzamide, *o*-, *m*-, and *p*-toluamides were prepared by the hydrogen peroxide hydrolysis[3] of the corresponding nitriles. ***o*-Ethylbenzamide, *p*-ethylbenzamide,** and **1,3-dimethylbenzamide-2** were prepared from the corresponding amines, using the method of Clarke and Read[4] in the preparation of the nitriles followed by the hydrolysis to the amides. The dimethyl compound, however, required refluxing for seventy-two hours with a saturated alcoholic potassium hydroxide solution for the hydrolysis to the amide.

The melting point of *p*-ethylbenzamide (see Table I) was found to be different from that reported in the literature. Upon hydrolysis, the acid was obtained melting at 112–113.5°. The amide was likewise prepared from the acid by treating with thionyl chloride followed by treatment with concentrated ammonia solution. The amide so obtained melted at 162.9–164.4°.

The amides, ***p*-propylbenzamide, *p*-*n*-butylbenzamide,** and ***p*-isobutylbenzamide** were prepared from bromobenzene and the corresponding bromides (obtained from the alcohols) by means of the Wurtz–Fittig synthesis. The alkyl benzenes were nitrated and reduced according to the method of R. R. Read and D. B. Mullin.[5] The

(1) Abstracted from a thesis submitted by C. Maresh to The Graduate School of The Pennsylvania State College in partial fulfillment of the requirements for the degree of Doctor of Philosophy. Presented before the Division of Microchemistry at the 97th meeting of the American Chemical Society, Baltimore, Md.

(2) Present address: Calco Chemical Division, The American Cyanamid Company, Bound Brook, New Jersey.

(3) C. R. Noller, "Organic Syntheses," Vol. 13, 1933, p. 94.

(4) H. T. Clarke and R. R. Read, "Organic Syntheses," Vol. 4, 1925, p. 69.

(5) R. R. Read and D. B. Mullin, THIS JOURNAL, **50**, 1763 (1928); D. B. Mullin, Thesis "The Disinfectant Power of Phenols," U. of Vermont, 1924.

TABLE I

ANALYSES AND PHYSICAL AND OPTICAL PROPERTIES OF AMIDES

Amides	Nitrogen, % Calcd.	Found	M. p.,[a] °C.	n_α	n_β	n_γ	Birefr.	Sign	2V	Optical orientations	Cryst. syst.	Habit
						Aliphatic Amides, λ = 5461 Å.						
Acet-			81.1 ±0.5	1.461[b]		1.507(n_ω)	0.046	−	0°	X = *c*	Hex.	Short, prismaticine.
Butyr-			114.1 ± .5	1.465[c,i]	1.482	1.530	.065	+	61°,[g] 63°[h]	X = *a*, Y = *b*, Z = *c*	Orth.	Mica-like pl.
Propion-			78.0 ± .5	1.445[d,i]	1.461	1.530	.085	+	52°,[g] 53°[h]	X = *a*, Y = *b*, Z = *c*	Orth.	Mica-like pl.
Isovaler-			125.9 ± .5	1.458[e,i]	1.466	1.498	.040	+	57°[h]	Ax. pl. (010)	Mono.	Mica-like pl.
n-Valer-			101.0 ± .7	1.466[f,i]	1.488	1.530	.064	+	75°,[g] 74°[h]	Ax. pl. (010)	Mono.	Mica-like pl.
						Aromatic Amides, λ = 5461 Å.						
Benz-			127.1 ±0.5	1.541	1.666	1.830	0.289	+	87°,[g,h] 88°[k]	Ax. pl. (010)	Mono.	Prism. pl.[g]
p-*n*-Butylbenz-	7.91	7.89	121.5 ± .4	1.547	1.577	1.700	.153	+	55°,[g] 56°,[h,k]	Ax. pl. (010)[m]	Mono.	Prism. ne.[g]
p-*s*-Butylbenz-	7.91	7.99	117.2 ± .5[g]	1.49 ±0.01	1.596	1.72 ±0.01	.23	−	85°,[g] 86°[k]	M. p. 128.4 ±1.5[j]	Mono.	Ne. + long rect. pl.[l,n]
2-Cyano-1,3-dimethylbenzene			89.5 ± .5	1.454	1.737	1.748	.294	−	20°[q,k]	X = *a*, Y = *b*, Z = *c*	Mono.	Long rect. cryst.[g]
1,3-Dimethyl-benz-(2)			137.3 ± .4	1.565	1.591	1.673	.108	+	61°[q,h,k]	Ax. pl. (010)[l]	Mono.	Long rect. pl.[g]
p-Ethylbenz-	9.49	9.62	164.2 ± .5	1.505	1.638	1.726	.221	−	72°,[g,h] 73°[k]	Ax. pl. (010)	Mono.	Tabular[n,g]
o-Ethylbenz-			153.0 ± .5	1.547	1.592	1.693	.146	+	71°,[g,k] 73°[h]	Ax. pl. (010)	Mono.	Rect. cryst.[n,g]
p-Isobutylbenz-	7.91	7.80	151.2 ± .2	1.464	1.605	1.724	.260	−	79°,[g,h] 78°[k]	Ax. pl. (010)	Mono.	Mica-like pl.[o,p]
p-Propylbenz-	8.59	8.58	128.4 ± .5	1.526	1.674	1.689	.163	−	33°,[g] 32°[h]	X∧*c* = ca. 40°, Y = *b*	Mono.	Rect. cryst.[q,p]
o-Tolu-			141.2 ± .2	1.470	1.715	1.761	.291	−	44°,[g] 42°[k]		Tri.?	Tablets[q]
m-Tolu-			93.7 ± .5	1.468	1.737	1.752	.284	−	23°,[k] 20°[q]	Ax. pl. (010)	Mono.	Prisms[q]
p-Tolu-			159.6 ± .5	1.510	1.708	1.734	.224	−	35°,[g] 38°,[h] 36°[k]	Z = *b* = *Bx*$_0$	Mono.	Square pl.[q]

[a] Melting points determined by usual capillary tube method with thermometer calibrated against Bureau of Standards' thermometers. The ± indicates the range, as: 127.1 ± 0.5 = 126.6–127.6°. [b] (n_ϵ). [c] 1.464 ± 0.005, Universal Stage. [d] 1.44 ± 0.01, Universal Stage. [e] 1.45 ± 0.01, Universal Stage. [f] 1.47 ± 0.01, Universal Stage. [g] Cryst. from H_2O. [h] Universal Stage. [i] Calcd. from 2V. [j] Cryst. from petroleum ether. [k] Indices. [l] X∧*c* = ca. 8°. [m] X∧*c* = 40°. [n] Elongated to *β*. [o] Mica-like plates crystallized from 50% ethyl alcohol; rect. plates from water. [p] Prisms from xylene–Canada balsam. [q] Melatopes.

amines were then diazotized, the nitriles prepared, and the amides formed by the hydrogen peroxide hydrolysis.

The Wurtz–Fittig synthesis was not successful in the preparation of *s*-butylbenzamide, and Eastman Kodak Co. *s*-butylbenzene was the starting material in the preparation of **secondary butyl benzamide.** The melting points from water and petroleum ether differed, and there is a possibility that the optical activity of the secondary butyl group is the explanation. The product from water was studied.

In nitrating, the position of the nitro group was in all cases checked by the preparation of the corresponding nitrobenzoic acid. The amides, *p*-propylbenzamide, *p*-butylbenzamide, *p*-isobutylbenzamide, and *p*-*s*-butylbenzamide, have not been reported in the literature.

The fractionations of the intermediates in the preparation of the aromatic amides were carried out with two columns packed with glass helices of the total condensing variable take-off type with electrically heated jackets 40 and 64 cm. long.

Apparatus and Technique.—A Spencer 35 petrographic microscope was used in all of the work except that involving the universal stage. In addition to the usual accessories, the microscope was fitted with a 1.8-mm. oil immersion (N. A. = 1.25) objective used in conjunction with an aplanatic wide angle condenser (N. A. = 1.40). A removable ocular micrometer in a Spencer 8x ocular was calibrated with both the 4-mm. and 1.8-mm. objectives for optic axial angle measurement against standardized mineral thin sections. As illustrated by W. M. D. Bryant,[6] the use of an oil immersion objective permits the measurement of the entire range of acute axial angles as well as smaller obtuse axial angles.

A Bausch and Lomb modified Fedorow universal stage was fitted on a Bausch and Lomb LC petrographic microscope for the measurement of optic axial angles and indices of refraction beyond the limit of the index oils as well as n_α in the case of the platy aliphatic amides. The universal stage was fitted with three pairs of hemispheres of refractive indices, 1.649, 1.559, and 1.516.

The indices of the liquids beyond the limit of the Abbé refractometer were determined by the method of minimum deviation using a constant temperature hollow prism[7] in conjunction with a single circle reflecting goniometer made by the R. Fuess Company. Monochromatic light was furnished by an 85-watt high intensity Westinghouse mercury vapor lamp Type H-3 along with suitable Corning filters (λ = 5461 Å.).

(6) W. M. D. Bryant, THIS JOURNAL, **60**, 1394 (1938).

(7) M. S. Buerger, *Am. Mineral.*, **18**, 325 (1933).

The principal refractive indices, α, β, and γ at 25° ±3° for λ = 5461 Å. were determined by the immersion method with axial illumination using interference figures in selecting the correct orientation for a given index.[8]

The optical study involved the examination of the crystals obtained from various solvents and from xylene–Canada balsam. In some cases crushed material was mixed with powdered glass preparatory to the examination. The determination of the optic axial angles by means of the universal stage was done on preparations made up in Canada balsam.

The universal stage was used in the determination of n_γ in the case of benzamide and n_α in the case of the platy aliphatic amides using the methods worked out by R. C. Emmons.[9] In the determination of the optic axial angles, the graphical method of T. A. Dodge[10] was used.

Optical Data.—Although metastable forms were encountered in this research, no attempt was made to determine their optical constants. $2V$ values were (a) obtained from melatope distances, (b) measured on the universal stage, and (c) calculated from the indices of refraction. The accuracy of the $2V$ values is given by the agreement of the values obtained by the three methods. The indices of refraction are given with an accuracy of ± 0.003 except where indicated.

Table I gives the data for the aliphatic amides. All of the aliphatic amides listed have been measured crystallographically, but only acetamide in its stable and metastable forms has been studied optically. The values recorded for the stable modification[11] (n_ϵ = 1.46, n_ω = 1.54) are not entirely in accordance with those reported here. The stable form of acetamide is trigonal uniaxial giving short prismatic needles from alcohol and does not fit in with the remainder of the series. The amides from propionamide through isovaleramide crystallize out in mica-like flakes which make it difficult to measure the lowest index.

E. Kahrs[12] states that the amides show good cleavage parallel to the front pinacoid (100), and the obtuse bisectrix is perpendicular to the prominent face of the crystals in the case of propionamide and butyramide, and leaning slightly toward (101) in the case of the two valeramides.

The first value for n_α given has been calculated from $2V$ values. The birefringence being small gives good results for the calculated index. The values given in footnotes are index values obtained on the universal stage by the method of R. C. Emmons.[9] They are good to ±0.01 except where noted.

In Table I are given the data for the aromatic amides studied. Only benzamide has been measured crystallographically. According to Groth[13] benzamide forms monoclinic prismatic crystals, β = 90° 38′; the acute bisectrix forms an angle of 40° with the c axis; and 2H = 100° 15′ (red), 2H = 102° 10′ (violet).

The plates obtained from water give beautifully centered optic axis figures which are practically straight. Twinning is prominent on this face. Rapid cooling during crystallization causes the formation of the metastable triclinic needles having $2V$ = 44°.

o-Toluamide from water gives tablets exhibiting oblique extinction, good cleavage, and off-centered Bx_0 figures. *m*-Toluamide from water crystallizes as monoclinic prisms with a maximum extinction angle of *ca.* 43°. They are elongated parallel to the c axis. The material used for optical determinations was fused beneath a cover glass, then crushed, and mixed with powdered glass. *p*-Toluamide from water crystallizes on the microscope slide as monoclinic square plates showing very good rectangular cleavage. Careful recrystallization from water gives monoclinic crystals elongated parallel to γ. *o*-Ethylbenzamide gives crystals showing both parallel and oblique extinction. From the melt a metastable form giving a well centered Bx_a figure rapidly reverts to the stable monoclinic form. *p*-Ethylbenzamide from water forms monoclinic tablets giving good Bx_0 figures and parallel extinction. *p*-Propylbenzamide from water shows very prominent cleavage parallel to the plane of the optic axes. *p-n*-Butylbenzamide from xylene–Canada balsam forms monoclinic prisms elongated parallel to the c axis. From water the prominent face is parallel to the plane of the optic axes with an extinction angle of 40°. *p*-Isobutyl benzamide from xylene–Canada balsam forms monoclinic prisms elongated parallel to the c axis. From water small plates representing sections parallel to the plane of the optic axes with an extinction angle of *ca.* 37° and with v-shaped cavities running in from the two ends are formed. The interference figure usually obtained for *p-s*-butylbenzamide is that of the optic axis section, not centered, however. Although 2-cyano-1,3-dimethylbenzene crystals

(8) K. E. Buck, "Outline for Examining Crystals," *Bull. Am. Ceram. Soc.*, **16**, 61 (1937).

(9) R. C. Emmons, *Am. Mineral.*, **14**, 441 (1929).

(10) T. A. Dodge, *ibid.*, **19**, 62 (1934).

(11) "International Critical Tables," Vol. I, p. 180.

(12) E. Kahrs, *Z. Kryst. Mineral.*, **40**, 475 (1905).

(13) P. Groth, "Chemische Krystallographie," Vol. IV, Leipzig, 1917, p. 523.

show only parallel extinction, they are monoclinic. The monoclinic needles are elongated parallel to the c axis and give perfectly centered Bx_a figures. 1,3-Dimethylbenzamide-2 from water forms needle-like plates giving Bx_a figures, and elongated parallel to c.

In Fig. 1 are given the optic axial angles of the aromatic and aliphatic amides. The aromatic amides plotted are para-substituted homologs of benzamide, and the abscissa gives the length of the carbon chain in the para position. In the case of the aliphatic amides the abscissa gives the length of the carbon chain attached to the $-CONH_2$ group.

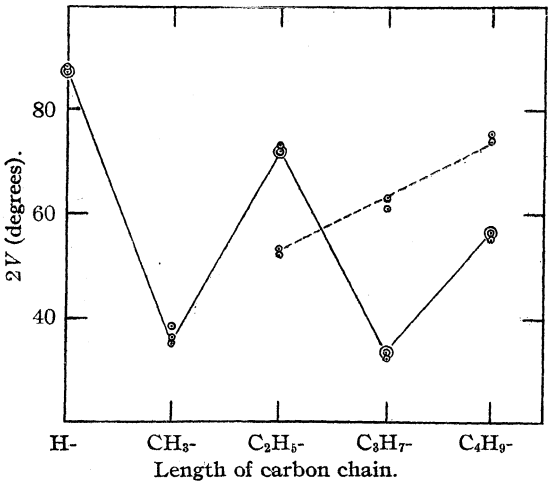


Fig. 1.—Optic axial angles: full lines represent $2V$ values of aromatic amides as a function of the carbon chain in the para position; dotted lines represent $2V$ values of aliphatic amides as function of the carbon chain.

The $2V$ value of acetamide has been omitted. Whereas the $2V$ values of the aliphatic amides vary in a regular manner, there is noted a fluctuation in the case of the aromatic para-substituted amides. The one with the odd number of carbon atoms in the aliphatic chain has a $2V$ value lower than the homolog containing the even number of carbon atoms. From the compounds investigated it appears that the evens and odds vary in a regular manner.

According to Müller and Shearer[14] the natural saturated alcohols have a zigzag structure while the carbon atoms in the natural saturated aliphatic acids have the alternate structure. It appears that the same two types of structure are present in the aromatic and aliphatic amides. Possibly the benzene ring is the cause of the alternate structure.

(14) A. Müller and G. Shearer, *J. Chem. Soc.*, **123**, 3156 (1923).

In Fig. 2 are plotted the refractive indices of the para-substituted normal aromatic amides as a function of the carbon content. As can be seen from the curves, there is a step-like decrease in the birefringence with an increase of the carbon chain which is what would be expected. The substance takes on an aliphatic character as the aliphatic chain is increased, a low birefringence being associated with the aliphatic amides and a higher birefringence with the aromatic amides.

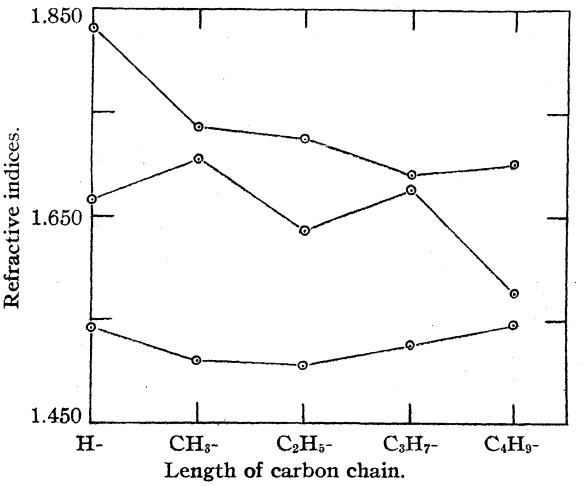


Fig. 2.—Refractive indices of benzamide and its para-substituted homologs: from top to bottom the lines represent n_γ, n_β and n_α; the length of the carbon chain in the para position is plotted as the abscissa.

It is noted from the figure that it is n_β which causes the fluctuation of the $2V$ values.

Acknowledgment.—The authors thank Dr. C. D. Jeffries of the Agronomy Laboratory for his counsel in the use of the universal stage and Mr. E. F. Williams of the Geology Department for the use of the universal stage and his counsel with its application. Thanks are also due The Research Council of this College for making a part of this research possible.

Summary

1. A homologous series of aromatic acid amides based on benzamide was prepared. Four of these have not been reported in the literature and another was reported incorrectly.

2. The optical data including the principal refractive indices, $2V$ values, optical character, crystal system, etc., was worked out for the aromatic amides as well as for a homologous series of amides based on acetamide.

3. The applicability of petrographic methods

including the use of the universal stage was shown.

4. Some attempt was made to explain the data in terms of structure and chemical constitution.

STATE COLLEGE, PA. RECEIVED DECEMBER 12, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF INORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, NO. 80]

The Reaction of Boron Fluoride with Aluminum Chloride or Bromide

BY E. LEE GAMBLE, PAUL GILMONT AND JOHN F. STIFF

Discussion

The comparative lack of volatility of aluminum fluoride (melting point 1040°) with respect to the other halides of aluminum may be taken advantage of for the preparation of various volatile halides. For example, this paper describes the preparation of boron chloride and of boron bromide by the action of boron fluoride on the corresponding aluminum halide.

$$BF_3 + AlX_3 = AlF_3 + BX_3$$

The ease with which the reactants are obtainable and the differences in volatility make this a simple means of preparation. It is possible that mixed fluorohalides of aluminum are intermediate products of this reaction, but they have not been isolated in a state of purity. The action of boron fluoride on aluminum iodide has produced small amounts of boron iodide but as yet the yields have been quite low. The development of this preparation is to be continued. Boron chloride or bromide is also produced when potassium fluoborate is heated with aluminum chloride or bromide but the yields obtained are not as satisfactory as when boron fluoride is used.

No fluorochlorides or fluorobromides of boron have ever been reported, nor have any been detected in this investigation. To determine whether the known fluorochlorides of silicon[1] could be prepared by this type of reaction, sodium fluosilicate was heated with aluminum chloride, the volatile products obtained proved to be only silicon tetrachloride and tetrafluoride, containing none of the fluorochlorosilanes.

The conversion of volatile fluorides into chlorides or bromides by means of aluminum chloride or bromide should prove to be somewhat general. From one point of view, the results of this reaction may be looked upon as the reverse of those of the Swarts reaction for the production of fluorides or mixed fluorohalides by means of antimony fluoride.[2]

Many of the methods described in the literature for the preparation of the boron halides have been repeated in this Laboratory.[3] It is felt that the preparation of boron bromide from boron fluoride and aluminum bromide is a simpler method than any hitherto described. Also, the preparation of boron chloride by this method may prove convenient.

Experimental

Reagents.—Potassium fluoborate was prepared by dissolving boric acid in 48% hydrofluoric acid and adding potassium carbonate. The product was recrystallized from hot water and dried at 110°.[4] Boron fluoride was prepared by the action of hot concentrated sulfuric acid on a mixture of potassium fluoborate and boric oxide.[5] The aluminum bromide was prepared by slowly adding bromine to an excess of aluminum, in an ordinary distilling flask cooled by water.

Reactions with Boron Fluoride.—The flask in which the reactions were carried on was dumbbell-like in appearance and was constructed by sealing a 1-liter round-bottomed flask to the bottom of a half-liter distilling flask by means of 25 cm. of 30-mm. tubing. The tube for the introduction of the boron fluoride passed through a one-hole cork stopper in the distilling flask and extended to the middle of the larger flask. The smaller flask served as a condenser to prevent large quantities of the aluminum halide from distilling over with the product. A weighed quantity of aluminum chloride was poured into the reaction flask, or aluminum bromide was distilled in from the flask in which it was prepared, and its weight determined by difference. The boron fluoride generator was connected to the reaction flask by means of a small bubbler containing concentrated sulfuric acid. The rate of flow of the boron fluoride was comparatively rapid, about thirty minutes for 2 moles of gas. After the apparatus was swept out with boron fluoride, the large flask containing the

(1) W. C. Schumb and E. L. Gamble, THIS JOURNAL, **54**, 3943 (1932); H. S. Booth and C. F. Swinehart, *ibid.*, **57**, 1333 (1935).

(2) F. Swarts, *Acad. roy. de Belgique*, **24**, 309 and 474 (1892); *Bull. soc. chim.*, [4] **35**, 1557 (1924).

(3) An effort was made to see whether, in the preparation of boron trichloride [BCl_3] by relatively low temperature reactions, some B_2Cl_4 was not formed at the same time. Careful distillation of the reaction products produced only negative results.

(4) "Inorganic Syntheses," Vol. I, McGraw-Hill Book Co., Inc., New York, N. Y., 1939, p. 24.

(5) Ref. 4, p. 23.

aluminum halide was heated gently by means of a free flame whereupon the reaction soon started. For the preparation of boron chloride gentle heating was found desirable as long as the reaction took place. Then, using two burners, both flasks were heated strongly with a stream of boron fluoride still passing through the reaction flasks. After continued heating, the aluminum fluoride fell from the sides of the flask as a light white powder. For the preparation of the boron bromide the aluminum bromide was refluxed gently in a stream of boron fluoride. The contents of the flask soon solidified and again the mass was strongly heated in boron fluoride. The effluent gases were passed into a U-tube cooled with solid carbon dioxide and alcohol, protected by a drying tube. When the reaction was over the U-tube was sealed off and its contents distilled. In the preparation of boron bromide small amounts of bromine were obtained but were readily removed by shaking with mercury. A little metallic aluminum added to the preparation flask decreased the amount of bromine formed. In order completely to remove boron fluoride from boron chloride or bromide, distillation in a good column was desirable. From one-half a mole of aluminum chloride and two moles of boron fluoride 80% yields of boron chloride have been obtained. Using comparable amounts of reactants, 70% yields of boron bromide have been obtained.

Pure aluminum fluoride was not obtained as the by-product of the reaction, appreciable amounts of chloride or bromide being present. Analysis has shown the amount of bromine to be as high as 40% (theoretical for AlF_2Br is 55%); but this was decreased very markedly when the solid product was heated strongly in a stream of boron fluoride.

Reaction with Potassium Fluoborate.—When either aluminum chloride or bromide was heated with potassium fluoborate, some boron chloride or bromide, together with boron fluoride, was formed. An excess of the aluminum halide increases the percentage conversion of the fluoborate.

In an apparatus somewhat similar to that described above, one mole of aluminum chloride and one-half a mole of potassium fluoborate were heated by means of an oil-bath for four hours, with the temperature slowly increasing from 150 to 175°. The product was condensed in liquid nitrogen. The recovery of pure boron chloride was 0.26 mole, a yield of 56%, based on the potassium fluoborate used. Under comparable conditions yields of around 30% of boron bromide have been obtained.

Summary

Boron fluoride and potassium fluoborate have been found to react with aluminum chloride or bromide to produce good yields of boron chloride or bromide. The conditions of the reactions are given and the use of boron fluoride is particularly recommended as a means of preparing boron bromide. No fluorochlorides or fluorobromides of boron have been isolated in this investigation.

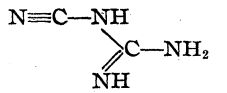
CAMBRIDGE, MASSACHUSETTS
RECEIVED FEBRUARY 19, 1940

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, NO. 767]

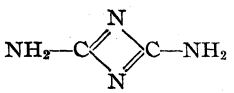
The Crystal Structure of Dicyandiamide

BY E. W. HUGHES

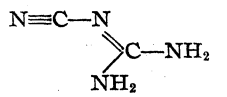
Several different structures have been proposed for the dimer of cyanamide but no absolutely conclusive evidence has ever been given for any one of them. In past years many people have preferred the cyanoguanidine[1] structure I.



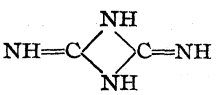
I



II



III



IV

But even fairly recently[2] arguments have been advanced in favor of the cyclic structure II. The closely related alternatives III and IV, which differ from I or II only in the disposition of hydrogens and double bonds, also have been proposed. I have made an X-ray examination of crystalline dicyandiamide for the purpose of resolving this long-standing controversy, with the results reported below.

Several previous crystallographic investigations have been recorded. In 1911 Heydrich[3] reported the crystals as monoclinic holohedral with $a : b : c = 1.1109 : 1 : 1.4213$, $\beta = 115° 20'$. He also found strong positive birefringence and that the acute bisectrix makes an angle of about 11° with c in the acute angle β'. The cleavage on {100} is excellent and that on {001} is good. In 1927 Baier[4] made an independent examination. Although he chose a different axial system, with $\beta = 90° 31'$, his axial ratios, $a : b : c = 1.0021 :$

(1) For a good summary of the arguments, as well as one of the more important original investigations, see Hale and Vibrans, THIS JOURNAL, 40, 1046 (1918).

(2) Bell, *Sci. Proc. Roy. Dublin Soc.*, 18, 207 (1926).

(3) Heydrich, *Z. Krist.*, 48, 278 (1910–1911).

(4) Baier, *ibid.*, 66, 719 (1927).

1 : 0.4854, are compatible with Heydrich's (within somewhat large experimental error) when recalculated for the older axial system. He confirmed Heydrich's crystal class and birefringence assignments. At the same time a superficial X-ray examination was made by Dehlinger.[5] On the basis of insufficient data, and following the axial system of Baier, he reported a cell with $a = 13.8$ Å., $b = 4.4$ Å., $c = 6.2$ Å. and $\beta = 90°$. The space group was said to be C_{2h}^3 $(= I2/m)$ with four molecules per cell. No structure was proposed.

The Unit Cell and Space Group

The material used in this examination was kindly supplied by Professor A. W. Browne of Cornell University. Crystals were grown from water solutions by evaporation in a thermostat at about 35°. They were lath-like needles elongated along b. Complete sets of oscillation photographs were made about b and c (Heydrich's axes) using Cu radiation. An additional oscillation picture was made about a to confirm the length assigned to that axis. One 5° oscillation photograph with Mo radiation was made about b to observe the reflection 12,08, which is beyond the range of Cu radiation, but of important intensity.

A preliminary attempt to index the b axis pictures using Dehlinger's unit showed that the latter was incorrect and that the dimensions had to be doubled in both the a and c directions, yielding a cell with sixteen molecules and an inconvenient type of centering. By reverting to Heydrich's axes a much simpler unit was obtained for which was found $a = 15.00$ Å., $b = 4.44$ Å., $c = 13.12$ Å. (all ±0.5%, CuKα, $\lambda = 1.540$ Å.) and $\beta = 115° 20'$ (Heydrich). This cell contains eight molecules of $H_4N_4C_2$. The calculated and observed (Heydrich) densities are 1.405 g./cc. and 1.404 g./cc., respectively. The only consistent extinctions, hkl when $h + k$ is odd and $h0l$ when l is odd, indicate the space group $C2/c$, thus confirming Heydrich's assignment to the holohedral class.

Two pictures were made for each oscillation range, their exposure ratios being always 6:1. From these the $h0l$, $hk0$ and $hk \pm 1$ intensities were carefully estimated visually and corrected for the Lorentz-polarization factor. The structure factors derived from them by taking their square roots are recorded in Tables I, II and III. They have been adjusted to approximately absolute scale by comparison with the corresponding values calculated from the final structure and are arranged in order of decreasing spacing. The $hk0$ and $hk \pm 1$ intensities are not as reliable as the $h0l$ values because in recording them the needle axis was perpendicular to the oscillation axis. However, the lath-like needle was extremely thin (not over 0.1 mm.) in the direction perpendicular to the {100} faces and about 0.3 mm. perpendicular to the {001} faces so bad absorption need be feared only for a few reflections for which the emergent beams were almost exactly parallel with the needle axis. These have been indicated in Table II.

(5) Dehlinger, *Z. Krist.*, **65**, 296 (1927).

TABLE I

STRUCTURE FACTORS OF THE ($h0l$) REFLECTIONS

$h0l$	$F_{calcd.}$	$F_{obsd.}$	$h0l$	$F_{calcd.}$	$F_{obsd.}$
200	+ 1	3	2.0,10	+10	< 7
002	+ 62	66	6,0,$\bar{12}$	−37	41
20$\bar{2}$	+ 62	66	806	−45	48
202	− 12	9	12,0,$\bar{10}$	−17	14
40$\bar{2}$	− 19	16	4,0,$\bar{12}$	−16	20
400	−142	126	14,0,$\bar{6}$	+14	< 8
20$\bar{4}$	− 21	24	10,0,4	+ 5	< 8
004	−109	121	14,0,$\bar{4}$	+ 7	< 8
40$\bar{4}$	+ 36	28	608	−10	13
60$\bar{2}$	+ 3	8	2,0,$\bar{12}$	− 1	< 8
402	− 80	88	10,0,$\bar{12}$	+44	56
204	+ 68	78	12,0,2	−11	14
60$\bar{4}$	− 62	62	14,0,$\bar{8}$	−14	10
600	− 5	9	14,0,$\bar{2}$	−14	7
40$\bar{6}$	− 23	25	4,0,10	− 6	< 8
20$\bar{6}$	− 32	28	0,0,12	+ 4	< 8
006	+ 22	21	14,0,$\bar{10}$	−29	29
60$\bar{6}$	− 20	21	12,0,$\bar{12}$	−18	17
80$\bar{4}$	+ 33	28	14,0,0	− 8	< 8
602	− 52	50	10,0,6	0	< 8
404	+ 29	24	16,0,$\bar{8}$	− 4	< 8
80$\bar{2}$	− 3	6	12,0,4	− 8	< 9
206	+ 36	36	6,0,$\bar{14}$	− 2	< 9
80$\bar{6}$	− 23	29	16,0,$\bar{6}$	−14	15
800	− 19	21	8,0,$\bar{14}$	+ 1	< 9
40$\bar{8}$	− 26	22	808	−27	27
20$\bar{8}$	− 1	< 5	2,0,12	+14	11
60$\bar{8}$	+ 33	25	16,0,$\bar{4}$	−23	24
604	− 31	26	4,0,$\bar{14}$	−18	23
10,0,$\bar{4}$	+ 35	38	10,0,$\bar{14}$	− 1	< 9
008	+ 39	34	14,0,$\bar{12}$	−13	9
10,0,$\bar{2}$	+ 1	< 5	6,0,10	− 9	< 9
80$\bar{8}$	− 18	16	14,0,2	+ 6	< 9
802	+ 40	42	16,0,$\bar{2}$	− 7	< 9
406	− 23	25	16,0,$\bar{10}$	− 3	< 9
10,0,$\bar{6}$	+ 13	9	2,0,$\bar{14}$	− 8	< 9
10,0,0	+ 8	9	12,0,$\bar{14}$	+ 3	< 9
208	− 4	< 6	4,0,12	− 2	< 9
10,0,$\bar{8}$	− 19	19	16,0,$\bar{12}$	+ 4	< 9
4,0,$\bar{10}$	− 9	5	16,0,0	+ 7	< 9
6,0,$\bar{10}$	− 10	9	0,0,14	+20	18
804	− 16	12	12,0,6	+24	24
12,0,$\bar{4}$	− 2	6	14,0,$\bar{14}$	− 3	< 9
2,0,$\bar{10}$	− 4	< 6	10,0,8	+10	14
12,0,$\bar{6}$	+ 26	25	18,0,$\bar{6}$	−18	17
8,0,$\bar{10}$	+ 31	32	18,0,$\bar{8}$	+20	19
606	− 8	8	14,0,4	+ 2	< 9
12,0,$\bar{2}$	+ 8	10	8,0,$\bar{16}$	+ 4	< 9
10,0,2	+ 20	19	18,0,$\bar{4}$	−21	17
408	+ 1	< 7	8,0,10	+13	13
0,0,10	− 7	11	6,0,$\bar{16}$	+22	25
10,0,$\bar{10}$	+ 26	26	10,0,$\bar{16}$	−19	18
12,0,$\bar{8}$	+ 21	16	18,0,$\bar{10}$	+17	16
12,0,0	+ 16	10	12,0,8	+23	21
8,0,$\bar{12}$	+ 27	28			

Determination of the Structure

Since there are eight molecules per cell it appears that each of the atoms of the molecule must

TABLE II

STRUCTURE FACTORS OF THE (*hk*0) REFLECTIONS

*hk*0	$F_{calcd.}$	$F_{obsd.}$	*hk*0	$F_{calcd.}$	$F_{obsd.}$
110	+ 55	61	040	+ 1	< 7
310	+118	109	240	− 2	< 7
510	+ 25	30	930[a]	−27	22
020	+ 2	4	440	+ 2	< 7
220	− 48	50	13,1,0	− 9	8
420	+ 8	10	12,2,0	+ 3	< 8
710[a]	+ 39	27	640	+ 2	< 8
620	+ 61	61	11,3,0	+ 9	10
130	+ 12	7	840[a]	− 7	9
910	− 12	10	15,1,0	− 8	< 8
330	− 4	4	14,2,0	+ 5	< 8
820[a]	− 9	8	150	− 4	< 8
530	+ 14	15	350	+ 2	< 8
11,1,0	+ 6	< 6	10,4,0	+ 4	< 8
730	− 12	12	13,3,0	+16	16
10,2,0[a]	+ 18	10	550[a]	+ 2	< 8

[a] Probably subject to absorption.

TABLE III

STRUCTURE FACTORS OF THE ($hk \pm 1$) REFLECTIONS

hk ±1	$F_{calcd.}$	$F_{obsd.}$	*hk* ±1	$F_{calcd.}$	$F_{obsd.}$
$11\bar{1}$	− 20	20	041	+ 2	< 7
111	− 85	83	$24\bar{1}$	+14	11
$31\bar{1}$	− 90	91	241	+ 3	< 7
311	−104	103	$93\bar{1}$	−20	12
$51\bar{1}$	− 39	40	$44\bar{1}$	−10	< 7
021	+ 28	26	$13,1,\bar{1}$	+ 4	< 7
511	+ 8	18	$12,2,\bar{1}$	− 9	< 7
$22\bar{1}$	− 9	11	441	−16	11
221	+ 2	11	931	−15	20
$42\bar{1}$	− 5	< 6	$64\bar{1}$	− 6	< 8
$71\bar{1}$	+ 34	26	13,1,1	− 4	< 8
421	− 6	< 6	641	+ 2	< 8
711	+ 52	55	12,2,1	− 1	< 8
$62\bar{1}$	+ 38	28	$11,3,\bar{1}$	− 7	< 8
621	+ 24	24	$84\bar{1}$	− 1	< 8
$91\bar{1}$	+ 9	8	11,3,1	− 5	< 8
$13\bar{1}$	+ 14	< 7	$15,1,\bar{1}$	+ 2	< 8
131	+ 20	18	$14,2,\bar{1}$	+ 5	< 8
$33\bar{1}$	+ 15	18	841	+ 9	< 8
$82\bar{1}$	+ 22	12	$15\bar{1}$	+ 2	< 8
331	0	< 7	151	+15	13
911	+ 13	8	$10,4,\bar{1}$	−10	< 8
$53\bar{1}$	− 3	< 7	$13,3,\bar{1}$	+24	19
821	− 7	9	$35\bar{1}$	0	< 8
531	+ 3	9	14,2,1	+14	16
$11,1,\bar{1}$	− 9	< 7	351	0	< 8
$73\bar{1}$	+ 5	< 7	15,1,1	− 3	< 8
$10,2,\bar{1}$	− 26	17	$55\bar{1}$	− 4	< 8
731	+ 6	< 7	10,4,1	+ 4	< 8
11,1,1	− 6	< 7	13,3,1	+10	12
10,2,1	− 27	23	551	−10	< 8

occupy one of the eightfold general positions of $C2/c$: (000 ; $\frac{1}{2},\frac{1}{2},0$) + x, y, z; $\bar{x}, \bar{y}, \bar{z}$; $\bar{x}, y, \frac{1}{2} - z$; $x, \bar{y}, \frac{1}{2} + z$. There are thus eighteen parameters to be determined, neglecting, as is customary, the hydrogens.

Because of the unusual shortness of the b axis, which is only slightly longer than the ordinary van der Waals separation of the atoms involved, it was decided to evaluate first the x and z coördinates which define distances perpendicular to this short axis. For this purpose, the $h0l$ intensities were used to prepare a Patterson projection onto (010). The series summed was $P(x, z) = \Sigma_h \Sigma_l F^2_{h0l} \cos 2\pi (hx + lz)$. The summation was effected by Beevers–Lipson strips[6] at intervals of $\frac{1}{60}\,a$ and $\frac{1}{30}\,c$, and the function is plotted as a contour map in Fig. 1. Since for $C2/c$, $h0l$ reflections always occur with both h and l even, only a fourth of the cell, containing only two molecules, need be considered.

This function tends toward maxima at values of x and z corresponding to the differences between the x and z coördinates of all the atoms of the cell taken in pairs. Because of the relatively large number of atoms involved, the extremely large number of such maxima possible superimpose and are not resolved individually. Each of the various peaks observed in Fig. 1 is the result of dozens of interatomic interactions falling near together and the interpretation of the result is consequently very difficult and uncertain. In the present instance, however, some simplification is introduced by the shortness of b. The smallest distance to be expected between two atoms in different molecules is about 3.0 Å., corresponding to a hydrogen bond >N—H. . . N<. Because every atom has others only 4.44 Å. above and below it in the y direction, the shortest possible component of this nearest approach parallel to the xz plane is easily calculated to be $\sqrt{3^2 - b^2/4}$ = about 2.0 Å. Consequently all interactions between atoms in different molecules are two or more ångströms from the corners of the plot. The area so blocked off is indicated in Fig. 1 by the heavy circles of two ångströms radius about the corners. The details inside these circles must be explained by the interactions arising inside single molecules and thus depend only on the shape and orientation of the molecules but not upon their positions.

The only striking point about this portion of the plot is that the large central peak at (0,0), which comes from the interaction of each atom with itself, is not symmetrical but is considerably elongated along a line making an angle of about 35° to c in acute angle β'. This indicates that a

(6) Lipson and Beevers, *Proc. Phys. Soc.*, **48**, 772 (1936).

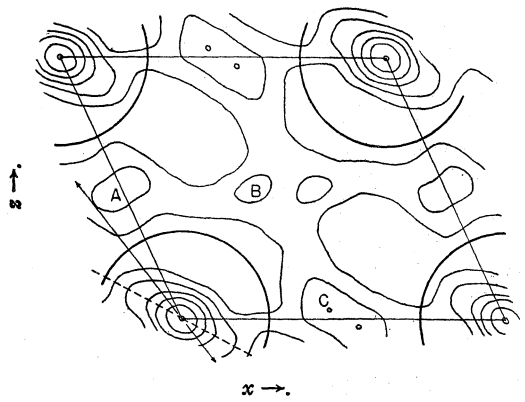


Fig. 1.—$P(x, z)$. The cell outlined is only a quarter of the true cell. P is in arbitrary units and negative contours have been omitted.

number of interatomic distances, probably chemical bonds, are oriented in this direction. The number can be estimated by approximately resolving the peak in the following way. The values of $P(x, z)$ along the ridge of the peak are plotted against distance from the origin and likewise the values of $P(x, z)$ in a direction perpendicular to the ridge, as in Fig. 2. If we assume that there are no important interactions exactly in the direction perpendicular to the direction of the ridge, this latter curve represents approximately the true shape of the central peak. The difference between the two curves (dashed curve) then represents the distorting maximum sought. It is seen to fall at about 1.2 Å. from the origin and is nearly half as high as the central peak, although these values are very uncertain because the base for the curves can only be estimated. Since the central peak corresponds to six atoms per molecule, the distortion must represent two or three atomic interactions and from their distance from the origin they must be the xz components of two or three nearly parallel chemical bonds. Now the direction of easiest polarization of the molecule, as given by the position of the acute bisectrix, is only 11° from c in acute angle β', as indicated in Fig. 1 by the arrow through the origin. We are thus led to a molecular model which has two or three bonds approximately parallel, but making an angle of about 24° with the direction of easiest polarization of the molecule on one side only of the latter. This eliminates quite clearly both cyclic formulas II and IV since their bonds are symmetrically distributed about the long axis of the molecule. Either I or III is acceptable, however. They differ very little as far as carbons and nitrogens are concerned and do in fact have three parallel or nearly parallel bonds making a suitable angle with the long way of the molecule. Such molecules are expected to be at least approximately coplanar. The orientation of the planes of the molecules was set approximately at plus and minus 45° to b, because Heydrich[3] had found the two smaller refractive indices of the crystal to be very nearly equal (α = 1.5212, β = 1.5493, γ = 1.8471, D lines). If the planes of the molecules were all even approximately parallel, one of these smaller indices would be considerably larger than the other

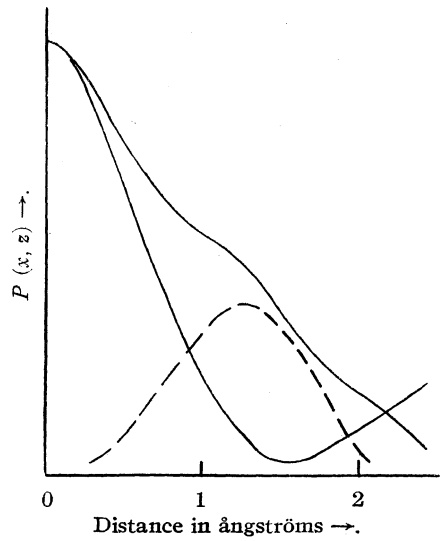


Fig. 2.—Cross section curves resolving the peak at the origin of Fig. 1.

The above arguments completely determine the approximate configuration and orientation of the molecule. The projections of the three parallel bonds are parallel to the long axis of the central peak, that of the long axis of the molecule is parallel to the acute bisectrix and the planes of the molecules make angles of about 45° alternately plus and minus with the b axis. All the interactions contributing to $P(x, z)$ which arise from within the same molecule were now marked on the plot as required by this model. Average bond distances and angles were used as no choice had yet been made between I and III. These interactions explained quite well the peak marked A but left the peaks B and C to be explained almost entirely by interactions arising between different molecules. An examination of the problem shows that these latter interactions form a pattern which depends only upon the shape and orientation of the mole-

cules. But the position of the pattern as a whole depends upon the position of the molecule. The pattern suggested by the above model was drawn to proper scale on tracing paper, placed in proper orientation on Fig. 1 and shifted about to obtain the best possible fit with the observed peaks, paying attention of course to the additional interactions produced from the pattern by the action of the symmetry elements of the projection. The possibilities are considerably restricted by the fact that all these interactions must fall outside the 2.0 Å. circles. The x and z coördinates of the atoms were determined from the position giving the best agreement. These parameters were then tested by computing the $h0l$ structure factors. The scattering factors of Pauling and Sherman[7] were used with a temperature factor of $e^{-B \sin^2\theta/\lambda^2}$, where $B = 2.00$. The factors for NH_2 were estimated by adding to those for N the differences between those for O and O″. These differed very little from nitrogen factors except at small scattering angles. In these early calculations model III was used to identify atoms but no significant error could be introduced in this way. The agreement between the observed F's and those calculated from the approximate parameters was unexpectedly good and it was possible to proceed at once to refine the parameters by Fourier syntheses.

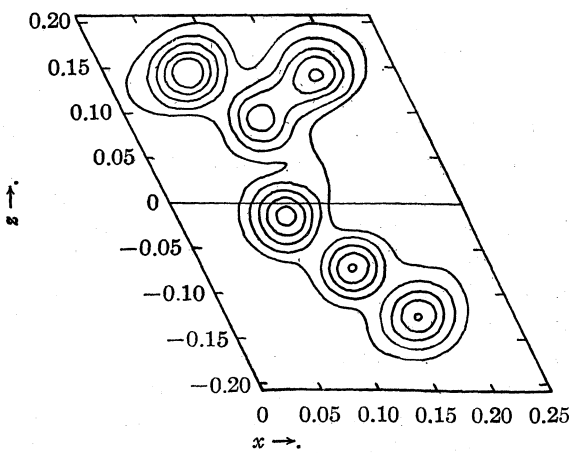


Fig. 3.—Projection of electron density on {010}. Contour intervals are approximately 2 electrons per sq. Å.

The summations of $\rho(x, z) = \Sigma_h\Sigma_l F_{h0l} \cos 2\pi (hx + lz)$ were carried out by Beevers–Lipson strips[5] at intervals of $1/120$ a and $1/120$ c. One-eighth of the final projection, which included all observed F's, is shown in Fig. 3. All atoms are satisfactorily resolved. The x and z coördinates were read from this plot to the nearest 0.0005 and are recorded in Table IV. The structure factors calculated from them are included in Table I and are seen to be in satisfactory agreement with the observed values.

TABLE IV

	C_1	C_2	N_3	N_4	N_5	N_6
x	0.1285	0.1145	0.1635	0.0920	0.1795	0.0705
y	.103	.171	−.037	.251	−.061	.334
z	−.0725	.0935	−.1265	−.0150	.1430	.1450

No assumption has been made so far with regard to the nature of the symmetry element at the origin of the Fourier plot. It may be a symmetry center at $y = 0$, one at $y = 1/4$ (lying between the c glide planes), a twofold axis or a twofold screw axis. A molecular model of average expected dimensions, adjusted in orientation to project exactly onto the Fourier peaks, was now moved along the y direction, assuming in succession each of the possible symmetry elements, and the interatomic distances to atoms in surrounding molecules produced by the symmetry elements were calculated as a function of the y coördinate of one of the atoms. It was found that satisfactory packing could not be obtained using symmetry axes at the origin. Nor did the center of symmetry between the glide planes give acceptable distances. Only when the origin was taken at a symmetry center in a glide plane did a structure with reasonable atomic separations result. In this way approximate y coördinates were obtained.

It was obvious at once from this approximate structure that there was no possible Fourier projection which would resolve any atom in such a way as to fix its y parameter. The six y coördinates had to be refined by the arduous trial and error procedure, using $hk0$ and $hk\pm1$ intensities. It seemed highly improbable that the four atoms of the guanidine group could be non-coplanar, or that the cyanimino group could be non-linear. The projection of the latter was in fact linear in the Fourier synthesis to the accuracy with which the plot could be prepared and read. Consequently, in refining the y parameters the trial adjustments were always made in such a way as to maintain the stated configurations. A survey of the final results indicates that even without these constraints the two groups would not have deviated from the expected shapes by more than the experimental errors.

(7) Pauling and Sherman, *Z. Krist.*, **81**, 1 (1932).

In comparing the calculated and observed structure factors no weight was given to those spectra believed to be influenced by absorption. The final accepted values are recorded in Table IV and the structure factors calculated from them (and the previously fixed x and z parameters) for $hk0$ and $hk\pm1$ are in Tables II and III. The agreement with observed values, while not as good as for the $h0l$ spectra, is satisfactory if one allows for the reduced reliability of the data.

Discussion

The resulting molecule is shown, as viewed parallel to and perpendicular to the plane of the guanidine group, in Fig. 4(a) and (b). The interatomic distances and bond angles are recorded on the figure (see also Table V). The underscored numbers give the heights of the atoms above the plane of the drawing in ångströms. The exact planarity of the guanidine group and the linearity of the cyanimino group have been imposed as described above, but the calculations indicate that unadjusted results would differ from these configurations by displacements not greater than the experimental errors. The probable error in the position of an atom is estimated to be about ±0.015 Å. and the probable error of a bond length consequently about ±0.02 Å. It is not very likely that any bond length is in error by more than ±0.04 Å.

TABLE V

INTERATOMIC DISTANCES

Chemical bonds		Hydrogen bonds	
1—3	1.22 Å.	6—4A, 4—6A	2.94 Å.
1—4	1.28	6—3C, 3—6D	3.02
2—4	1.36	5—3B′, 3—5B′	3.04
2—5	1.37	5—3C, 3—5D	3.16
2—6	1.34	5—6′, 6—5′	3.15

Van der Waals Contacts

$NH_2\cdots NH_2$		$NH_2\cdots C$	
5—5E	3.49 Å.	1—6A′	3.34 Å.
6—5E	3.62	2—5′	3.53
6—6A′	3.76	1—6A	3.68
		2—6A	3.85
$NH_2\cdots N$		2—6′	3.87
		2—6A′	3.88
6—4A′	3.47	6—1C	3.94
4—5′	3.61	1—5B	3.95
5—3B	3.62		
3—6A′	3.65	$N\cdots C$	
5—4A′	3.77		
		2—4A′	3.39
$N\cdots N$		2—3C	3.47
		2—3B	3.56
4—3B	3.56	2—4A	3.81
4—4A	3.69	1—3′	3.86
4—4A′	3.70	1—4′	3.94
3—3B′	3.73		
$C\cdots C$			
1—1B	3.56		

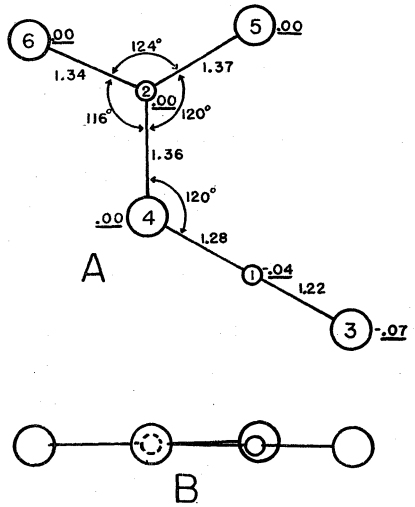


Fig. 4.—(a) View of the molecule perpendicular to plane of guanidine group. Underscored numbers are heights in ångströms of atoms above plane. (b) View of molecule parallel to same plane.

In a recent discussion[8] of double bond lengths it has been suggested that some of the double bond radii in common use recently have been too long. The present work supports this view. The previously accepted value for N=C was 1.28 Å. On this basis the 1.28 Å. bond of the cyanimino group would be a pure double bond and the corresponding structure $:\dot{N}=C=\dot{N}:$. This would require in turn that the other bond also be 1.28 Å. (or longer if one allows for the formal charge effect), whereas the observed value is 1.22 Å. If we accept the new constant for estimating double bond lengths, the theoretical C=N bond becomes 1.47 − 0.21 = 1.26 Å. and this value permits a satisfactory interpretation of both bond distances. If the cyanimino group resonates between the structures $:N\equiv C-\dot{N}:$ (25%) and $:\dot{N}=C=\dot{N}:$ (75%) the calculated bond lengths[9] become 1.22 Å. and 1.28 Å. in agreement with the observed values. These values differ from those previously predicted[10] for the cyanimino group, 1.20 Å. and 1.32 Å., respectively, partly because

(8) Stevenson, Burnham and Schomaker, THIS JOURNAL, 61, 2922 (1939).

(9) L. Pauling, "The Nature of the Chemical Bond," revised edition, Cornell University Press, Ithaca, N. Y., 1940, p. 171. The revised radii are listed on p. 164.

(10) Pauling and Sturdivant, *Proc. Nat. Acad. Sci.*, 23, 615 (1937).

of the revision in the C=N value but chiefly because in the earlier calculation it was assumed that the two resonating structures contribute about equally to the normal state. There is a special reason for the larger contribution of $:N{=}C{=}\ddot{N}\diagdown$ in the present structure. As we shall see below, the terminal nitrogen atom has three hydrogen bonds directed toward it. The structure $:N{\equiv}C{-}\ddot{N}\diagdown\!\!\diagdown$ has only one unshared electron pair to divide among these bonds which would therefore be weak, as in ammonia where a similar situation prevails.[11] But the alternative structure provides two unshared pairs and would permit much stronger hydrogen bonds. It consequently makes a larger contribution to the normal state, the final result being that the loss in resonance energy is more than made up by the gain in energy of the three hydrogen bonds. The structure $^{-2}\!:\!\ddot{N}{-}C{\equiv}N{-}$ which would provide even more electron pairs is probably of little importance because of the unfavorable bond angle, C—N—C = 120°. But the structure $^{-2}\!:\!\ddot{N}{-}\overset{+}{C}{=}N\diagdown$ may make a small contribution.

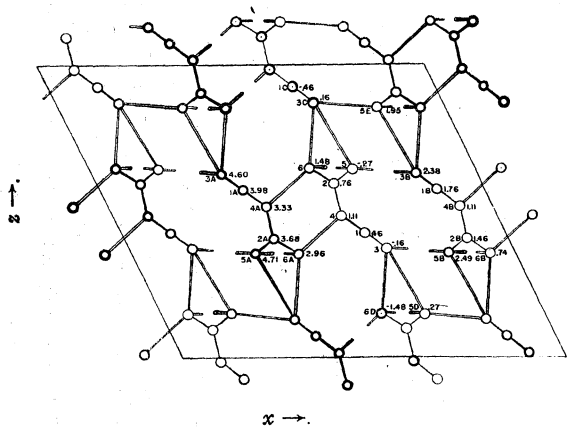


Fig. 5.—View of unit cell projected parallel to b. Numbers to right of atoms give heights in ångströms above {010}. Origin is at center of figure. Tubes represent hydrogen bonds.

In the guanidine group the double bond resonates to a certain extent into all possible positions.

$$-\ddot{N}\diagdown\!\!\diagdown C{-}NH_2, \quad =\ddot{N}\diagdown C{=}\overset{+}{N}H_2 \quad \text{and} \quad =\ddot{N}\diagdown C{-}NH_2.$$

The observed bond lengths 1.37, 1.36 and 1.34 Å. correspond to 23, 27, and 35% of double bond character, respectively, and the sum of these, 85%, comes fairly close to 100%. Moreover, the structure $=\ddot{N}\diagdown C^{+}{-}NH_2$ which involves no double bond is probably of some importance. Ordinarily we should expect the two amino groups to be equivalent and in fact the difference between their C–N bond lengths is of the order of the experimental error and may be without significance. This, however, will be discussed further in connection with the hydrogen bonds. The bond angles, which have a probable error of about ± 2½°, are compatible with the structures proposed. The deviation of the cyanimino group from the plane of the guanidine group, although probably exceeding experimental error, is quite small, corresponding to a rotation about the $\diagup\!\!\diagup N{-}C\diagdown\!\!\diagdown$ bond of only 2°.

The arrangement of the molecules in the unit cell is shown in Fig. 5. Here the atoms have been projected along the b axis, which is normal to the diagram, onto the {010} plane which is in the plane of the diagram. Numbers to the right of an atom give its height in ångströms above {010} while numbers and letters to the left identify the atoms. Numbers 1 to 6 indicate the atoms corresponding to the coördinates of Table IV, the origin being at the center of the figure. The suffix A, B, C, D or E indicates a molecule derived from the first by one of the symmetry operations of the space group. Primes, which occur in Table V, indicate atoms b(= 4.44 Å.) above or below corresponding unprimed atoms.

If one singles out sections of crystal parallel to (001) and one molecule thick all the molecules in alternate sections are approximately parallel to (310) while those in the interleaving sections are approximately parallel to (3$\bar{1}$0). These related planes make angles of about ± 45° with the horizontal and thus about 90° with each other. Within a section the molecules form strips, the atoms of the molecules of a strip all lying within ± 0.15 Å. of a plane parallel to (310) or (3$\bar{1}$0), depending upon what section the strip is in.

The arrangement about a single molecule is further shown in Fig. 6. Here the crystal has been projected onto the plane parallel to (310) which passes through symmetry centers at 0, ½, 0; ¼, ¼, 0; etc. Three of the molecules shown, which form part of a strip, lie almost in this plane, as indicated by underscored numbers

(11) Mark and Pohland, *Z. Krist.*, **61**, 532 (1925); de Smedt, *Bull. Acad. Roy. de Belgique*, **10**, 655 (1925).

which are the heights of the atoms above the plane in question. Portions of molecules in adjacent sections which are parallel to $(3\bar{1}0)$ are seen here edgewise at the top and bottom of the figure. Also are shown one molecule from each of the strips parallel to (310) but one layer above and below the plane of the drawing. The separation of these layers is 3.16 Å. Most of the interatomic distances between different molecules are 3.34 Å. or greater as shown in Table V, and correspond satisfactorily to expected van der Waals distances.[12] Five pairs of distances however are much shorter than van der Waals radii sums and these are indicated by dotted lines on Fig. 6 for the central molecule of the group. The lengths are also recorded there and in Table V. These are interpreted as hydrogen bonds and are represented in Fig. 5 by double lines or "tubes." Where one of these tubes ends before reaching a second atom it is generally directed at an atom b (= 4.44 Å.) above or below the atom at which it is directed but in some instances $2b$ (= 8.88 Å.) above or below.

These hydrogen bond distances are comparable with those found in ammonium azide,[13] 2.94 Å. and 2.99 Å.

Although the positions of the hydrogens cannot be found by X-ray diffraction effects, we may infer their positions from the arrangement of these short bonds. A hydrogen atom is to be placed, in accord with accepted stereochemical principles, on an atom at one end or the other of each short distance in such a way that there are four hydrogens per molecule. But in this case we have five pairs of bonds and only four hydrogens so we must assume that we have here another example of the so-called "bifurcated hydrogen bond" first reported in glycine.[14] In such a bond a hydrogen is attached to one atom with bond angles so arranged that it is directed equally well toward two other "acceptor" atoms on adjacent molecules. Because of this division of attraction the bonds are expected to be longer and in fact in glycine the two bonds of this type are on the average about 0.20 Å. longer than the other N–H...O bonds, but still definitely shorter than van der Waals approaches. This suggests that in dicyandiamide the two longest pairs of

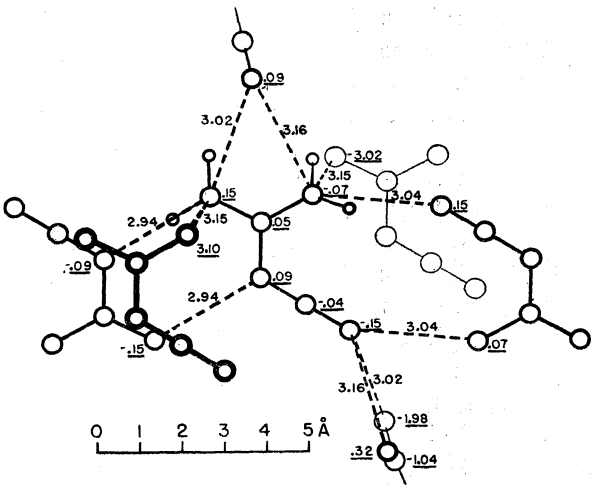


Fig. 6.—A normal projection of a portion of the structure onto (310). Small circles show probable positions of hydrogens. Underscored numbers are heights of atoms in ångströms above plane of diagram. Dotted lines indicate hydrogen bonds.

length 3.15 Å. and 3.16 Å. are the split bond and since they converge on atom 5 we place one hydrogen on it with the NH bond bisecting the angle between the two short distances. It was then found possible to distribute the three remaining hydrogens among the three remaining pairs of short distances in only one way without bringing hydrogen atoms on different molecules too close to one another. This way corresponds to the formation of two amino groups from atoms 5 and 6. The proposed positions thus found for the hydrogens are indicated (for the central molecule only) on Fig. 6 by small circles.

The N—H bonds were made to make angles of 120° with the C—N bonds (trigonal hybridization). The NH_2 group 6 is coplanar with the guanidine group and directs one of its hydrogens very nearly along (10°) the shortest hydrogen bond (2.94 Å.) while the other makes an angle of about 20° with the medium bond (3.02 Å.). The plane of NH_2 group 5 makes an angle of about 30° with the plane of the guanidine group. One of its hydrogens forms the bifurcated bonds (of lengths 3.15 Å. and 3.16 Å.) while the other makes an angle of about 25° with the second medium bond (3.04 Å.). The rotation of this NH_2 group out of the plane of the guanidine group would tend to force the resonating double bond somewhat out of this $\rangle C—NH_2$ bond and consequently more into the other. The observed C—NH_2 distances differ in the right direction for this

(12) Reference 9, p. 187.

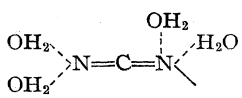
(13) Hughes, Thesis, Cornell University, 1935; Frevel, *Z. Krist.*, **94**, 197 (1936).

(14) Albrecht and Corey, THIS JOURNAL, **61**, 1087 (1939). See also discussion in reference 9, footnote p. 286.

effect and this small difference may therefore well be real. The loss in resonance energy would be compensated for by the energy of forming the second half of the split hydrogen bond. The excess in length of the medium bonds (3.02 and 3.04 Å.) over the short ones (2.94 Å.) is to be accounted for partly by the fact that the hydrogen is more exactly directed along the short bond but probably the chief source of weakness in the medium bonds is the fact that they both converge, along with one half of the split bond, upon a single nitrogen atom which, as already noted, does not have enough unshared electron pairs to provide one pair per hydrogen bond. This is not the case for the short bond. The 3.15 Å. component of the split bond is directed at the p_z orbital of an amino group 6′ of another molecule. This electron pair is involved in double bond formation only to the extent of 35% as indicated above. It thus provides about as good a terminus for a hydrogen bond as the end nitrogen of the cyanimino group.

The proposed structure satisfactorily accounts for the cleavages. The crystal may be cleaved parallel to {100} by breaking only four hydrogen bonds per cell (see Fig. 5), or 0.069 per (Å.^{2}). For the poorer cleavage on {001} the corresponding figures are eight per cell and 0.120 per (Å.^{2}). Any other cleavage will break even more bonds per unit area.

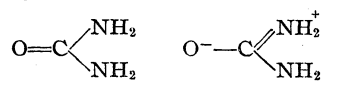
In water solutions the water molecules can form hydrogen bonds in equal numbers to both ends of the cyanimino group



Consequently, unlike in the crystal, the two contributing structures are probably of nearly equal energy and the resonance stabilization large. The addition of a proton at either end to form a cation would disturb this equality and so inhibit the resonance and decrease the stability. Moreover, the addition of a proton to an amino group would completely exclude the resonating double bond of the guanidine group from that atom and so would also cause a considerable decrease in stability. Consequently it is not surprising that the substance shows no basic properties whatever.

On the other hand, the removal of a proton from one of the amino groups to form an anion would destroy the equivalence of these two groups and although the effect would not be as drastic as that caused by adding a proton, the molecule would be destabilized to some extent by loss of resonance energy. It has been found that the acid properties are almost negligible. K_A is of the order[15] of 10^{-13} and the sodium salt, prepared in alcohol from sodium ethylate, is 95% hydrolyzed in 0.1 M solution in water. In liquid ammonia solution the conductivity of dicyandiamide reported[16] is exceedingly small so it would seem that even here there is very little dissociation despite the fact that some salts of dicyandiamide can be prepared in this solvent by reactions with metals or metal amides.

One may consider dicyandiamide to be an internal salt or zwitter ion in the same sense that urea may be so regarded. In urea the resonance of the double bond from oxygen to the amino groups transfers charges in such a way as to produce a high dipole moment:



In dicyandiamide the cyanimino group behaves like the oxygen of urea. In the crystal the hydrogen bonds from positive to negative groups tend to neutralize the charges and in fact the formal charge correction[17] has been ignored in calculating interatomic distances above. But in solution the substance would be expected to behave physically much like urea, producing an increase in the dielectric constant of the solution. This salt-like nature and the hydrogen bonds explain the high melting point (205°), low solubility in non-polar solvents, and high temperature coefficient of solubility in water and alcohol.

Crystals from alcohol were too poorly formed for goniometry but yielded a powder picture identical with that from crystals from water.

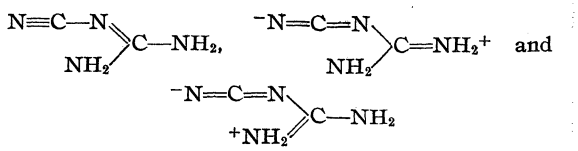
The dimensions found for the guanidine group are in good agreement with the C—NH_2 distance of 1.37 Å. found[18] in the closely related urea. But they do not agree with the corresponding distances reported[19] for the guanidinium ion, 1.20 Å. in guanidinium bromide and 1.18 Å. in the iodide.

(15) Grube and Krüger, *Z. physik. Chem.*, **86**, 85 (1914); Kameyama, *J. Chem. Ind. Japan*, **24**, 1263 (1921).
(16) Smith, THIS JOURNAL, **49**, 2162 (1927).
(17) Reference 9, page 164.
(18) Wyckoff and Corey, *Z. Krist.*, **89**, 462 (1934).
(19) Theilacker, *ibid.*, **90**, 51 and 256 (1935).

The author is indebted to Mr. P. A. Shaffer, Jr., who grew and mounted most of the crystals and assisted with the preparation and indexing of some of the photographs. Thanks are also due to Professor Pauling for encouragement and advice.

Summary

The crystal structure of dicyandiamide has been investigated. The monoclinic unit cell has $a = 15.00$ Å., $b = 4.44$ Å., $c = 13.12$ Å. and $\beta = 115° 20'$. The space group is $C2/c$ and there are eight molecules of $C_2N_4H_4$ per cell. The positions of the atoms have been found and correspond to a molecule which is a resonance hybrid, chiefly between structures



The packing of the molecules was found to be dominated by hydrogen bonds, one of which is of the rare bifurcated type. The properties of the compound have been discussed briefly in relation to the structure.

PASADENA, CALIF. RECEIVED MARCH 5, 1940

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 768]

An Electron Diffraction Investigation of the Molecular Structure of Tellurium Tetrachloride

BY D. P. STEVENSON AND VERNER SCHOMAKER

Introduction

It has been remarked by Pauling[1] that it is not known whether or not the unshared electron pair in molecules and complexes such as $SeCl_4$, TeC_4l, and $[AsCl_4]^-$ is stereochemically inert as it is in the compounds M_2SeBr_6, or stereochemically active as in ammonia-like compounds. From a discussion of the properties of the solid and dielectric constant measurements on dilute benzene solutions, Smyth, Grossman and Ginsburg[2] conclude that $TeCl_4$ has a large dipole moment. But this conclusion is insufficient to fix the structure of the molecule or to determine the steric effect of the unshared electron pair. Through the kindness of Professor J. H. Hildebrand, a pure sample of $TeCl_4$ which had been used for heat capacity determinations[3] was made available to us for the study of the structure of the molecule in the gas phase. The results of our study are reported in this paper.

Experimental

The apparatus used in this investigation has been described by Brockway.[4] The wave length of the electrons determined in the usual manner from transmission photographs of gold foil ($a_0 =$ 4.070 Å.) was 0.0618 Å. The photographs were taken with a camera distance of 10.86 cm.

The low volatility of the compound (b. p. 390°) necessitated the use of the high-temperature nozzle[5] in order to obtain sufficient gas pressure. The photographs were taken with the sample in the boiler at 250–350°. We believe that the material actually present in the diffracting jet of gas was monomolecular tellurium tetrachloride. Simons[6] has shown that tellurium tetrachloride vapor is not appreciably dissociated (into tellurium dichloride and chlorine) up to 500° and that below this temperature the vapor is unassociated. There is the possibility that some of the tellurium tetrachloride reacted with the various metallic parts of the boiler. The only probable volatile product of such reactions is tellurium dichloride. Moderate amounts of tellurium dichloride would have little effect on our determination inasmuch as the tellurium–chlorine distance[7] (2.36 ± 0.03 Å.) in tellurium dichloride is nearly the same as the value found here for tellurium tetrachloride, while the chlorine–chlorine scattering is small compared to the chlorine–chlorine scattering of tellurium tetrachloride.

The photographs show seven rings, two of which are asymmetric. Curve D of Fig. 1, to be dis-

(1) L. Pauling, "Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1939, p. 172.

(2) C. P. Smyth, A. J. Grossman and S. A. Ginsburg, THIS JOURNAL, **62**, 192 (1940).

(3) K. J. Frederick and J. H. Hildebrand, *ibid.*, **60**, 2522 (1938).

(4) L. O. Brockway, *Rev. Mod. Phys.*, **8**, 231 (1936).

(5) L. O. Brockway and K. J. Palmer, THIS JOURNAL, **59**, 2181 (1937).

(6) J. H. Simons, *ibid.*, **52**, 3488 (1930).

(7) W. Grether, *Ann. Physik*, **26**, 1 (1936).

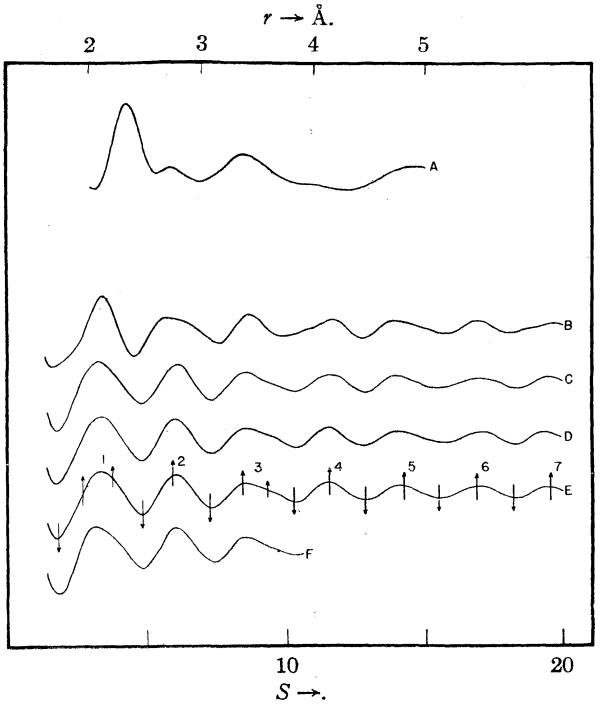


Fig. 1.—Curve A. Radial distribution function. Curve B. Regular tetrahedron, Te–Cl = 2.33 Å. Curve C. Trigonal bipyramid, Te–Cl = 2.33 Å., angles 90° and 120°. Curve D. Distorted trigonal bipyramid, Te–Cl = 2.33 Å., angles 93° and 120°. Curve E. Like D, but with temperature factor, $a = 0.003$, in coefficient of Cl–Cl terms. Curve F. Coplanar square. Te–Cl = 2.33 Å. Indistinguishable from curve E for S ⩾ 10.

cussed below, gives a good representation of the appearance of the photographs. The observed values of $s\left(s = \frac{4\pi}{\lambda}\sin\frac{\Theta}{2}\right)$ for the maxima and minima as well as the visually estimated relative intensities, I, are given in Table I.

Interpretation.—The radial distribution function[8] was calculated using the formula

$$D(l) = \sum_n C_n \frac{\sin ls_n}{ls_n} \qquad (1)$$
$$C_n = f(I_n, s_n)$$

The values of C_n were calculated in accordance with the recommendations of Schomaker[9] and are given in column 4 of Table I. The plot of $D(l)$ *vs.* l is given in Fig. 1, curve A. The strong peaks at 2.33 and 3.37 Å. undoubtedly correspond to interatomic distances in the molecule. The rather pronounced shoulder at 2.75 Å. is probably spurious, since the value 2.75 Å. does not correspond to an interatomic distance in any reasonable molecular model for tellurium tetrachloride. The 2.33 Å. peak corresponds to the Te–Cl distance (covalent radius sum, 2.36 Å.), while the other maximum at 3.37 Å. corresponds to a Cl–Cl distance. This interpretation leads to a bond angle of slightly more than 90° ($2.33\sqrt{2} = 3.30$). It is to be emphasized that there is only one maximum corresponding to a Cl–Cl distance. Several molecular models can now be eliminated from consideration. The molecule cannot have a regular tetrahedral structure, since for such a structure the Cl–Cl distance would be $2.33 \times \sqrt{8/3} = 3.82$ Å., while the radial distribution function gives 3.37 Å. for this distance. Models that can be derived by distortion of the regular tetrahedron with retention of the symmetry elements of the group C_{3v} would also be unsatisfactory. For example, a model with equal Te–Cl distances would have two equally important Cl–Cl distances, one greater than and the other less than 3.82 Å., in disagreement with the radial distribution function. A model having all equal Cl–Cl distances, three Te–Cl distances at the radial distribution function value, and one very much shorter Te–Cl distance (at about 1.7 Å.) would agree satisfactorily with the radial distribution function, but would be extremely improbable for structural reasons.

The radial distribution curve is compatible with models having equal or nearly equal Te–Cl distances, about four bond angles at 93°, and no more than one or two bond angles at any other value. Models satisfying these conditions can be

TABLE I

Max.	Min.	I_0	C_n	s_0	s_c[a]	s_c/s_0
	1	−10	− 4	1.80	1.72	(0.956)[b]
1		8	4	2.71	3.34	(1.232)[b]
	1a	− 2	− 1	3.19	...	...
1a		6	4	3.77	...	...
	2	−10	− 8	4.84	4.84	1.000
2		10	10	5.91	6.04	1.022
	3	− 7	− 7	7.23	7.30	1.010
3		7	8	8.40	8.50	1.012
	3a	− 2	− 2	8.79	...	...
3b		4	4	9.27	...	...
	4	− 7	− 8	10.21	10.30	1.009
4		10	11	11.50	11.45	0.996
	5	−10	−10	12.80	12.70	0.992
5		10	9	14.20	14.10	0.993
	6	−10	− 8	15.44	15.50	1.004
6		10	7	16.83	16.90	1.004
	7	−10	− 5	18.13	18.20	1.004
7		10	4	19.53	19.40	0.993
				Average		1.003±0.007

[a] From curve E. [b] Omitted because of unreliability of measurement.

(8) L. Pauling and L. O. Brockway, THIS JOURNAL, **57**, 2684 (1935).

(9) Verner Schomaker, A. C. S. Meeting, Baltimore, Md., April, 1939.

derived by unsymmetrical distortion of a regular tetrahedron retaining the symmetry elements of D_{2d} or C_{2v}. A very flat tetrahedron D_{2d} or C_{2v} (limiting case: the coplanar square) is such a model. A slightly distorted trigonal bipyramidal model (C_{2v}) in which the unshared electron pair occupies one of the equatorial positions is another. In these models the two Cl–Cl distances at values other than 3.37 Å. contribute little to the scattering, especially if different from each other, and might be expected not to appear on the radial distribution curve.

Theoretical curves were calculated for a variety of molecular models based on the interpretation of the radial distribution function given above, and are shown in Fig. 1, curves B-F. Average values of $Z_i - f_i$ were used in place of the more commonly used Z_i in the scattering formula

$$I(s) = \sum Z_i Z_j \frac{\sin l_{ij} s}{l_{ij} s} \qquad (2)$$

because of the great disparity in the functions $(Z - f)/Z$ for tellurium and chlorine. The effect of the variation of $(Z - f)_{Cl}/(Z - f)_{Te}$ with s was found to be negligible. The various symbols in equation (2) have their usual significance.[2] The values of f were obtained from the tables of Pauling and Sherman.[10] The intensity curves for the various models, except curve B, were all found to be satisfactory with regard to the qualitative features of the photographs, although none of the curves reproduces the unusually sharp appearance of the inner edge of the first maximum. Although we are unable to advance a satisfactory explanation of this discrepancy, we are quite sure that it is not due to our not having found the correct model for the structure of the molecule. Some of the curves were found to give more satisfactory quantitative agreement than others. Thus it was found that the models which had four of the bond angles equal to 93° gave curves for which the quantitative agreement was much better than those for which the angles were 90°. It was further found impossible to distinguish between models with two pairs of Te–Cl distances (2.27 and 2.40 Å.) from the corresponding models with all four Te–Cl distances equal to 2.33 Å., or between the flattened tetrahedral and the trigonal bipyramidal models of symmetry C_{2v}. The best quantitative agreement was attained when a temperature factor ($a = 0.003$) was introduced into the coefficients of the Cl–Cl terms as is suggested by the greater width of the Cl–Cl peak of the radial distribution function. The quantitative comparison with the most satisfactory curve (curve E, Fig. 1) is given in Table I.

The results of our electron diffraction study of $TeCl_4$ may be summarized as follows. The average Te–Cl distance is 2.33 ± 0.02 Å. The only important Cl–Cl distance is 3.37 ± 0.06 Å., corresponding to a bond angle of 93 ± 3°. The molecule cannot have a structure with symmetry C_{3v}. It may have any of a number of structures with symmetry D_{2d}, C_{2v}, or lower symmetry. The coplanar square structure seems unlikely because in it the important bond angles are at 90°. The value of a used in the effective temperature factor is comparable to the values found for other similar molecules investigated at high temperatures.

Discussion.—Among the possible configurations for $TeCl_4$ discussed above as being compatible with the electron diffraction photographs, only those of the "trigonal bipyramidal" type would be expected to lead to the large dipole moment (2.5 D)[2] found by Smyth, Grossman and Ginsburg. We accordingly believe that $TeCl_4$ molecules have a configuration derived from the trigonal bipyramid, one of the equatorial positions being occupied by the unshared electron pair. According to our electron diffraction investigation, the equatorial–axial bond angles are about 93°; the equatorial bond angle is probably considerably less than 120° but greater than 90°, as is suggested by the arguments given below; and the axial–axial bond angle is accordingly about 170°.

Our first argument regarding the equatorial bond angle is based on Pauling's theory of directed valence[1] and the assumption that the structure is based on the trigonal bipyramid with no significant distortion of the axial straight angle. If the four bond orbitals and the orbital occupied by the unshared pair are formed from the configuration sp^3d_z, as seems likely because of the greater stability of s and p, the equatorial bond angle will be 120° provided that p_x and p_y are distributed equally among the equatorial bonds and the unshared pair. It seems likely that the unshared pair orbital will have more than $1/3$ (s,d_z) character and less than $2/3$ p character because of the greater coulombic stability of s, and in spite of the lesser coulombic stability of d. This situation leads to an equatorial bond angle

(10) L. Pauling and J. Sherman, *Z. Krist.*, **81**, 1 (1932).

lying between 90 and 120°. On the other hand, the dipole moment (2.5 *D*) of $TeCl_4$ in benzene solution may be attributed to the free molecule also, and interpreted as the sum of four Te–Cl bond moments each having the value 2.3 *D* estimated by Smyth, Grossman and Ginsburg. For an axial–axial bond angle of 170° in the trigonal bipyramidal structure this interpretation leads to an equatorial bond angle of 102°.

The structure for $TeCl_4$ discussed here is in agreement with the prediction made by Pauling.[2] Kimball[11] suggested that $TeCl_4$ should have an "irregular tetrahedral" configuration of symmetry C_{3v}. This configuration is certainly incompatible with the results of our electron diffraction investigation; moreover, it would probably lead to a dipole moment much smaller than that found by Smyth, Grossman and Ginsburg. Kimball apparently assumed that in $TeCl_4$ the unshared pair occupies a pure *s* orbital. This assumption apparently is incorrect.

The Te–Cl distance, 2.33 Å., is but slightly less than 2.36 Å., which is the sum of the covalent radii.

(11) G. E. Kimball, *J. Chem. Phys.*, **8**, 194 (1940).

Summary

An electron diffraction study of gaseous $TeCl_4$ leads to the values 2.33 ± 0.02 Å. for the average Te–Cl distance, 3.37 ± 0.06 Å. for the only important Cl–Cl distance, and 93 ± 3° for the corresponding important bond angle. A distorted trigonal bipyramidal configuration with the unshared pair in one of the equatorial positions is compatible with these results and the known large dipole moment of the molecule. The equatorial bond angle is probably considerably less than 120°, but greater than 90°.

PASADENA, CALIFORNIA RECEIVED MARCH 18, 1940

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 769]

On the Molecular Structure of Sulfur Dioxide

BY VERNER SCHOMAKER AND D. P. STEVENSON

In the course of investigating the electron diffraction patterns of a number of simple molecules, we have obtained photographs of sulfur dioxide which are better than those previously obtained by Cross and Brockway,[1] in these Laboratories. Inasmuch as the interpretation of the new photographs leads to slightly different and probably more reliable values for the interatomic distances than those found by Cross and Brockway, we are reporting our results.

The apparatus and technique used in this investigation have been described by Brockway.[2] The camera distance was 10.85 cm. and the electron wave length 0.0611 Å. (a_0 = 4.070 Å. assumed for gold). The photographs showed seven rings of which six could be measured easily. The resulting *s* values $\left(s = \frac{4\pi}{\lambda}\sin\frac{\Theta}{2}\right)$ are given in Table I.

The radial distribution function,[3] curve A of the figure, was calculated according to the modified procedure recommended by Schomaker,[4] using the coefficients C_K given in Table I. The function has two peaks corresponding to an S–O distance of 1.435 Å., an O–O distance of 2.49 Å., and a bond angle of 121°.

TABLE I

Max.	Min.	C_K	s_0[a]	s_0[b]	s_c[c]	s_0/s_0[a]
	1	− 6	3.33	...	3.19	(0.958)[d]
1		10	5.54	5.63	5.48	(0.989)[d]
	2	−13	7.37	...	7.45	1.011
2		15	9.87	9.66	10.00	1.013
	3	−15	12.02	11.99	12.04	1.002
3		15	14.04	13.76	14.10	1.004
	4	−14	16.49	16.19	16.58	1.005
4		13	18.59	18.15	18.54	0.997
	5	−11	20.87		20.80	0.997
5		11	23.19		23.18	1.000
	6	− 7	25.33		25.13	0.992
6		6	27.50		27.58	1.003
					Average	1.002 ± 0.005

S–O = 1.002 × 1.43 = 1.433 ± 0.01 Å.

[a] This research.
[b] Cross and Brockway, ref. 1, S–O = 1.46 Å.
[c] From curve for model with ∠O–S–O = 120°.
[d] Omitted from average because of unreliability of measurement.

(1) P. C. Cross and L. O. Brockway, *J. Chem. Phys.*, **3**, 821 (1935).
(2) L. O. Brockway, *Rev. Mod. Phys.*, **8**, 231 (1936).
(3) L. Pauling and L. O. Brockway, THIS JOURNAL, **57**, 2684 (1935).
(4) V. Schomaker, A. C. S. Meeting, Baltimore, Md., April, 1939.

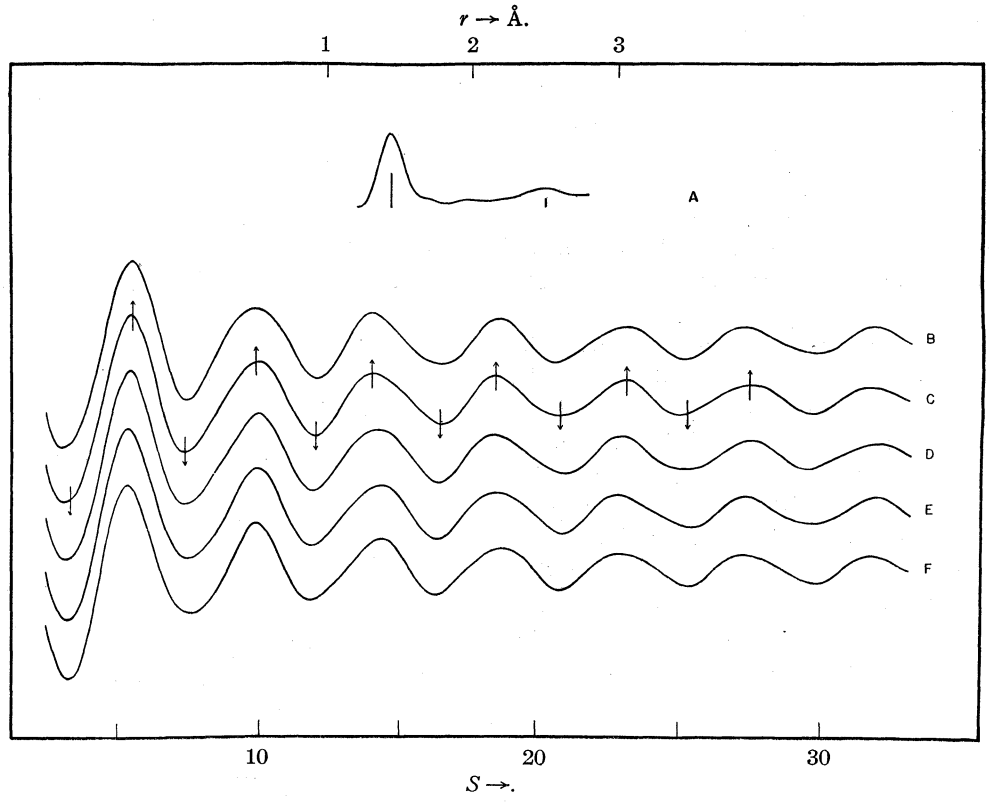


Fig. 1.—Theoretical intensity curves for sulfur dioxide: Curve A, radial distribution function; Curves B, C, D, E, F, simplified theoretical intensity curves with bond angles of 115, 120, 125, 130, 135°, respectively, and S–O = 1.43 Å. Observed s_0 values indicated by arrows.

Theoretical intensity curves, B–F of the figure, were calculated for five symmetrical models in which the bond angle was varied from 115 to 135°. It was found that the molecule could be regarded as rigid for the purposes of this investigation, and that the atomic numbers form satisfactory coefficients (Z_iZ_j) for the simplified intensity function. The curve for the 120° model (C) is the most satisfactory. Indeed, all of the other curves can be eliminated because of their appearance with respect to some or all of the following features: the width of the second maximum, the shape of the third maximum, the width and shape of the fourth maximum, and the width of the fifth maximum. Because the fifth, sixth and seventh rings of the photographs are quite faint, it is impossible to make any definite statements regarding the finer details of their appearance. The quantitative comparison of the observed and calculated s values is most consistent for the 120° model. This quantitative comparison for the 120° model is given in Table I and leads to the value 1.433 Å. for the S–O distance. The radial distribution function, and the qualitative and quantitative comparisons of the correlation method are thus in excellent agreement, giving for the S–O distance and the bond angle the values 1.433 ± 0.01 Å., and 120 ± 5°, respectively.

In previous electron diffraction investigations of sulfur dioxide Wierl,[5] whose pictures showed only one ring, found 1.37 Å. for the S–O distance, Cross and Brockway[1] found 1.46 ± 0.02 Å., and Pauling and Brockway,[3] interpreting the data of Cross and Brockway by the radial distribution method, found 1.43 Å.[6] for the S–O distance and 124 ± 15° for the bond angle. The observed s values of Cross and Brockway also are given in Table I. We feel that our s values, each of which is based on 20 to 30 measurements of a ring diameter, are the more reliable because our photographs (commercial ortho film) are much "cleaner" and show six more measurable features

(5) R. Wierl, *Physik. Z.*, **31**, 1028 (1930).

(6) The s value reported by Cross and Brockway for the first maximum of the sulfur dioxide photographs is too large, leading to a too small value for the interatomic distance. The discrepancy between the values (1.46 and 1.43) obtained from the same data by the two methods of interpretation arises largely because the first maximum was excluded from the average in the correlation procedure (C and B) but was given (excessively) great weight in the radial distribution function (P and B).

than the older photographs (X-ray film). (These differences are only typical, however, of the more or less gradual improvement which has occurred since 1933 in the electron diffraction technique employed in these Laboratories.) Moreover, it so happened that this investigation was undertaken concurrently with a very satisfactory series of check measurements on diatomic molecules[7] using the same technique and the same wave length calibrations.

There is some further information regarding the configuration of the sulfur dioxide molecule. Cross and Brockway[1] report the surprisingly consistent value 122 ± 5° as the bond angle obtained on fitting the three vibrational frequencies of the sulfur dioxide molecule to a two-constant, valence-force potential function. Much more important is the entropy determination of Giauque and Stephenson[8] which leads to the value (10.58 ± 0.99) × 10^{-116} g. cm.^{2} for the product of the three principal moments of inertia of the molecule. This value and our S–O distance give 121° as a fairly precise value for the bond angle, substantiating our electron diffraction determination. A variation of 0.1 cal. mol.$^{-1}$ deg.$^{-1}$ in the entropy (corresponding to the uncertainty in the product of the moments of inertia given above), or of 0.02 Å. in the bond distance, would produce a change of 4° in the value calculated for the bond angle. In the calculations leading to the results reported in this paragraph the current values[9] of N, h, and k were used. A correction of +0.2% was applied to our bond distance in order to compare it with the results of the entropy calculations based on the "new" constants. When the "old" values of the fundamental constants are used, the correlation of the entropy of sulfur dioxide with our bond distance leads to a bond angle value of 123°.

(7) Schomaker and Stevenson, to be published.

(8) W. F. Giauque and C. C. Stephenson, THIS JOURNAL, **60**, 1389 (1938).

Summary

The structure of sulfur dioxide has been reinvestigated by the electron diffraction method, with the following results: S–O = 1.43$_3$ ± 0.01 Å., and ∠ O–S–O = 120 ± 5°. This value for the bond angle is in excellent agreement with the value, 121 ± 5°, derived from the bond distance and the entropy.

(9) G. Herzberg, "Molecular Spectra. I," Prentice-Hall, New York, N. Y., 1939, p. 3.

PASADENA, CALIFORNIA RECEIVED MARCH 18, 1940

[CONTRIBUTION NO. 216 FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Aldehyde Complexes of Copper Salts

BY TENNEY L. DAVIS AND WALTER P. GREEN, JR.

As part of an investigation of the ability of compounds containing the carbonyl group to enter into coördinative combination, we have found that acetaldehyde and butyraldehyde combine with certain copper salts, and have prepared the compounds listed below and have determined their dissociation pressures at 0°.

TABLE I

DISSOCIATION PRESSURES AT 0° (MM. AT 20°)

$CuNCS \cdot CH_3CHO$	65.6
$3CuNCS \cdot 2C_3H_7CHO$	30.0
$2CuI \cdot CH_3CHO$	6.3
$3CuI \cdot C_3H_7CHO$	5.6
$Cu(OCOCH_3)_2 \cdot CH_3CHO$	89.9

For comparison with these dissociation pressures, we have determined the vapor pressure at 0° of pure acetaldehyde, 333.0 mm., and of pure butyraldehyde, 32.3 mm.

The formulas of the complexes show several interesting relationships. Cuprous thiocyanate combines (to form a complex which is fairly stable at 0°) with twice as many molecules of either aldehyde as cuprous iodide does. Two molecules of butyraldehyde are equivalent to three molecules of acetaldehyde in respect to the capacity of the aldehydes to combine with the cuprous salts.

When samples of the cuprous salts were exposed at 0° in closed vessels to atmospheres saturated with the vapors of the aldehydes, they absorbed the aldehydes rapidly in quantities much greater than correspond to the complexes listed above. Cuprous thiocyanate actually deliquesced in either aldehyde, and the crystals became covered with a layer of liquid. Cuprous iodide showed the same behavior with acetaldehyde, but

on exposure to butyraldehyde vapor it assumed a moist appearance but showed no distinct liquid phase after fifteen days. Different samples of the cuprous salts exposed to aldehyde vapors in the same vessel during the same interval of time absorbed different amounts of aldehyde, probably because of the formation of crusts. The results made it evident that pure complex compounds could not be produced conveniently by this procedure.

Cupric acetate absorbed acetaldehyde vapor more slowly than the cuprous salts; it remained dry in appearance but took on a deeper green color and absorbed about half a molecule of the aldehyde after five days.

Since the aldehydes attack mercury, the dissociation pressures could not be determined in an apparatus in which the vapors were allowed to come in contact with the mercury of a manometer. A torsion apparatus was used in which the pressure to be measured, within a spiral of very thin fused quartz tubing (without hysteresis), was balanced exactly by an external pressure measured with an ordinary manometer. The technique which had been used successfully in earlier researches[1] in this Laboratory, namely, that of adding to the dry salt an excess of the volatile component, pumping in the manometric apparatus, reading the equilibrium pressure, again pumping for a short time, again reading the equilibrium pressure, and so on until the equilibrium readings after successive pumpings were found to be the same, was satisfactory for determining the vapor pressures of the aldehydes but was found to be inapplicable to the complex compounds. The apparatus failed to come to equilibrium after standing for four or five days, evidently because dense, practically impervious crusts were formed which prevented the evaporation of the aldehyde from the interior of the mass.

The compositions of the complexes were determined by measurements of the weights of aldehyde retained by the dry salts. An excess of aldehyde was added to a weighed amount of the salt and the mixture was allowed to stand for several days at 0° in a closed container. The cuprous salts formed heavy, clay-like masses, while the complex of cupric acetate retained a granular texture. The materials were broken up and stirred over while the aldehyde evaporated freely at room temperature, until a complete change in the rate of evaporation of the aldehyde was noted, and dry, friable, meal-like masses were obtained. These were weighed, with the results indicated in Table II. The samples resulting from these experiments were used for the determinations of dissociation pressures. In the manometric apparatus they showed constant successive maximum equilibrium pressures after being successively pumped and allowed to stand. The pressures found in this way are reported in Table I.

TABLE II

COMPOSITION OF COMPLEX COMPOUNDS

Salt, g.	Aldehyde, g. Taken	Aldehyde, g. Retained	Molecular ratio aldehyde to salt	Complex compound
Cuprous thiocyanate and acetaldehyde				
4.3709	3.0755	1.5749	0.996	
3.4896	2.4832	1.2391	.981	CuNCS·
4.1038	3.3671	1.4235	.961 *i. e.* 1:1	CH_3CHO
Cuprous thiocyanate and butyraldehyde				
1.6179	1.3785	0.6586	0.690	
1.5700	1.3095	.6400	.689	
3.8064	3.5672	1.5476	.682	
3.9111	2.3847	1.5301	.662	
5.1654	7.9887	1.9969	.654	
3.9967	3.2817	1.5353	.649	3CuNCS·
3.5500	2.9417	1.3476	.641 *i. e.* 2:3	$2C_3H_7CHO$
Cuprous iodide and acetaldehyde				
5.4018	2.0247	0.6454	0.520	
4.9528	2.1453	.5810	.508	2CuI·
5.5608	1.9940	.6474	.504 *i. e.* 1:2	CH_3CHO
Cuprous iodide and butyraldehyde				
8.8736	2.5579	1.1691	0.348	
4.5774	3.0933	0.6010	.347	3CuI·
8.2229	1.9422	1.0243	.330 *i. e.* 1:3	C_3H_7CHO
Cupric acetate and acetaldehyde				
7.7980	3.8399	1.9353	1.022	
2.9960	1.3022	0.7170	0.986	$Cu(OCOCH_3)_2$·
6.1460	3.5703	1.4465	.972 *i. e.* 1:1	CH_3CHO

The aldehydes used in this work were purified from Eastman Kodak Co. "pure" materials. The acetaldehyde was treated with a small amount of 33% aq. sodium bisulfite solution for the removal of peroxides, allowed to stand six hours, and distilled through a Davis column; the upper fraction was dried with a mixture of sodium bicarbonate and anhydrous calcium sulfate, allowed to stand five hours, again distilled, and the middle fraction was taken. The butyraldehyde was distilled through a 3-foot (90-cm.) Podbielniak column to remove most of the acid and other high-boiling impurities; the middle fraction, b. p. 74.7–75.0°, was treated with sodium bisulfite for the removal of peroxides, washed with water, dried with anhydrous sodium and calcium sulfates, allowed to stand for two days at the temperature of dry-ice, and filtered clear from the impurities which had frozen out.

The vapor pressure of butyraldehyde at 0° has not been measured heretofore. The vapor pressure of acetaldehyde has been measured by de Leeuw[2] and by Emeleus,[3] whose data do not give straight lines on a semi-logarithmic chart,

(1) Davis and Batchelder, THIS JOURNAL, **52**, 4069 (1930); Davis and Ou, *ibid.*, **56**, 1061, 1064 (1934); Davis and Logan, *ibid.*, **58**, 2153 (1936).

(2) De Leeuw, *Z. physik Chem.*, **77**, 296 (1911).

(3) Emeleus, *J. Chem. Soc.*, 1735 (1929).

and by Gilmour,[4] who reported twenty-one values between +16.91° and −24.15°, and these values give a straight line on a semi-logarithmic chart which cuts the zero axis at a point corresponding to a value of 331.0 mm. for the vapor pressure of acetaldehyde at 0°. From Gilmour's data a writer in the "International Critical Tables"[5] has deduced a mathematical equation according to which we calculate the vapor pressure of acetaldehyde at 0° as 333.1 mm., in close agreement with our experimental value of 333.0 mm. Burton, Ricci and Davis[6] have recently reported the values 335.6 and 334.6 mm.

Summary

Complex compounds of cuprous thiocyanate and iodide with acetaldehyde and butyraldehyde, and of cupric acetate with acetaldehyde, have been prepared.

The dissociation pressures of the complexes at 0° and the vapor pressures of the pure aldehydes at 0° have been determined.

Cuprous thiocyanate at 0° forms a stable complex with twice as many molecules of aldehyde as does cuprous iodide.

Two molecules of butyraldehyde are equivalent to three molecules of acetaldehyde in respect to the capacity of the aldehyde to combine with cuprous salts.

CAMBRIDGE, MASS. RECEIVED MARCH 5, 1940

(4) Gilmour, *J. Soc. Chem. Ind.*, **41**, 293 (1922).
(5) *Int. Crit. Tables*, Vol. III, 1928, p. 215.
(6) Burton, Ricci and Davis, THIS JOURNAL, **62**, 265 (1940).

[CONTRIBUTION NO. 218 FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

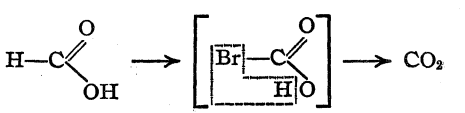
A New Reaction of Formic Acid

BY TENNEY L. DAVIS AND WALTER P. GREEN, JR.

If formic acid exists in the tautomeric form of dihydroxy divalent carbon, as has been suggested,[1] then it is possible that the reaction of formic acid with bromine might yield a certain amount of material produced from the tautomer, differing from any material which is likely to be produced from formic acid in its usual form. We find that the interaction of bromine and anhydrous formic acid produces a material (perhaps bromophosgene (carbonyl bromide) or, more probably, the hydrated form of bromophosgene, namely, dibromodihydroxy-methane) which reacts with aniline to form derivatives of urea, namely, carbanilide and brominated carbanilides, and conclude that the facts indicate with considerable probability that formic acid contains material of the formula $>C(OH)_2$.

The action of bromine on formic acid in dilute aqueous solution has been studied by Hammick, Hutchinson and Snell,[2] who concluded in 1925 that the reaction is of the second order and is essentially a reaction between bromine molecules and formate ions. They found that the influence of various reagents on the reaction is explained satisfactorily by a consideration of their effects upon the concentrations of the reacting molecules in accordance with the law of mass action. Jozefowicz[3] confirmed their results in 1929. Hell and Mühlhauser,[4] much earlier, in 1878, had studied the apparent catalytic effect of carbon disulfide on the rate of reaction of bromine with strong, but not anhydrous, formic acid. They postulated an intermediate compound but did not isolate it or assign any formula to it. In all these cases carbon dioxide was the product of the reaction, and the net result was as if the formic acid had been oxidized to carbonic acid.

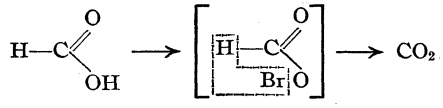
Formic acid in its usual structure may perhaps brominate by a mechanism which involves the primary substitution of either of its hydrogen atoms. If the hydrogen attached to the carbon is replaced by bromine, then the resulting intermediate compound will contain bromine and hydroxyl attached to the same carbon atom; and this is an arrangement which commonly splits off hydrogen bromide spontaneously: carbon dioxide will result.



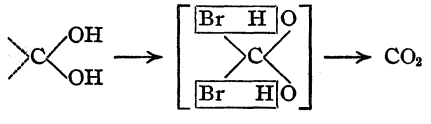
If, on the other hand, the hydrogen of the hydroxyl group is replaced by bromine, then an intermediate hypobromite will result which would

(1) Baly, Heilbron and Hudson, *J. Chem. Soc.*, **121**, 1080 (1922); Edith H. Ingold (Usherwood), *ibid.*, **125**, 1530 (1924); Scheibler, *Z. angew. Chem.*, **40**, 1072 (1927).
(2) Hammick, Hutchinson and Snell, *J. Chem. Soc.*, **127**, 2715 (1925).
(3) Jozefowicz, *Roczniki Chem.*, **9**, 309 (1929).
(4) Hell and Mühlhauser, *Ber.*, **11**, 241 (1878).

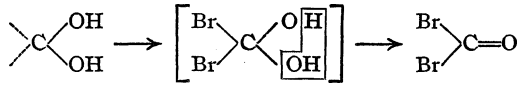
be expected to break up in the same manner that ethyl hypobromite breaks up, by the loss of hydrogen bromide from the bromine of the hypobromite group and the hydrogen attached to the same carbon atom: and again carbon dioxide will result.



The mechanism of the action of bromine on the tautomer of formic acid may perhaps involve first the addition of bromine to the two free valences, in the same way that bromine adds to carbon monoxide. The resulting intermediate dibromo-dihydroxy-methane may behave in three ways. (1) It contains bromine and hydroxyl on the same carbon atom, and would be expected to lose hydrogen bromide with the formation of carbon dioxide. This seems the most likely mode of its behavior, and the previously known comportment of formic acid with bromine may indeed occur through the intermediacy of this compound; and the formula of the tautomer explains the facts as conveniently as the more usual formula.



(2) There is however some chance, though a slight one, that this intermediate containing two hydroxyl groups on the same carbon atom, may lose the elements of water to form bromophosgene.



Since the other mode of decomposition seems more probable, and since bromophosgene is known to react readily with water, it is unlikely that more than traces of bromophosgene would be formed by the splitting out of water from a considerable amount of the intermediate. Bromophosgene reacts with aniline to form carbanilide; and a trace of bromophosgene indicates the probable presence in the original formic acid of at least some of the tautomer. (3) The intermediate itself would react with aniline to form carbanilide. There is also the possibility that the intermediate may not decompose at all to yield bromophosgene, but that while decomposing into hydrogen bromide and carbon dioxide, it may actually exist for a time in the presence of an excess of bromine with which it is probably in equilibrium.

When bromine and anhydrous formic acid were allowed to stand together at room temperature, and the mixture, still containing free bromine, was treated at room temperature or below[5] with an excess of aniline, a small quantity of carbanilide and of brominated carbanilide was formed. When a similar mixture was allowed to stand until the color of the bromine had disappeared, and was then worked up in the same way, no detectable carbanilide or brominated derivative of it was found. The substance from which the carbanilide was produced was therefore probably not bromophosgene but rather dibromo-dihydroxy-methane formed by the addition of bromine to the tautomeric form of formic acid.

Experiments

Anhydrous formic acid, m. p. 8.20°, was prepared by distillation with boric anhydride according to the method of Schlesinger and Martin,[6] who reported the melting point 8.26°.

6.9 Grams of bromine and 17.9 g. of anhydrous formic acid were allowed to stand together for thirteen days in a test-tube closed with a loosely fitting glass stopper. The mixture, which still consisted of two phases, was then frozen in dry-ice; 40.5 g. of purified and freshly distilled aniline was frozen in another tube; both tubes were allowed to warm somewhat, and the materials, partly frozen, were mixed with stirring and cooling. The temperature did not rise at any time above that of the room. The material was treated with aqueous sodium hydroxide in excess, and steam distilled for the removal of the aniline and of as much of the brominated aniline as possible. During the last part of the distillation a precipitate appeared in the flask. Precipitate and solution were extracted with ether, and the residue from the evaporation of the ether was recrystallized from alcohol, white crystals melting at 257–258° with some sintering at 230° (copper block). When this material was sublimed in the molecular still[7] it left about one-third of its mass behind in the form of tar. The sublimate, recrystallized from alcohol, yielded 0.0641 g. of material which melted at 260–265° dec., after another vacuum sublimation m. p. 278–281° dec., after another recrystallization from alcohol m. p. 279–281° dec., and further recrystallization did not raise the melting point. 2,4,2′,4′-tetrabromocarbanilide is reported[8] to melt at 281° dec. when heated rapidly. The purified product, now very small in amount, was heated with alcoholic ammonia in a sealed tube for twenty hours at 160°. The liquid on evaporation gave a tarry residue, the aqueous extract of

(5) The production of formanilide by the interaction of formic acid and aniline *in the cold* seems extremely unlikely, and hence unlikely the hypothesis that the carbanilide is formed from phenylisocyanate resulting from the action of bromine on formanilide.

(6) Schlesinger and Martin, THIS JOURNAL, **36**, 1589 (1914).

(7) Morton, Mahoney and Richardson, *Ind. Eng. Chem., Anal. Ed.*, **11**, 460 (1939), Fig. 2.

(8) Chattaway and Orton, *Ber.*, **34**, 1080 (1901).

which, acidified with hydrochloric acid, gave with xanthydrol solution a white precipitate insoluble in alcohol, evidently dixanthylurea.

Another experiment with 5.7 g. of bromine and 7.9 g. of anhydrous formic acid, twenty-four days of standing, 25.7 g. of aniline, etc., yielded 0.4 g. of material. This was extracted with cold concd. hydrochloric acid in an effort to remove the last portions of brominated aniline, then with alcohol and the residue from the evaporation of the alcohol was sublimed in the molecular still. The several fractions of the sublimate, recrystallized from alcohol, appeared to consist of mixtures of 4,4'-dibromo- and 2,2',4,4'-tetrabromocarbanilide. They were brought together and heated with alcoholic ammonia for five hours at 140–150°. The residue from the evaporation of the alcohol was extracted with water, and the aqueous solution, acidified with hydrochloric acid, gave with xanthydrol a white precipitate, insoluble in alcohol, m. p. 260° dec., showing the same behavior alone and in mixed melting point as a known sample of dixanthylurea prepared according to the directions of Werner and Fearon.[9]

Twelve grams of bromine and 30.7 g. of anhydrous formic acid were allowed to stand together for two days. The mixture, bromine being at the bottom, was allowed to run slowly from a dropping funnel into a solution of 108.3 g. of aniline in 300 cc. of benzene which was stirred vigorously with a mechanical stirrer. There was no considerable heating. A large amount of white precipitate appeared but this did not impede the stirring. The mixture, made alkaline, steam distilled, extracted with ether, etc., as described, yielded 0.2644 g. of crude product. Calculated as pure carbanilide this corresponds to 1.73% of the bromine. Fractional sublimation in vacuum and fractional crystallization yielded one fraction which consisted of impure carbanilide and another which consisted largely of brominated carbanilides. The first of these, recrystallized several times from alcohol, from dilute alcohol, and from water, and twice micro-recrystallized from alcohol, yielded carbanilide, m. p. 233.5–234.0°, identified by mixed m. p. 234.0–234.5° with a known sample, m. p. 234.5–235.0°. The other principal fraction was refluxed gently for forty-five minutes with 2 cc. of aniline in order that the brominated carbanilides by a "urea dearrangement" might be converted into carbanilide. The excess aniline was driven off by steam distillation, and the residue, dissolved out by ether, weighed 0.0341 g. In the molecular still it yielded 0.0199 g. of sublimate, light brown in color, and 0.0074 g. of residual tar. The sublimate, which evidently contained some brominated aniline, after several recrystallizations yielded carbanilide, m. p. 234.0–234.5°, mixed m. p. 234.5–235.0°, known m. p. 234.5–235.0°.

(9) Werner and Fearon, *J. Chem. Soc.*, **117**, 1360 (1920).

Summary

Bromine reacts with formic acid to produce a substance which, in the presence of an excess of bromine, reacts with aniline to form derivatives of urea, namely, carbanilide and brominated carbanilides.

The intermediate substance, evidently capable of existence only in the presence of free bromine, is probably dibromo-dihydroxy-methane formed by the addition of bromine to dihydroxy divalent carbon, the tautomeric form of formic acid.

CAMBRIDGE, MASS. RECEIVED FEBRUARY 10, 1940

[CONTRIBUTION NO. 219 FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY]

Metal Pyridine Complex Salts. VI. Cobaltous and Nickelous Dipyridine Salts of Fatty Acids

BY TENNEY L. DAVIS AND ALBERT V. LOGAN

In the preceding paper of this series[1] experiments were reported which showed that the pyridine in the pyridine complex cupric, cobaltous and nickelous cyanates is held by greater forces of affinity than the pyridine in the corresponding complex thiocyanates. The greater forces of chemical affinity are evident both from the lower dissociation pressures of the complex cyanates and from the greater shrinkages which occur when the complex cyanates, as compared with the complex thiocyanates, are formed from their component salts and pyridine. The thiocyanate radical to a greater extent than the cyanate radical exhausts the total affinity of the metal atom and leaves less of it available for coördinative combination with pyridine. The effect is due solely to the difference between a sulfur and an oxygen atom at the far end of the acid radical which is attached to the metal by an electrovalent linkage.

In the present paper we wish to report experiments on the dipyridine cobaltous and nickelous salts of acetic, propionic, butyric, isobutyric and valeric acids. We have determined their dissociation pressures over the temperature interval between 15–20° and 85–90° and the volume changes which occur at 25° when the complexes are formed by the combination of their compo-

(1) Davis and Logan, THIS JOURNAL, **58**, 2153 (1936).

TABLE I

DISSOCIATION PRESSURES, EXPERIMENTAL VALUES (MM. AT 20°)

Cobaltous Dipyridine								
Acetate	41.0°	48.0°	60.5°	71.0°				
	3.7	6.5	14.0	24.0				
Propionate	30.0°	45.0°	55.0°	65.0°	70.0°	80.0°		
	4.0	9.7	17.0	32.0	44.0	82.0		
Butyrate	30.0°	43.6°	54.0°	60.0°	70.0°	80.0°		
	3.0	7.0	14.5	20.0	38.5	76.0		
Isobutyrate	26.2°	43.0°	51.0°	60.0°	71.0°			
	2.9	8.0	13.0	21.2	41.5			
Valerate	40.0°	50.0°	60.0°	70.0°				
	10.0	18.0	35.2	75.0				
Nickelous Dipyridine								
Acetate	28.0°	40.0°	60.0°	70.0°	80.0°			
	1.0	1.5	3.0	7.4	16.5			
Propionate	30.0°	43.0°	48.0°	55.0°	60.0°	70.0°	80.0°	88.0°
	2.0	3.0	3.5	4.5	5.0	11.0	24.0	46.0
Butyrate	35.0°	45.0°	51.0°	60.0°	64.0°	70.0°	72.0°	80.0°
	1.8	2.5	3.0	4.0	5.0	8.0	10.0	18.0
Isobutyrate	18.0°	34.0°	50.0°	60.0°	70.0°	80.0°		
	1.2	1.9	3.2	4.5	9.5	19.5		
Valerate	15.0°	41.0°	50.0°	60.0°	70.0°	80.0°		
	2.7	5.6	7.0	9.0	21.0	44.0		

nent salts with pyridine. The results show the effect, upon the residual affinity of the metal atoms, of additional —CH_2— groups successively introduced into the acid radical.

Experimental Procedure

The dissociation pressures of the complexes were determined in the same way as in the earlier experiments of this series.[2]

Preparation of Compounds.—Cobaltous or nickelous carbonate was refluxed for several hours with the pure fatty acid, a small quantity of water was added, the solution was filtered and evaporated to dryness, and the crystalline residue was powdered and dried in vacuum over caustic potash for the removal of moisture and excess acid. When analysis showed that the material was the pure anhydrous salt, it was taken for the preparation of the complex.

The dry salts were converted into the complexes by treating them with chloroform and adding pyridine until everything went into solution. The lower members of the series of complex salts were found to be much less soluble in chloroform than the higher members, and a considerable excess of pyridine was found to be necessary to make them dissolve. The filtered solutions were allowed to evaporate in the hood, and the resulting crystals, dried between filter papers, were placed in a desiccator over caustic potash. The complex acetates and propionates were allowed to come to equilibrium with pyridine in an open vessel in the desiccator. When the same procedure was tried with the complex butyrates, isobutyrates and valerates, the crystals deliquesced and became wet with pyridine. The crystals of these complexes therefore were allowed to come to equilibrium, over caustic potash, with the pyridine which still adhered to their surfaces after they had been pressed between filter papers.

Cobalt was determined as sulfate, nickel as sulfate and sometimes by titration with potassium cyanide, and pyridine by the method of A. C. Houghton,[3] which we have used in earlier work and have found to be accurate to about 1%.

The five nickelous dipyridine complex salts consisted of bright greenish blue crystals. Cobaltous dipyridine acetate consisted of rose pink crystals, the propionate, butyrate and isobutyrate were more deeply colored, and the valerate crystallized in ruby red prisms.

Density Determinations.—The densities of the cobaltous and nickelous salts were determined by weighing in specific gravity bottles with dry benzene at 25°. Since it was expected that organic liquids would dissolve pyridine from the complexes, the densities of the latter were determined by using saturated solutions of the complexes in pyridine for the pycnometer liquids. The large effect of temperature on the solubility of the complex butyrates, isobutyrates and valerates in pyridine is probably the principal source of error in the determinations.

Experimental Results

The experimental data for the dissociation pressures, corrected for the expansion of mercury from 20°, are summarized in Table I. If these data are plotted on a semi-logarithmic chart, along with the data for the vapor pressure of pyridine (from our earlier experiments), they give good straight lines for the cobaltous complexes, lines which approach slowly at the higher tem-

(2) Davis and Batchelder, THIS JOURNAL, 52, 4069 (1930).

(3) A. C. Houghton, *Ind. Eng. Chem.*, 1, 698 (1909).

TABLE II

DISSOCIATION PRESSURES AT 25° (MM. AT 20°)

Di-pyridine	Acetate	Pro-pionate	Buty-rate	Iso-butyrate	Valer-ate
Cobaltous	1.5	3.0	2.3	2.7	3.7
Nickelous	0.9	1.7	1.3	1.5	3.6

peratures toward the straight line which represents the vapor pressure of pyridine. The data for the nickelous complexes yield straight lines which bend in the neighborhood of 60° and resume their straightness with a different slope, lines which approach the pyridine line both at the higher and at the lower temperatures. The dissociation pressures at 25°, estimated from the graphs, are shown in Table II.

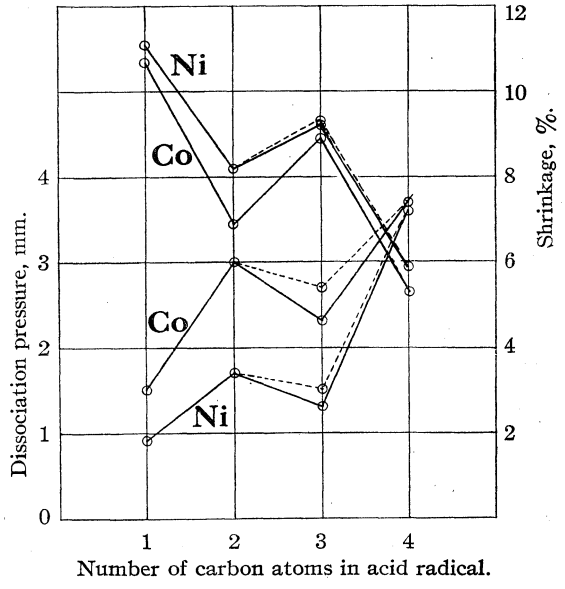


Fig. 1.—Dissociation pressures at 25° (lower), and shrinkages (upper) which occur at 25° during the formation of the complexes of cobaltous and nickelous dipyridine salts of fatty acids. (Dotted lines indicate isobutyrates.)

The results of analyses and of density determinations are summarized in Table III. In two cases the analytical figures represent single determinations; in all others they are averages of two check values.

The values reported for the densities are averages of two or of three determinations, and the "error" is the mean deviation from the average. From the densities and from our earlier data on the density of pyridine,[1] the molecular volumes were calculated and the contractions which occur when the simple salts combine with pyridine at 25° to form the dipyridine complexes were inferred. The decreases of volume per mole of complex are indicated in the last two columns of Table III.

Discussion of Results

From the positions of the dissociation pressure lines on a semilogarithmic chart (not reproduced), it is possible to conclude that, within the temperature range in which we have worked, the cobaltous dipyridine salts of the fatty acids are less stable at the higher temperatures. The nickelous compounds have a point of maximum stability in the neighborhood of 60°, and tend to decompose when they are warmed or cooled from that temperature. All of the nickelous and zinc pyridine complex salts which we have studied earlier have the remarkable property that they tend to decompose at low temperatures.

The greater forces of affinity which produce the greater decreases of volume during the formation of the complexes also result in the pyridine being more strongly bound to the metal and produce the lower dissociation pressures. The relationship is exhibited in the chart, Fig. 1, where the dissociation pressures at 25° and the volume–

TABLE III

ANALYSES, DENSITY DETERMINATIONS AND SHRINKAGES WHICH OCCUR AT 25° DURING THE FORMATION OF THE COMPLEXES

	Simple salt				Dipyridine complex					
	Metal, %		Density at 25°		Metal, %		Pyridine, %		Density at 25°		Volume decrease	
Cobaltous	Found	Calcd.	Average	Error	Found	Calcd.	Found	Calcd.	Average	Error	cc.	%
Acetate	33.17	33.31	1.7755	0.0005	17.45	17.59	46.61	47.17	1.4286	0.0003	28.0	10.7
Propionate	28.41	28.77	1.5475	.0003	16.21	16.24	43.41	43.54	1.3260	.0010	20.4	6.9
Butyrate	25.45	25.30	1.4011	.0012	15.26	15.08	40.11	40.21	1.3093	.0002	29.3	8.9
Isobutyrate	25.33	25.30	1.3509	.0007	15.25	15.08	40.09	40.21	1.2837	.0023	29.6	8.9
Valerate	22.63	22.58	1.3267	.0017	14.25	14.02	37.20	37.71	1.2342	.0050	18.9	5.3
Nickelous												
Acetate	33.24	33.22	1.7983	0.0004	17.34	17.53	46.88	47.21	1.4478	0.0025	28.8	11.1
Propionate	28.43	28.69	1.6163	.0003	16.23	16.18	43.44	43.56	1.3696	.0034	23.6	8.2
Butyrate	25.07	25.22	1.4476	.0006	15.01	15.02	40.30	40.44	1.3093	.0002	29.8	9.2
Isobutyrate	25.38	25.22	1.3617	.0000	14.89	15.02	40.33	40.44	1.2837	.0023	30.9	9.3
Valerate	22.49	22.51	1.3404	.0005	...	...	37.40	37.74	1.2499	.0009	21.3	5.9

decreases during formation at 25° are plotted as functions of the number of the carbon atoms in the acid radicals. Both curves show the sawtooth pattern which is a characteristic representation of many of the properties of fatty acids.

The acid radicals which contain two and four carbon atoms use less of the total affinity of the metals than do the acid radicals which contain three and five carbon atoms, and the corresponding complexes hold their pyridine more firmly, having lower dissociation pressures, their formation being accompanied by greater shrinkages.

Except for the effect of odd and even numbers of carbon atoms, the general effect of increasing the number of carbon atoms in the acid radical appears to be to reduce the residual affinities of the metal atoms and to leave less available for combination with pyridine.

The effect of a fork in the carbon chain is small.

The nickel atom has greater chemical forces available for coördinative combination with pyridine at 25° than has the cobalt atom, for the nickelous complex salts are formed with greater volume decreases, and have lower dissociation pressures, than the cobaltous compounds.

Summary

The dissociation pressures of cobaltous and nickelous dipyridine acetate, propionate, butyrate, isobutyrate, and valerate have been determined over the temperature range from 15–20° to 85–90°.

The densities at 25° of the complexes and of their component salts have been determined, and the volume changes which occur at 25° during the combination of the simple salts with pyridine have been calculated. The complexes of which the formation is accompanied by the greater shrinkages have the lower dissociation pressures.

The effect of groups upon the residual affinities of the metal atoms is discussed.

CAMBRIDGE, MASS. RECEIVED MARCH 5, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE CITY COLLEGE, THE COLLEGE OF THE CITY OF NEW YORK]

Alkanolamines. IX. Reducing and Hydrolyzing Action of the Ethanolamines on the Dichloronitrobenzenes

BY CHESTER B. KREMER AND AARON BENDICH

In a preceding article of this series,[1] an account was given of the reactions occurring between the isomeric dichloronitrobenzenes and monoethanolamine as carried out in neutral solvents. When these reactions are carried out in the absence of neutral solvents, the course followed is quite different, the condensing ability of the amino alcohol is considerably decreased and there is substituted the tendency toward reduction, hydrolysis and the formation of addition compounds. The finding of a combination of these tendencies, together with condensation, in a single run, is not infrequent. Insofar as the reductions involved, not only are the starting materials reduced to various stages, but there is also noted the reduction of an expected end-product. Under certain circumstances, it is found that when a dichloronitrobenzene is treated with monoethanolamine in the presence of anhydrous sodium carbonate, there can be isolated from the reaction mixture: (1) the condensation product, (2) a reduced product of the dichloronitrobenzene, either the azo or amino derivative, (3) the reduced condensation product, (4) an hydrolysis product of the dichloronitrobenzene, and in some cases (5) addition compounds of the type $x C_6H_3NO_2Cl_2 \cdot y NH_2CH_2CH_2OH$ where x and y are usually 1 or 2.

In order to make this survey more complete, the action of diethanolamine and triethanolamine upon the isomeric dichloronitrobenzenes was also studied. The ability of these ethanolamines to reduce, hydrolyze and form addition products with the isomers is, in most cases, greater than that of monoethanolamine. While condensations are possible in the case of diethanolamine, there was no instance of such reaction during the course of this work. Condensations involving this amino alcohol do occur when the reaction takes place in a neutral solvent; but even here the tendency is not great.

The fact that good yields of amino products can be obtained in these reactions is of interest since mononitro compounds are not generally re-

(1) Kremer and Bendich, THIS JOURNAL, 61, 2658 (1939).

duced to this stage in alkaline media. In this research, the reductions yielded only azo or amino compounds as final products, usually a mixture of the two. In only one or two instances was there any indication of the azoxy state and in no case were hydrazo compounds indicated.

Of the possible azo compounds derived by reduction of the dichloronitrobenzenes, only the 2,2′,5,5′-tetrachloroazobenzene is reported in the literature. This article reports the formation of two others, namely, 3,3′,4,4′-tetrachloroazobenzene and 3,3′,5,5′-tetrachloroazobenzene. It was not possible to isolate the azo compounds of the other isomers, tars being the main products in these cases. The presence of the azoxy state was suspected in several instances, but no satisfactory isolation was effected. The azo compounds obtained were orange solids, recrystallizable from benzene or petroleum ether–benzene mixtures.

Experimental

The isomeric dichloronitrobenzenes were prepared as previously described.[1] The ethanolamines were obtained from the Union Carbide and Carbon Corporation.

The experimental procedure followed in the major portion of this work can be summarized as follows. The apparatus used was a three-necked, round-bottom flask equipped with mechanical stirrer, reflux condenser and dropping funnel. The dichloronitrobenzene was introduced into the flask, along with any added alkali, and the whole gently warmed until the dichloronitrobenzene was melted. The ethanolamine was then added dropwise and the mixture refluxed for several hours. After refluxing, the reaction mixture was steam distilled until the distillate was clear. The latter was then freed of any solid or oil materials and extracted with ethyl ether and the ether extracts dried over anhydrous magnesium sulfate. The aqueous layers were made acid with hydrochloric acid and extracted with ethyl ether and these extracts were likewise dried.

The residue in the steam distillation flask was filtered from any resulting solid and alkaline and acid ether extracts made of the filtrate following the procedure described above.

The various extracts and residues were then systematically investigated and the results are summarized in Table I. All reactants are expressed in molar ratios although the actual amounts involved were usually fractions of those indicated.

Preparation of Azo Compounds. 3,3′,5,5′-Tetrachloroazobenzene.—In one run, monoethanolamine, 2,5-dichloronitrobenzene and anhydrous sodium carbonate in molar ratios were refluxed for approximately four hours. The reaction mixture was then subjected to steam distillation. 3,5-Dichloroaniline was detected in the steam distillate in a yield of about 20%. There remained in the distillation flask a very dark red solid which was filtered off. This was washed twice with hot alcohol and then recrystallized from benzene. The resulting product was orange in color and melted at 158.5° (cor.). Calculated % N for 3,3′,5,5′-tetrachloroazobenzene, 8.76; % N found, 8.88. The product was further identified by reduction with tin and hydrochloric acid. This yielded a white crystalline substance giving a primary amine test and melting at 51° (the melting point of 3,5-dichloroaniline). A mixed melt-

TABLE I

	Reactants: ratio of 1 mol 2,5-dichloronitrobenzene with	Hours refluxed	Products isolated	Yields, %
1.	2 mols M. E. A.[b]	4	4-Chloro-2-nitrophenol	1
	0.5 mol Na_2CO_3 (anhyd.)		2-(4-Chloro-2-nitro-anilino)-ethanol	85
			2-(4-Chloro-2-amino-anilino)-ethanol	2
			2,5-Dichloroaniline	5
2.	Same as in "1"	16	4-Chloro-2-nitrophenol	2
			2-(4-Chloro-2-nitro-anilino)-ethanol	65
			2-(4-Chloro-2-amino-anilino)-ethanol	2
			2,5-Dichloroaniline	15
3.	1.5 mols M. E. A.	20	4-Chloro-2-nitrophenol	5
	0.25 mols Na_2CO_3 (anhyd.)		2-(4-Chloro-2-nitro-anilino)-ethanol	10
			2,2′,5,5′-Tetrachloro-azobenzene	5
			2,5-Dichloroaniline	10
4.	2 mols M. E. A.	12	2-(4-Chloro-2-nitro-anilino)-ethanol	65
	2 mols $NaC_2H_3O_2$		2,5-Dichloroaniline	10
5.	1 mol T. E. A.[c]	5	4-Chloro-2-nitrophenol	30
	1 mol Na_2CO_3 (anhyd.)		2,5-Dichloroaniline	5
6.	1 mol D. E. A.[d]	5	4-Chloro-2-nitrophenol	20
	1 mol Na_2CO_3 (anhyd.)		2,5-Dichloroaniline	5
7.	1 mol M. E. A.	4	2-(4-Chloro-2-nitro-anilino)-ethanol	10
8.	1 mol D. E. A.	4	2,5-Dichloroaniline	20
9.	1 mol T. E. A.	4	2,5-Dichloroaniline	35
	Ratio of 1 mol 3,4-dichloronitrobenzene with			
1.	1 mol M. E. A.	4	2-(2-Chloro-4-nitro-anilino)-ethanol[a]	90
	1 mol Na_2CO_3 (anhyd.)			
2.	1 mol D. E. A.	4	2-Chloro-4-nitrophenol	1
	1 mol Na_2CO_3 (anhyd.)		3,4-Dichloroaniline	3
3.	1 mol T. E. A.	4	2-Chloro-4-nitrophenol	10
	1 mol Na_2CO_3 (anhyd.)		3,4-Dichloroaniline	7
4.	2 mols M. E. A.	4	2-(2-Chloro-4-nitro-anilino)-ethanol[a]	90
5.	2 mols D. E. A.	2	3,3′,4,4′-Tetrachloro-azobenzene	70
6.	2 mols D. E. A.	4	2-Chloro-4-nitrophenol	5
			3,4-Dichloroaniline	5
7.	2 mols T. E. A.	2	3,3′,4,4′-Tetrachloro-azobenzene	40
			3,4-Dichloroaniline	10
	Ratio of 1 mol 2,4-dichloronitrobenzene with			
1.	2 mols M. E. A.	2	Mainly tar formation	
2.	2 mols D. E. A.	2	2,4-Dichloroaniline	1
			Tar formation	
	Ratio of 1 mol 3,5-dichloronitrobenzene with			
1.	1 mol M. E. A.	4	3,3′,5,5′-Tetrachloro-azobenzene	60
	1 mol Na_2CO_3 (anhyd.)		3,5-Dichloroaniline	20
2.	2 mols D. E. A.	4	3,3′,5,5′-Tetrachloro-azobenzene	40

[a] Previously reported as 2-(6-chloro-4-nitroanilino)-ethanol. [b] Abbreviation for monoethanolamine. [c] Abbreviation for triethanolamine. [d] Abbreviation for diethanolamine.

ing point with a known sample of 3,5-dichloroaniline showed no deviation.

In another run, diethanolamine was employed without added alkali. No attempt was made here to identify other products than azo which was present in about 40% yield.

Preparation of 3,3′,4,4′-Tetrachloroazobenzene.—The 3,4-dichloronitrobenzene was, in most cases, refluxed with either di- or triethanolamine. The experimental procedure was the same as described above. The amount of 3,4-dichloroaniline recovered was small, usually under 10%. The azo product was recrystallized from a petroleum ether–benzene mixture giving a light orange product melting at 195.5° (cor.). Analyses indicated a persistent impurity, difficult to remove through successive recrystallizations: calculated % N for 3,3′,4,4′-tetrachloroazobenzene, 8.76; N found, 9.15, 9.07. Further identification was furnished by reducing the product with tin and hydrochloric acid. A white product giving a primary amine test and melting at 71° was obtained. A mixed melting point with a known sample of 3,4-dichloroaniline was unchanged.

Discussion

That reduction of the dichloronitrobenzenes occurs in definite stages is clearly borne out by some of the experiments. The one involving the action of diethanolamine on 3,4-dichloronitrobenzene is representative. When the two are refluxed together for a period of two hours, the only reduction product isolated is the azo compound; if heating is continued for four hours, no tetrachloroazobenzene can be identified, but reduction to the amino state is found to have taken place.

In previous work,[1] it was established that the 2,4-, 3,4- and 2,5-dichloronitrobenzenes were the most reactive of the isomers insofar as condensation reactions were concerned, while the 2,3- and 2,6- were much less reactive. When we examine the reducing tendency of the ethanolamines upon the various isomers, this general division still holds. The latter two compounds were much given to tar formation, from which tars little of interest could be extracted. For this reason most of the reported work dealt with the reactions of the 2,5-, 3,4- and 3,5-isomers, the 2,5- especially having been studied at length.

Hydrolysis of one of the chloro groups of 2,5- and 3,4-dichloronitrobenzenes was found to occur in certain of the reactions. That the chloro groups of these compounds are more active than the corresponding chloro groups of the other isomers already has been amply demonstrated.

Summary

1. Reduction to the amino and azo condition is found to occur when the isomeric dichloronitrobenzenes are reacted upon by the ethanolamines in the absence of a neutral solvent.

2. Condensation, hydrolysis and addition reactions are also found to occur.

3. Two new azo compounds, 3,3′,4,4′- and 3,3′,5,5′-tetrachloroazobenzene, are reported.

NEW YORK, N. Y. RECEIVED MARCH 16, 1940

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Ketene Acetals. V. The Reaction of Ketene Diethylacetal with Various Compounds Containing an Active Hydrogen[1]

BY HARRY M. BARNES,[2] D. KUNDIGER AND S. M. MCELVAIN

In the fourth paper[3] of this series the unusual hetero-enoid system that is present in ketene diethylacetal was discussed, particularly as it affected the polymerization of the compound. It was to be expected that the reaction of a compound having such a strong nucleophilic center as does ketene acetal with other substances containing an active hydrogen would be of considerable interest. The present paper is a report of the results obtained from a study of the reactions of a variety of compounds, in which hydrogen is found attached to halogen, oxygen, carbon and nitrogen, with ketene acetal.

At the time that the preparation of ketene acetal was first reported,[4] the vigorous reaction of both water and ethyl alcohol with it was noted. These reactions produce ethyl acetate and ethyl orthoacetate, respectively. The formation of the former compound probably, and the latter obviously, involves addition across the carbon to carbon double bond of ketene acetal, thus

$$CH_2{=}C(OEt)_2 + HOEt \longrightarrow CH_3C(OEt)_3$$

Secondary alcohols (*i*-propyl and *s*-butyl) react similarly, but *t*-butyl alcohol does not appear to

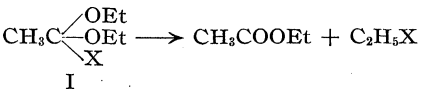
(1) This work was supported in part by grants from the Wisconsin Alumni Research Foundation.

(2) Wisconsin Alumni Research Foundation Scholar, 1935–1936.

(3) Johnson, Barnes and McElvain, THIS JOURNAL, **62**, 964 (1940).

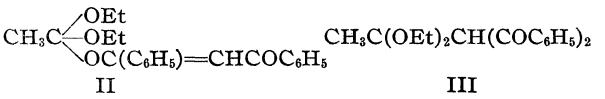
(4) Beyerstedt and McElvain, *ibid.*, **58**, 529 (1936).

react even after several hours of refluxing with the acetal. In a similar manner the halogen acids, carboxylic acids and phenol appear to add to ketene acetal. The reaction takes place at room temperature with the liberation of considerable heat. The addition product (I), however, is



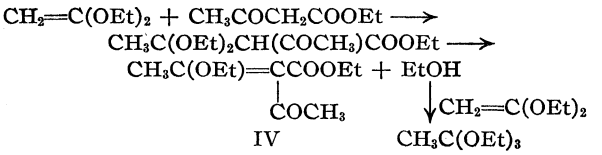
unstable and decomposes into ethyl acetate and C_2H_5X(X is —Br, RCOO—, or C_6H_5O—). In the case of the phenol reaction a small amount of I decomposes into phenyl acetate and ether.

In contrast to the behavior of phenol, the highly enolic dibenzoylmethane gives a stable addition product, (O-(α,α-diethoxyethyl)-dibenzoylmethane, (II) with ketene acetal. Reaction occurs at



25° and is practically quantitative. The reaction product melts at 87° (m. p. of dibenzoylmethane, 78°) and was shown to have the structure II by the fact that it reacted to only a small extent (16%) with a standard ethereal solution of sodium triphenylmethyl. The enolizable alternative addition product III, which would result from the addition of the dibenzoylmethane as H and CH(COC_6H_5)$_2$ to ketene acetal, would be expected to react quantitatively with this reagent as does dibenzoylmethane. When the product II is heated at 140° it decomposes into its components, dibenzoylmethane and ketene acetal. This is the same type of decomposition of an ortho-ester into a ketene acetal as that reported by Staudinger and Rathsam.[5] Indeed, II slowly decomposes at room temperature; a sample after standing in a vacuum desiccator over calcium chloride for three months was found to have reverted entirely into dibenzoylmethane.

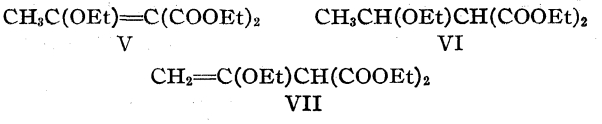
Acetoacetic ester, which contains a relatively small amount (7%) of the enolic form, shows an entirely different behavior with ketene acetal. While each of the reactants described above reacts with the acetal in the molecular ratio of 1:1, each mole of acetoacetic ester that reacts consumes two moles of the acetal. No apparent reaction occurs at 25° but after nine hours at 85° a 12% yield of ethyl (α-ethoxyethylidene)-acetoacetate (IV) and an equivalent amount of ethyl orthoacetate may be isolated. The product IV is probably formed by the addition of the keto-ester as H and CH($COCH_3$)COOEt to ketene acetal followed by the loss of alcohol from the addition product. This liberated alcohol then reacts with another equivalent of ketene acetal to produce the ortho-ester. These reactions are



The yield of IV from the above reaction may be increased to 55–60% of the theoretical by the addition of 1 mole per cent. of sodium ethoxide to the reaction mixture. A corresponding increase in the yield of ethyl orthoacetate also is obtained.

The structure of the ester IV was established by (a) carbon, hydrogen and ethoxyl analyses, (b) partial hydrolysis to ethyl diacetoacetate and (c) partial hydrolysis into alcohol, acetoacetic ester and acetic acid.

In the absence of sodium ethoxide malonic ester does not react with ketene acetal even after several hours of heating at temperatures as high as 200°. With 1 mole per cent. of this catalyst, however, a 55% yield of diethyl (α-ethoxyethylidene)-malonate (V) and the corresponding amount of ethyl orthoacetate may be obtained after sixteen hours at 125°. The structure of V was established by (a) analyses, (b) partial hydrolysis to diethyl acetomalonate and (c) catalytic reduction to diethyl (α-ethoxyethyl)-malonate (VI).



Differentiation between structure V and the alternative structure VII was made by ozonolysis.[6]

Methyl malonic ester could not be caused to react with ketene acetal under conditions that were effective for the reaction of malonic ester. The use of sodium ethoxide, in quantities of 1–50 mole per cent., or sodium triphenylmethyl as condensing agents together with temperatures

(5) Staudinger and Rathsam, *Helv. Chim. Acta*, **5**, 646 (1922).

(6) This ozonolysis was carried out by Mr. Howard Burkett of this Laboratory. He has found that a considerable amount of VII generally accompanies V as a product of this reaction. The combined yields of the two amount to about 80% of the theoretical. Their structures have been established by (a) ozonolysis and (b) alkylation of each to the same malonic esters, CH_2=C(OEt)C(R)(COOEt)$_2$, a series of which is being prepared and converted into the corresponding barbituric acids. This work will be reported in a future paper.

as high as 200° gave no appreciable reaction and in each case most of the starting materials could be recovered.

bis-(Phenylsulfonyl)-methane contains an acidic hydrogen, as shown by its solubility in alkali, but, presumably, is incapable of enolization. This disulfone gives no indication of reaction when treated with two equivalents of ketene acetal at 25°. When these reactants were heated together at 100° in dioxane solution for twelve hours and the solvent then removed by distillation, a glass-like residue remained. From this residue a considerable amount (42%) of the starting disulfone was separated, but no ketene acetal was recovered from the distilled solvent. The reaction product could be neither crystallized nor distilled. These facts indicate that this reaction was complicated by the polymerization of the ketene acetal. Similar results were obtained with these reactants when sodium ethoxide was used.

The nitrogen compounds used in this study were ammonia, aniline, ethylaniline and piperidine. In contrast to the vigorous reaction of water, ammonia shows no reaction with ketene acetal at 25°. At 100°, however, reaction between acetal and an excess of ammonia appears to be complete in three hours. For each mole of ketene acetal used, 1.68 moles of alcohol, 0.55 mole of acetonitrile (XI), 0.22 mole of acetamidine (X) and 0.02 mole of ethyl orthoacetate were isolated as reaction products. These products indicate that the following reactions occur

$$CH_2{=}C(OEt)_2 + NH_3 \longrightarrow \underset{\text{VIII}}{[CH_3C(OEt)_2NH_2]} \longrightarrow EtOH + CH_3C(OEt){=}NH$$

$$CH_3C(OEt){=}NH + NH_3 \longrightarrow EtOH + \underset{\text{X}}{CH_3C(NH_2){=}NH} \xrightarrow[-NH_3]{\text{IX}} \underset{\text{XI}}{CH_3CN} \quad (-EtOH)$$

The low yield of the ortho-ester suggests that the addition product VIII is sufficiently stable not to decompose into alcohol, which would convert the ketene acetal into the ortho-ester, until the ammonia has reacted with most of the acetal. The other alternative, *viz.*, that the imino-ether (IX) is formed from the ortho-ester and ammonia seems unlikely since some ortho-ester does remain in the reaction mixture in the presence of a large excess of ammonia.

Aniline reacts quite readily with ketene acetal at 25°. The main reaction product is ethyl N-phenyl iminoacetate (XIII) which is obtained in an 81% yield. An amount of alcohol equivalent to that required in the reactions below and a 7% yield of N,N'-diphenylacetamidine (XIV) is also obtained. No ethyl orthoacetate was isolated. The reactions that take place are

$$CH_2{=}C(OEt)_2 + H_2NC_6H_5 \longrightarrow \underset{\text{XII}}{[CH_3C(OEt)_2NHC_6H_5]} \longrightarrow \underset{\text{XIII}}{CH_3C(OEt){=}NC_6H_5} + EtOH$$

$$CH_3C(OEt){=}NC_6H_5 + H_2NC_6H_5 \longrightarrow \underset{\text{XIV}}{CH_3C(NHC_6H_5){=}NC_6H_5} + EtOH$$

Ethylaniline reacts with ketene acetal, slowly at 25°, but quite readily at 100° to give N-ethyl-N-(α-ethoxyvinyl)-aniline (XV) and ethyl orthoacetate. When the reactants are used in equivalent molecular quantities, one-half of the ethylaniline is recovered, indicating the following reaction course

$$2CH_2{=}C(OEt)_2 + C_2H_5NHC_6H_5 \longrightarrow \underset{\text{XV}}{CH_2{=}C(OEt)N(C_2H_5)C_6H_5} + CH_3C(OEt)_3$$

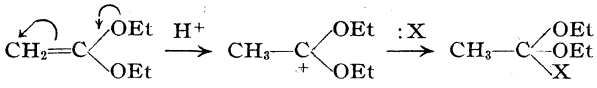
Whether or not an intermediate addition product of the type of VIII and XII is a precursor of XV is not known. The product XV was characterized by (a) analyses and (b) hydrolysis to ethylaniline, alcohol and acetic acid. It was not possible to partially hydrolyze XV to N-ethylacetanilide.

Piperidine shows no reaction with ketene acetal at 25°. When a mixture of a five-fold excess of the base with the acetal is refluxed for two hours, reaction takes place and 0.43 mole each of 1,1,1-tripiperidinoethane XVI and ethyl orthoacetate for each mole of ketene acetal used in the reaction may be isolated. The formation of these compounds is illustrated as follows

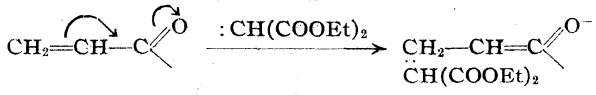
$$2CH_2{=}C(OEt)_2 + 3HNC_5H_{10} \longrightarrow \underset{\text{XVI}}{CH_3C(NC_5H_{10})_3} + CH_3C(OEt)_3 + EtOH$$

From the foregoing reactions it is seen that acids and, in general, compounds containing a replaceable hydrogen attached to oxygen (water, primary and secondary alcohols, enols, etc.) react readily with ketene acetal at ordinary temperatures. The reactivity appears to be related to the acidity of the compound. The same seems to be true for ammonia and its derivatives; the relatively strong bases (*i. e.*, weak acids), ammonia and piperidine, are decidedly less reactive than

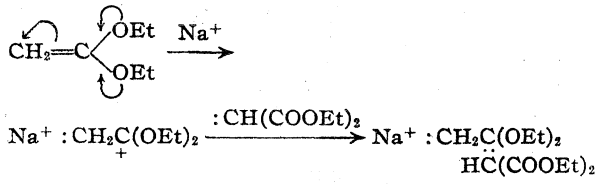
the very much weaker bases, aniline and ethylaniline. All of these reactions follow the course that would be expected, *viz.*, the attack of a proton on the nucleophilic center of a polarized molecule of ketene acetal, followed by the attachment of the negative portion of the addendum, :X, to the other carbon with an open sextet



The reactivities of the active methylene compounds, acetoacetic ester, malonic ester and methylmalonic ester, also decrease with the acidity of the ester but in these cases the reaction, when it occurs, is decidedly different in that it is catalyzed by sodium ethoxide and a new carbon to carbon bond is formed. It seems likely that the addenda in a case such as malonic ester are Na^+ and $:CH(COOEt)_2$, but whether the sodium cation or the anion is the attacking portion of the addendum is a matter of speculation. This reaction has some resemblance to a Michael reaction. The latter also involves the addition of an active methylene compound to a carbon to carbon double bond through the catalytic influence of sodium ethoxide. In this reaction it seems likely that the polarization of the carbonyl group of the unsaturated compound creates a center of low electron density at the carbon to which the addendum anion becomes attached



The hetero-enoid polarization of ketene acetal, however, is such that neither of the carbons acquires an electron deficit. It seems necessary to suppose, therefore, that the alkaline catalyst functions through the ability of the sodium cation to hold the electron increment that is built up on the methylene carbon until the anion portion of the addendum becomes attached to the other carbon which, after depolarization, would have the requisite electron deficit, thus



Another molecule of malonic ester could substitute a proton for the sodium cation, or a molecule of sodium ethoxide could be eliminated from the addition product, and the reaction continue through repetition of the steps above indicated. This formulation is similar to that used to explain the catalysis of cadmium chloride for the polymerization of ketene acetal.[3]

Since it has been shown[7] that active methylene groups in sulfones undergo the Michael reaction it was thought that *bis*-(phenylsulfonyl)-methane would behave similarly to malonic ester with ketene acetal. However, this was not the case. Even though it was not possible to isolate any product (except considerable of the starting disulfone) from this reaction it was quite obvious that it had taken a different course than that of the other active methylene compounds that were studied.

Experimental

The Reaction of Ketene Acetal with Acids and Enols

Hydrobromic Acid.—A solution of 18.6 g. (0.23 mole) of hydrogen bromide (from the bromination of xylene) in 200 g. of di-*n*-butyl ether was cooled to about 0° and treated dropwise, with vigorous stirring, with 26.7 g. (0.23 mole) of ketene acetal.[3] A yellow precipitate, which redissolved, was formed when each drop of the acetal entered the solution. A considerable amount of heat was evolved. After about one-fifth of the acetal had been added a red oil separated to the bottom of the reaction flask. This did not seem to increase in quantity during the reaction. After all of the acetal had been added, titration of the solution showed that 17% of the starting hydrogen bromide still was present. Distillation of the ether solution yielded 24 g. (85%) of the ethyl bromide and 12.7 g. (72%) of ethyl acetate.

3,5-Dinitrobenzoic Acid.—To 2.17 g. (0.01 mole) of 3,5-dinitrobenzoic acid, suspended in 30 ml. of ether, was added 1.7 g. (0.015 mole) of ketene acetal. The solution was evaporated on the steam-bath and recrystallized from alcohol. A yield of 1.8 g. (74%) of ethyl 3,5-dinitrobenzoate, m. p. 94–95°, was obtained.

Phenol.—To 47.0 g. (0.5 mole) of phenol in a flask attached to a condenser carrying a drierite tube, 58.0 g. (0.5 mole) of ketene acetal was slowly added with shaking. The temperature quickly rose to 80°. After standing for an hour, the reaction mixture was fractionated: 20.9 g. (59%) of ethyl acetate, b. p. 72–79°; 38.2 g. (78%) of phenetole, b. p. 162–169°, and 11.6 g. (17%) of phenyl acetate, b. p. 189–194°, were obtained.

Dibenzoylmethane.—To 14.0 g. (0.06 mole) of dibenzoylmethane, m. p. 77–78°, contained in a flask attached to a condenser carrying a drierite tube was added, with shaking, 14.5 g. (0.12 mole) of ketene acetal. In about thirty minutes the temperature of the solution had risen to 40°. After standing five to six hours the solution changed to a crystalline mass. The flask was then placed in an oil-bath at 60° and the excess of ketene acetal (6–7 g.) removed under 0.5 mm. pressure and collected in a cold trap.

(7) Connor, *et al.*, THIS JOURNAL, **58**, 1386 (1936).

The remaining 22 g. of residue was triturated in a mortar with 45 ml. of cold petroleum ether (60–68°) for ten minutes and then filtered by suction. The crystalline product so obtained was similarly washed with three other 18-ml. portions of petroleum ether and dried *in vacuo* to constant weight. The yield of product (II), melting at 86–87°, was 20.3 g. (95%). Its melting point remained unchanged after recrystallization from petroleum ether (60–68°); mol. wt. (cryoscopic in benzene), 335; calcd., 340.

Anal. Calcd. for $C_{21}H_{24}O_4$: C, 74.08; H, 7.11; OC_2H_5, 26.47. Found: C, 73.95; H, 7.06; OC_2H_5, 26.50.

The O-(α,α-diethoxyethyl)-dibenzoylmethane was characterized by the following reactions, (a) hydrolysis with 5% sulfuric acid converted it into ethyl alcohol, acetic acid and dibenzoylmethane; (b) pyrolysis of 20 g. of this product at 140° (38 mm.) under nitrogen produced 2.1 g. (31%) of ketene acetal as a distillate and left a rather tarry residue which, after washing with petroleum ether, and two recrystallizations from methanol yielded 8.3 g. (61%) of dibenzoylmethane, m. p. 77–78°; (c) simultaneous titration under nitrogen of a 1.2014 g. sample of the reaction product and a 0.4994 g. sample of dibenzoylmethane with a 0.0982 *N* solution of sodium triphenylmethyl[8] showed that the product used only 16% of a molecular equivalent while dibenzoylmethane used 100% of a molecular equivalent of the sodium triphenylmethyl before the red color of the solution of the latter compound persisted.

Ethyl (α-Ethoxyethylidene)-acetoacetate (IV).—To 22.8 g. (0.18 mole) of acetoacetic ester containing 1 mole per cent. of sodium ethoxide in a flask attached to a reflux condenser carrying a drierite tube was added 40 g. (0.36 mole) of ketene acetal. After heating for nine hours in an oil-bath at 85° the reaction mixture was fractionated. The following fractions were obtained, (a) 5.1 g. of a mixture of ethyl acetate and ethyl alcohol, (b) 21.8 g. (78% based on one-half of the ketene acetal used) of ethyl orthoacetate, b. p. 100–102° (200 mm.), (c) 1.5 g. of an intermediate fraction, and (d) 23.9 g. of a fraction boiling at 96–103° (1 mm.). Refractionation of fraction (d) gave 22.8 g. (68%) of IV, b. p. 96–98° (1 mm.); mol. wt. (cryoscopic in benzene), 208; calcd., 200.

Anal. Calcd. for $C_{10}H_{16}O_4$: C, 59.97; H, 8.06; OC_2H_5, 45.0. Found: C, 59.62; H, 8.02; OC_2H_5, 44.7.

When the above experiment was carried out in the absence of sodium ethoxide, a yield of only 12% of the theoretical amount of IV was obtained, even after twenty-four hours of heating at 85°.

Hydrolysis of 10 g. (0.05 mole) of IV with 1.8 g. (0.1 mole) of water in dioxane gave, after five hours of refluxing, 92% of the theoretical quantity of acetic acid (titration) and 2.0 g. of acetoacetic ester, b. p. 175–178°. Hydrolysis of 11.2 g. of IV with only one equivalent (0.95 g.) of water in 20 g. of dioxane gave, after thirty minutes of refluxing followed by fractionation, 3.7 g. of diacetoacetic ester,[9] b. p. 102–104° (15 mm.), the copper salt of which melted at 149–150°.[10]

(8) Hauser, *et al.*, THIS JOURNAL, **59**, 1823 (1937); **60**, 1960 (1938).

(9) Claisen, *Ann.*, **277**, 172 (1893).

(10) James, *ibid.*, **226**, 212 (1884).

Diethyl (α-Ethoxyethylidene)-malonate (V).—A mixture of 23.2 g. (0.2 mole) of ketene acetal, 16 g. (0.1 mole) of diethyl malonate and 0.1 g. of sodium ethoxide was heated in an oil-bath at 125° for sixteen hours, after which time the reaction mixture was fractionated. A yield of 13.2 g. (81%) of ethyl orthoacetate and 19 g. of a fraction boiling at 100–102° (1 mm.) were obtained. This fraction was cooled to −15° and rapidly filtered through a cold filter. The crystals so obtained amounted to about 70% of the weight of the fraction boiling at 100–102° (1 mm.). The crystalline product (V) weighed 12.7 g. (55%) and melted at 26–27°.[11] Mol. wt. (cryoscopic in benzene), 219; calcd., 230.

Anal. Calcd. for $C_{11}H_{18}O_5$: C, 57.37; H, 7.88; OC_2H_5, 58.7. Found: C, 57.62; H, 7.86; OC_2H_5, 58.6.

A mixture of 11 g. of V and 10 ml. of 2 *N* hydrochloric acid was heated, with intermittent shaking, for ten minutes on a steam-bath. The mixture was cooled and extracted with ether. The ethereal solution, after washing with sodium carbonate solution, was dried and distilled. A yield of 6.8 g. of diethyl acetomalonate, b. p. 65–70° (0.55 mm.); $n^{25}D$ 1.4435; d^{25}_{25} 1.0906, was obtained. Its copper derivative melted at 124–125° and showed no depression in melting point when mixed with the copper derivative of a known sample of diethyl acetomalonate prepared by the procedure of Nef.[12]

Diethyl (α-Ethoxyethyl)-malonate (VI).—A solution of 9.4 g. (0.04 mole) of diethyl (α-ethoxyethylidene)-malonate (V) in 15 ml. of absolute alcohol was hydrogenated at 100° under an initial hydrogen pressure of 2800 pounds in the presence of 1 g. of Raney nickel. Hydrogen absorption ceased in forty-five minutes after about 0.05 mole had been absorbed. Careful fractionation of the alcoholic solution, after filtering off the nickel catalyst, yielded 5 g. of VI, b. p. 66–67° (0.4 mm.); $n^{25}D$ 1.4198; d^{25}_4 1.0120; M_D calcd., 57.95; found, 58.0; saponification equivalent, calcd., 116; found, 118.

Anal. Calcd. for $C_{11}H_{20}O_5$: C, 56.68; H, 8.68; OC_2H_5, 58.2. Found: C, 56.84; H, 8.97; OC_2H_5, 56.1.

Attempted Reaction of Diethyl Methylmalonate with Ketene Acetal.—A mixture of 19 g. (0.11 mole) of diethyl methylmalonate, 12.8 g. (0.11 mole) of ketene acetal and 0.1 g. of sodium ethoxide was heated in an oil-bath under a reflux condenser at 125° for sixteen hours. Upon fractionation of the reaction mixture, 10.7 g. of ketene acetal, b. p. 80–85° (200 mm.), and 18.2 g. of diethyl methylmalonate, b. p. 86–87° (13 mm.), were recovered.

Reaction of *bis*-(Phenylsulfonyl)-methane with Ketene Acetal.—To 6.4 g. (0.025 mole) of the disulfone dissolved in 45 g. of dioxane was added 5.8 g. (0.05 mole) of ketene acetal and the resulting solution refluxed for twelve hours. The solvent was then allowed to evaporate spontaneously from a crystallizing dish in a vacuum desiccator, with the last traces of the dioxane being removed at 80° under 1 mm. pressure. The liquid removed by this evaporation was collected in an acetone–carbon dioxide snow cold trap.

(11) Diethyl (α-ethoxyethylidene)-malonate has been reported by Sah, THIS JOURNAL, **53**, 1836 (1931), as a product (yield 4%) of the reaction of ethyl orthoacetate and diethyl malonate in the presence of acetic anhydride at 140°. He describes it as a red, glycol-thick liquid, the color of which could not be removed by redistillation.

(12) Nef, *Ann.*, **266**, 105 (1891).

Upon distillation it was found to be dioxane with small amounts of materials boiling above ketene acetal but lower than the disulfone. No ketene acetal was found. The glassy residue remaining after the evaporation was extracted with three 20-cc. portions of ether. These extractions left a quantity of the original disulfone as a white powder, which after recrystallization from dilute alcohol weighed 2.7 g. (42%) and melted at 118–119°. Evaporation of the ether used to extract the reaction product left a thick oil which changed to a dark non-volatile tar on attempted distillation under 0.01 mm. pressure.

The use of 5 mole per cent. of sodium ethoxide in a reaction similar to that described above gave practically the same results.

Reaction of Ketene Acetal with Ammonia and Amines. Ammonia.—Into 28.4 g. of ketene acetal contained in a bomb tube, prepared for sealing and cooled in an acetone–carbon dioxide snow bath, 14 g. of dry ammonia was distilled and the tube sealed off. The two liquids are immiscible. The bomb tube then was heated for three hours at 110°, after which time it was cooled and opened. The ammonia was allowed to distil off at room temperature and collected in a cold trap; 9 g. was recovered. Fractionation of the remaining liquid through a Widmer column yielded the following fractions: (a) 23.5 g. of a mixture of ethyl alcohol, ammonia and acetonitrile, b. p. 71–76°; (b) 6.2 g. in receiver and cold trap boiling below 40° (8 mm.); (c) 2 g. of a residue of acetamidine. The residue (c) could be sublimed but was best purified by dissolving in a mixture of anhydrous alcohol and ether and precipitating as the hydrochloride with hydrogen chloride. After filtration and recrystallization this hydrochloride melted at 177–178°.

Anal. Calcd. for $C_2H_7N_2Cl$: N, 29.65; Cl, 37.6. Found: N, 30.2; Cl, 36.3.

This amidine hydrochloride was further characterized as follows. A 0.6667-g. sample was treated with a solution of 5 g. of sodium hydroxide in 200 cc. of water and the ammonia distilled into a standard solution of sulfuric acid. The solution remaining in the boiling flask was treated with 2 g. of silver oxide and 30 cc. of 6 *N* sulfuric acid. The acetic acid was distilled out and titrated. Yields of 0.234 g. (97.5%) of ammonia and 0.415 g. (97.8%) of acetic acid were obtained.

Redistillation of fraction (b) gave 2.1 g. of material boiling at 73–76°, which was added to fraction (a), and 1.0 g. of ethyl orthoacetate boiling at 130–145°. A 3.60-g. sample of fraction (a) was titrated with 0.5 *N* sulfuric acid to neutrality with a methyl red–methylene blue indicator; this titration showed 0.031 g. of ammonia to be present. The acetonitrile was hydrolyzed by boiling with a sodium hydroxide solution as described above and the total ammonia collected in standard sulfuric acid. The acetic acid was determined in the remaining solution, from which the ammonia had been distilled, by acidification with sulfuric acid followed by distillation. Yields of 0.365 g. of ammonia and 1.19 g. of acetic acid were obtained from the 3.60-g. sample of fraction (a). After deduction of the free ammonia that was present in this sample, the molecular ratio of the ammonia to the acetic acid from the hydrolysis was 1:1.010. These values indicate that 5.6 g. (56%) of acetonitrile was formed in the reaction.

Aniline.—The addition of 5 g. of ketene acetal to 4 g. of aniline caused a considerable evolution of heat. After heating the mixture on a steam-bath for two hours in order to assure a more complete reaction, it was distilled. The following fractions were collected, (a) 1.7 g. (86% of the theoretical) of ethyl alcohol, b. p. 75–80°, (b) 5.7 g. of ethyl N-phenyliminoacetate, b. p. 93–94° (9 mm.), and (c) 0.6 g. of residue. Fraction (c), which was N,N'-diphenylacetamidine, solidified on cooling and after recrystallization from 70% alcohol, melted at 132–133°.[13] Fraction (b) was characterized by conversion into N,N'-diphenylacetamidine according to the procedure of Lander.[14]

Ethylaniline.—A mixture of 7.3 g. (0.06 mole) of ethylaniline and 7.0 g. (0.06 mole) of ketene acetal was heated on a steam-bath for five hours. After this time the reaction mixture was fractionated and the following fractions collected, (a) 1.25 g. (0.01 mole) of ethyl orthoacetate, b. p. 30–50° (22 mm.), (b) 3.7 g. (0.03 mole of ethylaniline, b. p. 100–105° (22 mm.), (c) 0.53 g. of an intermediate fraction boiling at 105–125° (22 mm.), (d) 5.47 g. (0.029 mole) of N-ethyl-N-(α-ethoxyvinyl)-aniline (XV), b. p. 128–130° (22 mm.). Redistillation of fraction (d) gave a product that boiled at 129–130° (22 mm.); $n^{25}D$ 1.5232; d^{25}_{25} 0.9750.

Anal. Calcd. for $C_{12}H_{17}ON$: N, 7.32; OC_2H_5, 23.6. Found: N, 7.28; OC_2H_5, 23.0.

The N-ethyl-N-(α-ethoxyvinyl)-aniline on treatment with 0.2 *N* sulfuric acid evolves considerable heat, but careful attempts to isolate N-ethylacetanilide from a partial hydrolysis of it were unsuccessful. All attempts at hydrolysis resulted in complete cleavage into alcohol, acetic acid and ethylaniline.

Piperidine.—Addition of 5 g. (0.043 mole) of ketene acetal to 19.5 g. (0.230 mole) of carefully dried piperidine produced no indication of reaction. The mixture, therefore, was refluxed for two hours. After this time it was fractionated into (a) 13.4 g. of a mixture of alcohol and piperidine, b. p. 45–55° (200 mm.), (b) 3.0 g. (43%) of ethyl orthoacetate, b. p. 45–50° (19 mm.) and (c) 5.2 g. (43% based on the acetal used) of 1,1,1-tripiperidinoethane, b. p. 113–115° (1 mm.); $n^{25}D$ 1.5042; d^{25}_{25} 0.9520.

Anal. Calcd. for $C_{17}H_{33}N_3$: N, 15.0. Found: N, 15.2.

Hydrolysis of a 1.77-g. sample of the tripiperidinoethane was carried out by refluxing it for twenty-four hours in 10 cc. of 6 *N* sulfuric acid solution. On making this hydrolysis solution alkaline, 83% of the theoretical quantity of piperidine could be distilled out. Acidification of the remaining alkaline solution with sulfuric acid followed by distillation gave 110% of the calculated quantity of acetic acid.

Summary

The reactions that take place between ketene acetal and a variety of compounds, in which an active hydrogen is attached to halogen, oxygen, carbon and nitrogen, are reported. In most of these cases the primary reaction involves the addition of the hydrogen to the methylene

(13) *Cf.* Biederman, *Ber.*, **7**, 540 (1874).

(14) Lander, *J. Chem. Soc.*, **77**, 737 (1900).

carbon of the acetal followed by the attachment of the remainder of the addendum to the carbon carrying the ethoxyl groups. This primary reaction may be followed by one or more subsequent reactions.

In the cases of acetoacetic ester and malonic ester the reaction takes a different course. These compounds do not add as H and O—C(R)=CHCOR, as does dibenzoylmethane, but rather as H and $CH(COR)_2$ and the addition is strongly catalyzed by small amounts of sodium ethoxide. The function of the catalyst in this reaction is discussed.

MADISON, WISCONSIN RECEIVED MARCH 15, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

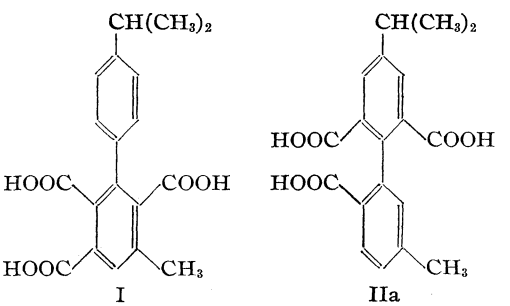
Acetylretene and 6-Retenol

BY WILLIAM P. CAMPBELL AND DAVID TODD

Acetylretene was first prepared by Bogert and Hasselstrom[1] and was shown[2] to have the acetyl group in the same position as the hydroxyl group of the β-retenol of Komppa and Wahlforss[3] by conversion into that substance. Evidence based on the coupling reaction, reduction potential data, and the Dimroth test, indicating that the β-retenol is either the 3- or the 6-derivative had been presented by Fieser and Young[4] and their view that the substituent probably is in the 6-position has been accepted in subsequent literature even though conclusive evidence was lacking. More recently there appeared a paper by Nyman[5] on acetylretene presenting evidence resulting mainly from oxidation experiments which he interprets as indicating that the acetyl group (and, therefore, the hydroxyl group of the β-retenol) occupies the 4- instead of the 6-position.

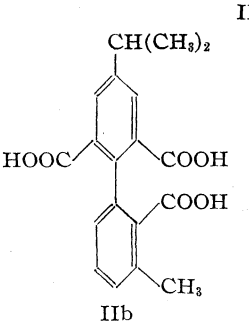
In the present research the possibility that these groups occupy the 6-position is definitely eliminated[6] by the preparation of 6-retenol (VII) of proven structure, which is different from the β-retenol. A careful study and reinterpretation of the results of Nyman[5] and of Fieser and Young[4] led us to the conclusion that the acetyl and hydroxyl groups must be in the 3-position in these compounds, and this view has been proven to be correct.

All of the arguments by which Nyman eliminated the various possible positions for the acetyl group in acetylretene seem valid with the exception of those regarding the 3-position. The point in question involves a distinction between I which would result from 3-acetylretene and IIa or b



I

IIa



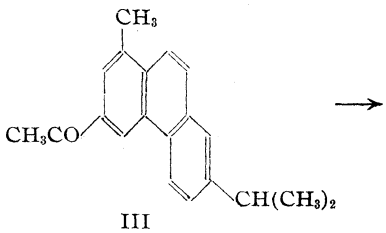
IIb

which would result from the 4-isomer. The evidence presented in favor of II was that the substance melts at a high temperature (277°) without apparent loss of water, and fails to form an anhydride on heating with acetyl chloride, although heating with acetic anhydride does produce the anhydride. There is ample contradictory evidence in the literature which can lead only to the conclusion that it is not possible to decide between these compounds on the basis of such evidence. For example, trimellitic acid, which is analogous to I, melts at 238° without apparent loss of water

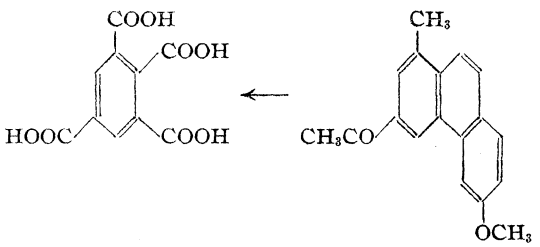
(1) Bogert and Hasselstrom, THIS JOURNAL, **53**, 3462 (1931).
(2) Adelson and Bogert, *ibid.*, **58**, 653 (1936).
(3) Komppa and Wahlforss, *ibid.*, **52**, 5009 (1930).
(4) Fieser and Young, *ibid.*, **53**, 4120 (1931).
(5) Nyman, *Ann. Acad. Sci. Fennicae*, **A48**, No. 6 (1937); *Chem. Abst.*, **33**, 8192 (1939).
(6) In a publication which reached us after this paper was written, Ruzicka and St. Kaufmann (*Helv. Chim. Acta*, **23**, 288 (1940)) arrived at this same conclusion by a comparison of the melting points of 6-ethylretene (prepared by way of 6-acetyldehydroabietic ester) and two of its derivatives with those reported by Bogert and Hasselstrom[1] for their ethylretene obtained from acetylretene. In the present paper, a direct comparison of the corresponding retenols by mixed melting point has been made.

and is only partially converted into the anhydride by three-hour boiling with acetyl chloride or acetic anhydride.[7] On the other hand retene diphenic acid, similar to IIa and b, forms an anhydride[8,9] with acetyl chloride at room temperature. Thus the work of Nyman indicates only that the acetyl group is in the 3- *or* 4-position.

The reduction potentials of retenequinone and the quinones from 2- and β-retenol as determined and interpreted by Fieser and Young[4] provide evidence that the hydroxyl group of β-retenol is either 3 or 6.[10] With the 6-position now eliminated the compounds of the β-series would on this evidence be the 3-derivatives. Proof of this structure was accomplished by the isolation of mellophanic (1, 2, 3, 5) acid (IV) as an oxidation product of acetylretene (III). That Nyman[5] was



III



IV V

unable to isolate this degradation product may be because he used a different method of oxidation.

On the basis of this structure for acetylretene, the cyclopenteno- and benzo-retenes prepared by Adelson and Bogert[11] must be written as the 2,3- or 3,4- instead of the 5,6-derivatives. By analogy with similar work on phenanthrene, the 3,4-position is most probable.

That the retene molecule directs the entering groups to the 3-position in the Friedel and Crafts reaction and to the 2-[4] and 3-positions in sulfonation is interesting in view of the similar behavior of phenanthrene.[12] In addition, dihydroretene undergoes sulfonation in the 2- and 3-positions.[13] Thus it appears that there is some orienting influence inherent in the ring system which overcomes any directive effect of the alkyl groups. On this basis one would expect the acetyl derivative of dihydroretene, which Nyman[14] showed not to be the 3-isomer, to be the 2-derivative.[15]

In the course of this work we had occasion to carry out a Friedel and Crafts condensation of acetyl chloride with 1-methyl-6-methoxyphenanthrene, and in this case also we obtained the 3-acetyl derivative, V. The structure was proved by oxidation to IV, and the compound was characterized by oxidation to the corresponding 3-carboxy derivative. This orientation is in contrast to the results of Burger and Mosettig[16] with derivatives of 6-(or 3-)phenanthrol. The 6-methoxyphenanthrene was converted into the 10-acetyl derivative under conditions similar to those used above. The acetyl group, however, entered the 3-position when the reaction was carried out on 6-acetoxyphenanthrene.

The 6-retenol (VII) was obtained in good yield (68%) by selenium dehydrogenation of methyl 6-hydroxydehydroabietate[17] (VI, R=H), and it has been characterized by the preparation of several derivatives.

The 6-retenol corresponds in its melting point and the melting point of seven of its derivatives with a retenol obtained by Brandt and Neubauer[18] from ferruginol and considered by them to be the 8-isomer. These authors placed the hydroxyl group in the 8-position because of the non-identity of their compound with the β-retenol (3-retenol) previously regarded as the 6-compound, and because the corresponding hydroxyquinone gave a positive Dimroth test. The same retenol has been obtained from hinokiol.[18,19] Table I gives a comparison of the melting points of 6-retenol and its derivatives with those of the retenol obtained from ferruginol and hinokiol. Although a direct comparison by mixed melting point determination

(7) R. P. Linstead, unpublished results.

(8) Adelson, Hasselstrom and Bogert, THIS JOURNAL, **58**, 871 (1936).

(9) Fogelberg, *Chem. Zentr.*, **98**, II, 2299 (1927).

(10) The 6-position was preferred by these authors because it is ortho to the isopropyl group whereas the 3-position, meta to the methyl group, was considered less likely.

(11) Adelson and Bogert, THIS JOURNAL, **59**, 399, 1776 (1937).

(12) Fieser, *ibid.*, **51**, 2460 (1929); Mosettig and van de Kamp *ibid.*, **52**, 3704 (1930).

(13) Komppa and Fogelberg, *ibid.*, **54**, 2900 (1932).

(14) Nyman, *Ann. Acad. Sci. Fennicae*, **A41**, No. 5 (1934); *Chem. Abst.*, **30**, 2958 (1936).

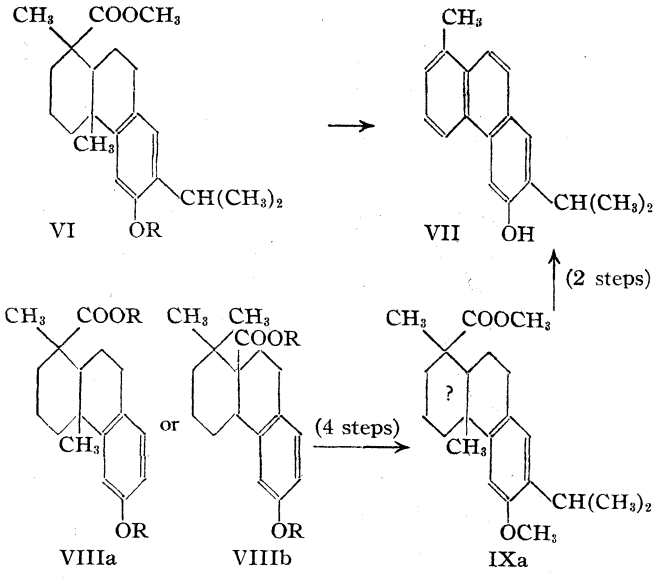
(15) Ruzicka and St. Kaufmann[6] have suggested the 6-position for this group.

(16) Burger and Mosettig. THIS JOURNAL, **56**, 1745 (1934); Mosettig and Burger, *ibid.*, **55**, 2981 (1933).

(17) Fieser and Campbell, *ibid.*, **61**, 2528 (1939).

(18) Brandt and Neubauer, *J. Chem. Soc.*, 1031 (1939).

(19) (a) Keimatsu and Ishiguro, *J. Pharm. Soc. Japan* (*Ger.*) **55**, 45 (1935); (b) Fukui and Chikamori, *ibid.*, **59**, 86 (1939).



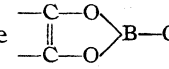
has not been made, the close correspondence of the melting points of all of the derivatives adequately establishes the identity of the substances.

TABLE I

MELTING POINTS

Compound	6-Retenol	Retenol from ferruginol and hinokiol
Retenol	179–180	179–180[19b]
Picrate	177.5–178	176–177[18,19a]
Acetate	91–92	90–91,[18] 94[19]
Methyl ether	78.5–79	80[19b]
Acetoxyquinone	186–189	188–189[18]
Hydroxyquinone	303–304 d.	285 d.,[18] 307[19]
Hydroxyquinoxaline	225–226	223[19a]
Acetoxyquinoxaline	195–196.5	194[19]

The hydroxyl group of 6-retenol is rather highly hindered since the substance is only slightly soluble in aqueous alkali and apparently methylates with difficulty.[18,19] After treatment with diazomethane in ether at 0° for three hours, the retenol was recovered quantitatively unchanged. In one experiment, no ether was obtained on treating the chloromagnesium salt with dimethyl sulfate in ether solution.

A positive Dimroth test, as reported by Brandt and Neubauer for the quinone corresponding to their retenol, was also obtained with the quinone from 6-retenol. This test consists of a comparison of the color of a solution of the hydroxyquinone in acetic anhydride with that of a similar solution containing added boro-acetic anhydride. If the hydroxyl group is ortho to the quinone carbonyl as in 1-hydroxyphenanthrenequinone the highly colored complex, X, is formed; otherwise simple acetylation takes place. As far as is known, the only example of an anomalous test is that reported by Fieser,[20] who found that morpholquinone (XI) gave a positive test. Two possible explanations were offered for this observation. The first postulated a reaction of the boro-acetic anhydride with the tautomeric form, XII, producing the complex, XIII. The second explanation involved the formation of a boron complex of the type  , with the two adjacent hydroxyl groups.

A comparison, made in the present work, of the colors produced when a series of hydroxyphenanthrenequinones were subjected to this test has given results (Table II) which favor the first of the two explanations and permit a slight extension of the idea. The colors were divided roughly into three groups, faint, medium, and intense, which are widely different and easily discernible, although the difference between those listed as "faint" and those

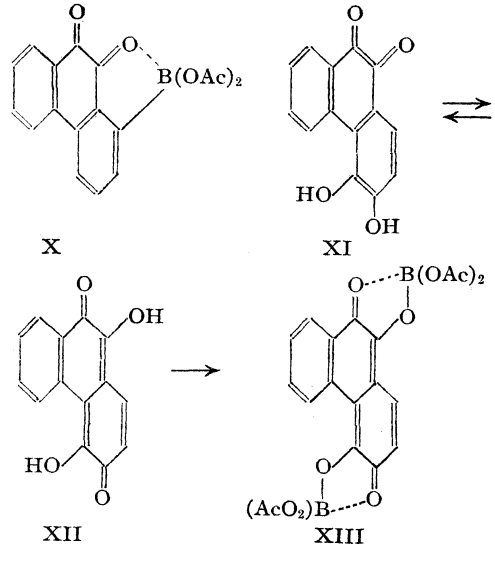


TABLE II

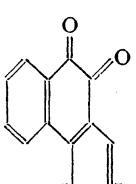
DIMROTH TEST ON HYDROXYQUINONES

Quinone from	Color
2,6-Dihydroxyphenanthrene[a]	None
3-Retenol[a]	None
3-Phenanthrol[a]	Faint
1-Methyl-6-phenanthrol	Faint
6-Retenol	Medium
Morphol[a]	Intense
1-Phenanthrol[a]	Intense

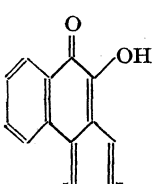
[a] Samples of these compounds were supplied by Professor L. F. Fieser.

(20) Fieser, THIS JOURNAL, 51, 2471 (1929).

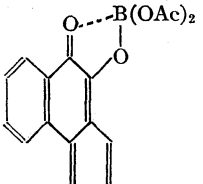
giving no color is not considered significant. If the development of color by the 3- and 6-hydroxyquinones is the result of the reaction of boro-acetic anhydride with the tautomeric form, the variation in the color produced can be qualitatively explained. An alkyl group substituted in the 5- or 7-position of XIV would exert only a negligible



XIV



XV



XVI

effect on the potential of the 9,10-quinone. The same substitution would, however, cause considerable lowering of the potential[21] of the tautomeric amphi-quinonoid form XV. The net effect would be an increase in the quantity of XV available for conversion into the colored complex, XVI, as a result of the increased stability of this form. Thus the quinone from 6-retenol (1-methyl-7-isopropyl-XIV), as would be expected, gives a deeper color than that from 1-methyl-6-phenanthrol. A hydroxyl group in the 5- or 7-position would produce an even greater lowering of the potential (roughly twice[21]) than an alkyl group, and the intense color obtained with morpholquinone (5-hydroxy-XIV) is in line with this view.

The results indicate that neither two ortho hydroxyl groups nor a hydroxyl group ortho to the quinone carbonyl is necessary for the production of color with boro-acetic anhydride, and that the reaction very probably takes place with the tautomeric amphi-quinonoid structure.

During the earlier stages of this research our first attempts to prepare 6-retenol by dehydrogenation of methyl-6-hydroxydehydroabietate met with little success. We sought, therefore, for a more productive source of the retenol and investigated the possibility of preparing the compound from podocarpic acid. In a recent investigation, Sherwood and Short[22] found that the resin acid could be dehydrogenated in good yield to 1-methyl-6-hydroxyphenanthrene, identified by synthesis. The formation of this phenanthrol on dehydrogenation locates all of the carbon atoms in the molecule except the methyl and the carboxyl groups which are eliminated in the reaction. Sherwood and Short considered formulas VIIIa and VIIIb (R=H) for podocarpic acid, favoring VIIIb because the carboxyl group is considerably more hindered than in the abietic acid series where the structure is similar to VIIIa.

Our plan for preparing 6-retenol from this substance involved the introduction of an isopropyl group into the 7-position and subsequent dehydrogenation. This was accomplished without difficulty by introducing an acetyl group into the 7-position by a Friedel and Crafts reaction. The reaction of the 7-acetyl compound with methylmagnesium chloride followed by dehydration and catalytic hydrogenation produced methyl O-methyl-7-isopropylpodocarpate (IXa). Dehydrogenation followed by cleavage of the methoxy group with hydrobromic acid yielded the same retenol (VII) as was obtained from 6-hydroxydehydroabietic ester. This latter reaction, in addition to confirming the location of the hydroxyl group, proved that the acetyl group entered the podocarpate molecule in the 7-position.

In connection with a suggestion advanced by Fieser and Campbell[17] concerning the structure of podocarpic acid, we were interested in comparing methyl O-methyl-7-isopropylpodocarpate (IXa) with methyl 6-methoxydehydroabietate (VI, R=CH_3). If podocarpic acid has the structure VIIIa, the two substances should be identical, providing the configuration in both molecules is the same. The melting points of the two compounds, however, are widely different and the mixed melting point showed considerable depression. The two substances, therefore, are either position- or stereo-isomers.

The methylation of methyl 6-hydroxydehydroabietate presented some difficulty. The hydroxyl group is highly hindered by the *o*-isopropyl group, since methylation of podocarpic acid proceeds with great ease. The phenol-ester is practically insoluble in aqueous alkali. In one experiment a small amount of the methyl ether was obtained by the action of dimethyl sulfate in alcoholic alkali but this could not be repeated. Attempts to prepare the ether by reaction with silver oxide and methyl iodide, with diazomethane (alone or with aluminum tertiary butylate), or by treating the sodium or potassium salt with dimethyl sulfate were all unsuccessful. The compound was unaltered by heating with potassium carbonate and dimethyl

(21) Fieser in Gilman, "Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1938, pp. 812–815.

(22) Sherwood and Short, *J. Chem. Soc.*, 1006 (1938).

sulfate in boiling xylene, although this method was used successfully[18] for the methylation of ferruginol. The ether was obtained in good yield, however, by the action of dimethyl sulfate on the chloromagnesium salt, prepared by treating the phenol with methylmagnesium chloride.

The authors wish to thank Professor L. F. Fieser for suggesting some of this work and for his helpful advice in connection with the interpretation of the results of the Dimroth test.

Experimental Part[23]

3-Acetylretene (III).—In this preparation nitrobenzene, instead of carbon disulfide,[1,2] was used for the solvent. To a solution of 25 g. of retene and 15 cc. of acetyl chloride in 100 cc. of nitrobenzene at −5° was added 29 g. of aluminum chloride. When about half of this material had been added, a deep red, finely divided complex separated accompanied by a slight rise in temperature. After stirring for five hours at −5° and standing at 5° for forty hours, the reaction mixture was poured into ice and 70 cc. of concentrated hydrochloric acid. The black residue remaining after steam distillation was treated with Norit in ether and crystallized from this solvent yielding 13.5 g. (45%) of pure acetylretene, m. p. 99.5–100° (cor.). From the mother liquor, 4.5 g. of product melting at 85–89° and 9.8 g. of a picrate melting at 127–132° were obtained. These materials are being investigated.

Oxidation of 3-Acetylretene to Mellophanic Acid.—A mixture of 0.5 g. of 3-acetylretene, 1 cc. of concentrated nitric acid and 2 cc. of water was heated for thirty-three hours in a sealed tube at 190–200°. Twice, during this time, the tube was opened and 1 cc. of concentrated nitric acid was added. The yellow sirup obtained by evaporation of the solution solidified on stirring with fuming nitric acid. The solid was removed by filtration and washed well on the filter with fuming nitric acid. This product was esterified with diazomethane and the ester was crystallized from methanol, m. p. 108–109°. Recrystallization from methanol raised the melting point to 108.5–109.5° (cor.). The melting point of a mixture of this material with an authentic sample of the tetramethyl ester of mellophanic acid (m. p. 110.5–111°) was 109–110.5° (cor.).

1-Methyl-6-phenanthrol.—This substance (m. p. 160–161°) was prepared by dehydrogenation of podocarpic acid (see below) by the method of Sherwood and Short.[22] It was also obtained from its methyl ether by boiling for four hours with hydrobromic-acetic acid.

1-Methyl-3-acetyl-6-methoxyphenanthrene (V).—This reaction was carried out in the same manner as the preparation of 3-acetylretene, above, using 0.95 g. of 1-methyl-6-methoxyphenanthrene,[22] 0.45 cc. (50% excess) of acetyl chloride, and 1.14 g. of aluminum chloride in 25 cc. of nitrobenzene. The time of reaction was sixty-five hours. The product was washed in ether solution with alkali and after drying the solvent was removed. The residue could not be induced to crystallize and was treated with 0.87 g. of picric acid in ethanol. The orange *picrate* which separated melted at 146–148.5° after two crystallizations from ethanol. Decomposition of the picrate by warming with aqueous sodium carbonate and crystallization of the resulting material from ethanol gave 0.25 g. (21%) of light feather-like crystals melting at 126.5–127°.

Anal. Calcd. for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10. Found: C, 81.90; H, 6.07.

For characterization the acetyl derivative (0.34 g.) was treated in dioxane–sodium hydroxide solution with iodine–potassium iodide solution until the iodine color persisted for two minutes at 60°. The **1-methyl-3-carboxy-6-methoxyphenanthrene** was obtained in a pure, crystalline condition after two precipitations from aqueous alkaline solution by hydrochloric acid, m. p. 233–235°. Recrystallization from aqueous ethanol did not change the melting point.

Anal. Calcd. for $C_{17}H_{14}O_3$: neut. equiv., 266. Found: neut. equiv., 266.

For proof of the structure, 0.07 g. of the acid was heated with 1 cc. of concentrated nitric acid and 2 cc. of water at 100° for one hour and at 180–200° for thirteen hours. The product obtained on evaporation of this solution to dryness was esterified in ether with excess diazomethane. The mellophanic tetramethyl ester, crystallized from aqueous ethanol, melted at 107–108° (cor.). Mixed with an authentic sample (m. p. 108.5–109.5°) it melted at 107–109° (cor.).

6-Retenol (VII).—A mixture of 2 g. of methyl 6-hydroxydehydroabietate and 2.1 g. of selenium powder was heated at 280–285° for twenty-four hours and then at 335° for four hours. The mixture was stirred continuously by passing a slow stream of nitrogen through it. The product was extracted with ether, washed with 5% sodium hydroxide, and dried. On concentrating the nearly colorless solution and adding hexane, 0.71 g. of 6-retenol, m. p. 177–178°, separated as thin, colorless flakes. A second crop of 0.27 g., m. p. 173–175°, separated from the concentrated mother liquor. Recrystallization from ether–hexane raised the melting point to 179–180°; yield 68%. In another run under the same conditions but without the nitrogen stirring, the yield was 43%. This product, mixed with the β(3)-retenol (m. p. 158–161°) melted below 138°.

Anal. Calcd. for $C_{18}H_{18}O$: C, 86.37; H, 7.25. Found: C, 86.58; H, 7.18.

6-Methoxyretene.—Dehydrogenation of 1.75 g. of methyl O-methyl-7-isopropylpodocarpate was carried out as described above using 1.85 g. of selenium. The ether solution, after clarification with Darco, was evaporated and the residue was taken up in methanol. One crop of crystalline material (m. p. 72–74°) was obtained from this solution. Recrystallization from methanol yielded 0.30 g. (22%) of 6-methoxyretene, m. p. 75–77°. By repeated crystallization from methanol the melting point was raised to 78.5–79°.

The non-crystalline residue from the first methanol mother liquor was refluxed for seven hours with 20 cc. of glacial acetic acid and 5 cc. of 48% hydrobromic acid. The product was washed and dried in ether and, after clarification with Darco, was purified by crystallization from ether–hexane. In this way 0.38 g. (30%) of 6-retenol, m. p. 172–175°, was obtained. Recrystallization from ether–

(23) The melting points are uncorrected unless otherwise specified.

hexane gave a product, m. p. 179–180°, which did not depress the melting point of the 6-retenol prepared from methyl 6-hydroxydehydroabietate.

Derivatives of 6-Retenol.—With the exception of the methyl ether, the derivatives of 6-retenol listed in Table I were prepared by methods previously described.[18,19] For the oxidation of 6-acetoxyretene to the quinone the conditions used by Fieser[20] for oxidation of diacetoxyphenanthrenes were found to be most suitable.

Podocarpic Acid (VIII, R = H).—This substance was prepared from "rimu" resin from *Dacrydium cupressinum*.[24] Two crystallizations of the crude resin from aqueous alcohol according to Sherwood and Short[22] gave acid melting at 193–200° in 85% yield. Methylation with methyl sulfate[22] of the material remaining in the mother liquors yielded an additional quantity of product as the more easily purified methyl O-methyl ester, bringing the total yield from the resin to more than 90%.

Methyl O-Methyl-7-acetylpodocarpate.—To a solution of 18 g. of methyl O-methylpodocarpate[22] and 9 cc. of acetyl chloride in 200 cc. of nitrobenzene at 0°, 16.2 g. of aluminum chloride was added over a half-hour period. After stirring at 0° for four hours the clear solution was let stand at 5° for one hundred hours, then at room temperature for five hours. The nitrobenzene was removed by steam distillation, after hydrolysis with ice and hydrochloric acid, and the residue was separated by filtration. The product was decolorized with Darco in hot ethanol solution and on cooling 16.3 g. (80%) of the acetyl derivative melting at 109–117° was obtained. A sample, after several crystalizations from ethanol melted constantly at 119–119.5°, $[\alpha]^{25}D$ + 142° (1.8% in ethanol.)

Anal. Calcd. for $C_{21}H_{28}O_4$: C, 73.23; H, 8.19. Found: C, 73.08; H, 8.26.

The oxime (m. p. 190–193° from ethanol) was prepared by treating the acetyl compound (0.1 g.) with a filtered solution of hydroxylamine hydrochloride (0.1 g.) and excess sodium bicarbonate in ethanol. Hydrolysis with dilute hydrochloric acid yielded the original ketone.

Methyl O-Methyl-7-(α-hydroxyisopropyl)-podocarpate.—A solution of 5 g. of the 7-acetyl derivative (m. p. 109–117°) in dry ether was added slowly to excess methylmagnesium chloride in ether and, after refluxing for one-half hour, hydrolysis was brought about by the addition of saturated ammonium chloride solution. The ether layer was washed, dried and evaporated and the residue was crystallized from hexane, yielding 4.6 g. of thick prisms melting at 146–150°. An additional 0.5 g. of product (m. p. 143–147°) was obtained from the mother liquor bringing the yield to 97%. Recrystallized from hexane, the product melted at 148–150°, $[\alpha]^{25}D$ + 119° (2.4% in ethanol).

Anal. Calcd. for $C_{22}H_{32}O_4$: C, 73.28; H, 8.96. Found: C, 73.15; H, 8.78.

(24) Samples of this resin for this and other investigations were very kindly supplied by Dr. John R. Hosking of Kent, England, and by Dr. H. J. Hardon, Buitenzorg, Java, to whom we are greatly indebted. We are also indebted to Dr. C. L. Mantell of the American Gum Importers Association, and to Dr. Jakobs, Buitenzorg, Java, for their courtesy in locating sources of material.—L. F. FIESER.

Methyl O-Methyl-7-isopropenylpodocarpate.—Dehydration of the hydroxyisopropyl derivative was accomplished by boiling 2 g. of the compound in 20 cc. of acetic acid for a few minutes. The residue remaining after evaporation of the solvent was washed and dried in ether and crystallized from hexane; yield, 1.5 g., m. p. 120–121°. A sample, recrystallized from hexane, melted at 120.5–121.5°, $[\alpha]^{25}D$ + 136° (2.1% in ethanol).

Anal. Calcd. for $C_{22}H_{30}O_3$: C, 77.16; H, 8.82. Found: C, 76.97; H, 8.85.

Methyl O-Methyl-7-isopropylpodocarpate (IXa).—Hydrogenation of 0.5 g. of the 7-isopropenyl derivative in 95% ethanol with 15 mg. of Adams catalyst proceeded to completion in thirteen minutes. After removal of the catalyst, water was added to the concentrated solution to incipient turbidity, and crystallization took place on cooling. The product (0.49 g.) melted at 109–109.5° and the melting point was not changed on further crystallization; $[\alpha]^{25}D$ + 124° (1.2% in ethanol).

Anal. Calcd. for $C_{22}H_{32}O_3$: C, 76.68; H, 9.38. Found: C, 76.78; H, 9.28.

Methyl 6-Methoxydehydroabietate (VI, R = CH_3).—Methyl 6-hydroxydehydroabietate (0.5 g.) was refluxed for one hour in dry ether with 2.3 cc. of 0.69 *N* methylmagnesium chloride solution. A solution of 10 cc. of freshly distilled dimethyl sulfate in dry ether was added slowly and refluxing was continued for eighteen hours. After decomposing the excess dimethyl sulfate with alkali, the ether solution was evaporated and the product was crystallized from aqueous ethanol. On recrystallization from the same solvent, there was obtained 0.32 g. (61%) of broad flakes melting at 65.5–66.5°, $[\alpha]^{25}D$ + 87° (1.6% in ethanol).

Anal. Calcd. for $C_{22}H_{32}O_3$: OCH_3, 18.01. Found: OCH_3, 17.82.

Summary

1. Acetylretene and β-retenol are shown to be the 3- instead of the 6-derivatives.

2. The preparation of 6-retenol is described and this substance is shown to be identical with the retenol, reported to be the 8-isomer, obtained from ferruginol and hinokiol.

3. The preparation and proof of structure of 1-methyl-3-acetyl-6-methoxyphenanthrene, and the corresponding 3-carboxy derivative are reported.

4. It is shown that suitably substituted 3-hydroxyphenanthrenequinones give a positive Dimroth test and a satisfactory explanation for this anomalous action is offered.

5. The 7-isopropyl derivative of podocarpic acid is not identical with 6-hydroxydehydroabietic acid.

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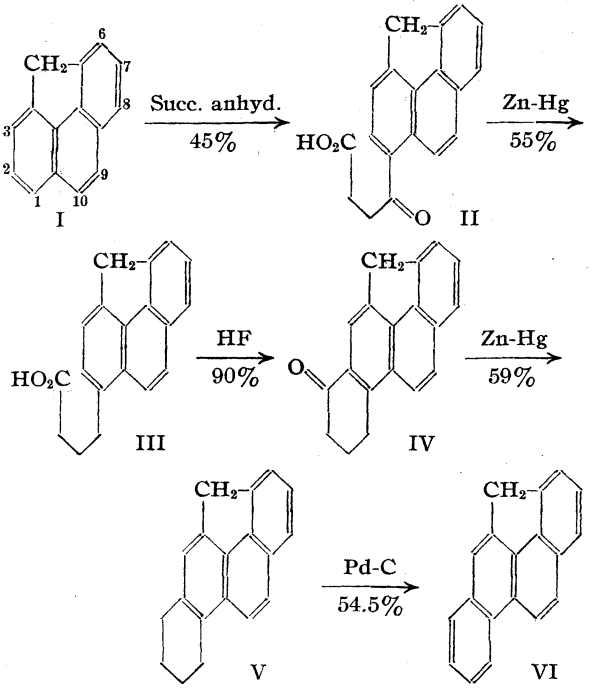
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

Synthesis of 4,5-Methylenechrysene and 1',9-Methylene-1,2-benzanthracene from 4,5-Methylenephenanthrene

BY LOUIS F. FIESER AND JAMES CASON[1]

4,5-Methylenephenanthrene (4,5-phenanthrylenemethane) was isolated in small amounts from coal tar by Kruber[2] in 1934 through the sodio and carboxy derivatives but has not as yet been made available by synthesis. We were interested in utilizing the substance as a starting point for the synthesis of higher hydrocarbons of possible carcinogenic activity and also in studying the orientation in a molecule combining special features of both the phenanthrene and the acenaphthene structures. An investigation along these lines has been possible through the courteous coöperation of Dr. O. Kruber, who kindly placed at our disposal a generous supply of the rare hydrocarbon.

In an initial study of the succinoylation of 4,5-methylenephenanthrene (I), it was found that with nitrobenzene and aluminum chloride at 5° there is produced a mixture of keto acids from which one isomer could be isolated in 45% yield and obtained in a completely pure form through the ester. On the basis of evidence to be presented below this substance is assigned the structure of the 1-acid (II). The same product was obtained by succinoylation in the presence of anhydrous hydrogen fluoride[3] but the reaction was less smooth and gave more tar. The reduced acid III was prepared by the Clemmensen reaction and purified by a novel and convenient method consisting in crystallization of the trinitrobenzene derivative and recovery of the acid by extraction with soda solution. By this means satisfactory material was easily obtained starting with partially purified keto acid. After cyclization with hydrogen fluoride[3] to the ketone IV, we tried aluminum isopropylate reduction to the carbinol and treatment with palladium charcoal, but in contrast to Bachmann and Struve's[4] experience with a tertiary carbinol, the results were unpromising. Clemmensen reduction and dehydrogenation proceeded more satisfactorily and gave a highly fluorescent hydrocarbon isomeric with the known 1',9-methylene-1,2-benzanthracene[5] and melting at 172.4–172.9°. The ultraviolet absorption spectrum, which will be reported later by Dr. R. N. Jones, closely resembles those of chrysene and 5-methylchrysene, indicating that the substance is 4,5-methylenechrysene as formulated (VI), and in view of the confirmatory chemical evidence to be presented there can be no doubt on this score. The hydrocarbon bears a certain resemblance to 3,4-benzpyrene in its chrysenoid form[6] and is being assayed for carcinogenicity.



Since the saturation of the 9,10-double bond of phenanthrene leads to homogeneous succinoylation in the 2-position,[7] this expedient was investigated. 9,10-Dihydro-4,5-methylenephenanthrene (VII) was first prepared in this Laboratory by R. C. Clapp and was found to correspond in spectrum to 9,10-dihydrophenanthrene. As with the parent hydrocarbon,[8] hydrogenation over copper chromite catalyst proceeds at a low

(1) Research Fellow on a grant from the National Cancer Institute.

(2) Kruber, *Ber.*, **67**, 1000 (1934).

(3) Fieser and Hershberg, THIS JOURNAL, **61**, 1272 (1939).

(4) Bachmann and Struve, *J. Org. Chem.*, **4**, 459 (1939).

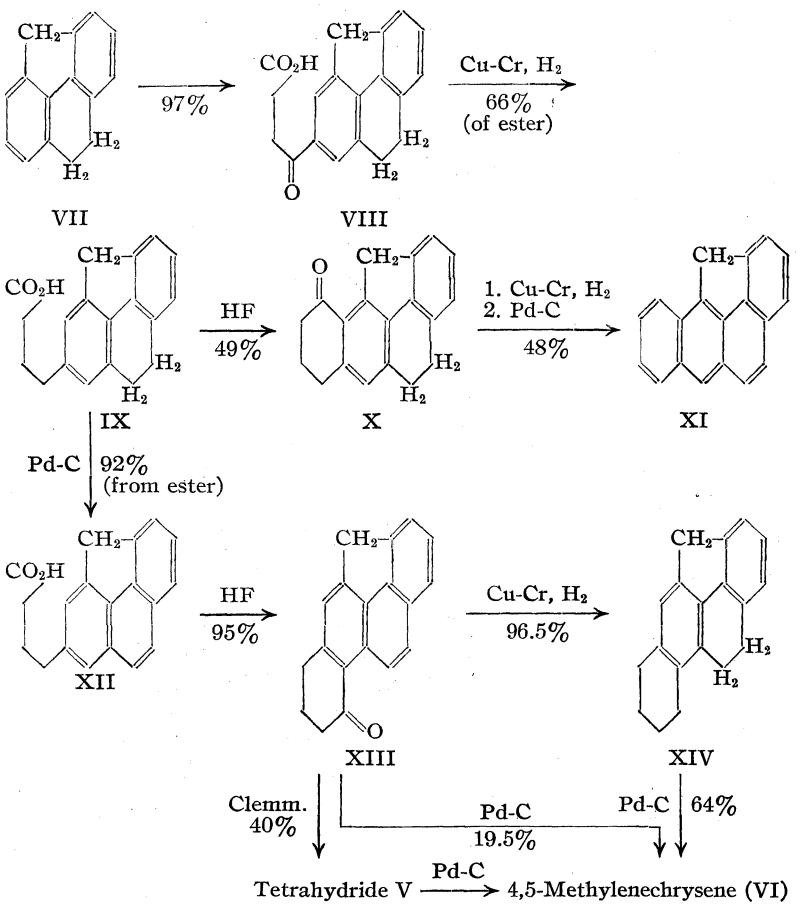
(5) Fieser and Cason, THIS JOURNAL, **61**, 1740 (1939); **62**, 432 (1940).

(6) Fieser and Seligman, *ibid.*, **60**, 170 (1938).

(7) Burger and Mosettig, *ibid.*, **59**, 1302 (1937); Fieser and Johnson, *ibid.*, **61**, 168 (1939).

(8) Burger and Mosettig, *ibid.*, **58**, 1857 (1936); Durland and Adkins, *ibid.*, **59**, 139 (1937); **60**, 1501 (1938).

temperature and affords VII in 85% yield. Succinoylation of the dihydride gave a single keto acid (VIII) in almost quantitative yield and this was reduced most satisfactorily by hydrogenation of an aqueous solution of the sodium salt over copper chromite catalyst. The resulting acid (IX) on cyclization afforded a ketone mixture from which a pure isomer (X) was isolated in only poor yield,



and since either the 1- or the 3-isomer could cyclize in only one direction this is an indication that the compound in question is probably the 2-acid (IX). Reduction of the ketone X by high pressure hydrogenation to a hexahydride followed by dehydrogenation, gave an aromatic hydrocarbon identical with the previously described 1′,9-methylene-1,2-benzanthracene[5] (XI), which proves that the dihydro acid (IX) is either the 2- or the 3-isomer. After this dihydro acid had been dehydrogenated in the form of the ester the aromatized acid (XII) underwent cyclization in a different direction, for the resulting ketone (XIII) on reduction and dehydrogenation afforded a fully aromatic hydrocarbon isomeric with 1′,9-methylene-1,2-benzanthracene. If the acidic side chain were located at the 3-position, cyclization could proceed in only one direction regardless of the degree of hydrogenation, and hence the chain must be attached at the alternate 2-position, as in formulas IX and XII. Since ring closure of the aromatized 2-acid XII does not occur in the 3-position, with the formation of a benzanthracene derivative, the reaction must involve the alternate 1-position and give 4,5-methylenechrysene (VI). The product obtained in this series of experiments was identical with that resulting as the end-product in the first series reported, and the chemical evidence of the structure of the hydrocarbon thus coincides with that derived from spectroscopy. A further inference can be drawn from the fact that the aromatized 2-acid XII of the second series is isomeric and not identical with the acid obtained by the succinoylation of 4,5-methylenephenanthrene and reduction. Since this acid gives rise to the 1,2-ring compounds, V and VI, identical with those from the 2-acid, it can only be the 1-acid (III).

The most practical route to the new 4,5-methylenechrysene is that starting with 9,10-dihydro-4,5-methylenephenanthrene and proceeding through VIII, IX, XII, XIII and XIV, and indeed the reactions all proceed so well that the over-all yield in the six-step synthesis from the hydrocarbon isolated from coal tar is 30%. In the next to last stage of this process the reduction of the carbonyl group of the ketone XIII is accomplished very satisfactorily by hydrogenation over copper chromite catalyst, and under the conditions required for effecting this change the 9,10-double bond is likewise attacked and the resulting hydrocarbon is a hexahydride (XIV). 4,5-Methylenechrysene was also obtained directly by heating the ketone XIII with palladium charcoal, as in a comparable case reported by Fieser and Joshel,[9] but the yield was quite poor.

The orientation of 4,5-methylenephenanthrene

(9) Fieser and Joshel, THIS JOURNAL, 61, 2958 (1939).

in the Friedel and Crafts reaction is quite different from that of the parent hydrocarbon. While phenanthrene is substituted chiefly at the 3-position (50–60%), with the formation of small amounts of the 2-isomers,[10] the 4,5-methylene derivative is attacked chiefly at the 1-position, a difference clearly attributable to the strong para directing influence of the 4-methylene group. This influence is similar to that operative in acenaphthene.

The exclusive 2-substitution of 9,10-dihydro-4,5-methylenephenanthrene parallels exactly the behavior of 9,10-dihydrophenanthrene,[7] the substituent in each case entering an unhindered para position in the diphenyl ring system. The direction of ring closure under the influence of hydrogen fluoride, however, is different in the two series. While γ-(2-phenanthryl)-butyric acid is cyclized largely (78%) in the 3-position,[11] the 2-acid XII undergoes reaction exclusively at the 1-position para to the methylene bridge, and while γ-(9,10-dihydro-2-phenanthryl)-butyric acid is cyclized by hydrogen fluoride solely at position 3,[12] the corresponding acid IX suffers ring closure at the 3-position only to the extent of 49% and evidently much substitution again occurs para to the methylene group. The 4,5-methylene bridge thus constitutes a dominant factor in directing the course of both the inter- and intramolecular acylations of 4,5-methylenephenanthrene.

Experimental Part[13]

β-(4,5-Methylene-1-phenanthroyl)-propionic Acid (II).—A solution of 8 g. of aluminum chloride in 40 cc. of nitrobenzene was cooled in ice and treated with 2.65 g. of powdered succinic anhydride followed by 5 g. of 4,5-methylenephenanthrene, the hydrocarbon being added in half-gram lots with swirling and cooling in ice after each addition. After standing at 5° for seventy-two hours the dark, opaque solution was treated with dilute hydrochloric acid and the solvent was removed with steam. The crude acid, obtained after washing and drying as a brown solid, was treated with Norit in 500 cc. of acetone and crystallized first from 125 cc. of this solvent and then from 150 cc., giving 2.85 g. of almost colorless needles, m. p. 203.5–205° dec. An additional 0.60-g. crop of the same quality was obtained from the mother liquor (total yield 45.4%).

This material consists almost entirely of the 1-acid but contains a trace of isomeric product which could not be separated by direct crystallization. Conversion to the methyl ester with diazomethane or methanol–hydrogen chloride gave material melting at 119–122°, and after four crystallizations from benzene–hexane (1:3) the pure 1-ester was obtained as slender, colorless prismatic needles, m. p. 124.8–125.5°. On systematic working of the mother liquors the yield of pure ester was brought to 60%.

Anal. Calcd. for $C_{20}H_{16}O_3$: C, 78.93; H, 5.29. Found: C, 78.99; H, 5.46.

On saponification of the pure ester and decoloration of the greenish hydrolyzate with Norit, the free acid crystallized from acetone in the form of colorless blades, m. p. 207–208°, dec.

Anal. Calcd. for $C_{19}H_{14}O_3$: C, 78.61; H, 4.86. Found: C, 78.80; H, 4.91.

Attempts to isolate another isomer by crystallization of the residual material as acid, ester, or salt were unsuccessful. The most nearly homogeneous material melted as the ester at 100–103° and as the acid at 178–184°.

On treating the hydrocarbon (1 g.) and succinic anhydride (0.53 g.) with hydrogen fluoride at room temperature for twenty hours there was recovered from the highly tarry reaction mixture 0.07 g. of the 1-acid, m. p. 203–204.5° dec. (no depression with above product), and very little additional acidic material.

γ-(4,5-Methylene-1-phenanthryl)-butyric Acid (III).—This was prepared most conveniently from the crude keto acid II, purification being accomplished more easily after reduction than before. The use of the methyl ester in the Clemmensen reduction was tried without success, the product being non-distillable. The most satisfactory procedure was essentially that of Martin[14]; a small amount of acetic acid[14] seemed better than a large quantity[4] or than none at all.

One gram of keto acid, m. p. 203.5–205° dec., was refluxed for twenty-four hours with 20 g. of amalgamated zinc, 15 cc. of water, 1 cc. of acetic acid, 20 cc. of toluene and a total of 65 cc. of concentrated hydrochloric acid. The crude acidic material was distilled at 2 mm. and converted in benzene solution into its stable **trinitrobenzene derivative.** Three or four crystallizations of this complex gave satisfactory material, m. p. 183.5–184.5°, whereas the free acid could be obtained pure only after seven to ten crystallizations. The recrystallized analytical sample formed yellow blades, m. p. 183.8–184.8°.

Anal. Calcd. for $C_{25}H_{19}O_8N_3$: N, 8.59. Found: N, 8.82.

By systematically working the mother liquors a total of 1.1 g. of pure trinitrobenzene derivative was obtained. This was dissolved in warm benzene and shaken out with sodium carbonate solution. After washing the carbonate extract three times with benzene the acid was precipitated, dried and crystallized from benzene, when it formed colorless plates, m. p. 176.6–177.6°; yield 0.52 g. (55%).

Anal. Calcd. for $C_{19}H_{16}O_2$: C, 82.58; H, 5.83. Found: C, 82.80; H, 6.00.

4,5-Methylene-7-keto-7,8,9,10-tetrahydrochrysene (IV).—The pure acid III (0.5 g.) was mixed with hydrogen

(10) Mosettig and van de Kamp, THIS JOURNAL, **52**, 3704 (1930); Haworth and Mavin, *J. Chem. Soc.*, 1012 (1933).

(11) Fieser and Johnson, THIS JOURNAL, **61**, 1647 (1939).

(12) Fieser and Johnson, *ibid.*, **62**, 575 (1940).

(13) All melting points are corrected. Microanalyses by Lyon Southworth. The 4,5-methylenephenanthrene employed (total used, 22 g.) was that supplied by Dr. O. Kruber of the Gesellschaft für Teerverwertung and melted at 114.4–115.2°.

(14) Martin, THIS JOURNAL, **58**, 1438 (1936).

fluoride (20 g.) and after twenty-two hours the residual reagent was largely removed in a stream of air and the residue was shaken with soda solution and benzene. The collected ketone crystallized from alcohol (Norit) as nearly colorless blades, m. p. 167.5–168.5° (0.42 g., 90%). Two further crystallizations gave a sample forming iridescent flat needles, m. p. 168–169°.

Anal. Calcd. for $C_{19}H_{14}O$: C, 88.34; H, 5.46. Found: C, 88.53; H, 5.43.

On reducing the ketone with aluminum isopropylate and heating the resulting carbinol for one hour with palladium charcoal at 300–320°, a dark product resulted from which only a small amount of impure 4,5-methylenechrysene could be isolated.

4,5-Methylene-7,8,9,10-tetrahydrochrysene (V). (a) From the 7-Ketone IV.—The ketone was reduced by the Clemmensen–Martin method and the product distilled at 2 mm. and crystallized once from alcohol, giving a 59.5% yield of the tetrahydride, m. p. 127.5–128.5°. This did not depress the m. p. of the purified sample described below.

(b) **From the 10-Ketone XIII.**—Following the same procedure, the yield of once crystallized hydrocarbon, m. p. 124–126°, was 40.5%, the lower yield possibly being due to greater hindrance. Six recrystallizations were required to give material of the constant m. p. 129–129.4° (colorless plates).

Anal. Calcd. for $C_{19}H_{16}$: C, 93.40; H, 6.60. Found: C, 93.37; H, 6.76.

The dehydrogenation of V is described below.

4,5-Methylene-9,10-dihydrophenanthrene, VII (with R. C. Clapp).—Fifteen g. of 4,5-methylenephenanthrene was hydrogenated at high pressure over copper chromite catalyst (KAF) at 160° without solvent, one mole of hydrogen being absorbed in about two and one-half hours. The product was separated from catalyst in benzene solution and then treated with Norit in alcohol and crystallized from this solvent. The first crop (12.2 g.) separated as large, colorless plates, m. p. 138–140° and the mother liquor afforded 0.7 g. of satisfactory material (yield 85%). The analytical sample after two more crystallizations from alcohol melted at 140.5–141.2°.

Anal. Calcd. for $C_{15}H_{12}$: C, 93.70; H, 6.30. Found: C, 93.67; H, 6.38.

β-(4,5-Methylene-9,10-dihydro-2-phenanthroyl)-propionic Acid (VIII).—The succinoylation was conducted as described for I, using 6.5 g. of the dihydride VII. A solution of the crude acid in warm sodium carbonate solution was clarified with Norit; the precipitated product was light gray and melted at 218–221°, dec.; yield 9.7 g. (99%). Three crystallizations from acetone gave colorless needles, m. p. 224–224.5°, dec.

Anal. Calcd. for $C_{19}H_{16}O_3$: C, 78.07; H, 5.51. Found: C, 77.99; H, 5.66.

It was found most convenient to isolate the acid in the form of the sodium salt as required for hydrogenation to IX. The carbonate solution obtained as above was treated at the boiling point with saturated sodium chloride solution until crystallization commenced, and the salt which separated on cooling was washed with 10% sodium chloride solution and with acetone. After recrystallization in the same manner the yield of almost completely colorless salt was 10 g. (95%).

The **methyl ester,** prepared by Fischer esterification of the crude acid and crystallized three times from methanol, formed colorless needles, m. p. 137.1–137.4°.

Anal. Calcd. for $C_{20}H_{18}O_3$: C, 78.42; H, 5.91. Found: C, 78.51; H, 6.03.

γ-(4,5-Methylene-9,10-dihydro-2-phenanthryl)-butyric Acid (IX).—A steel pressure bomb was charged with 7.5 g. of the sodium salt of VIII, 1 g. of copper chromite catalyst, 50 cc. of water, and a few drops of dilute sodium hydroxide. Hydrogenation was conducted at high pressure and 200° until two moles of hydrogen had been absorbed (five to ten hours). The product was extracted with warm water and the solution filtered with Super-cel, then with Norit, and the clear tan filtrate acidified, giving 5.0 g. of crude acid, m. p. 145–149°. Distillation at 2 mm. gave satisfactory material, and the analytical sample obtained by one crystallization from benzene–hexane (1:1) consisted of colorless blades, m. p. 154.5–155°.

Anal. Calcd. for $C_{19}H_{18}O_2$: C, 82.00; H, 6.50. Found: C, 81.98; H, 6.70.

Clemmensen–Martin reduction of the keto acid VIII proved less satisfactory, the yield of distilled product being 44%.

The **methyl ester,** prepared by Fischer esterification of the crude acid, was obtained on vacuum distillation as an almost colorless distillate which crystallized immediately on cooling to a solid, m. p. 53–57°; yield 4.6 g. (66% from the keto acid). Four crystallizations from methanol gave colorless plates, m. p. 59.3–60°.

Anal. Calcd. for $C_{20}H_{20}O_2$: C, 82.17; H, 6.88. Found: C, 82.15; H, 7.01.

8-Keto-1′,9-methylene-3,4,5,6,7,8-hexahydro-1,2-benzanthracene (X).—Cyclization of 0.5 g. of IX with hydrogen fluoride was conducted as described for the preparation of IV and the crude ketone was treated with Norit in 50 cc. of alcohol and crystallized from 25 cc. of this solvent. There separated 0.35 g. of large, colorless, feathery plates, m. p. 186–197° dec., which on fractional crystallization afforded 80 mg. of X, m. p. 201–203° dec., and 150 mg., m. p. 196–200° dec.; yield 49%. The m. p. of the top fraction was not altered by recrystallization; the fairly broad m. p. range apparently is due to decomposition.

Anal. Calcd. for $C_{19}H_{16}O$: C, 87.67; H, 6.19. Found: C, 87.54; H, 6.42.

1′,9-Methylene-3,4,5,6,7,8-hexahydro-1,2-benzanthracene was prepared by hydrogenation of 150 mg. of ketone X at high pressure as described below for ketone XIII. Distillation of the crude hydrocarbon gave a nearly colorless crystalline solid, m. p. 78–80°; yield 135 mg. (94.5%). Three crystallizations from alcohol gave 75 mg. of colorless, iridescent blades, m. p. 83–83.5°.

Anal. Calcd. for $C_{19}H_{18}$: C, 92.65; H, 7.35. Found: C, 92.78; H, 7.71.

1′,9-Methylene-1,2-benzanthracene (XI).—The mother liquors from the crystallization of the above hexahydride were evaporated to dryness and the residue, together with 50 mg. of pure material, was heated with 15 mg. of palladium charcoal for thirty minutes each at 220–265° and at 265–300° and finally for ten minutes at 300–320°.

After distillation, the pinkish material was converted to the picrate and this was crystallized twice from alcohol in the presence of excess picric acid and then decomposed by passage in benzene through a tower of alumina and Super-cel. Crystallization from alcohol then gave 50 mg. of 1′,9-methylene-1,2-benzanthracene, m. p. 120–121°, which formed a brilliant orange trinitrobenzene derivative, m. p. 161.5–162°. These two substances gave no depression when mixed with authentic samples.[5]

γ-(4,5-Methylene-2-phenanthryl)-butyric Acid (XII).—A mixture of 5.25 g. of the distilled methyl ester of γ-(4,5-methylene-9,10-dihydro-2-phenanthryl)-butyric acid (IX) and 0.60 g. of palladium charcoal was heated at 200–240° for thirty minutes, at 240–250° for thirty minutes, and at 250–265° for thirty-five minutes. The catalyst was removed by filtering a solution of the product in benzene and the ester was distilled at 2 mm., giving 5.05 g. of colorless distillate which soon solidified, m. p. 32.5–34.5°. A sample of this **methyl ester** when crystallized twice from methanol formed colorless, iridescent plates, m. p. 36.3–37.3°.

Anal. Calcd. for $C_{20}H_{18}O_2$: C, 82.74; H, 6.23. Found: C, 82.81; H, 6.56.

For saponification the ester was refluxed for forty-five minutes with 25 cc. of 1 *N* alcoholic potassium hydroxide and the solution was poured into 500 cc. of water (clear solution) and acidified. The light tan precipitated product (4.7 g.; m. p. 164–166°) was clarified in benzene and crystallized from 75 cc. of benzene and 50 cc. of hexane. After collecting a first crop of 4.4 g. of plates, m. p. 167–167.6°, the mother liquor afforded material which after two recrystallizations melted at 164–165.5° (0.10 g.); total yield 92%, from the dihydro ester. A sample crystallized twice more from benzene–hexane formed colorless blades and plates, m. p. 167.7–168.0°.

Anal. Calcd. for $C_{19}H_{16}O_2$: C, 82.58; H, 5.83. Found: C, 82.84; H, 6.10.

10 - Keto - 4,5 - methylene - 7,8,9,10 - tetrahydrochrysene (XIII).—Cyclization of 4.4 g. of the acid XII was conducted in hydrogen fluoride (120 g.) for sixteen hours and the product was isolated as described for the isomeric ketone IV, giving 3.70 g. of pale yellow plates, m. p. 171.5–173°, and 0.19 g., m. p. 169.5–171°; yield 95%. Two more crystallizations from alcohol gave highly iridescent plates with a yellowish reflex, m. p. 173–174°.

Anal. Calcd. for $C_{19}H_{14}O$: C, 88.34; H, 5.46. Found: C, 88.18; H, 5.69.

4,5 - Methylene - 7,8,9,10,11,12 - hexahydrochrysene (XIV).—One gram of the 10-ketone XIII in 7 cc. of absolute alcohol was hydrogenated at 160° under high pressure in the presence of 0.10 g. of copper chromite catalyst. The reaction proceeded rapidly and in less than one hour three moles of hydrogen had been absorbed; the absorption then became quite slow and the reaction was stopped. Distillation of the collected product gave 0.92 g. (96.5%) of almost colorless material which softened at 105° and melted at 110–115°. After three crystallizations from alcohol, the hydrocarbon formed clusters of colorless blades, m. p. 116.6–117.2°.

Anal. Calcd. for $C_{19}H_{16}$: C, 92.65; H, 7.35. Found: C, 92.63; H, 7.52.

4,5-Methylenechrysene (VI). (a) From the Hexahydride XIV.—The hexahydride (920 mg.) was heated with palladium charcoal (100 mg.) in a bath initially at 220°. The temperature was gradually raised to 265° in the course of one hour and held at 265–270° for fifty minutes. After separation from the catalyst the hydrocarbon was conveniently isolated as the trinitrobenzene derivative. Two crystallizations from alcohol gave 1.21 g. of complex, m. p. 193.5–194.5°, which was decomposed by reduction with stannous chloride. An initial crystallization of the recovered hydrocarbon from alcohol gave 480 mg., m. p. 172.4–172.9°, and 90 mg., m. p. 170–170.8°; total yield 64%. The compound crystallizes in highly iridescent colorless plates, many of them diamond shaped. Both the solid and its solutions show a violet fluorescence in daylight and give a particularly intense violet in ultraviolet light.

Anal. Calcd. for $C_{19}H_{12}$: C, 94.96; H, 5.04. Found: C, 95.10; H, 5.09.

The **trinitrobenzene derivative** crystallizes from alcohol in bright orange needles, m. p. 194–195°.

Anal. Calcd. for $C_{25}H_{15}O_6N_3$: N, 9.27. Found: N, 9.08.

The **picrate** forms bright red, flat needles from alcohol but is rather unstable.

(b) From the Tetrahydride V.—Dehydrogenation of 150 mg. of V with 20 mg. of palladium charcoal at 250–265° for one hour gave, after distillation of the product and crystallization from alcohol, 45 mg. of VI, m. p. 171.5–172.3°, and 12 mg., m. p. 169–170.2° (54.5%, no depression with above sample).

(c) From the 10-Ketone XIII.—A sealed Pyrex tube containing 200 mg. of XIII and 25 mg. of palladium charcoal was heated at 275–285° for six hours. (The yield was slightly lower on heating at 315° for three hours or at 265° for two hours.) The material was dissolved in benzene and the filtered solution passed through a column of alumina and Super-cel (1:1). In ultraviolet light the filtrate was brilliantly fluorescent and a yellow zone appeared at the top of the column, followed by a blue zone. The product recovered from the filtrate on distillation at 2 mm. gave 80 mg. of colorless crystalline distillate. Two crystallizations from alcohol afforded 45 mg. of hydrocarbon, m. p. 167–168.5°, which was combined with similar material from other runs and recrystallized four times. By systematic working of the mother liquors, with use of the trinitrobenzene derivative, there was obtained in all a 19.5% yield of pure 4,5-methylenechrysene, m. p. 172–172.5°, which gave no depression when mixed with the above samples.

Summary

By the Friedel and Crafts condensation of 4,5-methylenephenanthrene with succinic anhydride the 1-keto acid is obtained in 45% yield and affords a suitable intermediate for the synthesis of the new 4,5-methylenechrysene. 9,10-Dihydro-4,5-methylenephenanthrene undergoes succinoylation exclusively in the 2-position, and after reduction ring closure can be effected at the 3-position, providing in moderate yield a ketone

which can be converted into the known 1′,9-methylene-1,2-benzanthracene. γ-(4,5-Methylene-2-phenanthryl)-butyric acid is obtained in good yield by dehydrogenating the dihydro intermediate as the ester and it cyclizes exclusively at position 1, affording a very satisfactory route to 4,5-methylenechrysene in which the over-all yield from 4,5-methylenephenanthrene is 30%.

The structures of the different products are fully established by the transformations indicated.

In all of the inter- and intramolecular acylations observed in the 4,5-methylenephenanthrene series a strong para directive influence of the 4-methylene group is discerned.

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RECEIVED MARCH 20, 1940

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, NO. 221]

Certain Trialkylated Benzenes and their Compounds with Aluminum Chloride and with Aluminum Bromide

BY JAMES F. NORRIS AND JOHN N. INGRAHAM[1]

In a recent paper[2] methods were described for the preparation, with high yields, of mesitylene and *s*-triethylbenzene by the Friedel–Crafts reaction. By the use of similar conditions toluene and *m*-xylene were ethylated and methyldiethyl- and dimethylethylbenzene were prepared. It seemed highly probable that these hydrocarbons had the symmetrical structure, although the properties of some of their derivatives were not in accord with those recorded in the literature for the symmetrical hydrocarbons.[3]

The ethyldimethylbenzene has been restudied and additional evidence is presented in favor of the symmetrical structure of the hydrocarbon.

In the paper by Norris and Rubinstein results were given of the study of the product formed from toluene, aluminum bromide and hydrogen bromide. Since Gustavson[4] has reported that the compound containing *s*-triethylbenzene and aluminum bromide is a crystalline solid, the investigation of this substance was undertaken. It was formed by passing hydrogen bromide into a solution of aluminum bromide in the hydrocarbon. Heat was generated and a light red oil separated from the excess of hydrocarbon. When cooled the compound formed yellow crystals which melted at 64–66°. Analyses of the crystals gave results which checked with the formula proposed by Gustavson: $Al_2Br_6 \cdot 2C_6H_5(C_2H_5)_3 \cdot HBr$. The complex was held at 0.002 mm. pressure at room temperature. When it came to constant weight the residue was shown by analysis to contain the Al_2Br_6 and hydrocarbon in the ratio of 1 to 1.

When the crystalline complex was treated with acetyl chloride, the yield of methyltriethylphenyl ketone was 67%.

An attempt was made to prepare a compound having the formula $Al_2Br_6 \cdot 2C_6H_3(C_2H_5)_3 \cdot HCl$ by passing hydrogen chloride into a solution of the bromide in the hydrocarbon. Analyses of the product from time to time showed that the bromine in aluminum bromide was being replaced by chlorine. When aluminum chloride and the hydrocarbon were treated with hydrogen bromide, the chlorine was replaced and the complex containing aluminum bromide was formed.

A crystalline complex having the formula $Al_2Cl_6 \cdot 2C_6H_3(C_2H_5)_3 \cdot HCl$ was isolated. The complex prepared from mesitylene had the formula $Al_2Br_6 \cdot 3C_6H_3(CH_3)_3 \cdot HBr$ (m. p. 47–48°). When held at 0.002 mm. to constant weight the residue contained Al_2Br_6 and $C_6H_3(CH_3)_3$ in the molecular ratio 1:1.

The complex with pseudocumene contained three moles of hydrocarbon. The complex with benzene and aluminum bromide was very unstable. When held at 12 mm. pressure, nearly all the benzene was lost.

The complex prepared from toluene and aluminum bromide when held at 12 mm. to constant weight left a residue which contained one mole of the hydrocarbon to one of Al_2Br_6. When held at 0.002 mm., it lost nearly all the hydrocarbon. The compounds containing trimethyl and triethyl benzene (ratio to Al_2Br_6 1:1) were stable at this

(1) From a part of the thesis of John N. Ingraham submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy, 1938.

(2) Norris and Rubinstein, THIS JOURNAL, **61**, 1163 (1939).

(3) Jacobson, *Ber.*, **7**, 1430 (1874); Tohl and Geyger, *ibid.*, **25**, 1533 (1895).

(4) Gustavson, *Compt. rend.*, **140**, 940 (1905).

pressure. The results show that the stability of the complexes increases as the number of alkyl groups present increases.

Details of Experiments

Dimethylethylbenzene.—The hydrocarbon was prepared by the method of Norris and Rubinstein except that *m*-xylene, furnished by the du Pont Company, which contained less than 1% of isomers was used instead of commercial "metaxylene." The product, after fractionation only, boiled at 184–184.6°. The crude tribromo derivative melted at 86.5–88°, and after repeated recrystallization at 87–89°. Distillation in a molecular still did not change the melting point. The trinitro compound melted at 114–116° (uncor.). Oxidation of the hydrocarbon gave a mixture of acids from which the monobasic acid was recovered by steam distillation; it melted at 161–162° (uncor.). The melting point of 3,5-dimethylbenzoic acid is 165° (cor.) and that of the 2,4-isomer is 124°.

A sample of the crude hydrocarbon was sulfonated, hydrolyzed and distilled. There were obtained 6 cc. at 182–184°, 21 cc. at 184.0°, and 6 cc. at 184–185.6°. The fraction boiling at 184.0° (total immersion thermometer, pressure, 752 mm.) was redistilled without change in boiling point. The index of refraction taken of the distillate, from time to time, remained constant. The tribromo derivative melted at 89–89.5° and the trinitro derivative at 117–117.6°. The hydrocarbon was analyzed. Calcd.: C, 89.55; H, 10.45. Found: C, 90.35, 90.18, 89.66; H, 10.47, 10.46, 10.23.

A sample of the hydrocarbon was converted into the sulfonamide, which was crystallized; it melted at 123.0–123.6° (literature 126°). The hydrocarbon was recovered from the sulfonamide by hydrolysis and converted into the tribromo derivative, which melted at 88.0–88.5°, and the trinitro derivative which melted at 115–116°.

1,3-Dimethyl-4-ethylbenzene.—This compound has been prepared by a number of investigators, but the constants of its derivatives are not in good agreement. We prepared it by condensing pure *m*-xylene with acetyl chloride at 0° with aluminum chloride in the presence of carbon disulfide, and subsequent reduction of the ketone formed.

The hydrocarbon boiled at 187.8° (total immersion thermometer) and gave a tribromide derivative (m. p. 81–82°) and a trinitro derivative (m. p. 119–120°). The monobasic acid formed by oxidation melted at 123.5–124.0° (uncor.), the melting point of 2,4-dimethylbenzoic acid. The boiling points given in the literature for the hydrocarbon vary from 183 to 187°; the melting points of the tribromo derivative from an oil to 135° and of the trinitro derivatives from 119–127°. The sulfonamide was found by four investigators to melt at 148°. It was evident that our hydrocarbon was not 1,3-dimethyl-4-ethylbenzene.

Complexes Containing Aluminum Halides and *s*-Triethylbenzene.—In the preparation and manipulation of the complexes precautions were taken to exclude moisture. The aluminum bromide used was distilled in an all glass vessel into the tube in which the complex was made. The tube was then sealed off from the distilling apparatus. The compounds were manipulated, when necessary, in a stream of dry nitrogen.

Analyses of a complex were made by melting the latter, and drawing up a sample into a pipet. The liquid was run into a small flask of known weight, which was weighed again. The weight of complex used was about 1.5 g. Water and ice were added and the flask stoppered. During the decomposition of the complex the flask was kept in cold water. The aqueous solution was diluted to a definite volume, a part of which was titrated with standard alkali, using phenolphthalein as indicator, for the determination of acid. It was shown that the bromine in aluminum bromide could be accurately determined in this way. The solution was next treated with a slight excess of ammonia and heated. The aluminum hydroxide was separated and ignited. The amount of hydrocarbon in the complex was determined by decomposing it in a small Babcock bottle. Enough water was added to bring the hydrocarbon into the graduated neck of the bottle, which was then placed in a centrifuge to ensure complete separation of the two liquids. The volume of the hydrocarbon measured on the standardized scale gave results from which could be calculated the weight. In most of the analyses the complex was decomposed in the Babcock bottle and the same sample used for the determination of aluminum, halogen, and hydrocarbon. The total of the percentages obtained served as a check on the accuracy of the analysis. With the samples that contained both chlorine and bromine the halogens were determined, in separate portions of the solution, by precipitation with silver nitrate and by neutralization with an alkali.

The Complex $Al_2Br_6 \cdot 2C_6H_3(C_2H_5)_3 \cdot HBr$. Preparation and Analysis.—About 25 cc. of the complex was made by passing hydrogen bromide into a solution of aluminum bromide in *s*-triethylbenzene. Heat was generated and a red oil began to separate at once. When precipitation was complete the product changed to a mass of yellow crystals which melted at 64–66°. Without further treatment two samples were analyzed (Sample 1). The complex was washed with petroleum ether, the excess of the latter removed and the product held under diminished pressure (15 mm.) for five minutes (Sample II). A complex was made by forming it from a mixture of equal volumes of petroleum ether and the hydrocarbon. It separated as a fluffy precipitate, from which the liquid was poured off. It was washed with petroleum ether, dried by evacuation and analyzed (Sample III). The results are given in Table I. The duplicate analyses of each sample were made on different samples.

TABLE I

Sample	Al, %	Br, %	Hydrocarbon, %	Molecular ratios Al	Br	Hydrocarbon
I	5.94	61.23	32.13	1	3.46	0.9
	5.99	61.23	32.48			
II	5.97	61.23	32.64	1	3.45	.9
	6.03	61.28	32.52			
III	5.54	59.23	34.01	1	3.56	1.0
	5.75	59.60	34.55			
Calculated for $Al_2Br_6 \cdot 2C_6H_3(C_2H_5)_3 \cdot HBr$				1	3.5	1

Behavior under Reduced Pressure.—A sample of the complex which weighed 7.547 g. was held at room temperature and 0.002 mm. pressure of mercury, and weighed

at intervals. At the end of two hours the loss in weight was 0.273 g. Constant weight was reached in forty-five hours, when the loss was 1.775 g. The theoretical loss in weight should have been 1.823 if the residue had the compostion $Al_2Br_6 \cdot C_6H_3(C_2H_5)_3$. The residue was analyzed. The molecular ratio found was Al, 1, Br, 3.06, $C_6H_3(C_2H_5)_3$, 0.48.

Reaction of the Complex with Acetyl Chloride.—A mixture of 19.6 g. of complex and 6 cc. of acetyl chloride (molecular ratio 1 to 2) was allowed to stand in an ice-bath for two hours. After decomposition with water the oil was dried and distilled. The product solidified when cooled and melted at −17°. The yield of the mono-acetyl derivative of *s*-triethylbenzene was 5.5 g. (67%).

Reaction of the Complex with Ethyl Bromide.—A cold saturated solution of the complex in ethyl bromide was treated with petroleum ether; an oil was formed which crystallized when cooled with dry-ice. The oil was separated, held at 15 mm. pressure to remove solvent and analyzed. The sample used melted at about −20°. Bromine and aluminum were determined in the usual way. The liquid formed by decomposition with water was a mixture of triethylbenzene and ethyl bromide. To determine the amount of ethyl bromide present, the index of refraction of the mixture was determined and compared with a plot of the indexes of known mixtures of ethyl bromide and the hydrocarbon. The molecular ratios found were Al 1, Br 3.7, triethylbenzene 1.17, ethyl bromide 0.46. These results have led to further study. If the complex containing ethyl bromide is heated slightly above room temperature it decomposes with the evolution of hydrogen bromide.

Reaction of the Complex with Hydrogen Chloride.—An attempt was made to prepare a complex with the formula $Al_2Br_6 \cdot 2C_6H_3(C_2H_5)_3 \cdot HCl$ by passing hydrogen chloride into a solution of aluminum bromide in the hydrocarbon. At the end of ten minutes, when the reaction appeared to be complete, the product was washed and the vessel containing it was evacuated. The molecular ratios found were Al 1, Br 2.4, Cl 1.25, $C_6H_5(C_2H_5)_3$ 1.01. The result showed that bromine was being replaced by chlorine. The preparation was repeated and hydrogen chloride passed through the mixture for five hours. The product melted at 48–49° and an analysis gave the ratios: Al 1, Br 0.4, Cl 3.3, $C_6H_5(C_2H_5)_3$ 0.99. Repeated efforts failed to obtain a product free from bromine. It appears probable that the bromine of the aluminum bromide alone is replaced and not that in the hydrogen bromide in the complex. The molecular ratios in such a compound are: Al 1, Br. 0.5, Cl 3, $C_6H_5(C_2H_5)_3$ 1.

The product obtained as above was treated with hydrogen bromide. The mole ratios found were Al 1, Br 3.6, Cl 0, $C_6H_5(C_2H_5)_3$ 0.9. All the chlorine that had replaced bromine was removed from the compound.

Purity of the Triethylbenzene Recovered from Complexes.—It was found that the hydrocarbon recovered from complexes which had stood for not longer than two days had the correct index of refraction. In the case of the evacuation experiments which continued for several days, the index was about 0.0050 too high. Samples of the hydrocarbon from these experiments were combined and fractionated (180 cc.). A small amount of low- and high-boiling hydrocarbons was obtained along with 145 cc. of *s*-triethylbenzene which boiled at 215.4°.

The Complex $Al_2Cl_6 \cdot 2C_6H_3(C_2H_5)_3 \cdot HCl$.—Freshly sublimed aluminum chloride was covered with the hydrocarbon and hydrogen chloride was passed into the mixture. An oil was formed rapidly and on cooling changed to crystals that melted at 48–49°. The compound on analysis gave the following results: Al 8.66, 8.55%; Cl 40.33, 39.78%; $C_6H_5(C_2H_5)_3$ 52.85, 52.78. Calcd.: Al 8.60, Cl 39.66, $C_6H_5(C_2H_5)_3$ 51.69. The mole ratios found were Al 1, Cl 3.54, $C_6H_5(C_2H_5)_3$ 1.01.

The Complex Containing Mesitylene.—Experiments showed that apparently more than one complex was formed from mesitylene. Products were obtained in which the molecular ratios of the constituents changed when varying amounts of aluminum bromide and the hydrocarbon were used. When a large excess of the hydrocarbon was used the crystalline material obtained after cooling the reaction product was washed with petroleum ether and the vessel containing it was evacuated. The molecular ratios found were Al 1, bromine 3.6, $C_6H_3(CH_3)_3$ 1.6. These results are in fair agreement with the formula $Al_2Br_6 \cdot 3C_6H_3(CH_3)_3 \cdot HBr$. There was evidence of the formation of a complex which contained less of the hydrocarbon. The problem will be considered in a later paper.

The complex was treated with hydrogen chloride; a large percentage of the bromine was replaced by chlorine. The vessel containing a sample of the complex (10.22 g.) was evacuated to constant weight at 0.002 mm. in one hundred thirty-six hours. The loss in weight was 50%. If the residual compound had the composition $Al_2Br_6 \cdot C_6H_3(CH_3)_3$ the loss in weight would have been 52%. The hydrocarbon recovered from the complex after evacuation had the index of refraction $n^{14.7}D$ 1.5059 (literature for mesitylene at this temperature 1.4966 and for pseudocumene 1.5072). It was evident that on long standing the hydrocarbon had undergone a change.

Complex Containing Pseudocumene.—This was prepared in the usual way from the pure hydrocarbon. It separated as a red oil, which lost about one-fourth of its volume when washed with petroleum ether. When cooled in running water crystals were formed. The analysis gave the ratios Al 1, Br 3.44, $C_6H_3(CH_3)_3$ 1.5, which is in good agreement with the formula $Al_2Br_6 \cdot 3C_6H_3(CH_3)_3 \cdot HBr$.

Complex Containing Toluene.—The amounts of hydrogen bromide required to precipitate the complex containing aluminum bromide and toluene were determined. When the amounts of hydrogen bromide and aluminum bromide (Al_2Br_6) were in the ratio 1:1, precipitation was complete. With smaller amounts of hydrogen bromide the amount of precipitated oil decreased as the hydrogen bromide decreased. In these cases the addition of more hydrogen bromide brought about complete precipitation. The experiments confirm the view that the toluene complex contains aluminum bromide (Al_2Br_6) and hydrogen bromide in the ratio 1:1.

Complex Containing Benzene.—The complex was evidently very unstable and the analyses made did not fit accurately any definite molecular ratios. The precipitated oil gave the molecular ratios Al 1, Br 3.2, C_6H_6 3.05. An analysis of a second preparation gave 1:3.2:3.15.

These results indicate that the ratio of Al_2Br_6 to C_6H_6 is 1:6 and that the complex contains some hydrogen bromide.

When the oil was shaken with petroleum ether it decreased in volume. The residual oil gave on analysis the ratios Al 1, Br 2.9, C_6H_6 0.63. It appeared that the product contained Al_2Br_6 and C_6H_6 in the ratio 1:1.

The vessel containing a sample of the original oil was evacuated at 12 mm. Crystals soon appeared. This behavior is different from that of the complexes formed from the other hydrocarbons which gave no crystals but left a product containing the bromide and the hydrocarbon. The crystals appeared to be aluminum bromide. When 18.2 g. of the complex was held under diminished pressure, in about three hours the residue weighed 8.8 g., which is very close to the weight of the aluminum bromide in the complex.

In a second experiment the complex was held at 12 mm. for four hours and then at 0.002 mm. The loss at the latter pressure was 0.01 g. The residue was slightly impure aluminum bromide. The sum of the percentages of aluminum and bromine was 94.4%.

Summary

1. The ethyldimethylbenzene prepared by the Friedel and Crafts reaction from ethyl bromide and *m*-xylene has been restudied and evidence given that the hydrocarbon has the symmetrical structure.

2. The preparation and properties of complexes of certain aromatic hydrocarbons and aluminum bromide or aluminum chloride are described.

CAMBRIDGE, MASS. RECEIVED FEBRUARY 10, 1940

NOTES

Reaction between a Highly-Substituted Bromopyridine and Lithium

BY C. F. H. ALLEN AND G. F. FRAME

In view of the increasing interest in organometallic heterocyclic compounds[1] it seems advisable to record that lithium reacts slowly with the highly-substituted 2-bromo-3,4,6-triphenylpyridine. The resulting suspension does not seem to react with carbon dioxide, aldehydes, or ketones. Upon decomposition by acids, a 20–25% yield of 2,4,5-triphenylpyridine can be secured by distilling in a high vacuum. No conditions were found under which the highly-substituted 2,3,5-triphenyl-4-bromofuran would react with lithium. Neither of these substances reacts with magnesium.[2]

In the usual apparatus, swept by nitrogen, a mixture of 50 cc. of dry ether, 0.5 g. of lithium, and 13.8 g. of 2-bromo-3,4,6-triphenylpyridine was refluxed with stirring for four hours. A slow reaction was noted and the solution became a deep reddish-brown. After standing for several days practically all the metal had disappeared. The ether layer, which separated after adding iced hydrochloric acid, was removed, washed, dried, and the solvent evaporated. After efforts to induce crystallization had failed, the thick oil (1.2 g.) was distilled at 1.2–2 microns; a black tarry residue remained. The clear distillate (1.8 g.) crystallized when rubbed with alcohol. 2,4,5-Triphenylpyridine crystallizes in glistening, slightly iridescent rods, m. p. 112°, readily soluble in alcohol, ether and benzene.

Anal. Calcd. for $C_{23}H_{17}N$: N, 4.6. Found: N, 4.5.

EASTMAN KODAK COMPANY
ROCHESTER, N. Y. RECEIVED FEBRUARY 20, 1940

(1) Gilman and Spatz, THIS JOURNAL, **62**, 446 (1940).
(2) Allen and Rosener, *ibid.*, **49**, 2113 (1927).

The Carbonation of Organoalkali Compounds

BY HENRY GILMAN AND H. A. PACEVITZ

The kind and ratio of products obtained by carbonation of organometallic compounds are influenced markedly by the rate and temperature of carbonation. With organolithium compounds,[1] in particular, low temperature together with a large excess of carbon dioxide (conditions realized by pouring RM compounds jet-wise on crushed solid carbon dioxide) give predominantly the acid and little of the ketone or tertiary alcohol. Furthermore, carbonation by solid carbon dioxide depresses markedly the formation of malonic acids from benzylmetallic types. This is strikingly illustrated in studies submitted recently[2] with compounds like benzylsodium, benzylpotassium and 3,5-dimethylbenzylpotassium. These RM compounds when carbonated by solid carbon dioxide give almost exclusively the corresponding carboxylic acids; however, carbonation by gaseous

(1) Gilman and Van Ess, THIS JOURNAL, **55**, 1258 (1933). See, also, Gilman and Parker, *ibid.*, **46**, 2816 (1924).
(2) Gilman, Pacevitz and Baine, *ibid.*, **62**, June (1940).

carbon dioxide gives, in addition to the expected carboxylic acids, significant quantities of the malonic acids. The malonic acids probably owe their formation largely to a secondary metalation reaction of the active methylene group by the unused RM compound present in slow carbonation. The typical transformations may be illustrated by the studies of Ivanoff and Spassoff[3] with benzylmagnesium chloride.

$$C_6H_5CH_2MgCl + CO_2 \longrightarrow C_6H_5CH_2CO_2MgCl$$

$$C_6H_5CH_2CO_2MgCl + C_6H_5CH_2MgCl \longrightarrow [C_6H_5CHCO_2MgCl][MgCl] + C_6H_5CH_3$$

$$[C_6H_5CHCO_2MgCl][MgCl] + CO_2 \xrightarrow{[H_2O]} C_6H_5CH(CO_2H)_2$$

Our carbonation experiments with benzylalkali types[2] raise a question concerning benzylidene-dialkali compounds like $C_6H_5CHM_2$. If such compounds are formed in one way or another incidental to the several procedures[2] for the preparation of benzylalkali compounds, then it is possible, but somewhat unlikely, that they are not carbonated by solid carbon dioxide. We are at present of the opinion that they are either not formed or are formed to a subordinate extent, incidental to the preparation of benzylalkali types.

Of more immediate interest are the aliphatic types, $RCHM_2$, like amylidene-disodium.[4] From the experiments now reported, we find that the organosodium compound or compounds formed by interaction of *n*-amyl chloride and sodium give largely caproic acid with very little *n*-butylmalonic acid when carbonation is effected by solid carbon dioxide; and a mixture of caproic acid with large amounts of *n*-butylmalonic acid when gaseous carbon dioxide is used. Additional experiments may provide an answer to the question as to whether secondary metalations or other transformations, some of which have been reported,[4] are responsible for the reactions of compounds of benzylidene-dimetallic and amylidene-dimetallic types.

Experimental Part

In a typical experiment, a solution of 16.5 g. (0.155 mole) of freshly distilled *n*-amyl chloride (b. p., 107–108°) in 15 cc. of petroleum ether (b. p. 85–100°) was added dropwise over a one-hour period to 8.75 g. (0.38 g. atom) of sodium sand in 75 cc. of petroleum ether. The mixture was stirred at room temperature for four hours, after which it was carbonated by pouring jet-wise on solid carbon dioxide, the addition being completed within ten seconds. The products obtained (by isolation and weighing) were 6.9 g. or 38.5% of caproic acid and less than 1% of impure *n*-butylmalonic acid. In a check experiment on this carbonation by solid carbon dioxide the yield of *n*-caproic acid was 7.3 g. or 40.8%; and the yield of impure *n*-butylmalonic acid was again less than 1%. In a parallel experiment in which carbonation was effected by admitting gaseous carbon dioxide to the surface of the reaction mixture over a five-hour period at 27–28° and with stirring, the yield of *n*-caproic acid was 2.72 g. or 15.2%; and the yield of *n*-butylmalonic acid was 2.1 g. or 16.9%.

Again using the same quantities of reagents, two parallel experiments were carried out by first stirring at 27–28° for one hour and then at 42° for two hours. Rapid carbonation (solid carbon dioxide, ten seconds) yielded 6.52 g. or 36.4% of *n*-caproic acid, and less than 1% of impure *n*-butylmalonic acid. Slow carbonation (gaseous carbon dioxide, five hours) yielded 3.53 g. or 19.5% of *n*-caproic acid, and 1.83 g. or 14.8% of *n*-butylmalonic acid.

Acting on the suggestion that low boiling petroleum ether might give different results, parallel experiments were carried out with purified petroleum ether distilling over the range 28–38°. Rapid carbonation (solid carbon dioxide, five to ten seconds) yielded 51.5% of caproic acid and less than 2% of *n*-butylmalonic acid. Slow carbonation (gaseous carbon dioxide, four hours) yielded 17.3% of caproic acid and 31.4% of *n*-butylmalonic acid.

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(3) Ivanoff and Spassoff, *Bull. soc. chim.*, **49**, 19 (1931). See, also, Morton, Fallwell and Palmer, THIS JOURNAL, **60**, 1426 (1938), for the carbonation of benzylsodium.

(4) Morton and Richardson, *ibid.*, **62**, 129 (1940). Earlier references are to be had from this most recent article.

Agaric Acid and the Donnan Theory of Membrane Equilibrium

BY R. J. HARTMAN, E. W. KANNING AND J. E. WEBER[1]

The electromotive force of the following cell was measured at 25°.

Calomel electrode	Satd. KCl	Outside solution: dilute HCl	"Parlodion" membrane	Inside solution: agaric acid, 1.25%; $Ca(OH)_2$ or HCl, in varying quantities	Satd. KCl	Calomel electrode

The agaric acid was prepared by electrodialyzing "Noble Difco" agar agar for twenty-four hours under a potential of 110 volts according to the procedure of Hoffman and Gortner.[2] The procedure followed in making the electromotive force measurements was essentially the same as that used by Loeb.[3] After about twenty-four hours a true membrane equilibrium was established as

(1) This paper is constructed from a dissertation presented by Joseph Elliott Weber to the Faculty of the Graduate School of Indiana University in partial fulfillment of the requirements for the degree of Doctor of Philosophy in Chemistry.

(2) Hoffman and Gortner, *J. Biol. Chem.*, **65**, 371 (1925).

(3) J. Loeb, "Proteins and the Theory of Colloidal Behavior," Chapter XI, McGraw-Hill Book Co., New York, N. Y., 1924, p. 177.

TABLE I

MEMBRANE AND HYDROGEN ELECTRODE POTENTIALS FOR THE SYSTEM, AGARIC ACID/HYDROCHLORIC ACID

N $Ca(OH)_2$ in 50 ml. of agaric acid solution, ml.	Milliequivalents HCl in 50 ml. of agaric acid solution	Original pH	Final pH outside	Final pH inside	pH Out − pH In	H_2 elect. potential, mv.	Measured potential, mv.
50.0	..	3.95	4.00	3.93	0.07	4.1	3.85
25.0	..	3.64	3.73	3.64	.09	5.3	5.24
10.0	..	3.28	3.38	3.28	.10	5.9	6.00
6.0	..	3.13	3.26	3.14	.12	7.1	6.85
4.0	..	3.06	3.20	3.06	.14	8.3	8.59
3.0	..	3.02	3.19	3.03	.16	9.5	8.92
2.0	..	2.97	3.00	2.91	.09	5.3	4.82
1.0	..	2.70	2.71	2.68	.03	1.8	2.09
0.5	..	2.66	2.69	2.67	.02	1.2	1.16
..	0.0	2.48	2.48	2.47	.01	0.6	0.92
..	0.5	1.79	1.80	1.78	.02	1.2	.88
..	1.0	1.42	1.47	1.41	.06	3.6	1.19
..	2.0	1.20	1.23	1.20	.03	1.8	1.59
..	3.0	1.09	1.10	1.04	.06	3.6	2.85
..	4.0	1.01	1.02	0.94	.08	4.7	4.85
..	5.0	0.98	0.99	.91	.08	4.7	4.15
..	6.0	.94	.95	.90	.05	3.0	2.99
..	10.0	.72	.73	.71	.02	1.2	1.05
..	12.0	.71	.72	.70	.02	1.2	1.07

is shown in Table I where the observed P. D. (Measured Potential) is found to be in reasonably good agreement with the hydrogen electrode potential calculated from the pH values of the two solutions (measured at the end of the experiment). The membrane potential thus obtained arises from the unequal distribution of H^+ and Cl^- on opposite sides of the membrane. Tests of the hydrogen chloride solution revealed that neither Ca^{++} nor agarate ions passed through the membrane in detectable quantities.

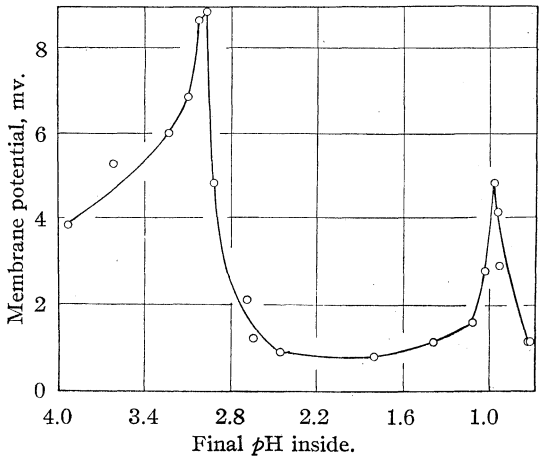

Fig. 1.—Relationship between pH and membrane potential.

When the final pH inside is plotted against the measured membrane potential, two maxima are found at pH values of approximately 3.0 and 1.0 (see Fig. 1). The second maximum is attributed to the hydrolytic decomposition of the agar. Since the membrane potential of such systems is a colligative property depending upon the number of discrete discontinuities of the dissolved constituent present, it is to be expected that the membrane potential will vary as a function of the concentration of the osmotically active particles. Agaric acid, a polyuronide, yields uronic acid units and reducing sugars.[4] Therefore, a second equilibrium is to be expected at pH values of approximately 1.0 where the agar complex is known to hydrolyze into simpler units.

(4) A. G. Norman, "The Biochemistry of Cellulose, the Polyuronides, Lignin, etc.," Oxford University Press, Oxford, England, 1937.

DEPARTMENT OF CHEMISTRY
INDIANA UNIVERSITY
BLOOMINGTON, IND.

RECEIVED DECEMBER 4, 1939

Melting Points of the p-Bromoanilides of Solid Fatty Acids[1]

BY DAVID F. HOUSTON

The melting points of the p-bromoanilides of certain solid fatty acids recently prepared in this Laboratory differ greatly from those in the literature.[1a] Several of our results agree with those previously ascribed to higher homologs. A graph of our values has the general form of the melting-point curves of aliphatic series; that of

(1) Not subject to copyright.

(1a) P. W. Robertson, *J. Chem. Soc.*, **115**, 1210 (1919).

TABLE I

ANALYSES AND MELTING POINTS OF THE *p*-BROMOANILIDES OF SOLID FATTY ACIDS

p-Bromoanilide	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found	Bromine Calcd.	Bromine Found	Melting point in °C. Lit.[c]	Melting point in °C. Found
Capric	58.92	59.03[a]	7.37	7.54[a]	24.6	24.7[b]	102	101.9
Lauric	61.02	61.02	7.94	7.93	22.6	22.5	104	106.7
Myristic	62.81	62.94	8.41	8.26	20.9	21.2	107	110.2
Palmitic	64.38	64.33	8.81	8.74	19.5	19.2	110(114)[d]	113.2
Stearic	65.72	65.63[a]	9.16	9.38[a]	18.3	18.4[b]	114	115.2

[a] Analyses by W. T. Haskins, National Institute of Health; all others by C. J. Rodden, National Bureau of Standards. [b] Pregl method. Other bromine analyses by Zacherl and Krainick method. [c] Robertson's values[1a] except *d*. [d] Acree and LaForge (*J. Org. Chem.*, 2, 308 (1937)). A sample of their material showed a melting point of 113.1° when determined by the writer by means of the Francis and Collins method.

the literature values has an opposite convexity. Hence it has seemed wise to publish our results.

The reagent quality acids were first recrystallized from concentrated sulfuric acid[2] until no further discoloration of the solvent occurred, and they were then repeatedly recrystallized interchangeably from acetone, benzene, and glacial acetic acid until no further change in melting point occurred. The acids were converted into their acid chlorides with thionyl chloride.

The *p*-bromoaniline was prepared (a) by the reduction of *p*-nitrobromobenzene (m. p. 126.3°), (b) by hydrolysis of *p*-bromoacetanilide (m. p. 168.6°) according to Vecchiotti,[3] and (c) by recrystallization of a commercial product from chloroform and then from aqueous alcohol to remove colored matter[4] and tribromoaniline, respectively. The three preparations of *p*-bromoaniline thus obtained had melting points between 63.5 and 64.0°, and gave products with palmitic acid which had identical melting points.

The chlorides were treated with a benzene solution of *p*-bromoaniline according to the procedure of Kuehn and McElvain,[5] with the single modification of first crystallizing the product directly from the benzene solution instead of evaporating the benzene. In the case of the long chain acids, this affords a more rapid purification.

The melting points were determined with a partial-immersion thermometer (calibrated at this Bureau) by the improved capillary-tube method of Francis and Collins.[6] This procedure, which maintains an extremely slow rate of temperature rise at the melting point, gives values that are somewhat lower than those usually obtained by capillary-tube methods (see footnote *d* of table). The results are, however, in better agreement with those obtained by equilibrium measurements on larger amounts of material.

NATIONAL BUREAU OF STANDARDS
U. S. DEPARTMENT OF COMMERCE
WASHINGTON, D. C. RECEIVED JANUARY 20, 1940

(2) F. Francis, F. J. E. Collins and S. H. Piper, *Proc. Roy. Soc. London*, **A158**, 706 (1937).
(3) L. Vecchiotti, *Gazz. chim. ital.*, **58**, 231 (1928).
(4) W. M. D. Bryant, THIS JOURNAL, **60**, 2748 (1938).
(5) M. Kuehn and S. M. McElvain, *ibid.*, **53**, 1173 (1931).
(6) F. Francis and F. J. E. Collins, *J. Chem. Soc.*, 137 (1936).

The Separation of Hydroxy from Non-hydroxy Fat Acids by Means of a Dibasic Acid Anhydride[1]

BY FLOYD E. KURTZ[2] AND P. S. SCHAFFER[2]

The methods used for separating hydroxy from non-hydroxy fat acids have been based for the most part on differences in physical properties of the acids or of the derivatives formed with the carboxyl group. When the fat acid mixture contains acids in which these differences are small, it becomes difficult to secure a separation by such methods. This is particularly true if one of the similar acids is present as a minor constituent while the other is present in a high concentration.

In the method proposed here, the mixed esters are heated with a dibasic acid anhydride, the reaction mixture is dissolved in petroleum ether, and the derivative formed with the hydroxy esters is extracted with alkali. Since this method consists in the separation of an alcoholic from a non-alcoholic compound rather than upon the separation of two acids, its efficiency is not affected by a similarity in the physical properties of the acids.

Of the most readily available dibasic acid anhydrides, phthalic anhydride was considered unsuitable because of the difficulty of freeing the recovered fat acids from phthalic acid. Maleic anhydride was thoroughly investigated. It formed derivatives with methyl ricinoleate and with 12-hydroxymethylstearate which could be extracted readily from petroleum ether solutions, less readily from ether solutions, by means of dilute potassium hydroxide. Since ricinoleic acid and 12-hydroxystearic acid represent two hydroxy acids with quite different physical properties, it is considered likely that similar results could be ob-

(1) The part relating to maleic anhydride was presented before the Division of Biological Chemistry at the 97th meeting of the American Chemical Society, April 3–7, 1939, at Baltimore, Maryland. (Not subject to copyright.)

(2) Division of Dairy Research Laboratories, Bureau of Dairy Industry, U. S. Department of Agriculture.

TABLE I

SEPARATION OF RICINOLEIC ACID FROM A NON-HYDROXY ACID

Experimental conditions					Ricinoleic acid, %		
Heated with		Equiv.	Time, hr.	Temp., °C.	Concn. in starting mat.	In hydroxy acid fraction Concn. sepd.	Orig. recov.
Maleic anhydride		6	18	120	5	47	63
		6	18	120	10	86	70
		1.5	6	100	50	95	84
Succinic anhydride with solvent	AmOAc	10	18	120	10	68	70
	Dioxane	10	18	120	10	73	47
	Pyridine	10	7	130	10	93	78
	Pyridine	10	18	130	10	92	86

tained with a large variety of hydroxy fat acids. Maleic anhydride is sufficiently soluble in esters, so that the reaction mixture can be made homogeneous by the addition of only a small proportion of dioxane and often without any solvent. Pyridine is not suitable as a solvent because of the formation of large amounts of a tarry precipitate. A disadvantage in the use of maleic anhydride was found in an unexpected side reaction which takes place to a certain extent between methyl oleate and maleic anhydride to form a saturated compound. Succinic anhydride does not have this disadvantage but because of its lower solubility in the higher esters a solvent is necessary. With dioxane low yields are obtained. With pyridine better yields are obtained, but on prolonged heating considerable quantities (though much less than with maleic anhydride and pyridine) of a tarry precipitate are formed. It is recommended that when the separation involves only saturated acids, maleic anhydride be used, and that when unsaturated acids are present, succinic anhydride be used.

Table I summarizes the results of some typical experiments. It is obvious from the data that, in most cases, more than one application of the separation would be necessary to secure the one type of acid free from the other. In the case of the castor oil acids, which contain about 85% of hydroxy acids, it was found that by two applications of the separation the hydroxy acids were obtained practically free from non-hydroxy acids.

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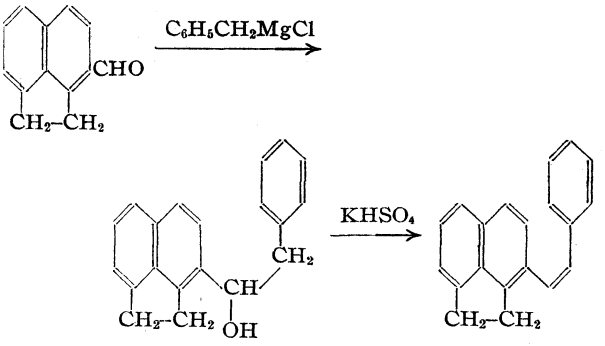
1-(β-Styryl)-acenaphthene

BY E. B. HERSHBERG[1] AND LLOYD M. JOSHEL[2]

The hydrocarbon mentioned in the title seemed of interest because in the *cis* form it constitutes an "opened" model of the carcinogenic cholanthrene from which it differs merely by the absence of one linkage connecting the benzenoid rings. The substance was synthesized by condensing 1-acenaphthaldehyde[3] with benzylmagnesium chloride and dehydrating the resulting carbinol. The hydrocarbon is crystalline and shows fluorescence in ultraviolet light.



Experimental Part[4]

1-Acenaphthylbenzylcarbinol.—A solution of 3.7 g. of 1-acenaphthaldehyde in benzene was added to the Grignard reagent from 3.5 cc. of benzyl chloride and 0.8 g. of magnesium in ether and after refluxing for one and one-half hours the mixture was decomposed with ammonium chloride and the solvents removed with steam. The product was taken up in ether and after washing and drying was obtained from ether–ligroin as needles, m. p. 107–109.5°, sufficiently pure for the next step; yield 4.9 g. (88%). A sample recrystallized for analysis from ether–ligroin (Norit) formed colorless needles, m. p. 109–110°.

Anal. Calcd. for $C_{20}H_{18}O$: C, 87.55; H, 6.61. Found: C, 87.62; H, 6.82.

1-(β-Styryl)-acenaphthene.—A mixture of 1.5 g. of the carbinol and about 0.1 g. of fused potassium bisulfate was heated at 200° until the evolution of water had ceased (ten minutes) and the product was then vacuum distilled and crystallized from absolute alcohol. The yield of twice crystallized hydrocarbon, m. p. 91.5–93°, was 1.0 g. (71%), but further recrystallizations were required to give material of the constant m. p. 93.2–94.0° (0.6 g.), possibly because

(1) Research Fellow on grants from the National Cancer Institute and the Eli Lilly Company.

(2) Fellow of the Finney-Howell Research Foundation.

(3) Fieser and Hershberg, THIS JOURNAL, **62**, 49 (1940).

(4) All melting points are corrected. Microanalyses by Lyon Southworth.

of the presence of *cis–trans* isomers. The substance exhibits a very strong blue fluorescence in ultraviolet light.

Anal. Calcd. for $C_{20}H_{16}$: C, 93.71; H, 6.29. Found: C, 93.62; H, 6.49.

A **dipicrate** was obtained from alcohol and crystallized as very dark red needles, m. p. 141.5–143°, dec.

Anal. Calcd. for $C_{20}H_{16}\cdot 2C_6H_3O_7N_3$: N, 11.76. Found: N, 11.61.

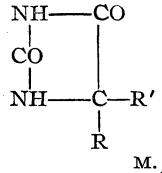
CONVERSE MEMORIAL LABORATORY
HARVARD UNIVERSITY
CAMBRIDGE, MASSACHUSETTS RECEIVED MARCH 27, 1940

Some New 5,5-Disubstituted Hydantoins

BY DAVID MARSH AND C. L. LAZZELL

It appears desirable to record data obtained on some six new 5,5-disubstituted hydantoins which have been prepared in this Laboratory following Bucherer's[1] method incidental to some other investigations. These substances were all recrystallized from 50% alcohol and were dried for five days at 85°. Except for the di-(*p*-dimethylaminophenyl) analog, which was yellow and soluble in benzene, they were all white crystalline solids, readily soluble in such organic solvents as acetone and 95% alcohol, but only moderately soluble in water.

TABLE I



—R	—R′	M. p. °C. (cor.)	Yield, %	Molecular weight Calcd.	Molecular weight Found	% Nitrogen Calcd.	% Nitrogen Found
Methyl	Cyclohexyl	204–205	48	199.31	200	14.1	14.1
Methyl	Styryl	217 d.	12	216.26	214	13.07	13.1
p-Dimethylaminophenyl	*p*-Dimethylaminophenyl	136–137	3	338.50	344	16.63	16.6
Methyl	2-Methylpropenyl	209–210	18	168.26	168	16.73	16.8
Methyl	*p*-Aminophenyl	100–101	36	205.33	202	20.57	21.0
Methyl	2-Methyl-2-hydroxypropyl	180–181	10	186.27	188	15.12	15.0

The yields obtained were rather low, but since it was only desired to obtain a pure sample of each hydantoin, no effort was made to improve them.

(1) Bucherer and Lieb, *J. prakt. Chem.*, [2] **141**, 5 (1934).

DEPARTMENT OF CHEMISTRY
WEST VIRGINIA UNIVERSITY
MORGANTOWN, WEST VIRGINIA
RECEIVED FEBRUARY 5, 1940

The Addition of Hydrogen Bromide to Methyl Methacrylate

BY CHARLES C. PRICE AND EUGENE C. COYNER

It has been found that methyl methacrylate adds hydrogen bromide to form methyl β-bromoisobutyrate exclusively. Only the β-bromo ester was produced even in pentane solution with peroxide catalysis, the conditions most favorable for reversing the mode of addition of hydrogen bromide to a double bond.[1]

This is in agreement with similar experiments with acrylic and crotonic acids and ethyl crotonate reported by Walling, Kharasch and Mayo and by Grimshaw, Guy and Smith[2] since the initiation of this investigation.

Since only the boiling points of the two possible addition products have been recorded, the two isomeric methyl bromoisobutyrates have been carefully characterized.

Methyl β-Bromoisobutyrate.—When redistilled methyl methacrylate[3] (10 g.) in hexane or carbon tetrachloride solution (50–100 cc.) was treated with hydrogen bromide at 0 or 25° in the presence of 1% of hydroquinone, benzoyl peroxide or "Lucidol"[4] or while exposed to direct sunlight in a quartz flask, nearly quantitative yields of methyl β-bromoisobutyrate were obtained; b. p. 67° (17 mm.),[5] $n^{20}D$ 1.4551; d^{20}_4 1.426; $M^{20}D$ (calcd.) 34.71; $M^{20}D$ (found) 34.47.

Anal. Calcd. for $C_5H_9O_2Br$: Br, 44.15. Found[6]: Br, 44.38.

No other product could be detected; even the first few drops of distillate had properties in agreement with those above. When methanol was used as a solvent no addition occurred at room temperature.

The hydrogen bromide was generated by dropping bromine into tetralin; it was bubbled through tetralin to free it from bromine vapor.

Methyl α-Bromoisobutyrate.—For comparison, the α-bromo ester was prepared by the Hell–Volhard–Zelinsky method. Bromine (102.5 g.) was added to 29.5 g. of

(1) Walling, Kharasch and Mayo, THIS JOURNAL, **61**, 1711 (1939).

(2) Walling, Kharasch and Mayo, *ibid.*, **61**, 2693 (1939); Grimshaw, Guy and Smith, *J. Chem. Soc.*, 68 (1940).

(3) E. I. du Pont de Nemours and Company, Wilmington, Delaware.

(4) Lucidol Corporation, Buffalo, New York.

(5) Vocke (*Z. physiol. Chem.*, **191**, 83 (1930)) reported the boiling point as 65–67° (12 mm.).

(6) Method described by Rauscher, *Ind. Eng. Chem., Anal. Ed.*, **9**, 296 (1937).

isobutyric acid and 5 g. of red phosphorus at 70–80°. The excess bromine was removed by evaporation under diminished pressure and the residue cooled in ice while 20 cc. of methanol was added. On fractional distillation, 14.4 g. (25%) of methyl α-bromoisobutyrate was obtained; b. p. 52° (19 mm.),[7] $n^{20}D$ 1.4410; d^{20}_4 1.331; $M^{20}D$ (calcd.), 34.71; $M^{20}D$ (found), 35.01.

Anal. Calcd. for $C_5H_9O_2Br$: Br, 44.15. Found[6]: Br, 43.14.

The physical properties of this ester changed appreciably on standing for a few hours since hydrogen bromide is evolved with extreme ease. This accounts for the low bromine content of the product. The physical properties recorded above were observed immediately after distillation.

(7) Wheeler and Barnes, *Am. Chem. J.*, **24**, 79 (1900).

NOYES CHEMICAL LABORATORY
UNIVERSITY OF ILLINOIS
URBANA, ILLINOIS

RECEIVED MARCH 20, 1940

The Identity of Obaculactone, Evodin and Dictamnolactone with Limonin[1]

BY MILTON S. SCHECHTER AND H. L. HALLER

Several investigators[2,3] have isolated from the extractives of the bark of the amur cork tree (*Phellodendron amurense* Rupr.) a colorless, crystalline, optically active compound, which melts with decomposition at 292–293° and possesses the properties of a dilactone. The compound was named "obaculactone" by Fujita and Wada,[2] who were the first to describe it. On the basis of combustion analyses and molecular weight determinations they assigned the formula $C_{15}H_{16}O_6$ to obaculactone, but subsequent studies have shown this formula to be in error. The molecular formula $C_{26}H_{30}O_8$ is now generally accepted as correctly representing the composition of the compound.

In 1934 Fujita, Kaku and Kutani[4] showed that obaculactone is identical with evodin and with dictamnolactone. Evodin was first isolated by Keimatsu[5] in 1902 from the benzene extractives of the fruit of *Evodia rutaecarpa* Hook. f. and Thoms., and subsequently by several investigators from the fruits of other species of *Evodia*. Dictamnolactone was first described by Thoms and his co-workers[6] who obtained it from the extractives of white dittany (*Dictamnus albus* L.). The latter workers surmised that evodin and dictamnolactone were identical but were unable to make a direct comparison. The identity of the three compounds was established[4] by mixture melting point determinations and specific rotations in neutral and alkaline solution. In acetone all three compounds are levorotatory; $[\alpha]_D$ about −123°. In ethanolic potassium hydroxide solution they are dextrorotatory; $[\alpha]_D$ about +30°.

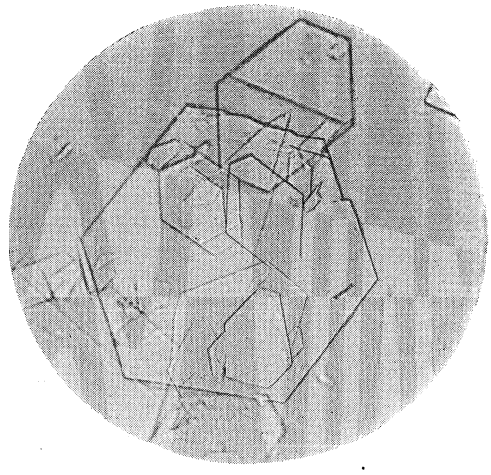
None of the early formulas assigned to the lactone were correct. In 1933 Chen and Chen[7] proposed the formula $C_{26}H_{30}O_8$. Mayeda[8] confirmed this and suggested that some of the previous difficulties in the determination of the molecular formula may have been due to the fact that the lactone crystallizes from acetic acid with one mole of acetic acid of crystallization. The lactone melts with decomposition, and melting points ranging from 280 to 293° have been reported for obaculactone, evodin and dictamnolactone by the several investigators.

A recent communication by Higby[9] describes the isolation of limonin from the pulp and seeds of the Valencia orange. This colorless, crystalline compound was first obtained by Bernay[10] in 1841 from the seeds of several varieties of citrus. Limonin has been shown to be an optically active dilactone, and combustion analyses and molecular weight determinations indicate it to possess the formula $C_{26}H_{30}O_8$. Koller and Czerny[11] have reported that limonin melts with decomposition at 280° (uncor.), whereas Higby found 292° (cor.). Citrolimonin, which is considered by Feist and Schulte,[12] by Koller and Czerny, and by Higby as being identical with limonin, is reported to melt with decomposition at 304° (Kofler micro melting point apparatus) by the first-mentioned workers.

In the course of our studies on the insecticidal properties of the fruit of the amur cork tree, the results of which will be reported elsewhere, obaculactone has been obtained from the ether and the acetone extracts of the fruit. The compound, when recrystallized by solution in acetone followed by the addition of ethanol, melted with decomposition at 299–300° (cor.).[13] When recrystallized from glacial acetic acid, it melted with decomposition at 297–298° (cor.). An aqueous

(1) Not subject to copyright.
(2) Fujita and Wada, *J. Pharm. Soc. Japan*, **51**, 506 (1931), (in German 52).
(3) Kaku, Cho and Orita, *ibid.*, **52**, 593 (1932), (in German 73).
(4) Fujita, Kaku and Kutani, *ibid.*, **55**, 67 (1935).
(5) Keimatsu, *ibid.*, No. **248**, 979 (1902).
(6) Thoms, *Ber. deut. pharm. Ges.*, **33**, 68 (1923).
(7) Chen and Chen, *J. Am. Pharm. Assoc.*, **22**, 716 (1933).
(8) Mayeda, *J. Pharm. Soc. Japan*, **55**, 90 (1935).
(9) Higby, THIS JOURNAL, **60**, 3013 (1938).
(10) Bernay, *Ann.*, **40**, 317 (1841).
(11) Koller and Czerny, *Monatsh.*, **67**, 248 (1936); **70**, 26 (1937).
(12) Feist and Schulte, *Ber.*, **69**, 1322 (1936).
(13) All the melting point determinations reported were made in open melting point capillaries, using a total immersion thermometer calibrated by the National Bureau of Standards, Washington, D. C.

Obaculactone (× 77).



Limonin (× 193).

Fig. 1.

ethanol solution of the lactone has an intensely bitter taste. It is insecticidally inert.

Some of the chemical properties recorded for obaculactone have been confirmed by us. It is a dilactone, dissolves in concentrated sulfuric acid with the formation of an intense red brown color, and does not absorb bromine in chloroform solution. It does not possess alkoxyl groups, or reactive carbonyl or hydroxyl groups. Contrary to the statement of Fujita and Wada,[2] it has been found that obaculactone absorbs hydrogen slowly on catalytic hydrogenation with the formation of a mixture of products. A study of these products will form the subject of a future communication.

Obaculactone recrystallized from a mixture of ethanol and acetone and then dried in an Abderhalden drier at 100° gave the following analytical data:

Anal. Calcd. for $C_{26}H_{30}O_8$: C, 66.35; H, 6.43; mol. wt., 470. Found: C, 66.39, 66.20; H, 6.52, 6.50; mol. wt. (Rast), 445; equiv. wt. (sodium hydroxide titration), 240. *Optical rotation:* 0.0888 g. in 10 cc. of acetone at 20.5° rotated −2.29°; l = 2.0 dm.; $[\alpha]^{20.5}D$ −129°. 0.0844 g. in 5 cc. of 0.5 N ethanolic potassium hydroxide and 5 cc. of water at 20.5° rotated +0.55°; l = 2.0 dm.; $[\alpha]^{20.5}D$ +32.6°.

The melting point, the rotation in neutral solution, the behavior toward alkali, and the identity of the molecular formula of obaculactone and limonin led us to believe that the two were the same. Through the courtesy of Dr. M. B. Matlack, Food Research Division, Bureau of Agricultural Chemistry and Engineering, U. S. Department of Agriculture, we obtained a sample of limonin isolated by him from orange seed. When recrystallized from ethanol or from glacial acetic acid the compound melted with decomposition at 297–298° (cor.). A mixture of equal parts of limonin and obaculactone also melted with decomposition at 297–298° (cor.).

The optical rotations of limonin in acetone solution and in 0.25 N aqueous ethanol potassium hydroxide solution were practically identical with the values obtained for obaculactone in these solvents.

Obaculactone and limonin recrystallized from ethanol consisted of colorless, micaceous, six-sided plates and were found to be identical microscopically.[14] Refractive indices (determined by immersion in oily liquids): n_α = 1.563; n_β = indet.; n_γ = 1.582; both ±0.002. In parallel polarized light (crossed nicols) the birefringence is moderate, usually first-order grays being shown. There appears to be no definite elongation. In convergent polarized light (crossed nicols) the plates were found to extinguish sharply, indicating that the plane of the optic axes is approximately parallel to the broad face of the plates so that interference figures could not be expected. Therefore, the refractive indices were determined by a variation of the statistical method, plates showing maximum double refraction for obtaining n_α and n_γ being selected.

The foregoing results indicate clearly that obaculactone and limonin are identical.

Since obaculactone, evodin, dictamnolactone, limonin, and citrolimonin are the same compound, it would appear desirable to retain one name and discard the others. As the compound was first

(14) We are indebted to George L. Keenan, of the Food and Drug Administration, U. S. Department of Agriculture, for the photomicrographs and for the optical crystallographic data reported here.

obtained by Bernay, who designated it "limonin," we suggest that this name be retained.

BUREAU OF ENTOMOLOGY AND PLANT QUARANTINE
U. S. DEPARTMENT OF AGRICULTURE
WASHINGTON, D. C. RECEIVED FEBRUARY 16, 1940

Mechanism of Nuclear Isomer Separation Process

BY G. T. SEABORG, G. FRIEDLAENDER AND J. W. KENNEDY

It has been shown that the energy released during the radioactive transition from an upper to a lower isomeric state of an atomic nucleus can be used to effect a chemical separation of two genetically related nuclear isomers and this discovery has provided a powerful method for the study of nuclear isomerism.[1,2,3,4] These so-called *isomeric transitions* have been the source of activation energy for many interesting chemical reactions and offer a unique method for a study of chemical activation.[1-6] We wish to report briefly some experiments which we have performed for the purpose of elucidating the mechanism of the chemical separation process.

The small amount of recoil energy, about 5.6 kcal. per mole,[7] acquired in the majority of the cases by the Br^{80} atom as the result of the emission of an internal conversion electron during an isomeric transition in a Br^{80} nucleus, seemed to be too small to account for the bond rupture and activation experiments (sometimes 100% efficient[1]) observed with bromine compounds. We have performed experiments with the isomeric transitions[3] in radioactive Te^{127} and Te^{129}, where the recoil energies are again very small. Internal conversion electrons are emitted in these cases and the recoil energies[3] of the tellurium atoms are 9.2 and 6.6 kcal. per mole for Te^{127} and Te^{129} respectively. We made a quantitative study of the change of telluric acid to tellurous acid which occurs when the radioactive Te^{127} or Te^{129} nucleus in the telluric acid undergoes a transition from its upper to its lower isomeric state. The experiments show, for both Te^{127} and Te^{129}, that the isomeric transitions effect reduction of telluric to tellurous acid with approximately 100% yield in aqueous solution at room temperature or even when frozen to the temperature of liquid air.

These experiments suggest, in view of the very small recoil energies involved, that the bond rupture and activation occurs, not as a result of the recoil energy, but as a consequence of the high state of electronic excitation which results from the vacancy in the K- or L-shell created by the emission of the internal conversion electron. A direct test of this view could be obtained by determining whether or not bond rupture could be initiated by an isomeric transition in which the transition gamma-ray undergoes very little internal conversion. Just such a case[8] is radioactive Zn^{69}, where the transition gamma-rays are largely *unconverted* and are of such an energy as to impart 40 kcal. of energy to the recoiling zinc atoms. We compared the effectiveness of the Zn^{69} transition in producing bond rupture with that of Te^{127} and Te^{129} under comparable conditions, namely, with the zinc and tellurium in the form of their gaseous diethyl compounds at 110°. The separation of the radioactivity corresponding to the lower isomeric state, as shown by its presence on the walls of the containing vessel (where fragments of the ruptured molecules collected), made it evident that again the isomeric transitions in Te^{127} and Te^{129} had been effective in producing an isomer separation process, while in the case of the zinc diethyl no separation was observed. The tellurium isomers were separated either in the presence or absence of electrically charged plates while the zinc isomers were not separable in any case. It is difficult to see how the isomer separations observed in tellurium compounds can be attributed to the recoil energy involved, since the recoil energy in the case of zinc is roughly five times greater and yet produces no separation in a similar molecule with similar bond energies.

These results lead to the not unexpected[6] conclusion that the state of high electronic excitation which exists after the loss of an internal conversion electron is responsible for the accompanying isomer separation process. For example, the tellurium atom is excited after K-shell conversion to the extent of 32 Kev. (740,000 kcal. per mole) or after L-shell conversion to 4.9 Kev. (110,000 kcal. per mole). During the electronic rearrangement which follows, the molecule should have ample opportunity to dissociate by reaching

(1) E. Segrè, R. S. Halford and G. T. Seaborg, *Phys. Rev.*, **55**, 321 (1939).
(2) D. C. DeVault and W. F. Libby, *ibid.*, **55**, 322 (1939).
(3) G. T. Seaborg, J. J. Livingood and J. W. Kennedy, *ibid.*, **57**, 363 (1940).
(4) A. Langsdorf, Jr., and E. Segrè, *ibid.*, **57**, 105 (1940).
(5) L. J. LeRoux, C. S. Lu and S. Sugden, *Nature*, **143**, 517 (1939).
(6) J. E. Willard, THIS JOURNAL, **62**, 256 (1940).
(7) G. E. Valley and R. L. McCreary, *Phys. Rev.*, **56**, 863 (1939).
(8) J. W. Kennedy, G. T. Seaborg and E. Segrè, *ibid.*, **56**, 1095 (1939).

either a repulsive state or an attractive state with sufficient vibrational energy (due to the operation of the Franck–Condon principle).

In some cases activation of a chemical reaction by an isomeric transition may follow from the formation of an undissociated molecular residue which, either before or after it regains an electron, is itself in a sufficiently reactive state. The irradiation of solutions by X-rays, wherein the same type of molecular excitation is produced, has also led to the observation of chemical decomposition and activation processes.[9]

(9) See H. Fricke, E. J. Hart and H. P. Smith, *J. Chem. Phys.*, **6**, 229 (1938), for bibliography.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF CALIFORNIA
BERKELEY, CALIFORNIA RECEIVED MARCH 20, 1940

Reaction of Sulfur with Mercuric Acetate in Glacial Acetic Acid

BY RICHARD E. VOLLRATH

When sulfur is heated with mercuric acetate in glacial acetic acid, no mercuric sulfide is formed but instead mercurous acetate. Quantitative experiments in which the reduction product was estimated as mercurous chloride and the oxidation product as barium sulfate indicate that the chief process taking place corresponds to

$$6Hg(C_2H_3O_2)_2 + S \longrightarrow 6HgC_2H_3O_2 + 6HC_2H_3O_2 + H_2SO_4$$

By carrying on the reaction in a sealed tube at 135°, over 90% of the mercury can be recovered as mercurous acetate. No more than a trace of mercuric sulfide was obtained after prolonged heating.

Prolonged heating of the mixture gives some mercurated acetic acid or related compound, as indicated by the fact that addition of sodium iodide no longer gives a precipitate of red mercuric iodide but instead a pale yellow iodide having the characteristics of an organic mercury compound. Further work is being done on this phase of the problem.

DEPARTMENT OF PHYSICS
UNIVERSITY OF SOUTHERN CALIFORNIA
LOS ANGELES, CALIFORNIA RECEIVED JANUARY 27, 1940

NEW BOOKS

Statistical Method from the Viewpoint of Quality Control. By WALTER A. SHEWHART, Ph.D., Member of the Technical Staff, Bell Telephone Laboratories, New York, with the editorial assistance of W. EDWARDS DEMING, Ph.D., Senior Mathematician, The Department of Agriculture, Washington. The Graduate School, The Department of Agriculture, Washington, 1939. ix + 155 pp. Illustrated. 16.5 × 24.5 cm.

Based on four lectures delivered in March, 1938, this book is a critique of statistical quality control, for readers who already have some acquaintance with the elements of statistical theory, and are more interested in applying than in developing it. Chemists and physicists will be interested in the analysis of the data on basic physical and chemical constants, in the light of which the incompatibilities pointed out by R. T. Birge may be evidence that statistical sins, even in high places, do not go forever unpunished. "When a scientist makes a mistake in the use of statistical theory, it becomes a part of 'scientific law'; but when an industrial statistician makes such a mistake, woe unto him for he is sure to be found out and get into trouble." The discussion of the specification of accuracy and precision will be a disappointment to readers who are looking for easy answers, "...neither the physical nor the numerical aspect of an operation by itself can be taken as a complete description of the operation." The table of contents by sections goes far toward atoning for the lack of an index, and the typography reflects credit on the Lancaster Press.

ELLIOT Q. ADAMS

Theoretical Qualitative Analysis. By J. H. REEDY, Associate Professor of Analytical Chemistry, University of Illinois. McGraw-Hill Book Co., Inc., 330 West 42d St., New York, N. Y., 1938. ix + 451 pp. 34 figs. 14.5 × 21 cm. Price, $3.00.

Most present-day Qualitative Analysis texts consist of companion sections on the theory of the processes of precipitation and separation, and on the characteristic reactions of the various ions, with the detailed analytical procedures. The author has followed this plan, presenting first some 150 pages of theory dealing with solutions, colloids, mechanics of precipitation, analytical operations, equilibrium, mass law, ionization and its applications, sulfide behavior, amphoterism, complex ions, hydrolysis, cell potentials, and the handling and balancing of equations. This list is a comprehensive and ambitious one for the space allotted; the treatment of each item is matter-

of-fact and necessarily brief, too much so at times, since many concepts and mathematical statements have to be introduced, considered and dismissed with little or no introductory background or explanation.

The qualitative analytical part of the book occupies the remaining 270-odd pages, consisting of the usual descriptive paragraphs on cations and anions (much more extensive than in most texts), the systematic procedures for the various groups, and short sections on dry (blowpipe) analysis and the dissolving of solid substances. The systematic cation procedure handles the silver group in the customary way, and the copper and tin group sulfides are divided with ammonium polysulfide. In the large iron–nickel family the whole group is precipitated as hydroxides and sulfides, and these are divided either with sodium hydroxide–peroxide, or by solution of all except cobalt and nickel in hydrochloric acid, followed by separation of the soluble members with sodium hydroxide (the phosphate–oxalate interference procedure also is given in some detail). The alkali earth cations are precipitated as usual with hot ammonium carbonate and then analyzed by a choice of methods: chromate–sulfate–oxalate, chromate–ferrocyanide–sulfate, chromate–chromate–oxalate, or the alcohol separation of the nitrates and chlorides. The Mg–Na–K group ions are identified by several methods, the phosphate–perchlorate–zinc uranyl acetate, and phosphate–perchlorate–fluosilicate (incorrect flow-sheet) methods being suggested. The anion analysis treatment is quite detailed, the radicals being classified on behavior into six groups: (I) insoluble silver salts (8), (II) slightly soluble silver salts (4), (III) silver and barium salts insoluble in dilute acid (11), (IV) soluble silver and barium salts (7), (V) barium salts insoluble in acids (3), (VI) silicates.

Every book contains factual and typographical faults or arguing points; in this text there might be mentioned: the use of certain unattractive (to the reviewer) plural and compound words, such as, mediums, equilibriums, deionization, saltlike, noncorrodible, nonoxidizing, timesaving, glycerin (glycerol preferred), nonionizing, nonaqueous, subreaction, semichemical, etc.; the unorthodox definition of molal solutions (p. 11); the unusual concept of "solid concentrations" (p. 50); the slightly severe treatment of the Arrhenius theory (pp. 72 ff.) (John Dalton has fared much better; did Arrhenius ever propose that ions actually existed as free simple atoms or groups?); the typographical oversight which has allowed the signs on anions to join end-to-end (preferably spaced or set up as $^{--}$ $^{=}$ or $^{---}$).

ALLEN D. BLISS

General Chemistry. Theoretical and Descriptive. By THOMAS P. MCCUTCHEON, Ph.D., Professor of Inorganic Chemistry, University of Pennsylvania, HARRY SELTZ, Ph.D., Professor of Physical Chemistry, Carnegie Institute of Technology, and J. C. WARNER, Ph.D., Professor of Chemistry, Carnegie Institute of Technology. Third edition. D. Van Nostrand Company, Inc., 250 Fourth Avenue, New York, N. Y., 1939. xiii + 685 pp. Illustrated. 14 × 22 cm. Price, $3.75.

This is a book which will appeal to the instructors who wish to give a full course in General Chemistry for the able student who has already had work in physics and chemistry. Hearing so much about the necessity of making chemistry simple arouses one's fears that teachers may choose texts which leave out the meat and that the chemical soup will be too dilute to satisfy the strong student. It is therefore encouraging to find another text, thorough in its presentation and accurate in detail, meet with sufficient support to warrant a third edition.

The subject matter is divided into two parts, following the plan of former editions. Part I, entitled "Chemical Principles and Theories," is complete in itself and would be received with favor for some uses if it were bound separately. This part is written with the viewpoint of the physical chemist and includes a good deal of the material ordinarily found in elementary physical chemistry texts. Nevertheless, the presentation is not too mathematical and a student who has had or is taking his first college mathematics, should comprehend fully any of the material presented.

Part II, entitled "Descriptive Chemistry," contains the usual factual information about the elements and their compounds. Following an introductory chapter on "Acids, Bases and Salts. Metals and Non-Metals," there are several chapters in which the non-metals and their compounds are presented in the conventional order. The metals are discussed in families following the order of the Periodic Table, two chapters on Organic Chemistry being included after group IVb.

The book has eight full-page portraits, about seventy-five excellent drawings, some seventy references (most of which are to more advanced texts) in Part I, no references in Part II, and a twenty-two-page two-column index.

It is the opinion of the reviewer that the text should have several fields of usefulness, such as: (1) a textbook for sincere and able students who have had some previous training in science; (2) a review for the upperclassman who wishes a logical presentation of chemical theory, which is not cluttered up with factual data about individual substances; (3) reading for teachers in related fields of Biology, Physics, Geology, and Mathematics, as well as Elementary Chemistry teachers, who for any of various reasons wish to be brought up to date in chemical thought and terminology.

C. R. CONARD

The Nature of the Atom. 115 pp. Illustrated. By G. K. T. CONN, M.A. (Aberdeen), B.A., Ph.D. (Cambridge). **The Wave Nature of the Electron.** 78 pp. Illustrated. By G. K. T. CONN. **The Nature of Crystals.** 114 pp. Illustrated. By A. G. WARD, B.A., Scholar of Trinity College, Cambridge. All three volumes published by Chemical Publishing Company, 148 Lafayette Street, New York, N. Y., 1939. 12.5 × 19 cm. Price, each, $1.50.

This series of little books is intended for the intelligent lay reader who desires a somewhat more thorough exposition of modern conceptions of the structure of matter than is to be found in the ordinary popular book on general physical science. Though the volumes belong naturally together, each is complete in itself, containing a carefully developed presentation of its subject. The ap-

proach is historical, in order to show why it has so frequently been necessary to abandon naive conceptions in favor of difficult and at first sight apparently fantastic abstractions. Assuming no special knowledge of mathematics on the part of the reader, the authors have been at pains to present their material in a way which should enable him to obtain, at the cost of a few hours of careful reading, some real comprehension and appreciation of the trends of recent Physics. The volume on crystals contains excellent illustrations and diagrams of the simpler lattice types, with directions for the construction of models which will undoubtedly, if followed, aid the reader to grasp the elementary theory of the crystal lattice. There is considerable discussion of modern views of different kinds of binding forces between molecules, atoms and ions. The volumes on the atom and the electron present what are now the standard results of wave mechanics.

A. S. COOLIDGE

A Short History of Chemistry. By J. R. PARTINGTON, M.B.E., D.Sc., Professor of Chemistry in the University of London, Queen Mary College. The Macmillan Company, 60 Fifth Avenue, New York, N. Y., 1937. xiv + 386 pp. 124 figs. 13.5 × 20.5 cm. Price, $2.50.

This Short History of Chemistry by Partington comes as a welcome addition to our somewhat meager list of really readable histories of chemistry. In the first portion the author has traced the beginnings of chemistry through the alchemical, iatrochemical and phlogiston periods in a most delightful manner, and has brought a fresh viewpoint on pre-Lavoisierian chemistry. His own investigations into original sources add a personal touch and the profuse illustrations are indeed refreshing. It is pleasing to note the emphasis and recognition given to that pioneer, van Helmont. The work on the discovery of gases by the group of British chemists is well described.

The main portion of the book, exactly one-half of the entire contents, is devoted to the period from Lavoisier down through the establishment of the valence theory. In giving account of the advances made and theories proposed during this badly confused period in the development of our science, the author has been only moderately successful. In the opinion of the reviewer, more definition might have been given to the interpretation of prevailing theories, in order to clarify the concepts, notations and viewpoints as they gradually evolved. In using this text with a class in the history of chemistry, the reviewer's students encountered this difficulty of interpretation. Yet, it might be said in justice to the author, that other histories of chemistry covering this epoch are likewise difficult to read and harder to understand; the authors are not entirely to blame, the period itself was chaotic.

The period of expansion following 1860, in which Inorganic Chemistry became definitely etsablished, Organic Chemistry greatly expanded and Physical Chemistry became differentiated as a separate branch of the science, is covered rather briefly by the author. For this brevity the author states in the preface "... this part of the subject is dealt with in the ordinary lecture courses on Chemistry, and need not be repeated in a book of this kind." For one seeking a concise (57 page) account of the development of chemistry from 1860 to relatively recent times, he will find it here.

On the whole, this book is one of the finest short histories of chemistry ever written. The reviewer commends it and congratulates the author in his accomplishment.

C. J. ENGELDER

Introduction to Practical Organic Chemistry. By FREDERICK GEORGE MANN, Sc.D. (Cantab.), D.Sc. (Lond.), F.I.C., Fellow and Lecturer, Trinity College, Cambridge, University Lecturer in Chemistry, and BERNARD CHARLES SAUNDERS, M.A., Ph.D. (Cantab.), B.Sc. (Lond.), Fellow and Charles Kingsley Lecturer, Magdalene College, Cambridge, University Demonstrator in Chemistry, Sometime Assistant Master, Eton College. Longmans, Green and Co., 114 Fifth Avenue, New York, N. Y., 1939. ix + 191 pp. Illustrated. 14.5 × 22.5 cm. Price, $1.50.

This book is "essentially a severely abridged version" of "Practical Organic Chemistry" by the same authors (*cf.* THIS JOURNAL, **61**, 1297 (1939)), and has been designed "to cover the essential requirements for the organic chemistry of the 1st M. B. examination at Cambridge and most other British universities, the various Higher School Certificate Examinations, the Chemist and Druggist Qualifying Examination of the Pharmaceutical Society, and examinations of a similar type. It is, therefore, directed at a specific group in Britain.

Inasmuch as the larger book has been competently reviewed, it seems that it remains only to point out the extent of abridgment. The section on methods and manipulation has been cut from 37 to 27 pages; preparations occupy 64 pages compared to 164 in the larger book; the section dealing with reactions and identification of organic compounds has been shortened from 79 to 57 pages; 24 pages instead of 77 are devoted to quantitative analysis, and the section on simple enzyme reactions has been deleted.

The use of a great deal of fine print does not increase the readability of the book, but if one desires a laboratory text in which preparations, reactions and identification of organic compounds and quantitative organic analysis are treated in the brief space of 172 pages, the text can be recommended. The exposition is clear and concise, and the choice of material good.

NATHAN L. DRAKE

Gmelins Handbuch der anorganischen Chemie. (Gmelin's Handbook of Inorganic Chemistry.) **Aluminiumlegierungen.** (Aluminum Alloys.) Collection of Patents. Edited by G. APEL, Regierungsrat in the Patent Office. First Supplement, Parts I–III. Verlag Chemie, G. m. b. H., Corneliusstrasse 3, Berlin W 35, Germany, 1939. VI + 1877 pp. Price, RM. 72 + 49.50 + 31.50.

This is a First Supplement to the Collection of Patents on Aluminum Alloys published in 1936 as an Addendum to the volume on Aluminum in Gmelin's Handbook. It covers all the patents on aluminum alloys which have appeared in England, France, Germany, Switzerland and the

United States during the succeeding three-year period, that is, from the beginning of 1935 to February, 1938. The same convenient system is followed as before, namely, listing the foreign constituents of each alloy alphabetically and putting all the alloys with the same final constituent in a single group arranged in the order of increasing complexity.

A list of the trade names of recognized aluminum alloys with their percentage composition and the name of the inventor or manufacturer is also provided.

The present collection, in spite of the short interval of time covered must include more than twice as many alloys as the original volumes. This is an indication of the extraordinary activity in this field.

ARTHUR B. LAMB

Rheological Memoirs. Volume I, Number 1, January, 1940. EUGENE C. BINGHAM, Editor. Experimental Investigations upon the Flow of Liquids in Tubes of Very Small Diameter. By Dr. JEAN LEONARD MARIE POISEUILLE, translated by WINSLOW H. HERSCHEL. Published by Rheological Memoirs, Easton, Pennsylvania. 101 pp. 10 figs. 15.5 × 23 cm. Price, $2.00; bound in cloth, $2.50.

The preface says in part: "There is no gainsaying that an adequate library is one of the most important of tools, even granting that research is highly dependent upon the laboratory. Even with the deployment of our scientific journals to cover every field, there still are memoirs which are not readily available. There are works which need to be made more accessible, not because of an existent demand and a probable financial return or for reasons of patriotism or other allegiance. There are some classical researches which are needed as tools of research and in education....

"It is now proposed, under the title of Rheological Memoirs, to publish in inexpensive form certain classical memoirs in rheology in the English language which are not only important but inaccessible to the majority of readers. For the rheologist, such a paper would be that of Poiseuille published in the *Mémoirs présentés par divers savants à l'Institut de France* in 1846. This paper was the one which brought to the world the knowledge of viscous flow and the data there given are still regarded as among the best available for the absolute determination of the viscosity of water....

"The attempt will be made to publish rheological memoirs from time to time in unbound numbers, exactly as are the journals. When a suitable number of these are published, it is proposed to bind them in book form. Subscriptions may be placed with the Rheological Memoirs, Lafayette College, Easton, Pa., or with the Secretary of the Society of Rheology in care of the American Institute of Physics, 175 Fifth Avenue, New York, N. Y. The publication is edited by Dr. Eugene C. Bingham, and each paper is passed upon by the Publications Committee of the Society of Rheology.

"A fund has been collected to initiate this project. The response of the public will determine whether this type of publication will support itself and be continued."

This monograph by Poiseuille, which was originally published in 1846, should be read by every chemist or physicist interested in the flow of liquids. Poiseuille, a man trained as a physician and physiologist who was primarily interested in the circulation of the blood in the human body, boldly challenged the accepted formulas of the hydraulic engineers and demonstrated that flow of liquids in narrow tubes obeys different laws than the flow in wide pipes. In addition to the great historical interest of this paper in opening a new branch of science, it is remarkable that nearly one hundred years ago Poiseuille evidently attained a precision in his experimental results which would be difficult to surpass at the present time even with the aid of modern equipment.

The translation has been done splendidly. A brief biography of Poiseuille and many critical notes add to the interest and value of the pamphlet. Our thanks are due to Eugene C. Bingham and to Winslow H. Herschel for making this masterpiece available.

Other memoirs on plasticity and lubrication are foreshadowed.

GRINNELL JONES

Molecular Spectra and Molecular Structure. I. Diatomic Molecules. By GERHARD HERZBERG, Research Professor of Physics, University of Saskatchewan. Translated with the Co-operation of the Author by J. W. T. SPINKS, Professor of Physical Chemistry, University of Saskatchewan. Prentice-Hall, Inc., 70 Fifth Avenue, New York, N. Y., 1939. xxviii + 592 pp. 181 figs. 16 × 23.5 cm. Price, $6.50.

The German edition of this book has been reviewed in the February, 1940, number of THIS JOURNAL. The English edition does not differ in any essential respect from the German, though some improvements have been made. The translation is adequate. The book provides an accurate and up-to-date account of the theory of diatomic molecules, especially those portions of immediate applicability to spectral analysis; some of the more difficult details and certain more complex portions of the theory are omitted. The theory is illustrated by many examples, a large number of which are discussed in detail. Table 36 summarizes the data on the ground states of the known diatomic molecules, including isotopic molecules, and has been revised as of July, 1939. The new values of the physical constants are used, instead of Birge's table of 1929. As most calculations in the literature are based on the older values, the reader using the data in the present volume will need to exercise some care in order not to introduce inconsistencies. The book is furnished with an excellent subject index. Altogether, it is a work which is indispensable to anyone who has a serious interest in the field covered.

O. K. RICE

Quantitative Biological Spectroscopy. By ELMER S. MILLER, Assistant Professor, Department of Botany, University of Minnesota. Burgess Publishing Company, Minneapolis, Minn., 1939. 213 pp. Illustrated. 21 × 27 cm. Price, $3.50.

This manual contains eighteen chapters. A brief history of optics and a summary of the theory of molecular spectra is given in chapters one and two. Chapter three

deals with thermopiles, photoelectric cells and amplifiers and chapter four with spectrophotometric instruments. In chapter five spectrophotometric methods for the determination of the absorption in the ultraviolet, visible and infrared regions of the spectrum are described and chapter six is devoted especially to photoelectric spectrophotometry. After having presented in chapter seven the basis of absorption spectroscopy including calibration and standards, the author has discussed in chapter eight the sources of error which may influence the accuracy of measurements. These chapters, which give a survey of the various types of spectroscopic apparatus and discuss the performance of absorption measurements represent a valuable collection of information otherwise obtainable only by wearisome search through scattered literature. They are enriched by fine illustrations.

The following chapters may be considered as a second part of the manual dealing with the applications of absorption spectroscopy: to chemistry (chapter nine); to the determination of molecular structure (chapter ten), and chapter eleven emphasizes the importance of infrared absorption spectroscopy for chemistry. Furthermore, chapters twelve to seventeen include the application of absorption spectroscopy to important biological material, such as absorption spectra of vitamins, cytochrome and other pigments; spectrophotometric studies of hemoglobin derivatives; absorption spectra applied to lipids and lipid metabolism; analysis of binary, ternary and quaternary mixtures (with special reference to chlorophylls and carotenoids); application of quantitative spectral analysis to plant pigment inheritance studies. The last chapter presents selected annotated references of spectrophotometric studies.

The compilation of these various applications of absorption spectroscopy will be of great value not only for those who intend to become acquainted with this field but also to those already familiar with the subject, especially with respect to the critically and clearly stated precautions which must be observed in investigations of this kind. It is unfortunate that the selected references given in the last chapter are not accompanied by a compilation of the references on these subjects for the past five years, particularly since many of them are given in the chapter bibliographies. Considering the significance of the application of absorption spectroscopy to biological problems this manual, written by a competent author, is welcome.

ADOLPH STERN

Thermodynamics for Chemical Engineers. By HAROLD C. WEBER, Associate Professor of Chemical Engineering, Massachusetts Institute of Technology. John Wiley and Sons, Inc., 440 Fourth Avenue, New York, N. Y., 1939. vii + 264 pp. Illustrated. 15 × 23.5 cm. Price, $3.25.

The author states in the preface that it is his purpose to present the more important thermodynamic relations in a manner particularly useful to the chemical engineer. The preliminary preparation expected of the students is indicated by the statement "Familiarity with the fundamentals of physics will be useful, and the simultaneous study of physical chemistry, as practiced in many schools, will be helpful." In the reviewer's opinion practically all of the book can be readily understood by most students without any previous or simultaneous study of physical chemistry. One exception is the chapter IV on phase relations which would be quite difficult for any student who had not made some study of the temperature–pressure–composition diagrams for binary systems. Many other sections of the book would involve unnecessary repetition for students who have taken a course in physical chemistry which even approximately covers the material in any standard text. As examples of this type of material may be cited portions of Chapters V, VI, VIII, and XVI.

In the preface it is suggested that the first fourteen or fifteen chapters include as much material as can be covered satisfactorily in a two semester course. Such a selection omits consideration of equilibrium constants, electrochemical effects, third law, and free energy as a function of temperature. The reviewer believes that these topics are of more importance in a course on thermodynamics than some other topics, such as fluid flow which is treated in considerable detail in chapter XI. Such topics are more suitable for a course in plant design than one in thermodynamics.

Objections to the material contained in the book are relatively few. Chapter XIX on electrochemical effects is probably the poorest in the book. In the first place the diagram on p. 241 does not even remotely resemble a workable cell. Then on p. 242 the author speaks of the cell reaction for a cell consisting of two hydrogen electrodes one in 0.1 molal hydrochloric acid and the other in 0.1 molal sodium hydroxide as being the transfer of hydrogen ion from a solution where its activity is a_1 to one where its activity is a_2. Actually the cell reaction is the formation of water from its ions. Later in the chapter the reader is left without any clear idea how to determine whether a given cell is functioning reversibly.

The numerous diagrams will be found an aid to the student. However, it is unfortunate that the author did not select a reaction for the figure on p. 27 which could be balanced at some pressure which can be contained by apparatus which is obtainable. Figure 9, p. 79 and Fig. 10, p. 81, both have entropy of vaporization as ordinates, it would be better to call it by this name rather than speak of an enthalpy function, especially since the term entropy is used elsewhere in the same chapter.

Those teachers who agree with Professor Weber as to the content of a course in thermodynamics for chemical engineers will probably be well satisfied with the book as it is. Those who believe more stress should be laid on the material covered in the last five chapters will have to amplify the book considerably.

G. K. ROLLEFSON

Colloid Chemistry. By ROBERT J. HARTMAN, Indiana University. Houghton Mifflin Company, 2 Park Street, Boston, Massachusetts, 1939. xxviii + 556 pp. 184 figs. 16 × 24 cm. Price, $4.75.

This textbook of colloid chemistry treats the subject under four general headings: surface chemistry (130 pages), lyophobic colloidal systems (225 pages), lyophilic colloidal systems (80 pages), and the biocolloids (100 pages). In the first section are treated the general char-

acteristics, theories, and applications of adsorption, including a chapter on contact catalysis. The second section is concerned primarily with the preparation, properties, and stability of sols, aerosols, emulsions, and foams. [Since a *sol* is by definition a colloidal system, the tautological expression *colloidal sol*, which the author uses frequently in this section, is not recommended.] The third section deals with lyophilic sols and with gels. The final section is devoted specifically to biocolloids and some colloidal aspects of organisms.

In the preparation of this book, the author has attempted "to present the important phases of colloid chemistry without overemphasizing one narrow phase of the subject at the expense of others which are to the average student and reader just as important." A specialist who writes a textbook is very likely to devote proportionately more space to the authoritative and critical analysis of that portion of the field in which he is directly interested; the remainder of the specialist's books will be less authoritative and is likely to be less critical. In this book the author has accomplished his worthy aim of avoiding overemphasis on some phase of colloid chemistry at the expense of others equally important; but unlike the specialist's book, this volume suffers throughout from the lack of a critical analysis on the part of the author of the large amount of material that he has compiled.

The book gets off to a good start with the section on adsorption phenomena. The survey of Langmuir's valuable contribution is especially good. Because of the space devoted to Langmuir, much less prominence could be given to the important work of Harkins, Bartell, and Adam.

For the purpose of "avoiding much possible confusion" the lyophobic and lyophilic colloidal systems are considered separately, although the author recognizes clearly that no exact line of demarcation can be drawn between them. On page 140, the author puts the oxide sols on the border line: "For example, the hydrosols of the oxides of such metals as iron, vanadium and chromium will tolerate the presence of more electrolytes than lyophobic colloids, such as suspended metals, before a state of instability is reached; and yet they are far more sensitive to electrolytes than lyophilic colloids such as protein suspensions." In the light of this statement the student unfamiliar with the various factors which influence the stability of sols, may be confused on finding on pages 260–261 that the precipitation value of sodium chloride, for example, is 28 for a certain gold sol and 9.25 for a certain ferric oxide sol. As a matter of fact, most of the oxide sols are not near the border line but are distinctly more lyophobic than lyophilic in their colloidal behavior. The gels are classified under lyophilic systems although dilute jellies of such lyophobic materials as platinum and cadmium have been prepared. In inorganic gels the capacity of the solid phase to form an interlacing structure may be much more important for gel formation than the lyophilic character of the solid phase.

The chapters dealing with the preparation and the physical, optical, and electrical properties of sols, are among the best in the book. The chapter on the stability of sols appears less satisfactory. Little attention is given to the constitution of colloidal particles and the discussion of the mechanism of the electrolyte coagulation process on which so many people have worked, is inadequate. No mention is made of the outstanding work of Verwey on this subject. The space devoted to biocolloids in this book is considerably greater than in most introductory treatises on colloid chemistry. For this reason it may be found of special use to students of biology and biochemistry.

The book is very attractively printed. The cuts include 40 excellent reproductions of photographs. The subject matter is well outlined by the generous use of section and paragraph headings. Throughout the book, distinctive terms appear in black face type. The interested instructor will be impressed by the good physical make-up of the book, but he will want to read it carefully to determine whether the choice and treatment of the subject matter are sufficiently critical to serve his purposes as a textbook for advanced undergraduate and graduate students.

HARRY B. WEISER

Die Ultrazentrifuge. Theorie, Konstruktion und Ergebnisse. (The Ultracentrifuge. Theory, Construction and Results.) By Prof. Dr. THE SVEDBERG and Dr. KAI O. PEDERSEN, Physical-Chemical Institute of the University of Upsala. Verlag von Theodor Steinkopff, Residenzstrasse 32, Dresden-Blasewitz, Germany, 1940. xii + 433 pp. 154 figs. 15.5 × 23.5 cm. Price, RM. 35; bound, RM. 37.

This comprehensive monograph is a thorough description of ultracentrifuges as developed in Professor Svedberg's laboratory at Upsala and of the results obtained with these machines by Svedberg and his pupils. Svedberg's development of ultracentrifugation is from every standpoint —technical, theoretical and in fruitfulness—one of the great triumphs of physical chemistry. For that reason his description within the confines of one book is of the widest importance.

The monograph is a coöperative effort of Svedberg and his pupils. General and introductory sections have been written by Svedberg himself; most of the sections on theory and method have been prepared by Pedersen. Special topics in theory and results have been written by several of Svedberg's pupils, and Bauer and Pickels have contributed a detailed description of their type of the air-driven ultracentrifuge.

The four principal parts of the book are devoted (1) to the theory of sedimentation, (2) to the construction of ultracentrifuges, (3) to the various methods of measurement with ultracentrifuges and (4) to the summary of results obtained with Svedberg's ultracentrifuges. The last of these parts without a doubt holds most interest for the general reader. Svedberg has a number of times summarized the data from his laboratory but this review, being more detailed and comprehensive, is of correspondingly wider usefulness. It should be read by all biochemists and physical chemists. Active workers with ultracentrifuges will probably find especially valuable the two chapters dealing with methods of measurement and with general theory. There is much useful technical information on design and construction, particularly of rotors, in the chapter describing the oil-turbine ultra-

centrifuge. This description makes apparent the enormous amount of work that has gone into developing the instrument; after studying it one can readily understand why more have not been built.

The few workers with ultracentrifuges who are not directly a part of the Svedberg school will find the book largely a record of the point of view, as well as the accomplishments, of one group. There is, of course, the greatest justification for this in the overwhelming role that Svedberg has played in demonstrating the usefulness of centrifugation in the study of macromolecules. At the same time this physical technique will reach its full usefulness only when it can be widely and freely employed and its methods modified by many people of varied interests. There is thus a real need to have ultracentrifugation, and its still unrealized opportunities as a research tool, presented in such a way as to encourage others to try to use it. Very high centrifugal fields are useful, not only as a step in molecular weight estimation, but also as a tool for the isolation and purification of macromolecular substances. The centrifuges necessary for such preparative work as well as for accurate measurements of sedimentation rates on the heavier proteins can be much less costly and complicated than those described in this monograph. Many persons feel that the air-turbine ultracentrifuge is important for the very reason that it makes possible instruments the average laboratory is equipped to build and operate. From this standpoint it may be regretted that the treatment of air-ultracentrifugation is restricted to a detailed description of one excellent but still very complicated, and costly, instrument.

RALPH W. G. WYCKOFF

BOOKS RECEIVED

March 10, 1940, to April 10, 1940

J. E. BELCHER AND J. C. COLBERT. "Properties and Numerical Relationships of the Common Elements and Compounds." Third edition. D. Appleton–Century Co., Inc., 35 West 32d St., New York, N. Y. 350 pp. $2.00.

J. E. BELCHER AND J. C. COLBERT. "Experiments and Problems for College Chemistry." Third edition. D. Appleton–Century Co., Inc., 35 West 32d St., New York, N. Y. 207 pp. $1.75.

MEYER BODANSKY AND OSCAR BODANSKY. "Biochemistry of Disease." The Macmillan Co., 60 Fifth Avenue, New York, N. Y. 684 pp. $8.00.

E. M. CHAMOT AND C. W. MASON. "Handbook of Chemical Microscopy." Volume II. Second edition. "Chemical Methods and Inorganic Qualitative Analysis." John Wiley and Sons, Inc., 440 Fourth Avenue, New York, N. Y. 438 pp. $5.00.

ERNEST CHILD. "The Tools of the Chemist." Reinhold Publishing Co., 330 West 42d St., New York, N. Y. 220 pp. $3.50.

THOMAS B. CRUMPLER AND JOHN H. YOE. "Chemical Calculations and Errors." John Wiley and Sons, Inc., 440 Fourth Avenue, New York, N. Y. 247 pp. $3.00.

WILLIAM LLOYD EVANS, ALFRED BENJAMIN GARRETT AND LAWRENCE LARKIN QUILL. "Semimicro Qualitative Analysis." Ginn and Company, 15 Ashburton Place, Boston, Mass. 246 pp. $2.00.

JOHN THEODORE FOTOS AND R. NORRIS SHREVE. "Advanced Readings in Chemical and Technical German." John Wiley and Sons, Inc., 440 Fourth Avenue, New York, N. Y. 304 pp. $2.50.

W. F. GERICKE. "The Complete Guide to Soilless Gardening." Prentice-Hall, Inc., 70 Fifth Avenue, New York, N. Y. 285 pp. $2.75.

E. HOPE, Editor AND F. W. ATACK, Founder. "The Chemists' Year Book 1939." Chemical Publishing Co., Inc., 148 Lafayette St., New York, N. Y. 1257 pp. $6.00.

J. S. LONG AND H. V. ANDERSON. "Chemical Calculations." Fourth edition. McGraw-Hill Book Co., Inc., 330 West 42d St., New York, N. Y. 266 pp. $1.75.

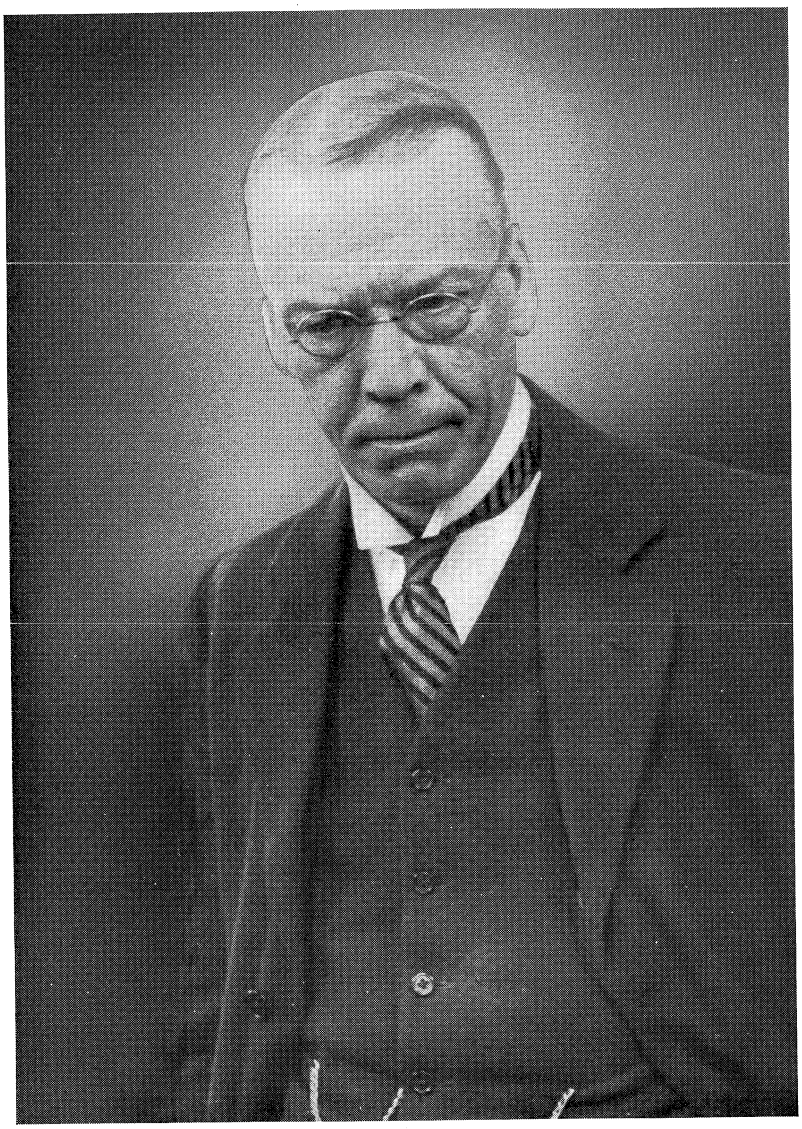
W. B. MANN. "The Cyclotron." The Chemical Publishing Co., Inc., 148 Lafayette St., New York, N. Y. 92 pp. $1.50.

KURT H. MEYER AND H. MARK. "Hochpolymere Chemie." Band 1. "Allgemeine Grundlagen der hochpolymeren Chemie." Akademische Verlagsgesellschaft m. b. H., Sternwartenstrasse 8, Leipzig C 1, Germany. 345 pp. RM. 22.20; bound, RM. 24.20.

MAXIMILIAN PFLÜCKE. "Periodica Chimica." Verlag Chemie, G. m. b. H., Sigismundstrasse 4, Berlin W 35, Germany. 208 pp. RM. 11.25.

LEON B. RICHARDSON AND ANDREW J. SCARLETT. "General College Chemistry." Henry Holt and Company, 257 Fourth Avenue, New York, N. Y. 683 pp. $3.75.

"Gmelins Handbuch der anorganischen Chemie." System-Nummer 68: "Platin." Teil C, Lieferung 2. "Verbindungen bis Platin und Caesium." Verlag Chemie G. m. b. H., Berlin W 35, Germany. 119 pp. RM. 14.25.



Sir William Jackson Pope

JOURNAL OF THE
AMERICAN CHEMICAL SOCIETY

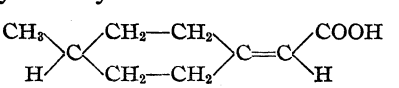
VOLUME 62 JUNE 8, 1940 NUMBER 6

SIR WILLIAM JACKSON POPE

1870–1939

William Jackson Pope was born on March 31, 1870 in London. He commenced the study of Chemistry in the Finsbury Technical College as one of the earliest students of the late Professor H. E. Armstrong, whom he followed in 1887 when the latter migrated to South Kensington. Ten years later he was appointed head of the Chemistry Department of the Goldsmiths Institute at New Cross. In 1901 he became Professor of Chemistry at the College of Technology in Manchester and seven years later was appointed to the Chair of Chemistry at Cambridge, where he remained until he died on October 17th, 1939.

Early as a student, Pope was attracted to the science of crystallography, and possessed the uncommon faculty of spatial visualization. At Manchester, in collaboration with Barlow, he published a series of interesting papers on the packing of atomic spheres as models of crystal structure. Whilst Pasteur, whose papers Pope studied with deep interest, in 1849, had clearly enunciated the fact that optically active substances, whilst not necessarily devoid of all elements of symmetry, were dissymmetric and possessed no plane of symmetry in their structure, this important generalization was in some danger of being forgotten in the attention given to the papers of van't Hoff and Le Bel in 1874. In these the concept of the asymmetric carbon atom, defined by van't Hoff as an atom to which four dissimilar groups were attached, as the criterion of dissymmetry and thus of optical activity, was somewhat unduly stressed. It is clear, however, that Van't Hoff visualised the possibility of optical dissymmetry in compounds such as allene derivatives which possessed no one asymmetric atom as defined by him. In collaboration with Perkin and Wallach, Pope prepared the first compound of such a type by synthesising and resolving 1-methyl-cyclo-hexylidene-4-acetic acid



He also showed that it was unnecessary for the asymmetric carbon atom to be attached to other carbon-containing groups for optical activity by preparing and resolving one of the simplest compounds possessing optical activity, *viz.*, HC(I)-(Cl)SO_3H. Up to 1899 optical activity had been associated with compounds which were either dissymmetric or contained an asymmetric atom of carbon, but in that year Pope opened what was virtually a new field in the chemistry of optical activity by preparing a compound in which the optical activity was due to an asymmetric atom of nitrogen by resolving benzylphenylallylmethylammonium iodide. In many of these resolutions he was assisted very materially by his discovery

and use with Kipping of the strong optically active acid α-bromocamphor sulfonic acid. This success was soon followed by the preparation of optically active compounds which owed their activity to asymmetric atoms of sulfur, selenium and tin.

At a later date there issued from the Cambridge Laboratories optically active compounds of arsenic, beryllium and zinc and still more recently compounds of platinum and rhodium. He was Longstaff Medalist of the Chemical Society in 1903 and Davy Medalist of the Royal Society in 1914; he was awarded the Dumas Medal of the Société de Chimie Industrielle in 1921 and the Messel Medal of the Society of Chemical Industry in 1932. He was elected an Honorary Member of the American Chemical Society at its 62nd General Meeting on September 7, 1921.

During the late war his breadth of knowledge and ability for getting things done resulted in a process for the direct synthesis of mustard gas and to drawing the attention of the authorities to a valuable source of toluene. For these services he was made a Knight of the British Empire in 1919. He was always keenly interested in the Goldsmiths Company, and attained high honor in this ancient Livery Company of the City of London. He took a lively interest in the metallurgical and chemical properties of the rare metals, gold, palladium and silver. After the late war his activity in research diminished although he still followed closely developments in dissymmetric molecular structure especially in the spirane configuration. Indeed, only a few weeks before his death he discussed with the writer the possible extension of a spirane configuration into a cyclol structure such as has recently been proposed by some as the basis of protein form.

The extent to which chemistry enters into the national economy impressed Sir William most forcibly during the period of the war, and it may be said that he devoted the rest of his life to rendering chemistry both more effective as a national asset, in the form of a Federal Council for Chemistry and as an important factor in international relations. It is generally recognized that the International Union of Pure and Applied Chemistry and the unique Solvay Chemical Conferences, in both of which he played a large part, owe much in vitality and mode of operation to Sir William Pope.

The criticism which has frequently been levelled at chemists that they are oblivious of other forms of culture could not be applied to Sir William, although it is true that this side of his life was presented only to his friends. His collections of pestles and mortars and of engravings of early alchemical discoveries are probably unique. He was also interested in ceramics and was no indifferent bibliophil. Whilst to some he appeared somewhat forbidding in aspect, to those who knew him and especially to those who had the privilege of being on his staff, he revealed himself as a man with a great sense of humour, of unusual kindness and generosity, possessed by an unexpected love of nature and withal somewhat shy. By his death International, British and Cambridge Chemistry have suffered a loss which will not easily be replaced.

ERIC K. RIDEAL

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, STANFORD UNIVERSITY]

Microtome Measurements of the Adsorption of Hydrocinnamic Acid in the Surface of its Aqueous Solutions*

BY J. W. MCBAIN, T. F. FORD AND G. F. MILLS

It has been demonstrated that the composition of a *moving* surface bears little relation to monomolecular adsorption or to the Gibbs theorem.[1] The microtome method[1,2] was developed for measuring adsorption at *static* air–water interfaces. In principle this method fulfills the Gibbsian requirement of equilibrium, and therefore can, theoretically, be made definitive as well as accurate. Results obtained with this apparatus are here reported for solutions containing 1.5 g. of β-phenylpropionic acid in 1000 g. of water. Humphreys,[2] Swain,[1] and two of the present authors (T. F. F. and G. F. M.) have each independently obtained a final value for the absolute adsorption per square centimeter of between 5.2 and 5.6 $\times 10^{-8}$ g.

It is disturbing to find that time appears to be a factor and that these equilibrium values appear to develop only on solutions that have been aged for several hours. However, it has been well established[3] by many methods and in several laboratories that the lowering of surface tension of these solutions likewise requires long periods of time for development. The Gibbs equation involves only quantities measured under equilibrium conditions. Hence, although it may be interesting that the final values for adsorption agree with the initial non-equilibrium values of surface tension obtained by the drop weight method,[3] they must properly be compared with the somewhat higher values obtained from the later more static measurements of surface tension.

Experimental

Apparatus.—The apparatus differs in a number of details from that previously used.[1,2] In order further to eliminate evaporation, both the inner and outer enclosures were rebuilt. In the inner enclosure the independent suspension of the trough was discarded. Instead, a silver sub-trough one inch (2.5 cm.) deep was set between the rails so as to seal the entire space and so designed that the trough rested directly upon it. The surface of the solution itself came into contact only with pure silver, except at the ends of the trough where the edges were coated with dicetyl. The glass side walls of the outer enclosures were replaced by brass ones heavily plated with silver, and all that space lower than the rails themselves was hermetically shut off from the outside by means of silver-plated aprons; the small cracks where the parts of the enclosure were fitted together were sealed on the inside with paraffin wax, and the glass covers were fitted on the cases with apiezon wax. After thus eliminating all leaks, it was found that, in the saturated atmosphere existing in the enclosure, water condensed in the guides in which the inner doors operate, and that capillary forces prevented their opening. The automatic feature of the doors as constructed had then to be discarded, and in these experiments the inner doors were operated manually by an assistant.

The sample of solution collected by the car was removed to the interferometer cell for analysis by means of a suitably shaped pipet, thus obviating the necessity of lifting the car from the tracks and reducing the evaporation loss. Also the whole length of the tracks beyond the outer enclosure was covered by a tunnel constructed of glass and of cardboard coated with shellac to make it possible for the car to be started and stopped in contact with a vapor similar to that inside the enclosures.

The silver stirrer previously used was replaced by one made of thin glass rods welded in the shape of a ladder with many rungs. This stirrer lies flat on the bottom of the trough and is manipulated through the holes in the covers of the outer and inner enclosures by means of a bent glass rod.

The tracks were surveyed and levelled where necessary, using a 15-inch (38-cm.) Pratt and Whitney gage, with which differences of 0.00005 inch (0.00127 mm.) per foot (30.5 cm.) may be estimated. Surveys were made before the experiments were started and again afterward to detect possible changes in level. The tracks within the enclosure were of pure block silver six feet long and were scraped true and level; the twenty-six feet of tracks outside the enclosure were of steel.

The microtome barrel in which the liquid skimmed off was caught was, like the trough itself, made of pure silver, burned together by autogenous welding to avoid contamination from solder. All fresh surfaces of solution were cut off many times to remove contamination. They were then very thoroughly stirred for several minutes and time was counted from the completion of stirring.

Experimental Procedure.—All apparatus was thoroughly washed and dried under cover before the experiment was started. No parts were handled more than could possibly be avoided. To prevent contamination being carried into the enclosure on the runners of the car, they and the tracks were washed with distilled benzene before each experiment.

A blank run, from which an approximate value of otherwise indeterminable experimental errors could be esti-

(*) Original manuscript received April 7, 1939.

(1) For references, see McBain and Swain, *Proc. Roy. Soc. London*, **A154**, 608 (1936); McBain and Wood, *ibid.*, 286 (1940).

(2) McBain and Humphreys, *J. Phys. Chem.*, **36**, 300 (1932).

(3) *Cf.* McBain, Vinograd and Wilson, THIS JOURNAL, **62**, 244 (1940).

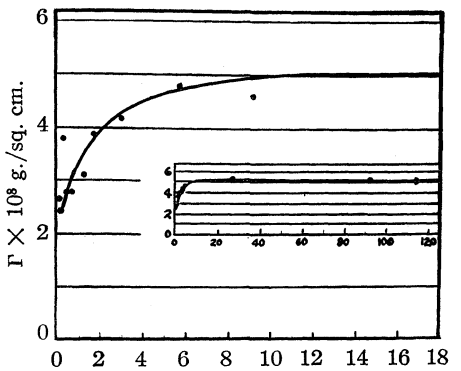


Fig. 1.—The measured adsorption of β-phenylpropionic acid in the surface of a solution containing 1.5 g./1000 g. water.

mated, was made by the usual procedure in which the sample placed in the microtome collecting chamber, or barrel, was of known original concentration. As a check the blank correction was divided into an evaporation and a dilution blank which were then added together. In the first, a known sample was poured into the barrel of the car after the car, wet with the same liquid, had been shot along the tracks; and this sample was then removed and analyzed. In the dilution blank the car was not shot at all, but a sample which differed by a known amount from the solution which had been used to rinse the barrel of the car was introduced into the barrel and removed again for analysis. The evaporation correction was −0.4, the dilution correction was +0.3, giving a composite blank correction −0.1 division of the interferometer dial for a 3-g. sample of 1.5 g./1000 g. hydrocinnamic acid. The corrections affect the final results by less than 4%. An 8-cm. Zeiss cell was used for analysis, reading to 0.1 division or 1.19×10^{-7} g. of hydrocinnamic acid to one gram of water.

A time schedule for a typical experiment was as follows. Three minutes after opening the inner doors only, the barrel of the car had been thoroughly rinsed with the stock solution. At 2, 3, 4 and 6 sec. later, respectively, the car was on the tracks, the outer doors opened, the car released, and the outer doors closed. At 21 and 51 sec., the sample had been placed in the interferometer cell and a sample of the liquid left in the trough had been removed and placed in the other compartment of the interferometer cell.

In the microtome measurements, the solutions were shielded from light or exposed during experiments only to the dimmest possible artificial light. Only dim indirect light was at any time permitted in the basement room in which the equipment was housed. This precaution was primarily to minimize temperature fluctuations, but it also guarantees the absence of light-induced polymerization of adsorbed solute. In the surface tension measurements in the same room, the solution was completely enclosed in an opaque box.

Results of Adsorption Measurements

The adsorption results for solutions containing 1.5 g./1000 g. water are collected in Table I and are shown graphically in Fig. 1. The table gives interferometer readings, Δ, for the surface liquid compared with that remaining in the trough from which the surface liquid had just been removed, and Γ the excess of solute found per square centimeter of the air–water surface over that corresponding to uniform concentration right up to the surface, where Γ = g./cm.^{2} = $\Delta Vk/A$, where k is the interferometer constant, V is the volume of shaving, and A is the area of surface removed by the microtome, 288 sq. cm. in every case.

TABLE I

THE ABSOLUTE AMOUNT OF ADSORPTION, Γ, PER SQ. CM. OF SURFACE OF AQUEOUS SOLUTION

Concentration: 1.5 g. of hydrocinnamic acid per kg. of water. Temperature: maximum variation in 24 hr. 21.30–21.70°; during the 2 weeks represented by the experiments, 20.10°, 21.70°.

Expt.	Time since stirring	Vol. of shaving	Δ	$\Delta_{cor.}$	Γ × 10⁸
10	7 min.	0.75±0.04	9.1	8.7	2.7
8	13 min.	1.0 ± .04	6.4	6.1	2.5
5	25 min.	2.53± .08	2.8	2.7	2.8
3	45 min.	2.15± .08	3.3	3.15	2.8
11	1 hr. 15 min.	1.90± .12	4.1	3.95	3.1
14	1 hr. 45 min.	0.49± .04	[a]	[a]	3.9
2	3 hr.	1.75± .08	6.0	5.8	4.2
6	5 hr. 45 min.	2.05± .08	5.8	5.65	4.8
4	9 hr. 20 min.	0.85± .04	13.5	13.15	4.6
9	27 hr.	0.49± .04	[a]	[a]	5.4
12	93 hr.	4.50± .25	2.9	2.8	5.2
13	116 hr.	1.65± .10	7.6	7.4	5.0

[a] Analyzed mixture with equal volume of standard solution.

Survey of the tracks before and after each set of experiments disclosed differences in level of less than 0.001 cm. throughout the length of the trough, so that complete films were certainly collected.

Effect of Evaporation.—Extensive tests of the effect of evaporation upon the experimental results were carried out both with solutions of hydrocinnamic acid and with more concentrated solutions of phenol, the latter being volatile. It was shown that a correct result can be obtained only when the solution in the trough is kept in such an atmosphere that its composition undergoes no change over long periods of time. This is in accordance with the Gibbs requirement of true equilibrium. For the experiments recorded in Table I, for example, the change in concentration of the solution in the trough was less than 1 division, or 1×10^{-6} g./cc. or 0.0006% of the original concentration, in a month.

Twelve measurements also were made upon solutions containing 5.2 g./1000 g. water. These data are not displayed here because at the low temperatures they were too near saturation. With the exception of two low values (including 0.14×10^{-8} g./cm.^{2} at age one minute), they averaged 6.6×10^{-8} g./cm.^{2}. The last four values obtained at ages from twenty-three to fifty-three hours averaged 7.7×10^{-8} g./cm.^{2}, which is still distinctly below the Gibbs value predicted from surface tension of aged solutions (see Table IV).

When the solution of hydrocinnamic acid in the trough was exposed to the atmosphere of the room, approximately 4 g. of water evaporated per hour, corresponding to an increase in concentration of 0.25 g./liter, and the value of apparent Γ found during this period was increased fivefold over the equilibrium value.

Phenol.—With Kahlbaum phenol solution (36 g./1000 g. solution in boiled out distilled water) the average equilibrium value of Γ was 8.3×10^{-8} g./cm.^{2}; and determinations during evaporation and condensation at known rates for this phenol solution gave an interpolated value of $\Gamma = 10 \times 10^{-8}$ at the point where both evaporation and condensation were suppressed. The Gibbs equation gives for phenol at this concentration $\Gamma = 4.7 \times 10^{-8}$, as calculated by Goard and Rideal.[4]

Experiments were made by L. A. Wood with pure water, at one hour and after two days, but no difference whatsoever could be observed in the interferometer, showing complete absence of contamination.

Surface Tension Determinations on Aqueous Hydrocinnamic Acid Solutions. Drop Weight Method.—It is commonly supposed that the static or final surface tension of a crystalloidal solution is established within a small fraction of a second.[5] In many cases, and especially for hydrocinnamic acid solutions, this certainly is not true. Nevertheless, it is generally felt that the few seconds required for drop weight determinations[6] represent a close enough approach to a static condition, and consequently such measurements have been universally used for calculation of adsorption by the Gibbs equation. In the two previous papers on the microtome apparatus[1,2] drop weight surface tension measurements were utilized for calculating Γ. The measurements were made independently by C. R. Bacon and R. C. Swain in 1932 and 1933, Dr. Bacon using a tip kindly furnished by Professor Harkins.

The effective radii of the tips were calculated from the drop weight of conductivity water (σ = 72.11 dynes at 24.6°). The radii, and the technique, were checked with repeatedly distilled benzene (density 0.879) dried over calcium chloride, and also with a solution of resublimed Kahlbaum "zur Analyze" *p*-toluidine (density 0.9983), containing 2.0 g. per 1000 g. of water. The results of these preliminary experiments are given in Table II; upper row by C. B., lower row by R. C. S.

TABLE II

CALIBRATION OF DROP WEIGHT

Tip radius cm. (calcd.)	Water drop wt., g.	Benzene Drop wt., g.	σ	*p*-Toluidine Drop wt., g.	σ
0.2955	0.08377 at 24.6°	0.03242 at 22.4°	28.54 28.56[a]	...	...
0.2932	0.08325 at 24.7°	0.03221 at 21.9°	28.50 28.63[a]	0.07300 at 22.1°	63.76[b]

[a] Calculated for check from values in "International Critical Tables, Vol. IV, p. 454.

[b] 65.34 at 20° obtained by Gans and Harkins[6]; 64.89 at 16° (in tap water) by Ferguson and Kennedy, *Proc. Phys. Soc.*, 44, 517 (1932); and 65.6 at 16.6° by Brown, *Phil. Mag.*, [7] 11, 689 (1931).

Solutions were prepared by Bacon and Swain from recrystallized Eastman Kodak Co. hydrocinnamic acid. The experimental results are given in Table III. The values of Γ are calculated by the approximate formula

$$\Gamma = -\left(\frac{c}{RT}\right)\left(\frac{d\sigma}{dc}\right)$$

TABLE III

DROP WEIGHT OF SOLUTIONS OF HYDROCINNAMIC ACID

Concentration g./1000 h. H_2O	$t°$	Mean drop weight	σ, dynes/cm.	$\sigma_{21.5°}$	$\Gamma \times 10^8$ g./cm.^{2}
0.5026[a]	22.7	0.07926	68.88	69.00	2.3
0.9617	22.2	.07673	66.39	66.49	3.8
1.5007	21.5	.07335	63.63	63.63	5.2
1.7506[a]	23.1	.06981	61.10	61.32	5.6
2.3515	21.9	.06801	59.20	59.25	6.2
3.0024[a]	22.1	.06375	56.06	56.14	6.7
4.1146	21.1	.05996	52.50	52.46	7.3
6.1291	21.5	.05380	47.24	47.24	8.5

[a] These done by R. C. S.; others by C. B.

Du Noüy Method.—In the ring apparatus of Harkins and Jordan[7] we have eliminated only the complicated device for bodily moving the bal-

(4) Goard and Rideal, *J. Chem. Soc.*, **127**, 1668 (1925).

(5) Bond and Puls, *Phil. Mag.*, [7] **24**, 864 (1937).

(6) Harkins and Brown, THIS JOURNAL, **38**, 246 (1916); **41**, 499 (1919); Gans and Harkins, *ibid.*, **52**, 2289 (1930).

(7) Harkins and Jordan, *ibid.*, **52**, 1751 (1930).

ance, by floating the large platinum dish containing the solution on water whose level can be exactly and smoothly adjusted. Since both glass and paraffin tend to contaminate the surface of water after long periods, Bakelite lacquer was used, twenty coats being applied, each baked on at 140°. This coating is not only completely impermeable, but has no tendency whatsoever to contaminate water even after a day or so. Both platinum dishes and Bakelite coated metal were used.

The arrangement of the apparatus is shown in Fig. 2. Evaporation was prevented by surrounding the solution with a closed dish (also floating) draped inside with cloth dipping into a surrounding reservoir of solution several centimeters deep, and with a small hole in the top of the vessel for the connection to the balance. This opening was closed except during the moments required for a measurement. After forty-five days a 2.5 g./liter solution of hydrocinnamic acid was found to be 2.46 g./liter.

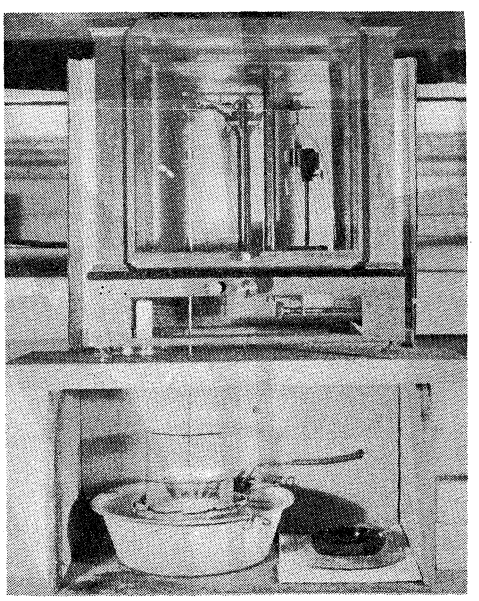


Fig. 2.—Modified ring method for measuring surface tension; outside container cut open to show interior, and wet draping also not shown.

In conducting an experiment, the solution dish was filled to overflowing and the surface twice swept with clean paper toweling, more solution added, the vapor chamber placed in position and the solution allowed to age for some hours. The du Noüy platinum ring was heated to white heat, the surface swept four or five times, the ring heated again in a clear alcohol flame, and then kept submerged beneath the surface except during measurements. A contact angle is observed when the ring approaches the surface from above, but not when it has been kept below. Conductivity water from a Barnstead still ($<0.4 \times 10^{-6}$ mhos) and specimens of hydrocinnamic acid purified by different methods were employed. It was shown that excess carbon dioxide, where permitted, did not affect the results, which are given in Figs. 3 and 4. The temperature was 22.5 ± 0.5°. The surface tension of water measured in the same apparatus remained completely constant for twenty-four hours. This may be contrasted with the changes found by du Noüy and by Klopsteg not using our precautions.

It is evident that the thirty seconds usually allowed in drop weight experiments is inadequate for the attainment of the static surface tension of such solutions. Actually the surface tension seems to change for days or weeks. This persistent time change agrees with observations by Adam and Shute,[8] studying 0.01% solutions of cetyltrimethylammonium bromide. They find big changes in surface tension with time by the sessile drop method, and Tartar and Reed and Cadle[9] find similar results for alkyl sulfonate solutions using capillary tubes. All these authors report changes persisting for periods of a week or more.

It is evident that ordinary processes of diffusion are almost infinitely faster than these surface tension effects. Application of the film balance to these solutions by McBain and Perry and Spencer[10] has shown that quite complicated phenomena occur in their surfaces. Measurements[3] with the PLAWM trough and pendant drop methods (at Stanford and at Massachusetts Institute of Technology) confirm this slow establishment of surface tension.

Discussion

The figures which have been given show that adsorption measured by the microtome method does not attain its final value immediately, but that several hours may be required. For solutions containing 1.5 g. of hydrocinnamic acid per kg. of water, the final or asymptotic value $\times 10^8$

(8) Adam and Shute, *Trans. Faraday Soc.*, **34**, 758 (1938).

(9) Tartar and Reed, This Journal, **58**, 322 (1936); Tartar and Cadle, *J. Phys. Chem.*, **43**, 1173 (1939).

(10) McBain and Perry, *Ind. Eng. Chem.*, **31**, 351 (1939); McBain and Spencer, This Journal, **62**, 239 (1940).

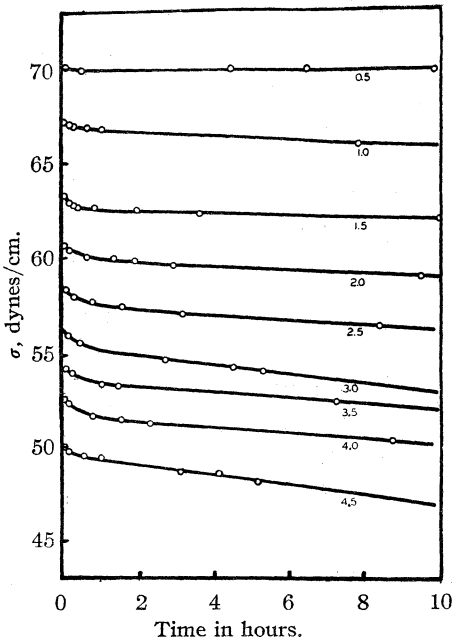


Fig. 3.—Change of surface tension of hydrocinnamic acid with time of solutions containing from 0.5 to 4.5 g. per liter.

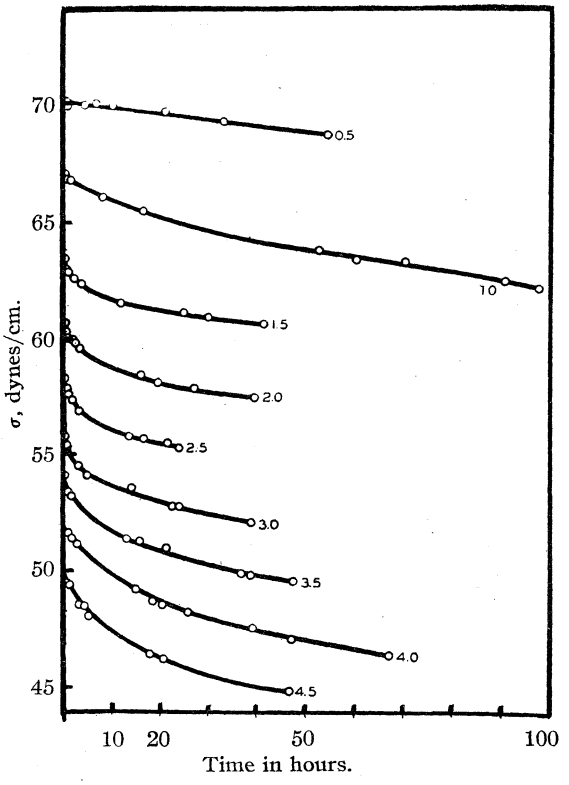


Fig. 4.—Change of surface tension of hydrocinnamic acid with time.

appears to be 5.2 ± 0.4, as compared with previous average values 5.2[1] and 5.6,[2] in experiments where time effects were not studied, and the apparatus had not been refined. Similarly, experiments with the interferometer[11] (by G. F. M.) have yielded a final value 5.2 attained after some hours. For solutions of 5.2 g./liter the final result appears to be at least 7.7×10^{-8} by the microtome method.

Having established the experimental values, the unexpected difficulty lies in finding what are the theoretical values predicted by the Gibbs theorem, since the surface tension changes so much and so slowly with time. Actually, although the surface tension falls for long periods, the slope of the surface tension–concentration curve and hence the predicted adsorption may change very little, and with the stronger solutions the amount of adsorption predicted from the Gibbs formula may even diminish with time, in contrast to the falling surface tension.

In Table IV are given data for the adsorption predicted for solutions containing 1.5, 4.0, 4.5 and 5.2 g./kg. of water, respectively, by the drop weight and by the ring method.

It appears that the actual equilibrium adsorption agrees very well with the value predicted from the non-equilibrium drop weight surface tensions, but is somewhat less than the proper values predicted from equilibrium surface tension.

TABLE IV

ADSORPTION, $\Gamma \times 10^8$ IN G./CM.², PREDICTED FROM GIBBS EQUATION, FOR SOLUTIONS OF HYDROCINNAMIC ACID OF DIFFERENT AGES OF SURFACES

Concentration g./1000 g. H_2O	Drop weight 30 sec.	Du Noüy 5 min.	Du Noüy 1 hr.	Du Noüy 9 hr.
1.5	5.2	5.9	5.9	6.3
4.0	7.3	9.0	8.8	8.8
4.5	7.7	10.2	9.1	9.1
5.2	7.6	..	..	..

In the adsorption experiments the solution was always thoroughly stirred before time was counted. The equations for ordinary diffusion are well known[5,12] and with the stirring employed the calculated time required for replenishment of the solution near the surface denuded by adsorption would be[12] about 10^{-1} second. The adsorption per square centimeter is 5×10^{-8} g., which comes from a solution which is 0.01 *N* and contains 1.5 g./liter. It therefore could deplete this to a depth of several Ångström units, and this would be restored to the extent of 90% in

(11) Ford and McBain, THIS JOURNAL, **58**, 378 (1936).

(12) Langmuir and Schaefer, *ibid.*, **59**, 2407 (1937); **60**, 2805 (1938).

0.003 sec. and to the extent of 99% in 0.3 sec. In only three experiments did we attempt a measurement until at least twenty minutes after stirring. As Doss has emphasized,[10,13] here the adsorption is delayed and therefore the diffusion "activated."

It is clear from all the phenomena referred to that the surfaces of ordinary solutions are far from being the simple structures commonly taken for granted. As was recently pointed out[10] the Gibbs equation is sometimes incompatible with their being monomolecular; for solutions of the simpler soluble fatty acids the Gibbs predicted adsorption remains constant with increase in concentration while the surface tension continues to drop. Much remains to be discovered about the depth, electrification and organization of surfaces of solutions.

(13) Doss, *Kolloid-Z.*, **86**, 205 (1939).

Summary

1. Even after efficient stirring, the experimentally determined adsorption of β-phenylpropionic acid in the surface of its aqueous solution as measured by the microtome method is not completed immediately, but may require several hours, whereas diffusion processes would require only about a tenth of a second.

2. The surface tension is not finally established until after much longer periods of time.

3. The final measured absolute adsorption seems to be slightly less than that calculated by the Gibbs theorem from surface tensions of comparable age and closest approach to equilibrium.

STANFORD UNIVERSITY, CALIF. RECEIVED MARCH 6, 1940

[CONTRIBUTION FROM THE GEOPHYSICAL LABORATORY, CARNEGIE INSTITUTION OF WASHINGTON]

The Effects of Pressure, Temperature and Chemical Composition on the Absorption of Light by Mixtures of Aromatic Amines and Nitro Compounds

BY R. E. GIBSON AND O. H. LOEFFLER

Introduction

It has been known for a long time that, when pure aniline and pure nitrobenzene are mixed, the solution immediately develops a deep orange color.[1] This is an example of a very general phenomenon, similar color changes being observed whenever primary, secondary or tertiary aromatic amines are mixed with aromatic nitro compounds,[2] aliphatic nitro compounds such as tetranitromethane,[2,3] nitroso compounds, quinones[4] or liquid sulfur dioxide,[5] etc. These color changes are due neither to adventitious impurities nor to irreversible reactions; addition of dilute hydrochloric acid to aniline–nitrobenzene mixtures discharges the color immediately, and the deep orange or red solutions of aniline or dimethylaniline in nitrobenzene freeze to very pale yellow solids which are immediately stained red when melting begins.[6] Furthermore, in the solutions we have studied, phototropic effects are not obvious although the mixtures do not differ greatly from some phototropic compounds.[7]

A satisfactory discussion of the changes in light absorption which occur when amines are mixed with *mono-nitro* compounds does not seem to have been given. It has been assumed that the colors observed are due to the formation of small amounts of intermolecular compounds in the solutions[8] and this has received some support from the known existence of a wide variety of stable, colored, solid intermolecular complexes between polynitro compounds and amines or hydrocarbons, substances which have been studied extensively.[9]

(1) I. Ostromisslensky, *Ber.*, **44**, 268 (1911). The phenomenon must have been noticed much earlier than this by such workers as Hepp (1882) or Kremann, but we have not been able to find any specific discussion of it in the literature.

(2) C. K. Tinkler, *J. Chem. Soc.*, **103**, 2171 (1913).

(3) D. L. Hammick and R. P. Young, *ibid.*, 1463 (1936).

(4) P. Pfeiffer, "Organische Molekulverbindungen," F. Enke, Stuttgart, 1927, p. 283.

(5) H. W. Foote and J. Fleischer, THIS JOURNAL, **56**, 870 (1934).

(6) For other examples see ref. 2.

(7) L. Chalkley, *Chem. Rev.*, **6**, 217 (1929).

(8) See P. Pfeiffer, ref. 4, pp. 358 and 384; G. M. Bennett and R. L. Wain, *J. Chem. Soc.*, 1108 (1936). Further references to articles supporting this view are given by D. L. Hammick and G. Sixsmith, *ibid.*, 972 (1939). In this paper we shall follow the customary practice and use the term "compound formation in solution" to mean the formation of covalent bonds between atoms in unlike molecules of the original components, as contrasted with general intermolecular attractions that result from dipole interaction or other polarization effects. A definite criterion, *viz.*, a measurable reaction velocity, has been proposed for this type of "compound formation" by D. L. Hammick and G. Sixsmith, *ibid.*, 580 (1935). Unless such a restriction is placed on the term "compound formation," it becomes too broad to be useful in the present state of our knowledge.

(9) (a) See P. Pfeiffer, ref. 4; (b) P. Pfeiffer, *Chem. Ztg.*, **59**, 205 (1935); (c) J. W. Baker and G. M. Bennett, *Ann. Rept. Chem. Soc., London*, **28**, 128 (1931); (d) D. L. Hammick and colleagues, papers in *J. Chem. Soc.* from 1935 to date; (e) G. Briegleb, *Z. physik. Chem.*, **B31**, 58 (1935); G. Briegleb and J. Kambeitz, *ibid.*, **B32**, 305 (1936); G. Briegleb, "Zwischenmolekulare Krafte und Molekulstruktur," F. Enke, Stuttgart, 1937.

Recent work, however, has shown that the stability of these solid addition compounds may be accounted for by the interaction energy arising from the mutual polarization of the molecules,[10] and their significance in supporting a theory of compound formation in the solution has consequently depreciated.

Furthermore, important differences in behavior indicate that the potential energy due to attractive forces between unlike molecules is less in systems containing mononitro compounds than in systems containing polynitro compounds, and that the former systems actually show positive deviations from ideality. For example, the freezing point curves of mixtures of aniline with (a) trinitrobenzene, (b) *m*-dinitrobenzene, (c) nitrobenzene indicate the formation of a congruently melting solid compound in case (a), of an incongruently melting compound in case (b) and no solid compound in case (c).[11] Linard's conclusion that a compound is formed in system (c) does not seem to be supported by his own diagram,[12] or by the disappearance of color when these solutions freeze. Tinkler[2] found a simple eutectic in the system *p*-chloronitrobenzene–diphenylamine, and, indeed, it has been stated categorically that no crystallized addition compounds of mononitro compounds are known.[13] The measurements of partition coefficients made by Moore, Shepherd, and Goodall[14] lead to the same conclusion. The fluidity–composition curves for mixtures of mononitro compounds and amines[15] show positive deviations from ideal behavior.[16] A small amount of heat is *absorbed* on the formation of aniline–nitrobenzene solutions[17] (132 cal./mole for a 50 mole per cent. solution at 14°) and we have already indicated that the volume changes on mixing at different pressures and temperatures make it unlikely that compound formation takes place in these solutions, and that if it did, the compound would be destroyed by rise of pressure.[18]

In this paper we give the results of some observations of the effects of pressure changes from 1 to 1500 bars and of temperature changes between 25 and 85° on the absorption of light by solutions of aniline, dimethylaniline, diphenylamine and triphenylamine in nitrobenzene, and by a number of solutions of related substances. The bearing of these observations on the problem of molecular interaction in solution, on the mechanism of the color changes to which we have referred, and on the role of intermolecular action in determining the color of organic compounds will be discussed.

Experimental

The effects of pressure and temperature on the absorption of light by the various solutions were measured in the same bomb and thermostat and with the same absorption cells that were used in our work on the determination of refractive indices under pressure.[19] Light from an incandescent tungsten strip filament entered the pressure bomb by one window, passed through the solution which was contained over mercury in the glass cell, and after emerging through the other window, impinged on the slit of a Hilger Type D2 constant deviation wave length spectrometer. The character of the incident light was varied to meet our requirements by adjustment of the filament temperature or by the use of suitable glass filters. The spectra of the transmitted light were photographed on Wratten panchromatic plates. An approximate scale of wave lengths was provided by similar photographs of the spectra of mercury and helium arcs, a spectrum of the mercury arc being superimposed on the transmission spectrum of each solution. The results of these experiments will be given in the form of microphotometer tracings of the photographs of the transmission spectra which were made on a Moll recording microphotometer.[20]

In these diagrams the abscissas give the approximate wave lengths and the ordinates are proportional to the logarithms of the intensity of the transmitted light over the ranges of intensity indicated by the vertical arrows in the right-hand margins.

The chief part of the experimental work consisted of comparing the transmission spectra at different pressures and temperatures with those at 25° and 1 bar, and care was taken to make the first and last photographs of any series with the solution under these standard conditions. In any pressure experiment the cell was filled with freshly prepared solution and the transmitted light was photographed

(10) L. Pauling, *Proc. Nat. Acad. Sci.*, **25**, 577 (1939); G. Briegleb, ref. 9e; B. R. Hamilton and D. L. Hammick, *J. Chem. Soc.*, 1352 (1938).

(11) R. Kremann, *Monatsh.*, **25**, 1271 (1904); R. Kremann and O. Rodinis, *ibid.*, **27**, 125 (1906). With *o*- and *p*-dinitrobenzene, aniline forms no solid compound.

(12) J. Linard, *Bull. soc. chim. Belg.*, **34**, 381 (1925).

(13) P. Pfeiffer, ref. 4, p. 358. Recently, however, G. P. Luchinskiĭ and A. I. Likhacheva, *J. Phys. Chem.* (*U. S. S. R.*), **7**, 723 (1936), have reported two eutectics in the system nitrobenzene–dimethylaniline.

(14) T. S. Moore, F. Shepherd and E. Goodall, *J. Chem. Soc.*, 1447 (1931).

(15) Computed from the data of R. Kremann, F. Gugl and R. Meingast, *Monatsh.*, **35**, 1365 (1914); R. Kremann and R. Ehrlich, *Sitzber. Akad. Wiss. Wien*, **116**, 786 (1907); D. E. Tsakalotos, *Bull. soc. chim.*, IV, **11**, 284 (1912).

(16) R. H. Ewell, *J. Chem. Phys.*, **5**, 967 (1937).

(17) R. Kremann, R. Meingast and F. Gugl, *Monatsh.*, **35**, 1235 (1914).

(18) R. E. Gibson and O. H. Loeffler, THIS JOURNAL, **61**, 2877 (1939).

(19) R. E. Gibson and J. F. Kincaid, *ibid.*, **60**, 511 (1938).

(20) We take this opportunity of thanking Dr. J. H. Hibben, formerly a member of this Laboratory, for his generous assistance in the use of this apparatus.

at different pressures in the following order, 1, 500, 1000, 1500 (in a few cases), 500 and 1 bar. All exposures to be compared were made on the same plate, the cell being left undisturbed whenever possible, and the exposure times were made long enough (30 to 60 sec.) to ensure adequate reproducibility. In the same way, when the effects of temperature changes were being studied, the exposures taken at the higher temperatures were bracketed between initial and final exposures at 25°. Except in rare cases when obvious causes were present, the photometer curves for exposures taken under the same conditions coincided within 2 mm. on a photographic record where the total possible excursion was 100 mm.

The Effect of Pressure on the Absorption of Light by Solutions of Amines in Nitrobenzene

The following observations were made on solutions of aniline, dimethylaniline, diphenylamine and triphenylamine in nitrobenzene, but it seems probable that conclusions drawn from them may be applied to solutions of any amine in a nitro compound. When the pressure is raised, the absorption of visible light by these solutions is increased much more than can be accounted for by the increase in the density of the solution. The effect is quite reversible and shows no time lag. Typical features of our results are to be seen in Fig. 1, which illustrates the results obtained with a 50% solution of dimethylaniline in nitrobenzene.

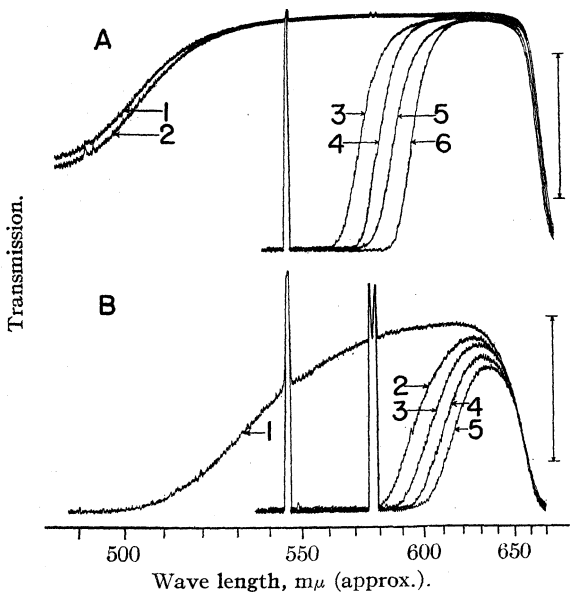


Fig. 1.—Transmission curves for a 50% solution of dimethylaniline in nitrobenzene at 45°: A1, aniline in 0.9-cm. cell; A4, solution in 0.9-cm. cell at 1 bar; A6, solution in 0.9-cm. cell at 1000 bars; A2, aniline in 0.5-cm. cell; A3, solution in 0.5-cm. cell at 1 bar; A5, solution in 0.5-cm. cell at 1000 bars; B1, same as A1; B2, solution at 1 bar; B3, solution at 500 bars; B4, solution at 1000 bars; B5, solution at 1500 bars.

Figure 1A shows the transmission spectra at 1 and 1000 bars with two different absorption cells: cell (a) 0.9 cm. thick and cell (b) 0.5 cm. thick. Curves 1, 4 and 6 refer to cell (a) and curves 2, 3 and 5 to cell (b). Curves 1 and 2 were taken with the cells full of pure aniline, no filter was used, the source of light being held at a low temperature in this series. Curves 3 and 4 were obtained at 1 bar and curves 5 and 6 at 1000 bars. The magnitude of the effect of pressure on the absorption of light by this solution may be estimated from a comparison of curves 3, 4 and 5, due allowance being made for the separation of curves 1 and 2. It will be seen that a 1.8-fold increase in the thickness of the absorbing layer does not increase the absorption by any means as much as an increase of pressure of 1000 bars even though the change in density due to the rise of pressure is less than 4%. In Fig. 1B, a systematic study of the effect of pressure on this system is given; cell (a) was used in this and in all the following experiments, and curves 2, 3, 4 and 5 give the transmission spectra at 1, 500, 1000 and 1500 bars, respectively. It will be noticed that at wave lengths where the solution is quite transparent at 1 bar, its absorption is considerable at 1500 bars, and that in the strongly absorbing regions on the short wave side of the transmission spectrum the logarithm of the intensity decreases linearly with rise of pressure.

Transmission curves for a 50% solution of aniline in nitrobenzene are given in Fig. 2A. The incident light (curve 1) passed through a filter of Corning Daylight Glass (5 mm.). Curves 2 and 3 represent different exposures at 25° and 1 bar and their reproducibility is typical. Curve 5 was obtained at 1000 bars. In one set of experiments with a photocell and galvanometer, it was found that the amount of light of wave length 546 mμ (mercury green line) transmitted by an aniline–nitrobenzene solution fell to 40% of its value at 1 bar when the pressure was raised to 1000 bars. From an examination of a series of mixtures of aniline and nitrobenzene over the whole range of concentration, it was concluded that there was no obvious influence of concentration on the effect of pressure on the absorption of light by these solutions.

The behavior under pressure of an 8.5% solution of triphenylamine in nitrobenzene is shown in Fig. 3A and that of an 8.5% solution of diphenylamine in Fig. 3B. The legend for the

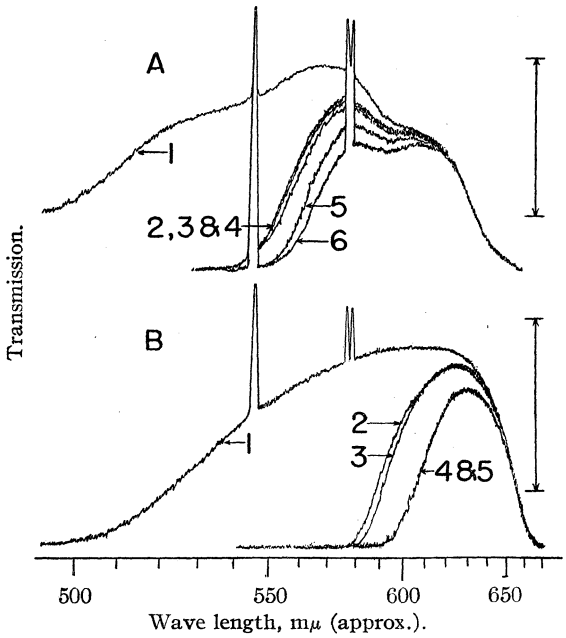


Fig. 2.—Transmission curves **A** for a 50% solution of aniline in nitrobenzene, **B** for a 49% solution of dimethylaniline in nitrobenzene: **A1** and **B1**, aniline in cell; **A2** and **A3**, solution at 25° and 1 bar; **A4**, solution at 85° and 1 bar; **A5**, solution at 25° and 1000 bars; **A6**, solution at 85° and 1000 bars; **B2**, solution at 85° and 1 bar; **B3**, solution at 25° and 1 bar; **B4** and **B5** (indistinguishable), solution at 25 or 85° and 1000 bars.

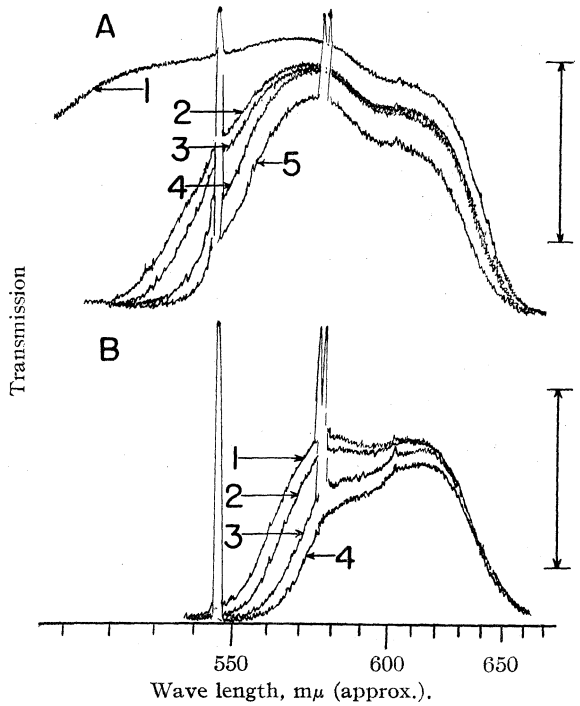


Fig. 3.—Transmission curves for 8.5% solutions of **A** triphenylamine in nitrobenzene, **B** diphenylamine in nitrobenzene: **A1**, aniline in cell; **A2**, solution at 85° and 1 bar; **A3**, solution at 25° and 1 bar; **A4**, solution at 85° and 1000 bars; **A5**, solution at 25° and 1000 bars; **B1**, solution at 85° and 1 bar; **B2**, solution at 25° and 1 bar; **B3**, solution at 85° and 1000 bars; **B4**, solution at 25° and 1000 bars.

figure identifies the curves. It will be noticed that as regards the effect of pressure on the absorption of light these solutions resemble those of the other amines in nitrobenzene. The transmission curve (A4) for the triphenylamine solution at 85° and 1000 bars is, however, anomalous in that it converges on the curve for 85° and 1 bar (A2) at a wave length of 580 mμ.

The Effect of Temperature on the Absorption of Light by Solutions of Amines in Nitrobenzene

We examined the transmission spectra of the solutions described in the previous section at 25, 55 and 85°. As the results at 55° were always intermediate between those at 25 and 85°, they are omitted from the published diagrams for the sake of clarity. The results are so diversified that each solution must be described separately. Figure 2A illustrates the results found with the aniline–nitrobenzene solution. At atmospheric pressure a rise of temperature from 25 to 85° produces a very small but reproducible *increase* in the absorption of light by this solution (curves 2, 3 and 4) which gains in significance when it is noticed that at 1000 bars the same rise of temperature causes a pronounced increase in the absorption of light by this solution, as a comparison of curves 5 and 6 will show. These observations apply to all the nitrobenzene–aniline solutions we have studied. The behavior of a 50% solution of dimethylaniline in nitrobenzene is shown in Fig. 2B. At 1 bar a rise of temperature from 25 to 85° causes a slight decrease in the light absorption particularly on the short wave edge of the transmission spectrum (curves 2 and 3). This change is reproducible and seems to be real. At 1000 bars the same rise of temperature produces no observable change in the absorption of light by the solution. As in the case of aniline–nitrobenzene mixtures, the effect of raising the pressure is to make the temperature coefficient of the absorption more positive. The curves given in Fig. 3 show that the absorption of light by the solutions of triphenylamine and of diphenylamine in nitrobenzene decreases quite significantly when the temperature is raised from 25 to 85° at both 1 and 1000 bars, and that there is no appreciable effect of pressure on the temperature coefficient.

At 85° and 1000 bars the specific volumes of all the solutions discussed in this section are approximately the same as at 25° and 1 bar. It will be seen from the diagrams, therefore, that rise of temperature at constant volume causes an increase in the absorption of light by all the solutions.

Miscellaneous Observations

In order to satisfy ourselves that the pressure effects just described were not due to some unexpected characteristic of our apparatus, we made similar observations on an 11% aqueous solution of potassium bichromate. No significant effect of pressure on the absorption of light by this solution was found (Fig. 4B). We also observed that the transmission of light by the apparatus, when the cell was filled with pure aniline, was not affected by pressure.

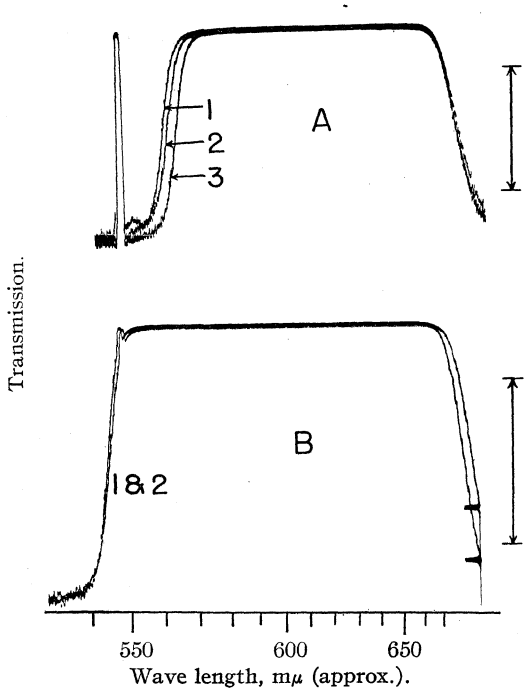


Fig. 4.—A. The transmission of light by a 3.1% solution of dimethylaminoazobenzene in benzene at 1 bar (1), 500 bars (2), and at 1000 bars (3). B. The transmission spectra of an 11% solution of potassium dichromate in water at 1 and at 1000 bars.

Solutions of *p*-nitrophenol in aniline absorb light less strongly in the visible than nitrobenzene–aniline solutions of the same molal composition, but their behavior under pressure changes is the same. On the other hand, the absorption of light by the *p*-nitrophenol solutions is notably increased by rise of temperature. The transmission curves at 25° (1) and 85° (2) for a 44% solution are given in Fig. 5, where it will be seen that the positive temperature coefficient is much larger than any other we have described.

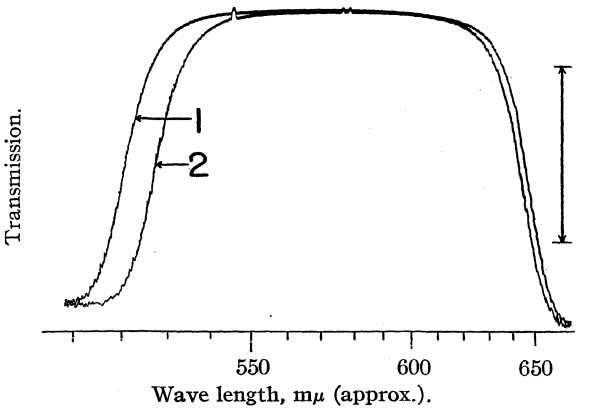


Fig. 5.—The effect of temperature on the transmission of light by a 44% solution of *p*-nitrophenol in aniline. Curve 1 was obtained at 25° and curve 2 at 85°, the pressure being 1 bar.

Solutions of nitrosobenzene in aniline and other amines are much more highly colored than the corresponding solutions of nitrobenzene. Figure 6A shows that rise of pressure increases the absorption of light by a dilute (1.1%) solution of nitrosobenzene in aniline. Similar results

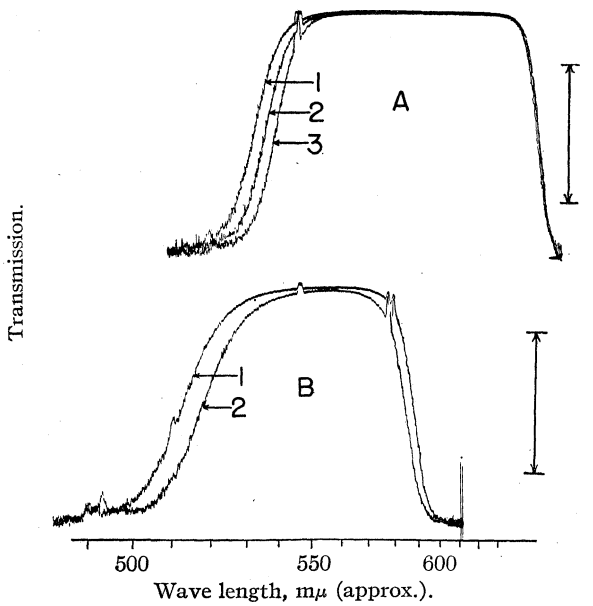


Fig. 6.—A. The transmission spectra of a 1.1% solution of nitrosobenzene in aniline at 1 bar (1), at 500 bars (2), and at 1000 bars (3). B. The effect of pressure on the transmission of light by an 18% solution of nitrosobenzene in benzene. Curve 1 was obtained at 1 bar and curve 2 at 1000 bars.

were obtained with solutions of nitrosobenzene in dimethylaniline. The absorption of light which gives rise to the well-known green color of solutions of **nitrosobenzene in benzene** also is influenced significantly by pressure changes (Fig. 6B).

We have observed an effect of pressure on the transmission curves of dilute solutions of **dimethylaminoazobenzene in benzene** (Fig. 4A) and of solutions of *o*- or *p*-nitroaniline in acetone (not illustrated). The pressure coefficients of the light absorption by these solutions are, however, not as large as those of solutions in which the NO_2 and NH_2 groups are on entirely separate molecules.

Solutions of *s*-Trinitrobenzene in Aniline.—These solutions absorb light much more strongly than any others we have discussed and it is known that a 1:1 solid addition compound is formed in this system.[21] Figure 7 shows that a 2.5% solution of trinitrobenzene in aniline behaves in the same way as mixtures of mononitrobenzene with amines under pressure changes and that the absorption of light is diminished by rise of temperature more rapidly than in the other cases we have studied. At constant volume, however, increase of temperature enhances the absorption of visible light by this solution. A comparison of Figs. 2, 3 and 7 shows that the stronger the absorption of visible light by the solution, the more negative is its temperature coefficient at atmospheric pressure.

Thermodynamic Discussion of Results

The experiments just described contribute strong evidence against the hypothesis that the colors of these solutions arise from the presence of small amounts of compounds that have been formed by the rearrangement of covalent bonds. A consideration of the temperature coefficients of the absorption of light by aniline–nitrobenzene solutions at different pressures, of the absence of time lag, of the data summarized in the introduction, and of the fact that the solutions all absorb more strongly when the temperature is raised at constant volume will show the improbability of such an assumption. On the other hand, the hypothesis that the colors of the solutions arise from the mutual polarizations of the unlike molecules when they are separated by distances which are short compared with the mean distance of separation, *i. e.*, during a collision, furnishes the basis for a fairly detailed account of our results.

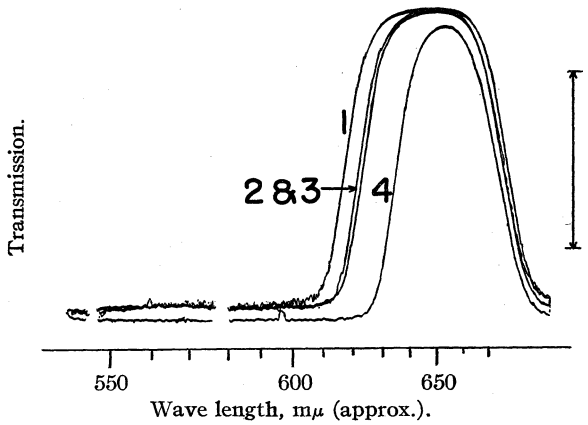


Fig. 7.—The effects of pressure and temperature on the transmission spectra of a 2.5% solution of *s*-trinitrobenzene in aniline. Curves 2 and 3 are from different photographs at 25° and 1 bar. Curve 1 gives the transmission at 85° and 1 bar, and curve 4 refers to 25° and 1000 bars.

We shall assume, therefore, that the absorption of visible light by the solution is proportional to the average time the active groups on unlike molecules spend very close to each other, *i. e.*, to the probability of finding two unlike molecules at very short distances apart and suitably oriented in the solution. The average time spent by the molecules at close distances may be correlated qualitatively with the pressure and temperature through the familiar model for liquids in which the thermal motion of the molecules is expressed in terms of the oscillations of a given molecule in a free volume, v_f, bounded by other molecules which are held stationary in their mean positions.[22] On the assumption that the potential energy of the molecule changes only during collisions, a formula for the oscillation frequency ν in such a system has been derived by Bradley and is essentially

$$\nu = Const.\ T^{1/2}/M^{1/2}V_f^{1/3} \qquad (1)$$

where T is the absolute temperature, M the molecular weight, and V_f the free volume per mole. From our thermodynamic data on aniline, nitrobenzene and their mixtures,[23] we can estimate V_f by means of a relation whose validity

(21) B. R. Hamilton and D. L. Hammick [*J. Chem. Soc.*, 1350 (1938)] have found that the absorption coefficients of solutions of aniline and *s*-trinitrobenzene in carbon tetrachloride diminish with rise of temperature.

(22) (a) J. O. Hirschfelder, D. Stevenson and H. Eyring, *J. Chem. Phys.*, **5**, 896 (1937); (b) R. S. Bradley, *Trans. Faraday Soc.*, **33**, 1185 (1937); *J. Chem. Soc.*, 1910 (1934); (c) N. F. Mott and R. W. Gurney, "Repts. on Progress of Physics," Vol. V, The University Press, Cambridge, 1939, p. 46; (d) J. Frenkel, *Trans. Faraday Soc.*, **33**, 58 (1937).

(23) R. E. Gibson and O. H. Loeffler, THIS JOURNAL, **61**, 2515, 2877 (1939).

has been made probable by Kincaid and Eyring[24] and which may be written in the form

$$V_f^{1/3} = 2R/V^{2/3}\,(\partial P/\partial T)_V \qquad (2)$$

At constant temperature we have found empirically that $V_f^{1/3}$ is inversely proportional to the pressure over a range of 1000 bars. By equation (1), therefore, the oscillation frequency of the molecules which determines the average time they spend in close proximity under these conditions should be directly proportional to the pressure, and, according to our hypothesis, the absorption of light of a given wave length should also vary directly with the pressure. This conclusion is in accord with the results given in Fig. 1A.

At constant volume we found empirically that the product $T^{1/2}(\partial P/\partial T)_V$ was constant over a range of 60° at least, whence it follows that $V_f^{1/3}$ is directly proportional to $T^{1/2}$ or to the mean square velocity of the molecules at their mean positions, and that the oscillation frequency is independent of the temperature (eqn. 1). This increase of free volume with temperature is due to the compressibility of the molecules,[25] their distance of closest approach during a collision depending on the velocity with which they collide, and on consequent changes in molecular distribution. As a result of this increasing interpenetration the molecules spend on the average a larger fraction of the time at very close distances as the temperature rises, even though the oscillation frequency computed from equations (1) and (2) remains constant, and the absorption of light of longer wave lengths increases. All the solutions we have studied show a marked increase in light absorption as the temperature is raised at constant volume.

The effect of increasing temperature at **constant pressure** is not so easy to predict, since the rapid increase in free volume reduces the probability that two unlike molecules will be close together, while the increase in the kinetic energy of the molecules and their closer approach on collision influences this probability in the opposite direction. It will be noticed that the influence of temperature at constant pressure on the absorption of light by all the solutions of amines in nitrobenzene is quite small, as might be expected when two opposing effects are at work. Calculations with equations (1) and (2) show that the oscillation frequency in aniline–nitrobenzene mixtures decreases when the temperature is raised at constant pressure, and that the decrease is slightly less rapid at 1000 bars than at 1 bar, owing to the fact that the thermal expansion of the solution diminishes with pressure. As the interpenetration effect may be presumed to be independent of pressure, the effects of pressure on the temperature coefficient of the light absorption shown in Figs. 2A and 2B are correlated with the thermodynamic properties of the solutions.

Another factor in determining the probability that two active groups on unlike molecules shall be in contact is the existence of short-range, specific attractive forces between groups in the respective molecules which will cause a temporary "sticking" when the molecule in our model collides with an appropriate spot on the walls of the "cage" of surrounding molecules. This effect is to be expected in systems showing negative deviations from ideality, especially those in which solid addition compounds are formed, and its importance decreases with rise of temperature according to the Boltzmann law.[26] In solutions where the mutually attracting groups are those intimately connected with the absorption of visible light this "sticking" effect will increase the absorption at low temperatures and produce a relatively large negative temperature coefficient of the light absorption. We consider this to be the state of affairs in solutions of *s*-trinitrobenzene in aniline and we shall refer later to the mechanism of the "sticking" effect in this system.

If, however, one or both of the mutually attracting groups is not directly connected with the absorption process, the probability of color-producing collisions will fall, the solution will absorb light to a less extent at low temperature (other things being equal) and the temperature coefficient of absorption will have a relatively large positive value. Solutions of *p*-nitrophenol in aniline provide, we think, an example of this effect, the strong specific attraction being between the OH and NH_2 groups. The behavior of these solutions suggests that a phenomenon akin to complex isomerism in some solid addition compounds[27] is appearing in the solutions. We recognize two separate intermolecular actions in these solutions: (a) interaction between the NO_2 and NH_2 groups giving rise to the color, and (b)

(24) J. F. Kincaid and H. Eyring, *J. Chem. Physics*, **6**, 620 (1938).

(25) For a definition of this term see R. E. Gibson and O. H. Loeffler, THIS JOURNAL, **61**, 2520 (1939), or ref. 22c.

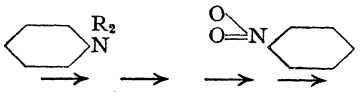
(26) The short-range attractions between groups on like molecules must not be overlooked in this discussion.

(27) E. Hertel and K. Schneider, *Z. physik. Chem.*, **A151**, 413 (1930); **B13**, 387 (1931).

interaction between the NH_2 and OH groups tending to inhibit (a) at lower temperatures and giving rise to solid addition compounds. It is well known that mixtures of phenol and aniline[28] and of *p*-nitrophenol and aniline[29] have relatively high viscosities, show large negative departures from Raoult's law, and deposit solid addition compounds at lower temperatures, but that these deviations from ideal behavior diminish rapidly as the temperature is raised.[30]

The Effect of Composition on the Absorption of Light by the Solutions

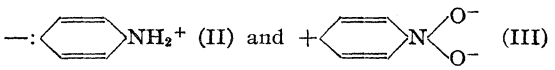
In the systems we have studied, reactions involving a transfer of electrons from the amino group of an *aromatic* amine[31] to the nitro or nitroso group of the other component (*e. g.*, oxidation–reduction or acid–base reactions) are possible, and, although they do not actually proceed under the conditions of our experiments, we suggest that the primary inductomeric or electromeric polarizations[32] associated with these reactions do occur and are responsible for the color changes. Kinetic studies of the reduction of nitrobenzene derivatives[33] have shown that the rate of reduction increases when the inductive and resonance[34] effects of the nuclear substituents tend to diminish the negative charge on the nitro group and hence to increase its attraction for external electrons. We shall assume, therefore, that a drift of electronic charge from the NR_2 group to the oxygens of the NO_2 group with consequent displacements of negative charge in the N:O bond and in the polarizable aromatic nuclei in the direction indicated by the arrows in formula I takes place when an aromatic amino group and a nitro group come very close together in the solution.



(I)

Hammick[35] and his collaborators already have suggested the same polarization mechanism in their assumption that the primary activation in the formation of solid addition complexes between polynitro compounds and aromatic hydrocarbons is a driving of electronic charge from the oxygen to the nitrogen of the NO_2 group.

In demonstrating from qualitative considerations of the inductive and resonance effects of substituents in either compound that the absorptions of the solutions are pushed to longer wave lengths (a) as the electron attraction power of the oxygen of the NO_2 group increases and (b) as the electron mobility in the aromatic amine increases, we should first note that the configurations



(II) and (III)

which, together with the orthoquinonoid forms, contribute significantly to the structure of aniline and of nitrobenzene,[36] actually oppose the polarization we have suggested. We should emphasize, therefore, that the electron drift in formula I is presumed to occur in aniline–nitrobenzene solutions only when the molecules are brought into very close contact by their thermal motion (*cf.* the discussion of the temperature coefficient).

Electron-attracting groups such as NO_2, Cl or CO_2CH_3 in the ring of the nitro compound promote the electronic drift by reducing the negative charge on the NO_2 group. This gives rise to short-range attractions and affords an explanation of the differences in behavior between solutions of polynitro compounds and those of mononitro compounds in amines or hydrocarbons mentioned in the introduction and accounts for the greater absorptions of the polynitro solutions. It will be recalled that dilute alkalies cause color changes in polynitrobenzenes but not in pure nitrobenzene.[37]

Electron-repelling groups such as NH_2 or CH_3 in the ring of the nitro compound reduce its ability to polarize the amino compound both by their inductive effects and, in *o*- and *p*-positions, by their resonance effects. We found from

(28) F. A. H. Schreinemakers, *Z. physik. Chem.*, **29**, 577 (1899). R. Kremann, *Monatsh.*, **25**, 1234 (1904); *ibid.*, **27**, 91 (1906).

(29) R. Kremann and O. Rodinis, *ibid.*, **27**, 125 (1906).

(30) See, for example, the effect of temperature on the viscosity–composition curves of mixtures of phenol with amino compounds studied by A. Bramley, *J. Chem. Soc.*, **109**, 10 (1916).

(31) We have found that no significant color change occurs when α-phenylethylamine, a stronger base than aniline, is mixed with nitrobenzene. This observation suggests strongly that the amino group must be attached to the ring either directly or through a conjugated bond system, if a color change is to be produced.

(32) See J. R. Johnson, "Organic Chemistry," H. Gilman, Editor, J. Wiley and Sons, Inc., New York, N. Y., 1938, Chap. 19; C. K. Ingold, *Chem. Rev.*, **15**, 225 (1934).

(33) See N. V. Sidgwick, T. W. J. Taylor, and W. Baker, "The Organic Chemistry of Nitrogen," Clarendon Press, Oxford, 1937, p. 255.

(34) See J. R. Johnson, ref. 32; G. W. Wheland and L. Pauling, THIS JOURNAL, **57**, 2086 (1935); L. Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1939, p. 141. The "mesomeric" effect of Ingold (ref. 32) is now generally referred to as the resonance effect.

(35) D. L. Hammick and G. Sixsmith, *J. Chem. Soc.*, 580 (1935); D. L. Hammick and A. Hellicar, *ibid.*, 761 (1938); T. T. Davies and D. L. Hammick, *ibid.*, 763 (1938).

(36) L. Pauling, ref. 34, p. 192.

(37) See N. V. Sidgwick, T. W. J. Taylor, and W. Baker, ref. 33, p. 259

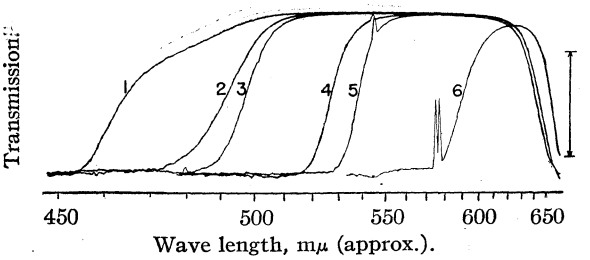


Fig. 8.—A comparison of the transmission of light by equimolecular solutions of (1) *p*-nitroaniline in nitrobenzene, (2) aniline in nitrobenzene, (3) *p*-nitroaniline in aniline, (4) diphenylamine in nitrobenzene, (5) dimethylaniline in nitrobenzene, and (6) *p*-phenylenediamine in nitrobenzene.

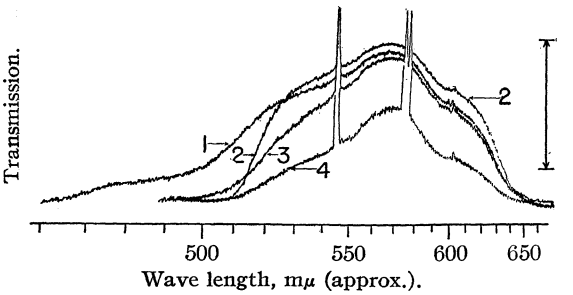


Fig. 9.—A comparison of the transmission curves of 0.22 molar solutions of *p*-nitroaniline (1), *o*-nitroaniline (2), aniline (3), and *m*-nitroaniline (4) in nitrobenzene.

curves similar to those in Fig. 9 that the absorption of visible light by 0.31 molar solutions in aniline increased in the order *p*-nitroaniline < nitrobenzene < *m*-nitroaniline. Quinonoid structures being impossible in *m*-nitroaniline,[38] this result shows that the inductive effect of the NH_2 group does not compensate for the loss of the resonance effect when nitrobenzene is changed to *m*-nitroaniline and that the resonance in nitrobenzene does diminish its interaction with aniline.[39]

As regards the effects of substituents in the amine nucleus, Fig. 9 shows that 0.22 molar solutions of the nitroanilines in nitrobenzene increase in light-absorbing power in the order *p*-nitroaniline ~ *o*-nitroaniline < aniline ≪ *m*-nitroaniline. The effect of an absence in the meta compounds of possible quinonoid configurations is again striking and indicates that resonance involving these configurations does reduce the interaction of aniline with nitro compounds as formula I suggests. A comparison of the transmission curves of equimolecular solutions of aniline, *m*-nitroaniline and *p*-nitroaniline in nitrobenzene, on the one hand, and of nitrobenzene, *m*-nitroaniline and *p*-nitroaniline dissolved in aniline, on the other, showed that absorptions of light are more influenced by the resonance effect of the NO_2 group than by that of the NH_2 group, a conclusion which is supported by the interaction dipole moments of aniline and nitrobenzene.[40] A transmission curve of a solution of *p*-nitroaniline in nitrobenzene is shown also in Fig. 8, curve 1. The sharp bend in this curve about 465 mμ is a feature of interest, because the absorption below this wave length is sensitive to pressure changes and hence of intermolecular origin, whereas the absorption at longer wave lengths is not sensitive to pressure changes, being due presumably to the nitroaniline itself. By their inductive effects, groups such as NH_2 or CH_3[41] increase the potential concentration of electronic charge on the amino group. This effect on the absorption of light is strikingly shown by the curve for a dilute solution of *p*-phenylenediamine (a much stronger reducing agent than aniline) in nitrobenzene in Fig. 8 (curve 6). The exposure from which this curve was made was four times as long as that of any of the other amines in this diagram.

In acetanilide and *p*-nitroacetanilide the configurations $C_6H_5NHC(CH_3)=O$ and $C_6H_5{}^+NH=C(CH_3)O^-$ contribute to the structure,[42] and the resonance introduced lowers the possibility of the formation of a double bond between the nitrogen and the ring and renders the NH group less polarizable. The interaction of the NH group with external or internal NO_2 groups is, therefore, reduced by the attachment of the acetyl group. We have observed, on the one hand, that acetanilide and *p*-nitroacetanilide (a *white* solid) dissolve in nitrobenzene without any appreciable color change, and, on the other, that the transmission spectra of *p*-nitroacetanilide–aniline solutions resemble closely those of nitrobenzene–aniline solutions, being quite different from the spectra of *p*-nitroaniline–aniline solutions of the same molar concentration.

The electron mobility in the N-substituted amines, as measured, for instance, by the interaction dipole moments (resonance contribution to the dipole moment) of their *p*-substituted

(38) N. V. Sidgwick, T. W. J. Taylor, and W. Baker, ref. 33, p. 74.

(39) In alkaline solutions *m*-nitroaniline is reduced much more rapidly than the *o* and *p* isomers. H. Goldschmidt and M. Eckardt, *Z. physik. Chem.*, **56**, 424 (1906).

(40) L. Pauling, ref. 34, p. 146.

(41) B. R. Hamilton and D. L. Hammick (*op. cit.*) showed that the absorption coefficients of carbon tetrachloride solutions of *s*-trinitrobenzene and different amines decreased in the order *o*-toluidine > *m*-toluidine > *p*-toluidine > aniline > chloroaniline.

(42) See L. Pauling, ref. 34, p. 192.

derivatives, increases as the number of methyl groups on the nitrogen increases.[43] Our results show that the absorption of light by nitrobenzene solutions of these N-substituted amines is pushed to longer wave lengths as the solute changes from aniline to dimethylaniline (curves 2 and 5, Fig. 8). It is of interest to note that the heats absorbed on the formation of 50 mole per cent. solutions of nitrobenzene in aniline, ethylaniline and diethylaniline are, respectively, 132, 27 and −15 cal./mole.[17]

In accord with the well-known fact that nitrosobenzene is much more readily reduced than nitrobenzene,[33] we have observed that the colors of liquid mixtures of amines and nitrosobenzene are much more intense than those of the corresponding mixtures with nitrobenzene. Both these facts may be explained by the recognized existence of the NO_2 group itself as a resonating structure[44] to which several configurations stabilizing the electronic charge on the oxygen contribute. We conclude from our observations of the effect of pressure on the absorption of light by solutions of nitrosobenzene in benzene that part, at least, of this absorption is due to intermolecular action. The interaction of a polarizable benzene molecule with a nitroso group is apparently large enough to bring the light absorption into the visible region, whereas the action of benzene on a nitro group is apparently not large enough. The role of the amino group seems to be that of a liaison between the polarizable aromatic nuclei and the oxygen atoms of the NO_2, NO, SO_2, etc., groups, the amino group focussing the polarization, and the difference between the interactions of aromatic hydrocarbons and of aromatic amines with these oxygens is, therefore, only one of degree.

Without a quantum mechanical treatment, methods of which are, however, rapidly developing,[45] it is difficult to locate exactly the electron system responsible for the absorption of visible light by these solutions. The behavior of tetranitromethane shows that the aromatic part of the nitro compound is not essential to the phenomenon. Sklar[46] has shown theoretically that the weak 2500 Å. band in benzene is intensified and shifted toward the red when the symmetry of the ring is distorted by the resonance effects of substituents. It seems improbable, however, that any intermolecular polarization of the type we have discussed can cause distortions in the aromatic ring as large as those produced intramolecularly in nitrobenzene or nitroaniline, whose absorptions in the green or yellow are very much less than those of the solutions. Furthermore, the behavior of hydrocarbons suggests that the amino group is not absolutely essential, so that we are left with the N:O group as the most probable seat of the absorption. It will be seen from our picture in formula I that the proximity of the polarizable amine or hydrocarbon lowers the energy of a state in which an ionic binding such as $^{-}N—O^{+}$ exists in the N:O group.[47]

Our hypothesis that the colors of the solutions discussed in this paper arise from preliminary polarizations in oxidation–reduction reactions suggests comparison with other labile intermediate oxidation–reduction products such as quinhydrone, Wurster's salts, or semiquinones in general,[48] whose strong absorptions have been ascribed to charge-resonance involving odd electrons.[49] Nitrosobenzene and *p*-nitrosodimethylaniline are also relatively unstable, deeply colored intermediate steps in oxidation–reduction series, but they differ from the semiquinones in that they are diamagnetic[50] and have, presumably, no odd electrons. The apparent similarities in origin and behavior of the semiquinones, the nitroso compounds and the colored solutions are, however, sufficiently striking to merit further investigation, even though a theoretical picture embracing all these types of systems is not immediately obvious.

If our assumption that the changes in the absorption of light by these solutions are due to prereaction polarizations is substantiated, interesting possibilities of investigating reaction mixtures under different thermodynamic conditions by ultraviolet and visible absorption spectroscopy arise. Indeed, the large accelerating effect of pressure on reactions such as the addition of isopropyl iodide to dimethylaniline[51] is exactly

(43) G. M. Bennett and S. Glasstone, *Proc. Roy. Soc.* (London), **A145**, 71 (1934). R. J. B. Marsden and L. E. Sutton [*J. Chem. Soc.*, 599 (1936)] give 0.95 and 1.86 × 10^{-18} e. s. u. for the interaction dipole moments of *p*-nitroaniline and *p*-nitrodimethylaniline, respectively.

(44) L. Pauling, ref. 34, p. 186.

(45) L. Pauling, *Proc. Nat. Acad. Sci.*, **25**, 577 (1939); R. S. Mulliken, *J. Chem. Phys.*, **7**, 570 (1939), the latest of a series; A. L. Sklar, *ibid.*, **7**, 984 (1939). G. N. Lewis and M. Calvin [*Chem. Rev.*, **25**, 273 (1939)] give a comprehensive survey of the data and the theories of the color of organic compounds, and advance a theory of color based on empirical and quantum considerations.

(46) A. L. Sklar, ref. 45.

(47) R. S. Mulliken, *J. Chem. Phys.*, **7**, 123 (1939).

(48) L. Michaelis, *Chem. Rev.*, **16**, 243 (1935).

(49) L. Pauling, ref. 34, p. 259.

(50) E. B. Wilson, THIS JOURNAL, **56**, 747 (1934).

(51) M. W. Perrin and E. G. Williams, *Proc. Roy. Soc.* (London), **A159**, 162 (1937).

paralleled by the effects of pressure on the absorption of light by similar solutions.

Summary

We have found that the absorption of visible light by solutions of aromatic amines in nitro or nitroso compounds is pushed very significantly toward the longer wave lengths when the hydrostatic pressure over the solutions is raised at constant temperature, and also when the temperature is raised at constant volume. The absorption of light by these solutions may increase, decrease or remain constant as the temperature is raised at constant pressure. These results have been correlated into a consistent theory which avoids any assumption of the formation of colored compounds by the hypothesis that the colors of the solutions arise from the mutual polarizations of the molecules when appropriate groups are in close proximity, account being taken of the influence of pressure and temperature on the collision frequency, the distance of closest approach and the effect of short-range attractions between groups.

We have also shown from orienting experiments that substituents in the nitro compound and in the amine influence the absorption of light by the solutions in a way that parallels closely their effects on the reducibility of the NO_2 or NO group on the one hand, and the electron mobility in the amino compound on the other. It is suggested that the polarizations which give rise to the colors of the solutions may be regarded as primary steps in possible reactions, such as oxidation and reduction, involving transfer of electrons from the aromatic amine or hydrocarbon to the oxygen of the nitro or nitroso group.

WASHINGTON, D. C. RECEIVED FEBRUARY 21, 1940

[CONTRIBUTION FROM THE MULTIPLE FELLOWSHIP OF THE COTTON RESEARCH FOUNDATION, MELLON INSTITUTE]

Composition of Cottonseeds. III. Solubility of Proteins in Alkaline Solutions of Neutral Salts[1]

BY H. S. OLCOTT AND T. D. FONTAINE

Oil-free cottonseed meats contain approximately 8.5% nitrogen (50–55% protein). Water will extract 25–30% of the nitrogen compounds. Dilute solutions of neutral salts extract 75–85% of the total. The materials not dissolved by water but extracted by salt are the cottonseed globulins. Osborne and Vorhees[2] and Jones and Csonka[3] have recorded some of the properties of these proteins. Their extraction by salt and alkaline solutions has been described more recently.[4]

Methods were sought for isolating the globulin fraction on a large scale. Extraction with salt solutions was efficient but means of recovery therefrom did not appear to be practical. Dilution required relatively large amounts of water, and precipitation with acid, though easily effected, yielded an insoluble product. The cottonseed globulins, like several other vegetable globulins, are very readily denatured in acid solution.

Extraction with alkali at *p*H 10.0 and precipitation by the addition of acid to the isoelectric point (*p*H 6.5–7.0) was found to be a satisfactory procedure but suffered from the disadvantage that cottonseed pigments are easily oxidized in alkaline solution, yielding brown products which affect the color of the protein.

A consideration of the theories of protein solubility suggested that the globulin might be extracted at lower *p*H levels in the presence of low concentrations of salt; that is, that the two methods, salt peptization and alkali solution, would be mutually additive. Experimentally, however, it was found that the opposite was true; in the presence of low concentrations of salt, the solubility of the protein at a *p*H below the maximum for extraction was actually depressed. The phenomena observed were of sufficient interest to invite further investigation.

Experimental

Data were obtained in the following manner. Ether-extracted cottonseed meats[4,5] were used. A sample was

(1) Presented in part before the Division of Biological Chemistry of the American Chemical Society at Boston, Mass., Sept. 11–15, 1939.

(2) Osborne and Vorhees, THIS JOURNAL, **16**, 778 (1894).

(3) Jones and Csonka, *J. Biol. Chem.*, **64**, 673 (1925).

(4) Olcott and Fontaine, THIS JOURNAL, **61**, 2037 (1939).

(5) The amount of nitrogen extracted under a given set of conditions varied for different preparations of cottonseed meal. With the two meals used in the present investigation, alkali at *p*H 9.0 extracted 83% of the nitrogen from one, 77% from the other.

shaken thoroughly with 40 times its weight of water containing sufficient salt and alkali (as indicated by preliminary titrations) to bring the mixture to the required *p*H and salt concentration. Several drops of chloroform were added to prevent spoilage and the mixtures were allowed to stand, with occasional shaking, for sixteen to twenty-four hours. To determine the amount of protein extracted, the suspension was centrifuged, filtered, and aliquots were analyzed for nitrogen by a modified Kjeldahl method. *p*H was determined with the glass electrode.[6]

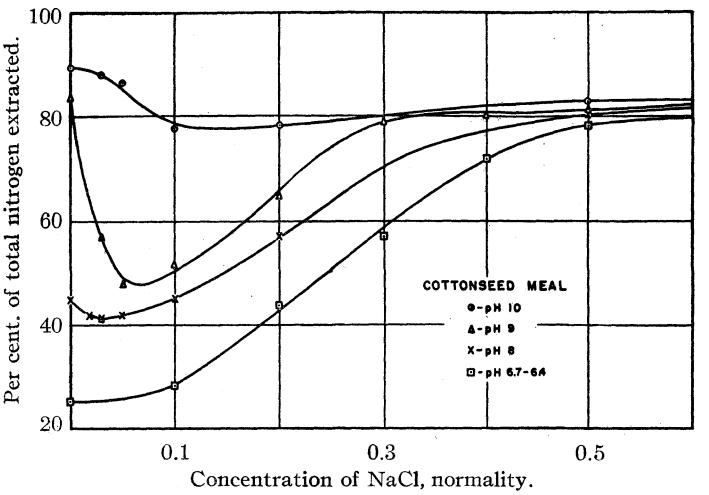


Fig. 1.—Effect of sodium chloride concentration on the extraction of cottonseed proteins from the meal at different *p*H levels. Sodium hydroxide was used to bring the mixtures to the proper *p*H.

The effect of sodium chloride on the extraction of the nitrogen compounds of cottonseed at various *p*H levels is indicated in Fig. 1. The solubility of the protein at *p*H 10 was depressed only slightly by the presence of salt. At *p*H 9, the amount of protein extracted reached a minimum in 0.05–0.07 *N* salt, the solubility again increasing with increasing concentration of salt. At *p*H 8, the antagonistic effect of the salt was only slightly evident. The lowest curve represents the extractability of the cottonseed proteins in solutions of salt to which no alkali had been added. The *p*H of such extracts varied from 6.7 in the absence of salt to 6.4 in 0.5 *N* solution.

That the behavior of cottonseed meal under the conditions described could be attributed specifically to the globulins was demonstrated by duplicating the experimental procedure with the isolated protein (Fig. 2). The material was prepared by leaching cottonseed meal with water to remove water-soluble constituents, then extracting the residue with 0.5 *N* sodium chloride. After centrifugation, the protein was precipitated by dilution with 5 volumes of water. The precipitate was repeatedly washed with distilled water to remove residual salts, separated each time by centrifugation, and finally dried in thin layers on a glass plate in a current of air. Sixty-four % of the product so obtained was soluble at *p*H 9.0, but only 22% could be peptized at the same *p*H in the presence of 0.05 *N* sodium chloride. A solution of the protein at *p*H 9.0 or 9.5 could be partially precipitated by the addition of the correct amount of salt.

The effect of several other inorganic salts on the solubility of the cottonseed proteins was investigated under similar conditions (Fig. 3). In the case of the sodium salts, the important part played by the anion was evident. In contrast to the chloride, the sulfate and iodide caused only a slight depression in the solubility curve. Sodium fluoride is a poor peptizing agent; whereas, in neutral solution, most inorganic salts (0.5 *N*) peptize 75 to 85% of the nitrogen of cottonseed meal, sodium fluoride peptizes only 57%. The results obtained with potassium chloride and sulfate were almost identical with those observed with the corresponding sodium salts (Table I).

The effect of alkaline earth salts was more pronounced. Inasmuch as water alone extracts 25 to 30% of cottonseed nitrogen, the 0.03–0.05 *N* solutions of calcium chloride and magnesium sulfate apparently suppressed entirely the solubility of the globulin. This fact was also demonstrated with the isolated protein. A quantitative method for the separation of the globulin from an alkaline extract of cottonseed meal is suggested, based upon the addition of calcium, magnesium, or barium salts in the correct concentration. The precipitation is not dependent upon a decrease in *p*H.

The data for experiments typical of those which have been plotted on the graphs are shown in Table I. Preliminary runs were used to determine how much alkali was necessary to bring the mixture to the required *p*H. It will be noted that increasing amounts of alkali were needed with increasing concentrations of salt.[7]

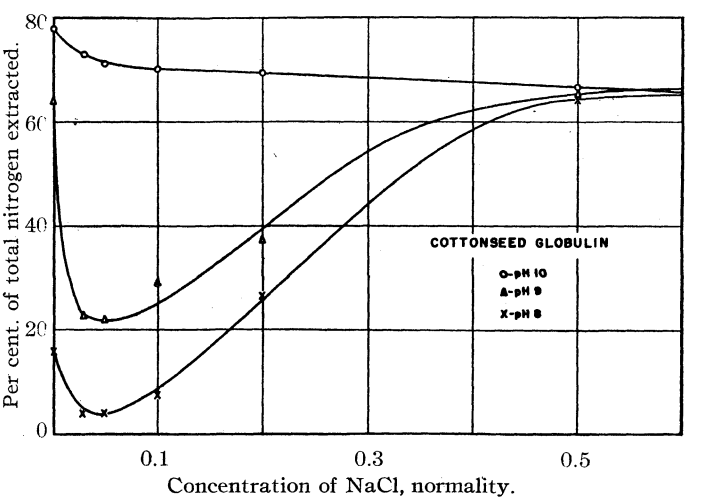


Fig. 2.—Effect of sodium chloride on the solubility of a cottonseed globulin preparation at different *p*H levels.

The effect of sodium and calcium chlorides, in the concentrations resulting in minimum solubility, on the extrac-

(6) Coleman electrometer, model 3D.

(7) This result was observed in every series of experiments. The complete data have been omitted for the sake of brevity.

TABLE I

EXTRACTION OF NITROGENOUS SUBSTANCES FROM ETHER-EXTRACTED COTTONSEED[a]

Salt concn.,[b] N	NaCl NaOH Milli-equiv.	NaCl pH	NaCl % N extd.	KCl NaOH Milli-equiv.	KCl pH	KCl % N extd.	Na_2SO_4 NaOH Milli-equiv.	Na_2SO_4 pH	Na_2SO_4 % N extd.	K_2SO_4 NaOH Milli-equiv.	K_2SO_4 pH	K_2SO_4 % N extd.	$MgSO_4$ NaOH Milli-equiv.	$MgSO_4$ pH	$MgSO_4$ % N extd.
..	1.35	9.00	83.6	1.40	8.95	77.4	1.40	8.95	77.4	1.40	8.95	77.4	1.45	9.00	83.6
0.01	..	..	..	1.41	8.88	71.4	1.51	8.92	74.1	1.41	8.90	74.8	1.55	8.95	30.8
.02	..	..	..	1.45	8.88	58.8	1.56	9.00	73.5	1.45	8.93	71.6	1.60	8.90	28.2
.03	1.40	9.10	57.3	1.47	8.90	57.6	1.61	9.00	73.3	1.47	8.88	68.6	1.65	8.92	27.2
.05	1.45	9.05	48.7	1.51	8.88	50.5	1.66	8.97	69.5	1.51	8.90	67.2	1.75	8.90	31.8
.10	1.52	8.95	52.0	1.55	8.85	52.8	1.75	9.05	75.6	1.55	8.90	67.2	1.90	8.88	47.2
.20	1.62	8.90	65.2	1.60	8.85	62.3	1.82	9.05	78.5	1.60	8.88	75.5	2.05	8.90	67.5
.30	1.65	8.95	79.6	1.61	8.95	74.2	..	..	..	1.61	9.00	76.0	2.20	8.95	71.5
.40	1.66	8.88	80.5	1.62	8.95	75.4	..	..	..	1.62	9.00	76.3	..	..	..
.50	1.67	8.90	81.5	1.63	8.82	75.5	1.90	9.00	79.0	1.63	8.85	76.0	2.25	8.92	82.8

[a] Five g. of meal was extracted with 200 cc. of solution for sixteen to twenty-four hours. The amount of nitrogen contained in a filtered aliquot of the extract was calculated to 200 cc. to obtain the data. [b] Cottonseed meal contains 8% ash, more than half of which is soluble in water. The extractability of the protein is probably influenced somewhat by the presence of these salts of unknown nature.

tion of the nitrogenous compounds from cottonseed meal throughout the *p*H range 3 to 11 is shown in Fig. 4. For purposes of comparison, the curves showing the efficiency of extraction with 0.5 *N* sodium chloride and in the absence of salt are repeated from the earlier publication.[4] The specific antagonistic effect of 0.07 *N* sodium chloride is marked in the *p*H range between 8 and 10, while that of calcium chloride does not disappear until a *p*H of 11 is attained.

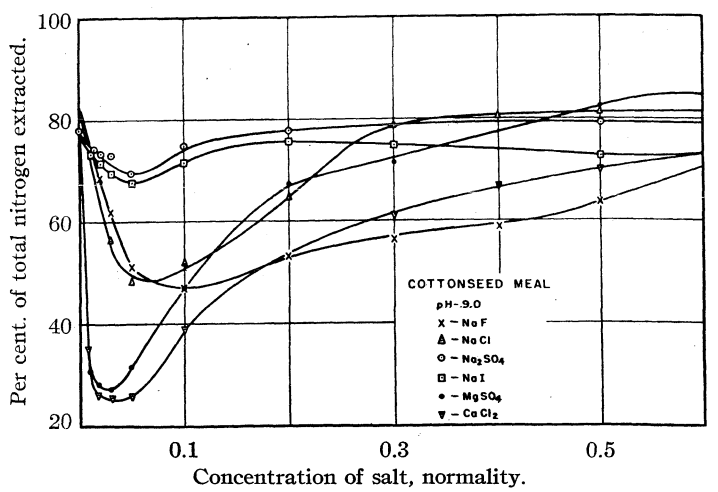


Fig. 3.—A comparison of the effect of several inorganic salts on the extraction of cottonseed proteins from the meal at *p*H 9.0.

The results shown graphically in Fig. 5 were obtained with ether-extracted hempseed meal under experimental conditions similar to those used with cottonseed meal. The absolute amounts of nitrogenous substances peptized differ from those observed with cottonseed meal but the shapes of the curves are somewhat similar. The antagonistic effect of sodium sulfate was more marked than in the case of cottonseed meal but was still less than that of sodium chloride.

Discussion

The phenomena of protein solubility have recently been reviewed by Edsall.[8] According to the investigators cited, neutral salts invariably *increase* the solubility of globulins on the alkaline side of the isoelectric point.

Sörensen and Sladek[9] concluded, from their carefully controlled experiments, that the solubility of casein varied directly with the concentration of sodium chloride in solutions alkaline to the isoelectric point. However, in the series in which the largest amount of alkali was used, a depression of solubility is recorded at a concentration of 0.025 *N* sodium chloride, as shown in Table II. This discrepancy is not commented upon in the original paper nor by Green[10] in her interpretation of the results. If the data are significant, they would indicate that, within a limited *p*H range, low concentrations of salt may antagonize rather than increase the solubility of casein in alkali. There is no suggestion in Green's[10] solubility determinations of hemoglobin in alkaline salt solutions of any parallelism with the phenomena described in this paper. The *p*H, how-

TABLE II

EFFECT OF SALT ON THE SOLUBILITY OF CASEIN IN ALKALI[a]
(Data of Sörensen and Sladek)[9]

Concn. of NaCl, N	*p*H (cor.)	% of total casein in solution
0.01	5.50	69.3
.025	5.40	63.5
.05	5.31	65.4
.10	5.24	82.2
.25	5.17	97.5

[a] In each case 91.6 milligram equivalents of casein nitrogen and 0.85 milligram equivalent of surplus NaOH were present in 1000 cc. of the mixture.

(8) Schmidt, "The Chemistry of the Amino Acids and Proteins," Charles C. Thomas, Springfield, Ill., Chapter XVI, 1938.

(9) Sörensen and Sladek, *Compt. rend. trav. lab. Carlsberg*, **17**, No. 14 (1927–1929).

(10) Green, *J. Biol. Chem.*, **93**, 517 (1931).

ever, did not vary by more than 1 *p*H unit from the isoelectric point, nor were salts other than phosphate buffers investigated. In the case of the cottonseed globulin, the region of maximum

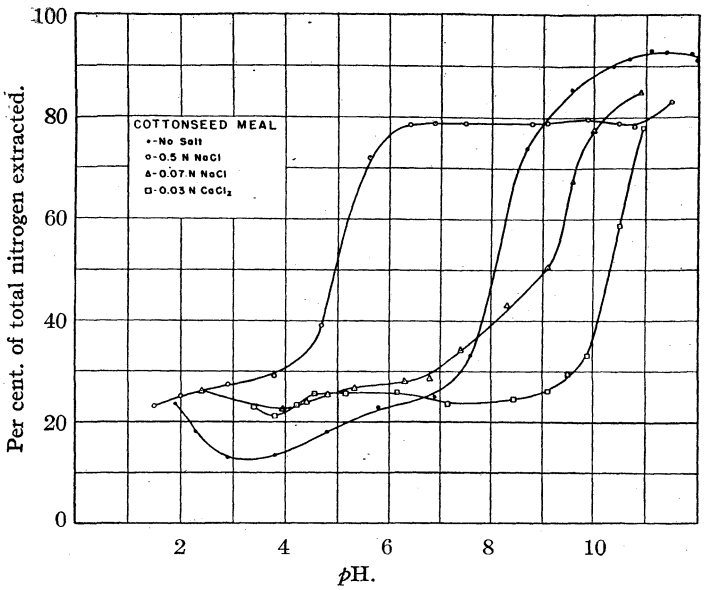


Fig. 4.—Extraction of proteins from cottonseed meal. Sulfuric acid and sodium hydroxide were used to adjust *p*H.

antagonism appears to be 2 *p*H units higher than the isoelectric point of the protein.

Edsall[11] observed that a clear gel of myosin in alkaline solution was precipitated by the addition of a small amount of salt. Upon the addition of further salt the precipitate dissolved. No quantitative data were recorded.

The data of Smith, Brother and Circle[12] can be interpreted as indicating a direct parallelism between soybean meal and cottonseed meal proteins (Fig. 6). More protein can be extracted from soybean meal with distilled water than with dilute salt solutions. Minimum solubility occurs at a concentration of 0.1 *N* sodium chloride (1 part meal:40 parts water). The isoelectric point of the principal soybean protein lies in the *p*H range 4.2–4.7; therefore the solubility behavior in neutral salt solutions (*p*H 6.7–6.0) was measured at approximately 2 *p*H units above the isoelectric point. While there was no attempt to maintain a constant *p*H level, the variations were probably not large enough to change essentially the character of the solubility curves.

(11) Edsall, *J. Biol. Chem.*, **89**, 289 (1930).

(12) Smith, Circle and Brother, THIS JOURNAL, **60**, 1316 (1938).

That the results obtained with soybean meal are a reflection of the behavior of the soybean globulin is indicated by the data shown graphically in Fig. 7. In this case the equilibrium was approached from the solution in dilute alkali.

A fresh precipitate of purified soybean globulin[13] was washed thoroughly with water, then dissolved by the careful addition of sodium hydroxide to *p*H 6.7. Upon the addition of different amounts of sodium chloride to aliquot portions, some cloudiness appeared but no precipitate could be removed by centrifugation. Quantities of acid sufficient to lower the *p*H to approximately 5.7 were then added to each aliquot, the several samples were centrifuged, and portions of the supernatant solution were analyzed for nitrogen. The sodium chloride concentration for minimum solubility appeared to be 0.1 to 0.15 *N*[14] or about twice that indicated by Smith, *et al.*,[12] for the meal. However, the solution contained approximately 3% protein, whereas with the meal, at maximum solubility, the protein was present to the extent of only 1.25%. The data for calcium chloride were obtained after the salt had been added to the solution at *p*H 6.7. In this case, no further addition of acid was necessary. The concentration of calcium chloride

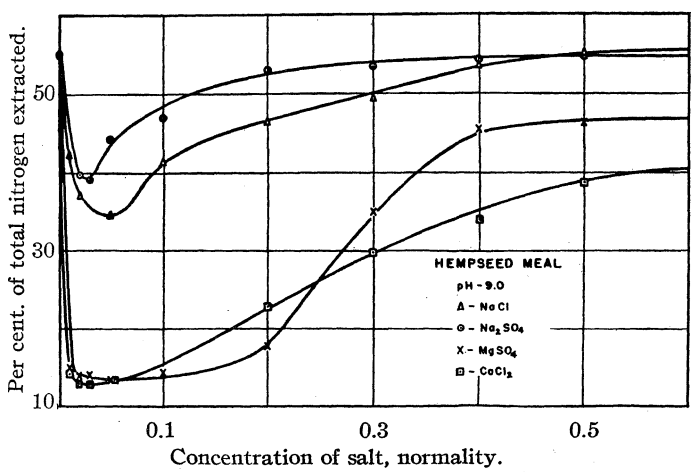


Fig. 5.—Effect of several inorganic salts on the extraction at *p*H 9.0 of the proteins from ether-extracted hempseed meal.

(13) Kindly supplied by Dr. N. J. Beaber, Mellon Institute.

(14) The salt concentrations are approximations. It was not determined how much of the sodium hydroxide used to bring the protein into solution had been required to neutralize adsorbed sulfuric acid.

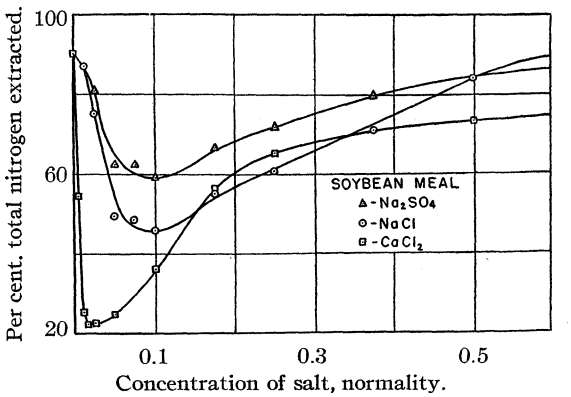


Fig. 6.—Data of Smith, Brother and Circle[12] on the extraction of soybean proteins by aqueous salt solutions. The *p*H was not held constant but probably varied from 6.7 to 6.3 with sodium chloride and from 6.7 to 5.2 with calcium chloride.

necessary to ensure minimum solubility was also approximately twice that required for the meal.

The solubility of cystine in water is increased in the presence of salt. Cystine is also soluble in dilute alkali. This resemblance to the behavior of globulins, which has been discussed by Cohn,[15] suggested that the antagonism might be observable with the amino acid. However, in a short series of determinations, in which the sodium chloride concentration was varied from 0.1 to 2.0 *N* and the *p*H maintained at 8.0, the solubility was found to vary directly with the salt concentration.

A complete interpretation of the physical and chemical reactions involved in the antagonism of small amounts of salts to alkaline extraction of the several globulins does not seem possible at present. In the case of the alkaline earth salts, the inference that metallic proteinates are precipitated appears justified. The insoluble proteinate either may again be peptized in the presence of higher concentrations of salt or may react to form more soluble compounds containing larger amounts of calcium, barium, or magnesium or consisting of double salts of the metallic proteinate and the salt.

In the case of the sodium and potassium salts, the anion plays an important role.[16] Thus the sodium proteinate which is insoluble in sodium chloride solution (0.05–0.1 *N* at *p*H 9.0), is soluble in sodium sulfate or sodium iodide when these salts are present at the same concentration.

(15) Cohn, *Chem. Rev.*, **19**, 241 (1936).

(16) It has been suggested that the results may be interpreted in terms of electrokinetic potential changes. However, in the simplest application of such an explanation, it would be expected that a divalent anion (sulfate) would be a more effective precipitant than a monovalent ion (chloride), which is contrary to the observations.

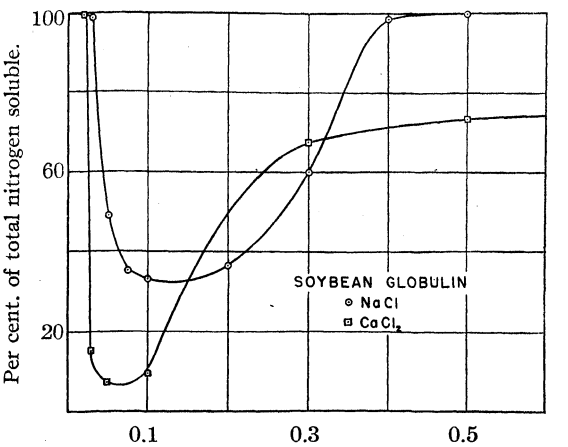


Fig. 7.—Effects of salts on the solubility of a soybean globulin preparation. The *p*H varied from 5.8 to 5.63 in the sodium chloride series and from 6.48 to 6.25 in the calcium chloride series.

As the proteins discussed in this communication, except myosin, are known to be mixtures of several individual entities, the possibility that the solubility phenomena observed with sodium chloride may be ascribed to a fractionation requires further investigation. A comparison of the physical and chemical properties of the precipitate and the soluble portion would be of interest. The data obtained with hempseed meal suggest that edestin would be a suitable purified protein for a more critical investigation of the phenomenon.

Inasmuch as it is not possible at present to continue this work, the attention of other investigators is invited to the possibilities for study of protein behavior suggested by these observations.

Summary

At *p*H 9.0 small amounts of sodium chloride markedly depress the solubility of cottonseed protein, as determined by extraction studies with cottonseed meal. Greater or smaller concentrations of salt permit the peptization of larger amounts of the total nitrogen. The alkaline earth salts are particularly effective precipitants; under the conditions used, 0.03–0.05 *N* calcium or magnesium salt solutions suppress the solubility of the globulin at *p*H 9.0 completely. The effects of several other salts on the solubility of the nitrogenous constituents of cottonseed meal have been determined. That the observed phenomena can be ascribed to the globulins and not to other constituents of the meal is shown in experiments with isolated globulin preparations.

Analogous results have been obtained with hempseed meal.

The data of Smith and co-workers[11] have been interpreted to indicate that the influence of salts on the solubility of soybean proteins in the neutral *p*H range is a parallel phenomenon.

The observations cited are exceptions to the hitherto-accepted generalization that the solvent action on proteins of salts and alkali is additive.

PITTSBURGH, PA. RECEIVED JANUARY 22, 1940

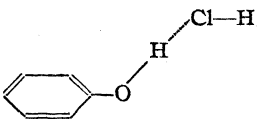
[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

Increases in the Acid Strength of Hydrogen Chloride in Dioxane Brought about by Phenols and Alcohols

BY PAUL D. BARTLETT AND HYP J. DAUBEN, JR.

Some years ago Meerwein and his co-workers[1] showed that the metallic chlorides which catalyze the rearrangement of camphene hydrochloride into isobornyl chloride are all capable of forming complexes with hydrogen chloride which are stronger acids than hydrogen chloride itself. This property was demonstrated by a method introduced by Hantzsch.[2] A solution of hydrogen chloride in dry ether was made just too dilute (0.02 *N*) to redden the indicator butter yellow (*p*-dimethylaminoazobenzene). The addition of equivalent stannic chloride (which alone at this concentration did not redden the indicator) now turned the indicator red, and a dilution of 120-fold was necessary to restore the yellow color. This was clearly due to the fact that in ether an acid of the type H_2SnCl_6 is stronger than hydrochloric acid. Meerwein concluded that the catalytic activity of the chloride and its acid-strengthening power were closely related manifestations of its complex-forming ability.

By Hantzsch's method it can be shown that the phenols, which also catalyze the rearrangement of camphene hydrochloride, conform to this generalization in that they, too, increase the acid strength of hydrogen chloride in ethereal solution. The effect is much less than with stannic chloride, but quite definite. We are forced to the conclusion that phenols, like the complex-forming inorganic chlorides, can form complexes with hydrogen chloride in which the phenol is attached to the chlorine and encourages the separation of this as an ion. The only probable manner in which a phenol can form such an attachment is through hydrogen-bond formation at its hydroxyl group



and we thus have a method of making some quantitative measurements on the relative tendencies to hydrogen bonding by a series of hydroxyl compounds.

This subject is of particular interest at the present time in view of the attention directed by G. N. Lewis[3,4] to the general aspects of the acid–base relationship. Any molecular species X which can form a coördinate link with the chloride ion, $X:\ddot{\underset{\cdot\cdot}{Cl}}:^-$, is functioning as an "acceptor" center, in the terminology of Sidgwick,[5] while the chloride ion functions as a "donor." Lewis prefers to substitute the terms "acid" and "base" for "acceptor" and "donor," and says of the Sidgwick notation: "This expressive nomenclature I should be glad to adopt if I did not hope to show that his classification coincides absolutely with the classification of acids and bases, so that the need for new names disappears."[3,4]

Now in the present instance we have a substance, a phenol, which can function as an acid in the Brönsted sense by donating a proton to some acceptor; it can also function as an acid in the Lewis sense, as an acceptor, by forming a complex with the chloride ion or with hydrogen chloride through its chlorine. If these two kinds of acidity run completely parallel in a series of phenols, being governed by exactly the same structural features, then we have no need to differentiate between them. However, as we shall show, the Lewis

(1) Meerwein, Hammel, Serini and Vorster, *Ann.*, **453**, 16 (1927); Meerwein, *ibid.*, **455**, 227 (1927).

(2) Hantzsch, *Z. Elektrochem.*, **29**, 226 (1923); *Ber.*, **58**, 627, 631 (1925).

(3) G. N. Lewis, *J. Franklin Inst.*, **226**, 293 (1938).

(4) Lewis and Seaborg, THIS JOURNAL, **61**, 1886, 1894 (1939).

(5) Sidgwick, "The Electronic Theory of Valency," Oxford University Press, New York, N. Y., 1929.

acidity and the Brönsted acidity do not run completely parallel and much interest is attached to their separation and comparison. Therefore we cannot absorb the one class of acids completely into the other. Rather than to use a new term for proton-donors, which are now generally designated by the term "acid," it seems to us best to retain this term in its accepted sense and to adopt Lewis's second choice by calling the Lewis acids "acceptors." At least this practice will contribute to clarity in the present paper. Ingold's useful term, "electrophilic reagent," is of course synonymous with "acceptor."

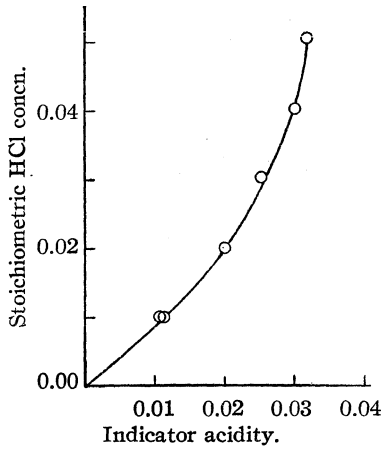


Fig. 1.

For exploring the relationship between acid strength and acceptor activity among the phenols it was desirable to have a quantitative method which should be sensitive to small differences in the latter property. Accordingly, series of colorimetric measurements were made using a one-color indicator, and comparing the specific color intensity of a standard solution of hydrogen chloride with those of weaker hydrogen chloride solutions containing progressively greater concentrations of a phenol. Because of its volatility, ether would be an objectionable solvent for this purpose, and we used carefully purified dioxane instead. As an indicator pentamethoxy red (2,2′,2″,4,4′-pentamethoxytriphenylcarbinol) proved well adapted to our purpose. This indicator turns from colorless to red at such a point that a 0.02030 *M* solution of hydrogen chloride in dioxane is a convenient standard. This standard solution, containing six drops of a 0.005 *M* solution of the indicator in 50 cc. of solution, was compared with series of solutions 0.001578 *M* in hydrogen chloride and from 0.05 to 4.0 *M* in the phenol containing the same amount of indicator. For each phenol–hydrogen chloride solution readings were taken at different times and with thermostatic control, so that temperature effects were eliminated and time effects could be shown to be absent. In each case we established the absence of color in solutions of the phenol and indicator more concentrated than any used in the work.

The expressing of our results in terms of a hydrogen ion activity or H_0 scale[6] is rendered undesirable by the fact that our indicator reaction forms water

$$\underset{\text{Colorless}}{ROH} + BH^+ \rightleftharpoons \underset{\text{Colored}}{R^+} + H_2O + B$$

Although our solvent and materials were as anhydrous as possible, it is unjustified to assume that the water formed as a result of this reaction is the only water present. Accordingly, no attempt is made to use a true measure of acidity. The quantity called "indicator acidity" in Fig. 1 is the molarity of hydrogen chloride in the standard solution multiplied by the ratio of color intensities in the test solution and the standard. Figure 1 shows the relationship of this indicator acidity to the stoichiometric concentration of hydrogen chloride in a series of solutions containing no phenol.

Figure 2 shows the plots of indicator acidity against phenol concentration for several phenols studied. These curves are not all the same shape, and do not appear to approach the same limiting value of the ordinate. This is not surprising since we are dealing with a solvent of dielectric constant only 2.2,[7] and adding to it relatively large amounts of substances which will raise the dielectric constant and probably alter the behavior of electrolytes. It can be seen that the early parts of the

TABLE I

COMPARISON OF ACCEPTOR ACTIVITY AND ACID STRENGTH FOR HYDROXYL COMPOUNDS

Compd.	Slope	pK_a
p-Cyanophenol	0.432	7.89
p-Chlorophenol	.097	9.39
o-Chlorophenol	.045	9.11
Phenol	.036	10.00
p-Cresol	.032	10.17
o-Cresol	.0294	10.20
s-Trichlorophenol	.0123	7.59
Methanol	.0085	17.00
Ethanol	.0064	19.14
i-Propanol	.0020	
Acetic acid	.0102	4.73

(6) Hammett and Deyrup, THIS JOURNAL, **54**, 2721 (1932).
(7) Kraus and Fuoss, *ibid.*, **55**, 21 (1933).

phenol curves are very nearly linear and differ among themselves markedly in slope. This slope of the initial part of the curve of indicator acidity

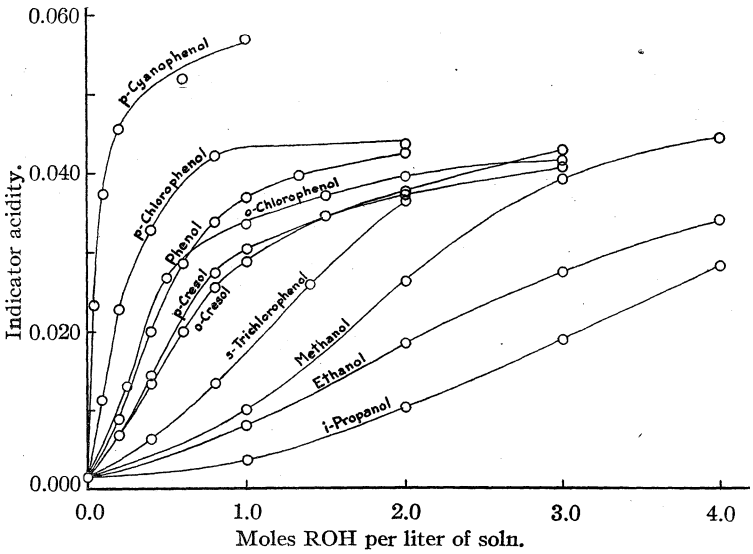


Fig. 2.

against phenol concentration seems about the best comparative measure of the acceptor activities of the different phenols. We have no way of determining to what extent the slope reflects the acid strength of the HCl–phenol complex as contrasted with the actual extent of conversion of the HCl molecule into the complex. Since these two effects are almost certain to run parallel in any series of closely related hydroxyl compounds, there is some justification in referring to the slope of our curve as a measure of the acceptor activity of the phenol.

In many instances the logarithms of the rate or equilibrium constants for two reactions shown by compounds containing the same series of radicals have been found to be linearly related.[8] Although we have no equilibrium constant for a reaction involving the phenols as acceptors, it is of interest to plot the logarithm of the slope, our measure of acceptor activity, against the logarithm of the acid dissociation constant of the same phenol. Figure 3 shows such a plot including points for all the hydroxyl compounds measured. The acid dissociation constants taken are those recorded for aqueous solutions.[9] It is not too much to expect that the phenols will fall in the same order of acid strength in dioxane as in water, in view of the fact that acids *of the same type* have been found to have the same order of acidity in solvents of quite different character.[10]

All the phenols measured except *o*-chlorophenol and 2,4,6-trichlorophenol yield points which fall on a straight line in the figure. These chlorophenols deviate largely from the linear relationship, especially the symmetrical trichlorophenol, which has a K_a of 2.6×10^{-8}, the highest of the series, but is definitely the weakest acceptor of the group. The mere fact that these ortho-substituted phenols are known to have intramolecular hydrogen bonds[11] is not sufficient to explain why the acceptor activity should suffer in comparison to the acid strength, for if free rotation of the hydroxyl group were possible any restraint against

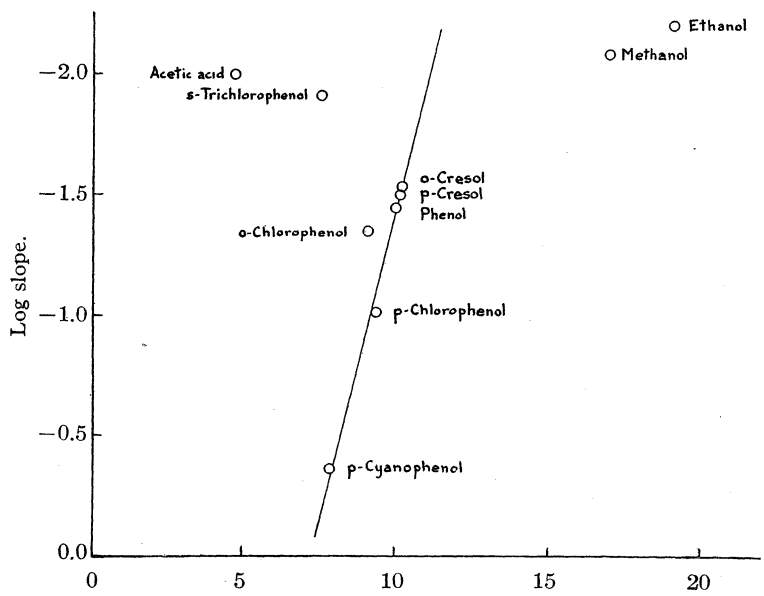


Fig. 3.

(8) See Hammett, *Chem. Rev.*, **16**, 67 (1935); **17**, 125 (1935).

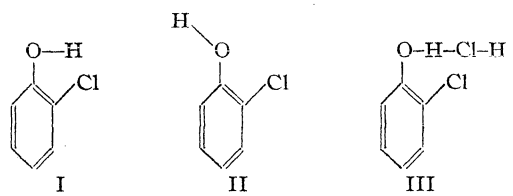
(9) Scudder, "Conductivities and Ionization Constants of Organic Compounds," D. Van Nostrand Co., New York, N. Y., 1914; Lucas, "Organic Chemistry," American Book Co., New York, N. Y., 1935; Boyd, *J. Chem. Soc.*, 1540 (1915).

(10) See, for example, Wooten and Hammett, THIS JOURNAL, **57**, 2289 (1935).

(11) Huggins, *J. Org. Chem.*, **1**, 407 (1937); Sidgwick and Callow, *J. Chem. Soc.*, **125**, 527 (1924).

the formation of an outside hydrogen bond (limitation of acceptor activity) would be attended by an equal restraint against the complete donation of the proton to an outside base (acid activity). What needs to be explained is a *selective* operation of the ortho-effect against the acceptor activity of the phenol.

An attractive explanation is to be found based upon Pauling's interpretation[12] of the infrared absorption spectra of the chlorophenols.[13] The evidence is that *o*-chlorophenol exists as an equilibrium mixture of the two spectroscopically distinguishable forms, I and II



without detectable amounts of forms resulting from random rotation of the hydroxyl group about the C–O bond. The possibility of forming a hydrogen bond in the "*cis*" form, I, results in its predominance (estimated as 10 to 1) over the "*trans*" form, II, but the force restraining free rotation arises from the contribution of structures having carbon–oxygen double bond character, and hence requiring the hydroxyl group to lie in the plane of the ring. There is presumably no hindrance to acceptor activity in the *trans*-form. In the *cis*-form the breaking of the intramolecular hydrogen bond and forming of one outside results in a congested structure, III, for it amounts to placing the outside donor, in this case chlorine, on an extension of the O—H bond contiguous to the aromatically bound chlorine atom. We must suppose that this makes the formation of such a hydrogen bond less probable but not impossible. Trichlorophenol, which can have no "*trans*" form, still shows an acceptor activity about one-third as great as that of phenol, and one-fortieth of that to be predicted from its acid dissociation constant. *o*-Cresol, in which for obvious reasons the *trans*-form would be expected to predominate over the *cis*-, shows normal acceptor activity in terms of its acid strength.

Now, in the transfer of a proton to another base, the reaction whose equilibrium constant expresses the acidity of the phenol, a phenol must form a *transition state* resembling the phenol–hydrogen chloride complex, in its chemical and geometrical nature. In the case of the *o*-chlorophenols this transition state, too, would be hindered. If the acid dissociation were something whose rate we could measure, we should expect to find this rate retarded according to our present hypothesis of the ortho-effect. However, this reaction in normal cases proceeds too fast to measure, and as long as the hindrance to the formation of the transition state is not absolute, the equilibria of proton-transfer will continue to be established. Since the transition state appears on either side of the equilibrium, *the equilibrium of proton transfer should be exempt from this particular kind of ortho-effect.* Rates of acid-catalyzed reactions should not be exempt, for here any hindrance to a transition state in proton transfer will show itself in a lowering of the rate.

The work of Farinacci and Hammett[14] on the solvolysis of benzhydryl chloride in alcohol–water mixtures, and the interpretation of the work of Olson and Halford and of W. Taylor[15] in its light, make it seem highly probable that water, and to a lesser extent, alcohols, can also form hydrogen bonds with the chloride ion and so facilitate its removal from organic combination. We investigated methyl, ethyl and isopropyl alcohols with the results shown in Fig. 2. Here the initial rise is slow and not perfectly linear. In evaluating the slope use was made of the first point, but this is open to criticism since we do not know that this represents the true limiting slope. The points for methyl and ethyl alcohols have been included in Fig. 3. Here the assignment of abscissas is made on the basis of existing data[16] on the self-ionization of the pure liquids. It is, of course, difficult to compare these acid dissociation constants with the others determined in water solution. According to Faurholt,[17] the ionization constant of methanol in water solution is $10^{-15.5}$ at 18°, or 1.5 pK units greater than the figure we have plotted. This assignment is made in the belief that it cannot be far enough in error to bring the alcohol points onto the phenol line, and this is of some interest. It means that the alcohols are, in proportion to their acid strengths, far better acceptors than the phenols.

(12) Pauling, THIS JOURNAL, **58**, 94 (1936).
(13) Wulf and Liddel, *ibid.*, **57**, 1464 (1935).
(14) Farinacci and Hammett, *ibid.*, **59**, 2542 (1937).
(15) Olson and Halford, *ibid.*, **59**, 2644 (1937); see Watson, *Ann. Reports*, 215 (1938).
(16) Bjerrum, Unmack, and Zechmeister, *Kgl. Danske Videnskab. Selskab. Math. fys. Medd.*, **5**, No. 11, 34 (1925); Danner and Hildebrand, THIS JOURNAL, **44**, 2824 (1922).
(17) Faurholt, *Z. physik. Chem.*, **126**, 85 (1927).

Meerwein found that benzoic and other organic acids had the ability to increase the acidity of ether–hydrogen chloride solutions. Acetic acid under our conditions shows an acceptor activity similar to that of the alcohols. A comparison with the phenols on the basis of acid strength in water may be misleading since if the acetic acid exists as double molecules in dioxane, then it is not present as the same species whose acid strength has been determined.

The results of Farinacci and Hammett indicate that water is a stronger acceptor than alcohol. Unfortunately, we are unable to demonstrate this with our present system, since water is a component of the indicator-equilibrium. The curve obtained with water is shown in Fig. 4. Its curious shape, which has been repeatedly checked, suggests a superposition of various effects. Among these we might expect to find the acceptor activity of water, its participation in the indicator-equilibrium, its basicity, and the fact that the addition of any quantity of it to dioxane multiplies the dielectric constant of the solution and accordingly greatly alters the state of ions in solution. The first and last of these effects might operate to give the curve a positive slope, while the two other effects would tend to make the curve descend as it does.

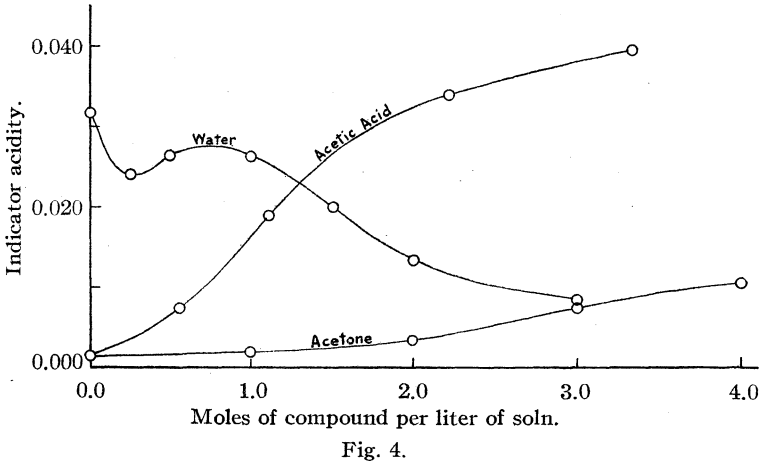


Fig. 4.

The carbonyl group has been demonstrated to have both donor and acceptor activity, arising out of its dipolar character. Toward the cyanide ion it functions as a pure acceptor,[18] while strong acids bring out its donor activity. In general, the reagent employed determines which type of activity will be displayed. Toward hydrogen chloride in dioxane the behavior of acetone is that of a feeble acceptor whose effect (Fig. 4) is so slight that it may be purely a solvent effect. Gordy[19] has presented data which indicate that acetone and dioxane are bases of about the same strength.

Several of the properties of dioxane as a solvent are worthy of comment for the way in which they determine the behavior of our system. In the first place, the basic strength of dioxane is sufficient to assure us that the hydrogen chloride occurs entirely chemically combined with the solvent, as dioxanonium chloride. This same basicity of dioxane causes phenol to be largely combined with the dioxane in which it is dissolved and not associated, as it would be in non-basic solvents of low dielectric constant.[20] When we speak of the phenols as if they were free, we refer to a small fraction which must be free in order to have acceptor activity, since there is no evidence that hydrogen can be attached to more than two other atoms at once.

The conductivity data of Chesterman[21] and Mounajed[22] show that in solutions of hydrogen chloride in ether the diethyloxonium chloride is only slightly dissociated into free ions. The dielectric constant of dioxane is still less (2.2) than that of ether (4.6) so that in our present system we may expect a great deal of ion association, not only into pairs but into clumps of greater size.[23]

The well-known "leveling" effect of a basic solvent, that of converting into its own conjugate acid all stronger acids which might be formed in solution, is important in bringing out the effects which we have observed. In a completely non-basic solvent, alcohols are known to behave as bases toward hydrogen chloride, and this effect, if present here, would completely conceal the acceptor properties of the alcohols. These acceptor properties appear here because there is practically no hydrogen chloride present, but only the much

(18) Lapworth, *J. Chem. Soc.*, **83**, 995 (1903).
(19) Gordy, *J. Chem. Phys.*, **7**, 93 (1939).
(20) Meisenheimer and Dormer, *Ann.*, **482**, 130 (1930); M. and R. Freymann, *Bull. soc. chim.*, [5] **4**, 944 (1937); Belluci and Grassi, *Gazz. chim. ital.*, **43**, 712 (1913); Morgan and Pettet, *J. Soc. Chem. Ind.*, **54**, 22 (1935).
(21) Chesterman, *J. Chem. Soc.*, 906 (1935).
(22) Mounajed, *Compt. rend.*, **197**, 44 (1933).
(23) Fuoss and Kraus, THIS JOURNAL, **55**, 2387 (1933); Kraus and Vingee, *ibid.*, **56**, 511 (1934).

weaker acid, dioxanonium chloride, from which methyl or ethyl alcohol is incapable of taking a proton.[19] Hence the acceptor properties of the alcohols are not overlaid. If these experiments were carried out in benzene, it would surely be impossible to detect the acceptor properties of the alcohols or of acetone, and we might even find phenols displaying basic character.

It is equally obvious that if any base is to be used as solvent which, like dioxane, combines completely with hydrogen chloride, the solvent must not be one which allows complete ionization of the resulting salt. Such ionization would mean that the maximum acidity of which the system was capable was already reached, and complex-formation by the acceptors would not be detectable by the indicator method.

It is of interest that the acceptor properties of phenol have been utilized[24] in promoting the elimination of hydrogen bromide from 9,10-dibromo-9,10-dihydroanthracene.

Experimental

Apparatus.—A Bausch and Lomb colorimeter (No. 2504) of the Dubosque type was used. Water-jacketed all-glass cups were clamped firmly in place and provided with machined brass caps with felt linings which fitted the plungers and minimized the entrance of moisture from the air. Water at 25.00 ± 0.05° from a thermostat was circulated through the jackets.

1,4-Dioxane.—The technical product was purified by refluxing for eight to fifteen hours with concentrated hydrochloric acid to destroy acetals, drying, refluxing with sodium until no reaction occurred, and distilling. The fraction used boiled at 101.1–101.3° and melted at 11.8°.[25] It was stored in a nitrogen atmosphere over sodium wire in a bottle closed with a paraffin-treated cork.

***p*-Dimethylaminoazobenzene** from the Eastman Kodak Co. was recrystallized three times from ethyl alcohol and carefully dried before use. It melted at 115–116°.

2,2′,2″,4,4′-Pentamethoxytriphenylcarbinol was prepared by the method of Lund.[26] Several recrystallizations from hot ethanol gave well formed white crystals of m. p. 145.5–146.5°.

Phenols.—With the exception of *p*-cyanophenol the phenols were prepared by the fractional distillation of good commercial grades. The *p*-cyanophenol[27] was synthesized and purified by crystallization from hot water and melted at 111.5–112.5° after careful drying. To obtain *p*-chlorophenol free from hydrogen chloride it was necessary to extract it with water, dry, and distil under diminished pressure. The fraction used boiled at 119.2–119.7° under 27 mm. pressure. The *o*-cresol boiled at 105.9–106.0° under 50 mm. pressure. The other phenols were fractionally distilled at atmospheric pressure. The phenol melted at 40.6° and boiled at 178.0–178.4°. The *p*-cresol boiled at 202.4–202.5° at atmospheric pressure. The *o*-chlorophenol boiled at 174.8–174.9° at 756 mm. The *sym*-trichlorophenol melted at 66.5–67.5°. All the phenols were stored in an atmosphere of nitrogen.

Methanol.—A commercially available "acetone-free" product was refluxed with sodium hydroxide and iodine, distilled, dried by refluxing with magnesium and a little iodine, and finally distilled. It gave no precipitate with aluminum ethoxide.

Ethanol (absolute, from the Commercial Solvents Co.) was refluxed with silver nitrate and potassium hydroxide for seven to eight hours, distilled, and finally dried by the magnesium method. It also gave a negative test with aluminum ethoxide.

Isopropanol was heated under reflux for thirty hours with its weight of quicklime and distilled. The middle fraction, which boiled at 82.2°, was used.

Acetone (alcohol-free) was refluxed with potassium permanganate and a little sodium hydroxide for a few hours and distilled. The middle fraction of the distillate was shaken with freshly dried potassium carbonate for about twelve hours. The product distilled at 56.2°.

Acetic acid, provided by Rolf Altschul, had been heated with chromic anhydride and a little acetic anhydride and distilled through a six-foot (1.8-meter) packed column. The fraction used boiled at 118.3° at 764 mm. and had a freezing point of 16.6° just before use.

Summary

Seven phenols and three alcohols have been investigated and all found to increase the acid strength (measured by an indicator) of solutions of hydrogen chloride in dioxane. This is interpreted as due to the formation of a hydrogen bond with the chlorine atom of the hydrogen chloride by the hydroxyl group of the phenol or alcohol. A composite quantitative measure of this effect is had from colorimetric determinations. The hydrogen bond formation appears to run parallel to the acid strength in the series of phenols except for phenols with ortho-substituents capable of intramolecular hydrogen bonding, which are far less efficient "acceptors" than would be expected from their acid strength. This deviation is regarded as an argument against the diversion of the term "acidity" to cover activity as an electron acceptor.

This property of hydroxyl compounds is correlated with the mechanisms of the Wagner–Meerwein rearrangement and the solvolysis of secondary and tertiary halides. Measurements on acetic acid and acetone are included for comparison.

CAMBRIDGE, MASSACHUSETTS
RECEIVED FEBRUARY 27, 1940

(24) Barnett and Cook, *J. Chem. Soc.*, 1084 (1924).

(25) Eigenberger, *J. prakt. Chem.*, **130**, 75 (1931); Scatchard and Benedict, THIS JOURNAL, **58**, 837 (1936); Hess and Frahm, *Ber.*, **71**, 2627 (1938).

(26) Lund, THIS JOURNAL, **49**, 1346 (1927).

(27) Ahrens, *Ber.*, **20**, 2953 (1887).

[CONTRIBUTION FROM THE CONVERSE MEMORIAL LABORATORY OF HARVARD UNIVERSITY]

Kinetics of the Reaction of *p*-Methoxybenzhydryl Chloride with Methanol in Dilute Nitrobenzene Solution

BY PAUL D. BARTLETT AND RICHARD WILSON NEBEL

Much of the kinetic work on the reaction of organic halides with hydroxyl compounds has been done with the hydroxyl compounds as solvents.[1] These conditions obscure the manner in which the hydroxyl compound participates in the rate-determining step, which has been the subject of much debate. The present work is an effort to obtain unambiguous evidence on this point by carrying out the alcoholysis of a suitable halogen compound in an inert solvent, in which the alcohol concentration can be kept low and varied, and in which the reaction can be freed from competing reactions and made irreversible. The first of these conditions has been met in a series of experiments described by W. Taylor[2] since the inception of our work.

The dielectric constant has been considered by some to be an important factor in the effect of changing medium on the rate of solvolysis of secondary and tertiary halides.[3] With this in mind we chose an inert solvent with approximately the same dielectric constant as the alcohol taking part in the reaction. Nitrobenzene ($E = 36.1$)[4] and methanol ($E = 33.7$)[5] were selected. Nitrobenzene has the further advantage of being thoroughly inert to the kind of substances expected to be present. It was necessary, however, to establish the limits within which methanol acts as a normal, unassociated solute in nitrobenzene. This was done by a series of vapor pressure measurements, by the dynamic method, of methanol–nitrobenzene solutions at 25°. Absorption of the alcohol vapor in sulfuric acid and weighing was found precise enough to give this information. The plot of partial pressure of methanol against its formal concentration, shown in Fig. 1, indicates constancy of the size of the dissolved unit up to 0.6 molar, which means that methanol is unassociated under these conditions.

Since in dilute alcohol solutions alcoholysis of a chloride is incomplete at equilibrium, it was desirable to make the reaction irreversible if this could be done without disturbing its course. The trials for the selection of a suitable chloride were therefore made in the presence of excess piperidine, which was converted into its hydrochloride as the reaction progressed and could be titrated as a means of following the reaction. After various trials, *p*-methoxybenzhydryl chloride was selected as a halide which reacted at a convenient rate with these low concentrations of methanol. It was found, however, that there was an appreciable rate of reaction with piperidine in the absence of any methanol, and piperidine accordingly was replaced by triethylamine, which was shown to be free from this difficulty. Only after standing for a matter of months was there appreciable reaction at room temperature between the chloride and triethylamine in nitrobenzene. This great preference on the part of a secondary chloride for reacting with the weakly basic methanol rather than the more strongly basic triethylamine or even piperidine emphasizes the difference in mechanism of reaction between secondary and primary chlorides to which Ingold and Hughes have repeatedly directed attention.

In view of recent results and discussions of sol-

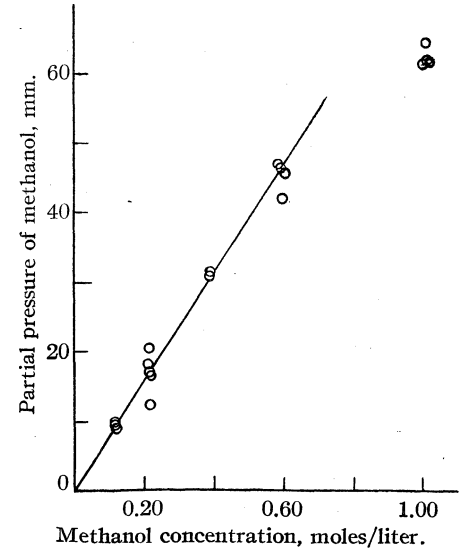


Fig. 1.

(1) Hughes, *J. Chem. Soc.*, 255 (1935); Olson and Halford, THIS JOURNAL, **59**, 2644 (1937).

(2) Read and Taylor, *J. Chem. Soc.*, 479 (1939); Taylor, *ibid.*, 1853 (1937); THIS JOURNAL, **60**, 2094 (1938).

(3) Scatchard, *J. Chem. Phys.*, **7**, 657 (1939); Hughes, ref. 1, but see Farinacci and Hammett, THIS JOURNAL, **59**, 2542 (1937).

(4) Walden, *Z. physik. Chem.*, **54**, 129 (1906).

(5) Tereschin, *Ann. phys.*, **36**, 792 (1889).

volysis it seemed possible that, even though the chloride did not react directly with triethylamine, the reaction in the presence of both triethylamine and methanol might lead to a substantial fraction of the quaternary ammonium salt. To test this, the following experiment was performed. A solution was prepared of 0.953 g. of *p*-methoxybenzhydryl chloride with two equivalents of methanol and 1.25 equivalents of triethylamine in 50 cc. of nitrobenzene, and this solution was allowed to stand overnight. The precipitate (triethylamine hydrochloride) was filtered off and the solution was extracted three times with 10% hydrochloric acid. Then 10 cc. of the solution was concentrated under 2 mm. pressure to about 0.5 cc. and the last of the solvent removed by steam distillation. The oily residue crystallized on seeding and standing at 0°, yielding 0.195 g. of crystals melting at 19–20°, identified as impure *p*-methoxybenzhydryl methyl ether by mixed melting point with a pure sample, m. p. 27–28°. The theoretical yield was 0.189 g. of the ether. If any quaternary ammonium salt had been formed it would have passed into the water extract and the quantity of ether isolated would have been correspondingly diminished. We conclude that in titrating the amine we are following the rate of reaction between *p*-methoxybenzhydryl chloride and methanol, no reaction being involved between the chloride and the amine.

Runs carried out in the presence of only the chloride, the alcohol and the amine did not at first show good second order kinetics. The liberation of hydrogen chloride was at first excessively rapid, and the bimolecular plots did not become linear until the run was well under way. It was noted that the point of straightening of the curve in each case coincided approximately with the time at which triethylamine hydrochloride began precipitating from the solution. Apparently the building up of salt concentration was attended by a slowing of the specific reaction rate. This was confirmed by saturating the solvent in advance with triethylamine hydrochloride, which resulted in the second order plots being linear over the entire measurable reaction (in some cases more than 90%). The runs reported in this paper were all made in solutions saturated with triethylamine hydrochloride.

The solubility of triethylamine hydrochloride in nitrobenzene is markedly dependent upon the methanol concentration, even when this is small. Table I shows the solubility under the conditions of the kinetic runs.

TABLE I

SOLUBILITY OF TRIETHYLAMINE HYDROCHLORIDE IN NITROBENZENE CONTAINING METHANOL AND TRIETHYLAMINE AT 25.0°

Concentrations in moles per liter		
Methanol	Triethylamine	Triethylamine hydrochloride
0	0	0.0157
0	0.101	.0147
0.0833	.102	.0236
.167	.102	.0356
.250	.102	.0468

The slight effect of 0.1 molar triethylamine upon the solubility of triethylamine hydrochloride suggests that the large effect in the case of methanol is due to its chemical union with one of the ions of the salt, presumably with the chloride ion, to give a new and more soluble molecular species. The solubility in the solutions containing triethylamine is well expressed by

$$0.0145 + 0.1086[CH_3OH] + 0.0854[CH_3OH]^2$$

This is consistent with the idea of practically constant solubility for the molecular species $C_6H_{15}N\cdot HCl$ and the appearance of soluble $C_6H_{15}N\cdot HCl\cdot CH_3OH$ and $C_6H_{15}N\cdot HCl\cdot(CH_3OH)_2$ in amounts governed by the methanol concentration. From the solubility data we can estimate equilibrium constants

$$K_1 = \frac{[S][CH_3OH]}{[S\cdot CH_3OH]} = 0.119, \text{ and}$$

$$K_2 = \frac{[S\cdot CH_3OH][CH_3OH]}{[S(CH_3OH)_2]} = 1.27$$

where S represents triethylamine hydrochloride. This would mean that at all concentrations of methanol in nitrobenzene saturated with triethylamine hydrochloride, about 11% of the methanol is bound to the salt in a mono-alcoholate, while in the most concentrated solution about a further 4% of the methanol is bound in a di-alcoholate. This fits with the other observations made in this work and offers a satisfactory interpretation of the effect of low concentrations of methanol on the solubility of the salt.

Despite the apparent bimolecular nature of the reaction in individual runs, the bimolecular velocity constant varied markedly as the concentration of methanol was altered. A change of the methanol concentration from 0.0737 to 0.2129 caused a change in the bimolecular rate constant from 0.153 to 0.233. From the experimental results of Farinacci and Hammett[6] and the calcula-

(6) Farinacci and Hammett, *loc. cit.*

tions of Winstein,[7] it seemed possible that there might be, superposed upon the bimolecular reaction, a trimolecular reaction involving the attack of two molecules of alcohol upon one of the chloride. The trimolecular reaction, if simultaneous with the bimolecular one, would gain in importance at higher alcohol concentrations. An equation for such superposed reactions has been derived and found to fit the present results.

If the chloride is present at a concentration x and the alcohol at a concentration $(x + c)$, and the chloride is disappearing irreversibly by a bimolecular and a trimolecular path, then

$$-dx/dt = k_2x(x + c) + k_3x(x + c)^2$$

If the ratio k_2/k_3 be denoted by r, the integrated equation is

$$k_2t = \frac{1}{c} \ln \frac{x + c}{x} - \frac{1}{(c + r)} \ln \frac{x + c + r}{x} + \text{constant} \quad (1)$$

Two tests of this equation are possible. A value of r should exist such that the same values of k_2 and k_3 are obtained from all the runs, and the plots of Equation (1) should be linear in all cases. By successive approximations we arrived at the value $r = 0.221$, which meets these conditions. Table II summarizes the results of applying this equation to our kinetic data.

TABLE II

BIMOLECULAR AND TRIMOLECULAR VELOCITY CONSTANTS FOR THE REACTION OF *p*-METHOXYBENZHYDRYL CHLORIDE WITH METHANOL IN NITROBENZENE AT 25°, ASSUMING $k_2/k_3 = 0.221$

Initial concentrations of Chloride	Methanol	Triethylamine	k_2	k_3	% reaction covered
0.0712	0.0737	0.0908	0.131	0.593	82
.0758	.0780	.0934	.131	.593	84
.0723	.1435	.0881	.136	.615	86
.0820	.1450	.0926	.136	.615	85
.0408	.1477	.0901	.131	.593	94
.0738	.1549	.1736	(.102)	(.461)	76
.0705	.1622	.2352	(.091)	(.411)	79
.0797	.1950	.0869	.134	.606	68
.0780	.2129	.0851	.127	.575	77
		Average	.133	.599	

The values of the rate constants, in parentheses, for the runs containing 0.1736 and 0.2352 M triethylamine, are not included in the average, since these large increases in the amine concentration appreciably diminish the rate of the alcoholysis. This fact and the slightly reduced solubility of triethylamine hydrochloride in the presence of tenth molar triethylamine in nitrobenzene (for which no "common ion effect" can be responsible) both suggest a slight association between methanol and triethylamine to give some such species as

$$(C_2H_5)_3N \ldots HOCH_3$$

in which the hydroxylic hydrogen is not available for hydrogen bonding and hence unable to promote either the solution of the hydrochloride or the rate of the alcoholysis.

From the average values of k_2 and k_3, we conclude that with 0.1 M methanol the reaction is proceeding 69% by the bimolecular and 31% by the trimolecular path. In this same case when the reaction is 75% complete, these percentages become 90 and 10, respectively. It is not surprising that the simple bimolecular formulation seems to fit these runs, since in the later stages of the reaction, when the distinction between orders of reaction is easiest to draw, the deviation from bimolecular kinetics is slight.

For reasons which have been reviewed recently,[8] we favor the interpretation of the solvolysis of secondary and tertiary halides given by Farinacci and Hammett[6] in that the rate-determining step is the removal of halogen by the alcohol or water as a solvated anion. Our present results are in harmony with this mechanism. If the solvation of a halide ion is regarded as a chemical process, there is a series of possible solvated ions involving one, two, three, etc., molecules of alcohol. The alcohol can be attached by a hydrogen bridge through any or all of the electron pairs of the halogen ion, and polymeric clusters of alcohol molecules can take the place of single alcohol molecules. By our solubility and kinetic measurements on dilute solutions we seem to have detected the ions with one and two molecules of alcohol of solvation. There is reason to suppose that at somewhat higher concentrations, where association of the alcohol becomes important, the formation of more highly solvated ions will introduce terms of higher order into the rate equation. The "polymolecular" reaction of Farinacci and Hammett would then be the predominant one in the pure alcohols and in alcohol–water mixtures.

Experimental

***p*-Methoxybenzhydryl chloride** was prepared according to Norris and Blake.[9] After purification by distillation it solidified and was recrystallized from benzene–hexane solution. It melted at 62–63°.

(7) Winstein, THIS JOURNAL, **61**, 1635 (1939).

(8) Bartlett and Knox, *ibid.*, **61**, 3187, 3188 (1939).

(9) Norris and Blake, *ibid.*, **50**, 1811 (1928).

Nitrobenzene, m. p. 5.7°, was freshly distilled from phosphorus pentoxide immediately before each run. It was very light yellow in color.

Triethylamine, b. p. 89°, was kept over magnesium sulfate and distilled before each run from zinc and sodium.

The **methanol** used was an analytical grade giving no precipitate with aluminum ethoxide.

Triethylamine hydrochloride was prepared by passing hydrogen chloride gas into an ethereal solution of triethylamine. The product was recrystallized from alcohol, washed with ether, and dried for several days in a vacuum desiccator over calcium chloride.

Vapor Pressure Measurements.—Solutions of methanol in nitrobenzene were prepared by breaking weighed ampoules of methanol into weighed amounts of nitrobenzene. The solutions so prepared were placed in absorption towers filled with glass beads. The amount of solution used was such that in removing enough methanol for a vapor pressure determination the concentration of the methanol was not altered by more than 2%. Dried air was drawn through the absorption towers immersed in a thermostat at 25°, and then through a U-tube filled with glass beads wet with sulfuric acid. Pure nitrobenzene gave a gain in weight of the absorption tube of 0.0011 g. per 100 cc. of air passed, and a proportional blank correction was applied to each run to determine the methanol absorbed. Seventeen runs were made, at molar concentrations of methanol from 1.015 down to 0.117. Table III summarizes the results.

While these results are not very precise, the plot in Fig. 1 shows clearly the linear relationship between concentration and partial pressure of methanol up to 0.6 molar.

The solubility determinations were made by stirring the solutions of methanol and triethylamine in nitrobenzene with finely powdered triethylamine hydrochloride for several hours in the thermostat, extracting measured portions of the solution with water and titrating with standard silver nitrate. The solid phase present at saturation was identified as the original triethylamine hydrochloride, without any solvent of crystallization.

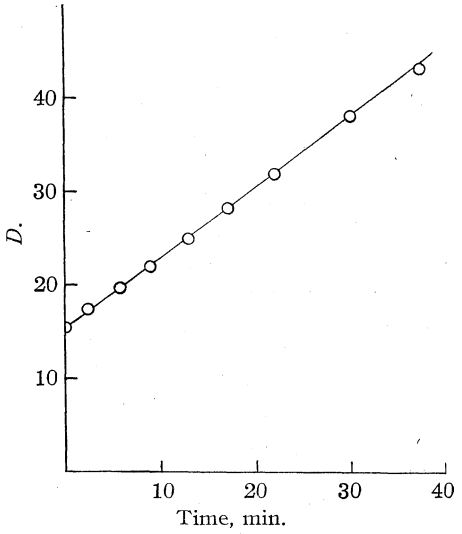


Fig. 2.

TABLE III

Methanol concentration	Air (S. T. P.), cc.	Methanol (cor.), g.	V. p. of methanol (mm. Hg)
1.015	86.8	0.0117	62.1
1.007	99.4	.0135	62.3
1.003	90.8	.0127	64.8
0.996	83.4	.0111	61.6
.601	96.8	.0094	46.0
.596	105.1	.0093	42.3
.589	131.4	.0129	46.7
.581	114.0	.0113	47.2
.389	168.6	.0107	31.4
.386	140.3	.0090	31.0
.217	153.2	.0052	16.6
.216	140.3	.0035	12.3
.215	143.6	.0050	17.1
.213	154.8	.0065	20.5
.211	150.7	.0055	18.1
.121	309.5	.0056	9.0
.119	328.0	.0065	9.8
.117	308.2	.0059	9.4

Technique of Velocity Determinations.—The titrations of triethylamine were satisfactorily carried out in acetone as a titration medium using a standard solution of hydrogen chloride in ether and brom phenol blue as indicator. A solution of triethylamine was freshly prepared by adding about 0.77 cc. of it to 60 cc. of nitrobenzene and mixing. Then 55 cc. of this solution was delivered into a 125-cc. glass-stoppered Erlenmeyer flask and a weighed ampoule of methanol was broken into it. Excess solid triethylamine hydrochloride was added and the solution was shaken for several hours at 25° to attain saturation with the salt. A 5-cc. sample was then pipetted out and titrated in 50 cc. of acetone with 0.025 *N* hydrogen chloride–ether solution. The reaction was started by the addition of a weighed quantity (about 0.9 g.) of *p*-methoxybenzhydryl chloride to the 50 cc. of solution which had been brought to temperature in the thermostat. The solid dissolved rapidly, and the stop watch was started at the time of complete solution. Samples of 5 cc. were withdrawn at successive times with a pipet and titrated. The end-points were sharp and showed no tendency to drift. One 5-cc. sample was sealed in a tube and heated at 100° for several hours to get the titer corresponding to complete reaction. This provided a check on the purity of the chloride, which

TABLE IV

RUN G-14

0.3787 g. of methanol and 0.9154 g. of *p*-methoxybenzhydryl chloride in 50 cc. of nitrobenzene containing excess triethylamine and saturated with triethylamine hydrochloride. Samples of 4.99 cc. titrated with 0.02740 *N* ether–HCl solution.

Minutes	Titer	x	$x + c$	D	Per cent. reaction
0	15.50	0.0780	0.2129	0.1541	0
2.42	13.57	.0674	.2023	.1749	12
5.75	11.94	.0584	.1934	.1973	25
8.83	10.60	.0511	.1860	.2195	34
12.83	9.15	.0431	.1780	.2494	45
17.00	7.90	.0363	.1712	.2821	53
21.92	6.78	.0301	.1650	.3187	61
29.92	5.31	.0224	.1574	.3809	71
37.17	4.55	.0179	.1529	.4312	77

proved to be better than 95%, and also on the consistency of the other measurements.

We present in Table IV the data for a typical run. The quantity D in the table is

$$\log_{10}\frac{x+c}{x} - \frac{c}{c+r}\log_{10}\frac{x+c+r}{x}$$

which, according to the kinetic equation used, is expected to be proportional to time. Figure 2 shows the plot of this quantity against time.

Summary

The rate of the reaction between methanol and *p*-methoxybenzhydryl chloride in dilute nitrobenzene solution under irreversible conditions has been studied as a function of the methanol concentration from 0.07 to 0.21 *M*. There is a bimolecular reaction involving one molecule of the chloride and one of methanol and at the same time a trimolecular reaction involving one molecule of chloride and two of methanol. It is suggested that mechanisms of higher order appear as the alcohol is made more concentrated, as seems probable also from the work of Farinacci and Hammett.

Vapor pressure measurements have been made, showing that methanol is not associated in nitrobenzene solutions of the strength used.

The solubility of triethylamine hydrochloride in nitrobenzene is altered markedly by small concentrations of methanol. A series of solubility measurements are interpreted as giving evidence of specific solvation of the chloride ion by one and by two molecules of methanol.

Triethylamine is inert toward *p*-methoxybenzhydryl chloride in nitrobenzene solution, at least in comparison to like concentrations of methanol. This makes it possible to use triethylamine to combine with hydrogen chloride liberated in the alcoholytic reaction and thus to make the reaction effectively irreversible.

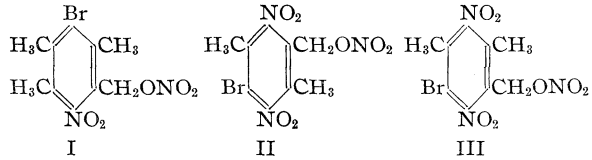
CAMBRIDGE, MASSACHSETTS RECEIVED MARCH 27, 1940

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE UNIVERSITY OF MINNESOTA]

Polymethylbenzenes. XXVI. The Nitration of Bromopentamethylbenzene

BY LEE IRVIN SMITH AND JAMES W. HORNER, JR.[2]

When bromodurene is nitrated under certain circumstances, the product is 6-nitro-3-bromo-2,4,5-trimethylbenzyl nitrate, I.[3] Similarly, 5-bromopseudocumene or its 3,6-dinitro derivative can be attacked at the side chain by nitric acid,[4] and the product has been shown to consist of an inseparable mixture of two benzyl nitrates, II and III.[5]



These nitrates usually can be converted into aromatic nitro compounds by action of sulfuric acid. Peculiar orientation effects frequently are observed when polyalkylbenzenes are converted into substitution products by reactions in which an alkyl group is simultaneously removed or replaced.[6] The most striking of these effects is perhaps that shown by the nitration of pentamethylbenzene[7] and of pentaethylbenzene[8] to dinitrotetraalkylbenzenes in yields of over 70%, and with an ortho orientation of the nitro groups in the methyl derivative and a para orientation in the ethyl derivative. The easy decomposition of benzyl nitrates to nitro compounds indicates that these substances may well be intermediates in those reactions in which alkyl groups are replaced by nitro groups and that the peculiar orientation effects observed in such reactions are due to factors which determine which one of several alkyl groups will be attacked.

In order to study further these effects, the nitration of bromopentamethylbenzene (IV) has been examined. When fuming nitric acid was added to a solution of IV in chloroform, there resulted an oily solid from which was isolated a mixture of two isomeric bromotetramethylbenzyl nitrates, V

(1) XXV, THIS JOURNAL, **62**, 771 (1940).

(2) Abstracted from a thesis by James W. Horner, Jr., submitted to the Graduate Faculty of the University of Minnesota, in partial fulfilment of the requirements for the Ph.D. degree, January, 1940.

(3) (a) Smith and Tenenbaum, THIS JOURNAL, **57**, 1293 (1935); (b) Smith, Taylor and Webster, *ibid.*, **59**, 1082 (1937).

(4) Huender, *Rec. trav. chim.*, **34**, 25 (1915).

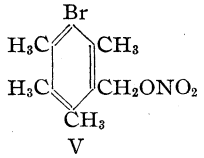
(5) Rinkes, *ibid.*, **57**, 1405 (1938); *ibid.*, **58**, 218, 538 (1939).

(6) (a) Baur, *Ber.*, **27**, 1614 (1894); (b) Barbier, *Helv. Chim. Acta*, **11**, 152, 157 (1928); (c) de Cappeller, *ibid.*, **11**, 426 (1928); (d) Battegay and Kappeler, *Bull. soc. chim.*, **35**, 989 (1924).

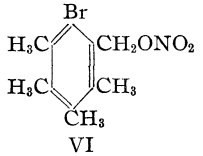
(7) Smith and Harris, THIS JOURNAL, **57**, 1289 (1935).

(8) Smith and Guss, unpublished work.

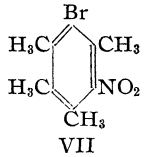
and VI, and a substance A, melting at 66.5–70° containing halogen but no nitrogen. The two benzyl nitrates formed an inseparable mixture and like the inseparable mixture of II and III, the mixture of V and VI could not be converted into any separable mixture of isomers. When the



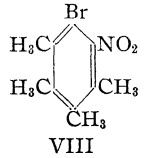
V



VI



VII



VIII

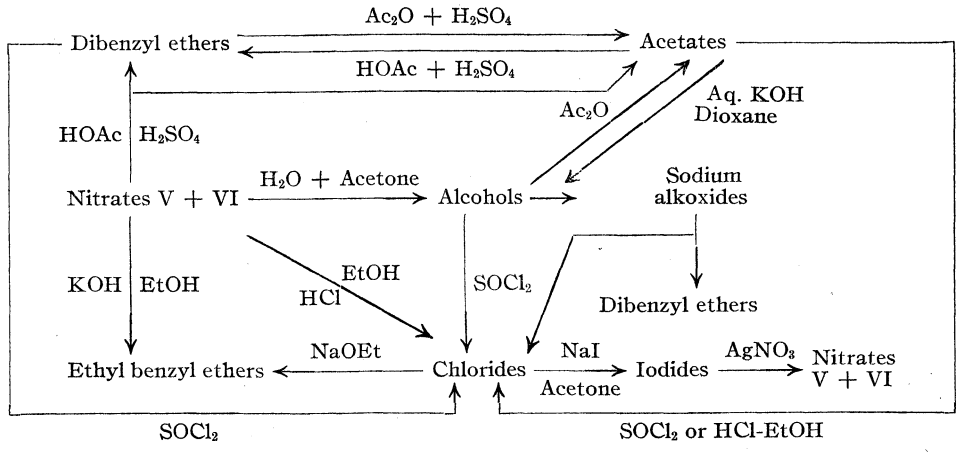
nitrates were subjected to the action of sulfuric acid, there resulted an inseparable mixture of bromo nitro tetramethylbenzenes, VII and VIII. When this mixture of nitro compounds was reduced by tin and hydrochloric acid, the product was a mixture of bromoaminoisodurene (IX) and aminoprehnitene (X), the halogen having been removed from the *o*-halo nitro compound, and not from the *m*-isomer.[9] The two amines produced in this way were separated; the mixture yielded approximately 0.6 mole of IX and 0.4 mole of X. No trace of any derivative of durene could be obtained from the mixture of amines. It followed, therefore, that the mixture of bromo nitro compounds contained about 60% of VII and 40% of VIII, and, in turn, that the nitration of bromopentamethylbenzene gave, as one of the products, a mixture of the nitrates V and VI containing about 60% of V.

The reactions of the nitrates and their derivatives are summarized in the chart. It is particularly noteworthy that these nitrates, in contrast to I, II and III, never produced any aldehydes upon hydrolysis.[10]

Substance A was obtained from the mother liquors after the crude nitration product was crystallized from methanol. Acetylation of A produced the same acetate mixture as that obtained from V + VI. This fact made it possible to prepare all the benzyl derivatives described above directly from the entire solid nitration product rather than from the purified nitrates only. These properties of A, together with the low melting point and the analysis, indicated that A was a mixture of the benzyl methyl ethers derived from V and VI.

The complete series of compounds (chlorides, iodides, acetates and nitrates) derived from each of the bromotetramethylbenzenes, was synthesized. In every case, the melting point of the derivative from bromopentamethylbenzene was not depressed by addition of the synthetic derivative from either prehnitene or isodurene, but a marked change in the melting point resulted when the durene derivative was added.

REACTIONS OF THE BENZYL NITRATES V + VI



Experimental Part[11]

Nitration of Bromopentamethylbenzene.—Fuming nitric acid (d. 1.52, 22 cc.) was added over a period of fifteen minutes to a vigorously stirred solution of bromopentamethylbenzene (10 g.) in chloroform (150 cc.) at −11°.

(9) Nicolet, *et al.*, THIS JOURNAL, **43**, 2081 (1921); **49**, 1796, 1801, 1806, 1810 (1927).

(10) (a) Nef, *Ann.*, **309**, 126 (1899); (b) Klason and Carlson, *Ber.*, **39**, 2752 (1906); *ibid.*, **40**, 4183 (1907); (c) Carlson, *ibid.*, **40**, 4191 (1907).

(11) Microanalyses by J. W. Opie and E. E. Renfrew.

During the reaction, the temperature rose to −1°; the mixture was poured immediately into cold water. The chloroform layer was removed and washed with carbonate (5%) and then with water. Removal of the solvent left a yellow oily solid (13 g.) which was crystallized from methanol (80 cc.) at room temperature. Succeeding crops of crystals were obtained by evaporating the filtrates to half their volume and cooling in ice. In this way the following material was obtained: first crop, 3.56 g., m. p. 69–83°; second crop, 3.00 g., m. p. 53–59°; third crop, 0.77 g., m. p. 55–56°; fourth crop, 0.41 g., oily, m. p. 50–67°; residue, 3.73 g., orange oil. The first crop was principally V + VI. This could be recrystallized from methanol, ethanol, ether, acetic acid, ethyl acetate or petroleum ether. After the two crystallizations from petroleum ether, it melted at 78–84°. Further crystallization sometimes gave a product with a slightly higher melting point, but the melting point range was not decreased.

Anal. Calcd. for $C_{11}H_{14}O_3NBr$: C, 45.83; H, 4.90. Found: C, 46.00; H, 4.90.

After three crystallizations of the fourth crop from methanol, the substance A, m. p. 66.5–70°, was obtained. This substance was most likely a mixture of benzyl methyl ethers. It was not a mixture of the alcohols (m. p. 170°) and bromopentamethylbenzene (m. p. 160°) because a mixture of these two substances melted at 160–164.5°.

Anal. Calcd. for $C_{12}H_{17}OBr$: C, 56.03; H, 6.61. Found: C, 55.57; H, 6.11.

The nature of the nitration product depends greatly upon the amount of acid used, and upon the time allowed for the reaction. More vigorous conditions yield a very oily product from which only the product of exhaustive nitration, 4-bromo-5,6-dinitrohemimellithene, can be isolated. As an example, the following may be cited: pentamethylbromobenzene (29.3 g.) in chloroform (130 cc.) was added slowly (two hours) to a well-stirred mixture of sulfuric acid (381 cc.), fuming nitric acid (d. 1.52, 88 cc.) and chloroform (500 cc.) at 25–31°. The product (34 g.), isolated as in method 1, consisted of 4-bromo-5,6-dinitrohemimellithene, m. p. 201–202° (5.9 g.) and an oil (27.7 g.) which on standing in sulfuric acid slowly deposited more of the bromo dinitro compound. The solid was identified by comparison with an authentic specimen of 4-bromo-5,6-dinitrohemimellithene,[12] and by analysis.

Anal. Calcd. for $C_9H_9O_4N_2Br$: C, 37.38; H, 3.12. Found: C, 37.74; H, 3.49.

The Dibenzyl Ethers.—The nitrates (3.43 g.) were refluxed in acetic acid (50 cc.) containing water (50 cc.) and sulfuric acid (2 *N*, 5 cc.) for four hours. The cooled reaction mixture deposited a white solid (2.27 g.) melting at 80–165°. Extraction of this material with hot ethanol left a residue of the ether mixture (0.83 g.) melting at 202–218°. Crystallization of this material from chloroform–ethanol or benzene did not give a product with a sharper melting point. This mixture of dibenzyl ethers had the widest melting point range of any of the derivatives of the nitrates; since it is derived from two molecules of V and VI, three benzyl ethers probably are present.

(12) Smith and Moyle, THIS JOURNAL, **58**, 9 (1936).

Anal. Calcd. for $C_{22}H_{28}OBr_2$: C, 56.40; H, 6.03; active H, 0; carbonyl, 0. Found: C, 56.44, 56.45; H, 5.79, 6.33; active H, 0; carbonyl, 0.

The alcoholic extract, when concentrated and cooled, deposited the acetates (0.86 g.) melting at 72–78°.

The Acetates. (a) The **benzyl ethers** (0.55 g.) were allowed to stand for seventeen hours in acetic anhydride (10 cc.) and sulfuric acid (5 drops). The solution was poured into water and the solid (0.65 g., 100%) was removed and crystallized from petroleum ether. It then melted at 82–83.5°.

Anal. Calcd. for $C_{13}H_{17}O_2Br$: C, 54.73; H, 6.01. Found: C, 54.92; H, 6.27.

(b) The **alcohols** (0.19 g.), after the above treatment, gave the same acetate, m. p. 77.5–83.5° after one crystallization from methanol.

(c) The **chlorides** were largely unchanged when treated as above, but the **iodides** (0.15 g.) were readily converted into the acetates by refluxing in acetic acid (5 cc.) with potassium acetate (0.21 g.) for two hours. The product melted at 81–86°.

When the acetates (0.21 g.) were refluxed for eleven hours in acetic acid (4 cc.) containing water (3 cc.) and sulfuric acid (5 drops), the product (0.17 g.), m. p. 140–170°, was the **dibenzyl ether** mixture. After two crystallizations from chloroform–ethanol, it melted at 211–219°.

(d) Substance A (0.63 g.) was allowed to stand for thirty-five minutes in acetic anhydride (5 cc.) and concentrated sulfuric acid (5 drops). The mixture was poured into water and the solid was removed and crystallized three times from methanol. It weighed 0.21 g., melted at 78–82°, and gave no depression in m. p. when mixed with the acetates prepared in other ways. Similarly, substance A (0.18 g.), hydrolyzed with acetic acid (2 cc.), water (2 cc.) and sulfuric acid (2 *N*, 0.2 cc.) gave an impure product which melted at 60–120°. Acetylation of this material produced the acetates (0.13 g.) melting at 77.5–81.5° without any purification.

(e) The entire nitration product, consisting of the nitrates and substance A, was subjected to successive hydrolysis and acetylation as described under (d). The acetates were obtained in good yield, although apparently there was an impurity present throughout which was best removed by steam distillation before the final acetylation. Further, the crude hydrolysis product could be converted into the alcohols in good yield by the dioxane–potassium hydroxide method, but again the rather persistent impurity was best removed by steam distillation before the final hydrolysis to the alcohols.

The Alcohols.—(a) The acetates (0.67 g.) were refluxed for six hours in dioxane (10 cc.) and potassium hydroxide (25%, 10 cc.). The solution was diluted with water and the solid was removed and crystallized first from ethanol and then from methanol. It weighed 0.35 g. (61%) and melted at 168–171°. It crystallized sometimes as brittle glassy rods, sometimes in clumps of heavy white needles.

Anal. Calcd. for $C_{11}H_{15}OBr$: C, 54.31; H, 6.22; active H, 1 mole; carbonyl, 0. Found: C, 54.30; H, 6.08; active H, 1.0 mole; carbonyl, 0.

(b) The **nitrates** (0.52 g.) were heated with acetone (9 cc.) and water (4 cc.) to 200–240° in a sealed tube for

twenty-three hours. The product, after crystallization first from benzene and then from methanol, melted at 168.5–170°.

The chlorides. (a) The **alcohols** (0.97 g.) were refluxed with thionyl chloride for fifteen minutes. Excess reagent was pumped off and the residue (1.04 g., 100%), if it melted below 110–113°, was crystallized from methanol or ethyl acetate.

Anal. Calcd. for $C_{11}H_{14}ClBr$: C, 50.48; H, 5.40. Found: C, 49.88, 50.12; H, 5.47, 5.59.

(b) The **acetates** (0.20 g.), heated with thionyl chloride (3.2 cc.) in a sealed tube at 112° for twenty hours, gave the **chlorides,** m. p. 109–110.5°. When a solution of the acetates (0.40 g.) in ethanol (12 cc.) and hydrochloric acid (4 cc.) was refluxed for five hours, the **chlorides,** m. p. 108–112.5°, were produced.

(c) The **dibenzyl ether** (0.14 g.) was heated for forty-two hours at 122° in a sealed tube with thionyl chloride (3 cc.). The product (0.097 g., 62%) was the chloride. After crystallization from ethanol it melted at 105–110.5°.

(d) The **nitrates** (1.51 g.) were refluxed for a day in ethanol (24 cc.) and hydrochloric acid (8 cc.). The solution was poured into water and the solid (0.18 g.) was removed and crystallized from ethanol. It was the chloride, m. p. 111–112°. The aqueous filtrate contained 1.21 g. of orange oil from which some solid material, m. p. 75–100°, could be isolated, but it could not be purified further. The oil gave an immediate precipitate with silver nitrate.

When the chloride (0.25 g.) in toluene (5 cc.) was refluxed for five hours with the sodium derivative of the alcohols (prepared by refluxing the alcohols (0.23 g.) with sodium (0.023 g.) in toluene (5 cc.) until the white sodium derivative was formed), the product was the **dibenzyl ether.** The reaction mixture was filtered, water was added to the filtrate and the toluene was removed by steam distillation. The residue was extracted with chloroform and crystallized from methanol or benzene. The product melted at 200.5–211°.

The Iodides.—The chlorides (1.04 g.) were warmed briefly with an acetone solution of sodium iodide (10%, 20 cc.) and the solution was then allowed to stand for an hour. Addition of water precipitated a solid (1.34 g., 95%) which was removed and crystallized from acetone or ethyl acetate. It then melted at 133.5–136°.

Anal. Calcd. for $C_{11}H_{14}BrI$: C, 37.40; H, 4.00. Found: C, 37.25; H, 3.97.

The Benzyl Ethyl Ethers.—The nitrates (1.00 g.) were refluxed for eighty-five minutes with ethanol (25 cc.) containing potassium hydroxide (2.19 g.). The inorganic precipitate contained 1.8% of nitrite. The alcoholic filtrate was diluted with water and the solid was removed and crystallized twice from aqueous methanol. It melted at 51–53.5°.

Anal. Calcd. for $C_{13}H_{19}OBr$: C, 57.55; H, 7.06. Found: C, 56.70; H, 7.30.

When the chlorides (0.11 g.) were refluxed for seven hours with sodium ethoxide in ethanol (0.21 g. of sodium, 10 cc. of dry ethanol), the product was the benzyl ethyl ether, m. p. about 50°.

The Bromonitrotetramethylbenzenes, VII + VIII.—Sulfuric acid (8.3 cc.) was added slowly at room temperature to a vigorously stirred solution of the nitrates (0.72 g.) in chloroform (7 cc.). The chloroform layer was removed at once (seven minutes after starting the reaction), washed with carbonate (5%), then with water, and evaporated to dryness, pumping off the last traces of the solvent. The residue, after crystallization from ethanol (charcoal), weighed 0.14 g. (22%) and melted at 163–174.5°. Recrystallization from petroleum ether gave a product melting at 174–177°.

Anal. Calcd. for $C_{10}H_{12}O_2NBr$: C, 46.51; H, 4.69. Found: C, 46.38; H, 4.81.

The mixture of VII + VIII (0.57 g.) in acetic acid (6 cc.) was refluxed for ten hours with granular tin (1.25 g.) and hydrochloric acid (5.5 cc.). The reaction mixture was made strongly alkaline and was steam distilled. The solid (0.25 g.) was removed from the distillate and was sublimed *in vacuo*, first at 100° and then briefly at 150°. The first portion of the sublimate (0.05 g.) melted at 57–62°; the second portion (0.06 g.) melted at 115–136°, and the residue (0.09 g.) melted at 144–147°. The first sublimate, after crystallization from petroleum ether, melted at 64.5–67.5°, gave no depression in m. p. when mixed with aminoprehnitene (m. p. 66–68°), but did give a depression when mixed with aminodurene (m. p. 71.5–74.5°). The residue from the sublimation, after crystallization from petroleum ether, melted at 146–148°. It gave no depression in m. p. when mixed with bromoaminoisodurene (m. p. 145.5–147°). Considering the first sublimate to be pure aminoprehnitene, and the residue to be pure bromoaminoisodurene, and assuming that the midpoint (125°) of the melting range of the second sublimate is a linear function of the mole fractions of aminoprehnitene (m. p. *ca.* 70°) and bromoaminoisodurene (m. p. *ca.* 147°) present, then the mole fractions of these two amines in the second sublimate are 0.286 and 0.714, respectively, and their respective weights are 0.012 g. and 0.048 g. Hence the total weights of aminoprehnitene and bromoaminoisodurene in the reduction product were 0.062 and 0.138 g., which corresponds with 0.107 g. (41%) of bromonitroprehnitene and 0.156 g. (59%) of bromonitroisodurene in the original mixture of VII + VIII.

The Pure Isomers.—The preparations are described in detail for one set of isomers; other results are given in Table I.

TABLE I

DATA ON PREPARATION OF PURE BROMOTETRAMETHYLBENZYL DERIVATIVES

Bromotetramethylbenzyl derivative	Yield, %	Analyses, % Calcd. C	Calcd. H	Found C	Found H
4,2,3,5,6-chloride	42	50.48	5.40	50.14	5.52
5,2,3,4,6-chloride	45.5	$C_{11}H_{14}ClBr$		50.22	5.53
6,2,3,4,5-chloride	36			50.74	5.62
4,2,3,5,6-iodide	95	37.40	4.00	37.41	4.27
5,2,3,4,6-iodide	100	$C_{11}H_{14}BrI$		37.30	4.36
6,2,3,4,5-iodide	99			37.84	4.37
4,2,3,5,6-acetate	95	54.73	6.01	54.87	6.60
5,2,3,4,6-acetate	84	$C_{13}H_{17}O_2Br$		54.66	6.04
6,2,3,4,5-acetate	93			54.74	5.92
4,2,3,5,6-nitrate	65	45.83	4.90	46.26	5.18
5,2,3,4,6-nitrate	72	$C_{11}H_{14}O_3NBr$		46.27	5.14
6,2,3,4,5-nitrate	92			45.56	4.61

TABLE II

MELTING POINTS (°C.) OF BROMOTETRAMETHYLBENZYL DERIVATIVES

	Chloride	Iodide	Acetate	Nitrate
1. Durene series	105.5–107.5	118.5–120	119.5–122	113–114.5
2. Isodurene series	114–114.5	132.5–134	88.5–90	105–106.5
3. Prehnitene series	114–116	142–143.5	96.5–98	90–92.5
4. Mixture from bromopentamethylbenzene	110–113	133.5–136	82–83.5	78–84
1 + 2	96–101	114–128	89–116	111–114.5
1 + 3	94–100	118–133	97.5–109	84–110
2 + 3	111.5–113	134.5–136	81–92	78–85
1 + 4	Below 99	115–127	83–116	82–110
2 + 4	110–114	134–134.5	83–86	80–91
3 + 4	112.5–114.5	136.5–137	80–94	81–89

Chloromethylations.—The bromohydrocarbon (2.5 g.), hydrochloric acid (10 cc.) and formalin (10 cc., 40%) were stirred vigorously and heated on a water-bath for thirty-two hours while a stream of dry hydrogen chloride was passed through. Occasionally during the reaction, more formalin (total 10 cc.) was added in 2–3 cc. portions. The reaction mixture was extracted with chloroform and the organic layer was washed with water. Removal of the solvent left the solid reaction product, which was crystallized once or twice (charcoal if the product was colored) from ethyl acetate.

Iodides.—The chloride (1.28 g.) was dissolved in a solution of sodium iodide in acetone (20 cc., 10%) and allowed to stand for forty-five minutes to one hour. The solution was poured into water and the solid was removed by filtration or chloroform extraction and crystallized from acetone.

Acetates.—The iodide (0.30 g.) was refluxed for three to five hours in acetic acid (12 cc.) containing potassium acetate (0.50 g.). The mixture was poured into water and the precipitate was removed and crystallized from ethanol.

Nitrates.—The iodide (0.30 g.) was refluxed in dry dioxane (10 cc.) containing powdered silver nitrate (1.50 g.). The reaction mixture was poured into water and the solid was isolated by filtration or, better, by chloroform extraction. It was crystallized from petroleum ether (b. p. 60–68°).

In Table II are given the melting points of the pure substances and their binary mixtures (approximately 50–50) with each other and with the corresponding derivatives (mixture) from bromopentamethylbenzene. It is apparent that many of the mixtures do not show great depressions in melting points, but in all cases the melting points of mixtures of the isodurene and prehnitene derivative are almost identical with, and do not depress, the melting points of the corresponding mixture obtained from bromopentamethylbenzene.

Bromonitrodurene.—A mixture of chloroform (3.5 cc.) and fuming nitric acid (d. 1.57, 1.3 cc.) was added rapidly (4.5 minutes) to a cooled (0°) and well-stirred mixture of chloroform (17 cc.) sulfuric acid (5.5 cc.) and bromodurene (5 g.). The reaction mixture was immediately poured into water, the chloroform layer was removed and partially evaporated. Ethanol was added to replace the chloroform until the hot solution began to crystallize, after which the mixture was chilled. The product (4.03 g., 66%) consisted of light yellow needles which melted at 179–180° after crystallization from chloroform–ethanol.

Anal. Calcd. for $C_{10}H_{12}O_2NBr$: C, 46.51; H, 4.69. Found: C, 46.19; H, 5.14.

Bromonitroisodurene was prepared as above from bromoisodurene (4 g.). The product (2.97 g., 61%), after crystallization from chloroform–ethanol, formed light yellow needles which melted at 176.5–177.5°.

Anal. Calcd. for $C_{10}H_{12}O_2NBr$: C, 46.51; H, 4.69. Found: C, 46.13; H. 4.90.

Bromonitroprehnitene was prepared as above from bromoprehnitene (3.81 g.). The product (1.51 g., 33%) after two crystallizations from chloroform–ethanol formed light yellow needles which melted at 180–181.5°.

Anal. Calcd. for $C_{10}H_{12}O_2NBr$: C, 46.51; H, 4.69. Found: C, 46.88; H, 4.83.

Aminodurene.—Bromonitrodurene (3.28 g.) in acetic acid (35 cc.) was refluxed for four hours with granular tin (7 g.) and hydrochloric acid (32 cc.). The reaction mixture was made strongly alkaline and steam distilled. From the distillate there was isolated 1.45 g. (75%) of aminodurene which, after vacuum sublimation, softened at 68.5° and melted at 71.5–74.5°.[13] A mixture of aminodurene and aminoprehnitene (m. p. 66–68°) was entirely liquid at 51°.

Bromoaminoisodurene.—Reduction of bromonitroisodurene (1 g.) as above gave 0.70 g. (79%) of bromoaminoisodurene which melted at 145.5–147° after crystallization from petroleum ether.

Anal. Calcd. for $C_{10}H_{14}NBr$: C, 52.62; H, 6.19. Found: C, 52.87; H, 6.29.

Aminoprehnitene.—Reduction of bromonitroprehnitene (1.27 g.) as above gave 0.55 g. (75%) of aminoprehnitene, which after vacuum sublimation melted at 66–68°.[14]

Summary

1. The action of fuming nitric acid upon bromopentamethylbenzene produced an inseparable mixture of two benzyl nitrates, 5-bromo-2,3,4,6-tetramethylbenzyl nitrate (V) and 6-bromo-2,3,4,5-tetramethylbenzyl nitrate (VI) in the approximate ratio of 3 to 2. These nitrates were converted into nitro compounds, bromonitroisodurene (VII) and bromonitroprehnitene (VIII), by sulfuric acid.

2. The action of a mixture of fuming nitric

(13) Ref. 3a, p. 1294; ref. 12, p. 6.

(14) Limpach, *Ber.*, **21**, 644 (1888); Töhl, *ibid.*, **21**, 905 (1888).

and sulfuric acids upon bromopentamethylbenzene gave 4-bromo-5,6-dinitrohemimellithene, in which two methyl groups had been replaced by nitro groups.

3. The benzyl nitrates V and VI were intermediates in the replacement of methyl groups by nitro groups; this may possibly be the course of other aromatic nitrations in which alkyl groups are replaced by nitro groups.

MINNEAPOLIS, MINNESOTA RECEIVED FEBRUARY 12, 1940

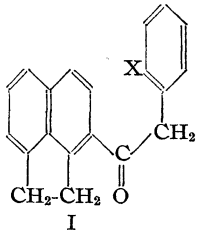
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

7-Cholanthroic Acid

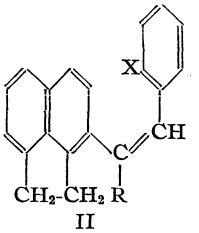
BY LOUIS F. FIESER AND GLEN W. KILMER[1]

The recently described preparation of 1-acetoacenaphthene by the acetylation of the hydrocarbon in the presence of liquid hydrogen fluoride[2,3] has rendered this ketone far more readily available as an intermediate for synthesis than any other 1-substituted acenaphthene, and the present research was undertaken to determine whether this or other 1-acyl derivative obtainable with the use of hydrogen fluoride could be employed as the starting point for the construction of the cholanthrene ring system.

The ready availability of the 1-aceto compound, which in large scale preparations has now been obtained in yields as high as 45% of the theory, is dependent upon the formation of a large proportion of the 1-isomer and also upon the fact that this is less soluble than the 3-ketone present in the mixture and is very easily separated. This favorable combination of factors has not been encountered in such other hydrogen fluoride acylations as have been investigated,[2a] for in the benzoylation, succinoylation and condensation of the hydrocarbon with crotonic acid by the hydrogen fluoride method, the amount of 1-substitution is small or negligible and no greater than in the Friedel and Crafts reaction. Although the prospects of obtaining other 1-acyl derivatives easily by direct hydrogen fluoride acylation are thus none too great, some trial was made of the condensation with phenylacetic acid derivatives with the thought that ketones of the type I might afford a short synthetic route to cholanthrenes. Thus a derived unsaturated compound (II) might be convertible to a cholanthrene by Pschorr ring closure (X = NO_2) or by the alkali fusion method employed by Hewett[4] (X = Br).



I



II

In a preliminary trial the hydrogen fluoride acylation of acenaphthene with phenylacetic acid itself was found to give a difficultly separable ketone mixture which on fractional crystallization afforded in 30% yield a pure compound identified as 3-phenylacetoacenaphthene by hypoiodite oxidation to the corresponding acid. The desired 1-isomer (I, X = H), which was similarly characterized as to structure, was isolated with difficulty and in only small amounts through the picrate. *o*-Bromophenylacetic acid, prepared from *o*-bromobenzoic acid by the Arndt–Eistert[5] reaction in 61% over-all yield, behaved similarly and gave a mixture from which two apparently pure compounds were isolated but only by tedious processing and in very small amounts. In view of these unfavorable indications, this approach was abandoned.

We then undertook to prepare intermediates of the type II starting with 1-acetoacenaphthene (III). Two routes were explored for the conversion of this ketone into 1-acenaphthylacetic acid (VII), the first being via the acid chloride and diazo ketone by the Arndt–Eistert procedure.[5] While the over-all yield of 50% is adequate, the process is time-consuming and not well adapted to the preparation of a quantity of the acetic acid derivative. Furthermore, the purified product probably was contaminated with a trace of the more sparingly soluble 1-acenaphthoic acid, for the melting point was not quite as high as that of

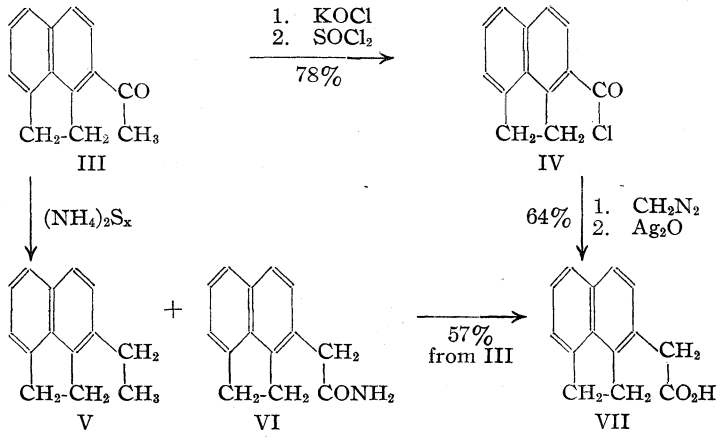
(1) Du Pont Graduate Fellow, 1939–1940.

(2) (a) Fieser and Hershberg, THIS JOURNAL, **61**, 1272 (1939); (b) **62**, 49 (1940).

(3) Fieser and Cason, *ibid.*, **61**, 1740 (1939).

(4) Hewett, *J. Chem. Soc.*, 1286 (1938).

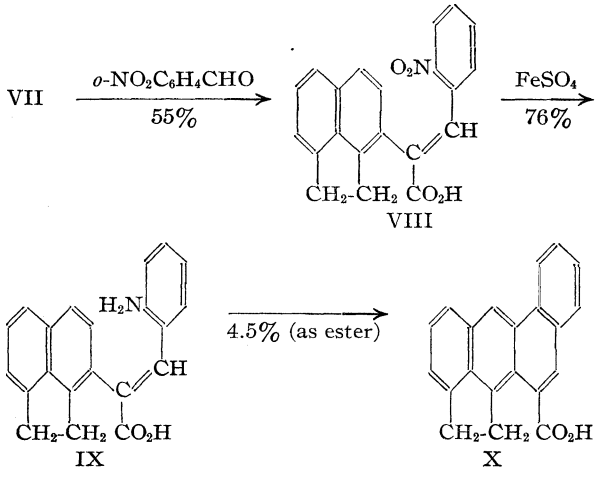
(5) Arndt and Eistert, *Ber.*, **68**, 203 (1935).



material prepared by the Willgerodt reaction,[6] which proved to be generally more satisfactory. This in the simplest case consists in heating a methyl ketone with yellow ammonium sulfide and results in the formation of an amide derivative, $ArCH_2CONH_2$, and in a certain amount of reduction. In a number of small scale experiments conducted in sealed tubes it was found that with 1-acetoacenaphthene the results are improved by the use of added dioxane and by conducting the reaction at a temperature (160°) considerably lower than recommended by Willgerodt. In the best case the yield of slightly colored but sharply melting acid (VII), isolated after hydrolysis of the crude amide, was 57%. This result could not be matched in large scale preparations conducted in an autoclave, for in the best case the yield of 1-acenaphthylacetic acid was 37% and considerable 1-ethylacenaphthene (47%) was produced. In one run in the autoclave the yield of the hydrocarbon was 67% of the theoretical. Cook, Haslewood and Robinson[7] prepared this hydrocarbon in a different way and reported the melting point of a purified sample as 30°. The redistilled material from the Willgerodt reaction had the m. p. 34.8–35.1° (constant) after a single crystallization from methanol.[8]

The Perkin condensation of 1-acenaphthylacetic acid with *o*-chlorobenzaldehyde proceeded satisfactorily (55%) to α-(*o*-chlorobenzal)-1-acenaphthylacetic acid (II, X = Cl, R = CO_2H), but fusion of this substance with potassium hydroxide or refluxing with potassium hydroxide in quinoline gave tars from which only traces of starting material could be isolated. Although these experiments were conducted with only rather small quantities of the chloro acid, the results discouraged further attempts to effect cyclization by this route. The case is comparable to an unsuccessful trial in the chrysene series.[9]

The Pschorr reaction then was tried, the intermediate α-(*o*-nitrobenzal)-1-acenaphthylacetic acid (VIII) being obtained by the Perkin condensation and reduced satisfactorily with ferrous sulfate and ammonia. Hydrogenation of the nitro compound in the presence of Adams catalyst



was less successful, for the yield of the amine IX was poorer (53%) and two unidentified neutral products were formed, one in 18% yield. The Pschorr ring closure proceeded poorly under all conditions tried, the procedure eventually adopted consisting in diazotization with isoamyl nitrite and treatment with Gattermann copper. The reaction gave a tarry acidic product which could not be purified as such, but by esterification with diazomethane and purification of the ester by

(6) Willgerodt, *Ber.*, **20**, 2467 (1887); **21**, 535 (1888); *J. prakt. Chem.*, **80**, 183 (1909); Willgerodt and Merk, *ibid.*, **80**, 192 (1909); Willgerodt and Hambrecht, *ibid.*, **81**, 74 (1910); Willgerodt and Scholtz, *ibid.*, **81**, 382 (1910); Willgerodt and Albert, *ibid.*, **84**, 387 (1911). Also Weitzenbock and Lieb, *Monatsh.*, **33**, 564 (1912); Cook, *J. Chem. Soc.*, 2524 (1931); Mosettig and van de Kamp, THIS JOURNAL, **55**, 3442 (1933).

(7) Cook, Haslewood and Robinson, *J. Chem. Soc.*, 667 (1935).

(8) Willgerodt and Merk (ref. 6) heated phenyl isobutyl ketone with yellow ammonium sulfide and isolated in 14–15% yield a substance melting at 118° and regarded as α-methyl-γ-phenylbutyramide. We prepared the ketone both by the Friedel and Crafts reaction (56%) [Claus, *J. prakt. Chem.*, **46**, 490 (1892)] and from benzamide and isobutyl bromide (59%) and tried the Willgerodt reaction under various conditions. The best yield of amide, isolated as glistening plates, m. p. 121–122° was 1.8%. Saponification and conversion to the anilide gave fine needles, m. p. 137–138°, with softening at 130°. Krollpfeiffer and Schäfer [*Ber.*, **56**, 620 (1923)] report the m. p. 140° for the anilide of α-methyl-γ-phenylbutyric acid, while the anilide of the β-methyl isomer is given as 101° [Anschütz and Motschmann, *Ann.*, **407**, 88 (1915)].

(9) Fieser, Joshel and Seligman, THIS JOURNAL, **61**, 2134 (1939).

chromatographic adsorption, distillation and crystallization, methyl 7-cholanthroate was isolated as a nicely crystalline product of sharp melting point in small yield (4.5%). Hydrolysis gave 7-cholanthroic acid (X), the alkali salts of which are moderately soluble in water, and the substance is being tested for carcinogenic activity. While the pure acid seemed rather resistant to decarboxylation by heating with basic copper carbonate (at least on a micro scale), the crude acidic product of the cyclization was converted by this catalyst into cholanthrene, identified by mixed melting point determination and by the preparation of the picrate. The yield of cholanthrene from the amino acid IX was 8.1%.

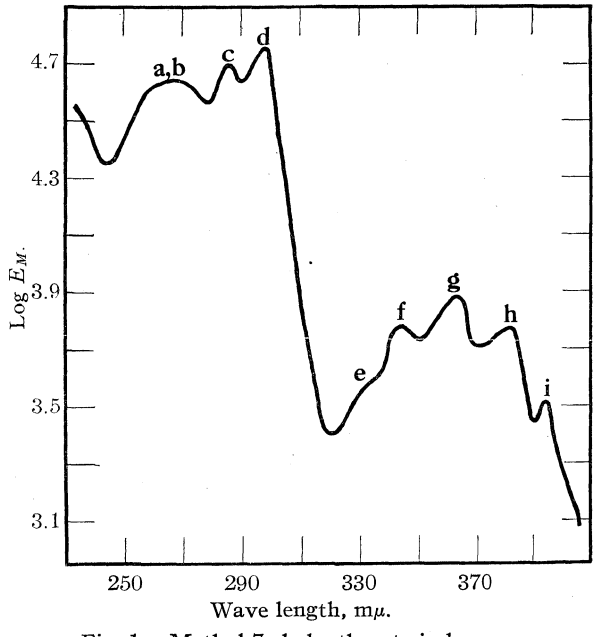


Fig. 1.—Methyl 7-cholanthroate in hexane.

The ultraviolet absorption spectrum of methyl 7-cholanthroate (Fig. 1), kindly determined by Dr. R. N. Jones, corresponds in general form and detail with that of cholanthrene,[10] although some resolution is lacking. A comparison of the wave lengths and intensities of the principal maxima with those of cholanthrene is given in Table I.

TABLE I

ULTRAVIOLET ABSORPTION MAXIMA

Maxima	Cholanthrene λ, mμ	Cholanthrene Log E_M	Methyl 7-cholanthroate λ, mμ	Methyl 7-cholanthroate Log E_M
a, b	(265.5)	4.6	265.5	4.65
c	284.5	4.8	285.5	4.69
d	295	4.9	297.5	4.75
e	328	4.6	(328)	(3.53)
f	342	3.8	344	3.78
g	358	4.0	362	3.89
h	377	3.8	381	3.77
i	(388)	(3.5)	394	3.52

(10) Fieser and Hershberg, THIS JOURNAL, **60**, 940 (1938).

Experimental Part[11]

Acylation of Acenaphthene with Phenylacetic Acid.—A mixture of 10 g. of the hydrocarbon, 9.3 g. of phenylacetic acid, and 130 g. of anhydrous hydrogen fluoride was allowed to stand at room temperature in a platinum container for ten and one-half hours and poured onto ice. The greenish, amorphous precipitate was ground in a mortar with sodium carbonate solution to neutralize adhering acid, then washed and dried, giving 16.9 g. of gray-green powder, m. p. 65–95°. Repeated crystallization from benzene and from ethyl acetate–hexane gave **3-phenylacetoacenaphthene,** m. p. 111.5–113°, in 30% yield. The picrate, prepared in alcohol and crystallized from benzene–hexane, formed somewhat unstable, yellow-orange needles, m. p. 107.5–108.5°. The ketone recovered from the picrate with the use of an alumina adsorption tower crystallized from ethyl acetate–hexane in the form of colorless prisms, m. p. 113.5–114°.

Anal. Calcd. for $C_{20}H_{16}O$: C, 88.20; H, 5.92. Found: C, 87.96; H, 5.99.

By oxidation of 1 g. of this ketone in dioxane with sodium hypoiodite solution there was obtained 121 mg. of 3-acenaphthoic acid, m. p. 218–219°. The m. p. was not raised by recrystallization from alcohol and the acid showed no depression with an authentic sample.

The residual ketonic mixture on repeated crystallization afforded a small amount of substance melting at 73–90° which was converted into the picrate in benzene. After crystallization from ethyl acetate–hexane, this derivative was obtained as brilliant yellow needles which seemed to undergo a change in form at 130.5–131° and melted at 133–134°. **1-Phenylacetoacenaphthene** was recovered from the picrate with the use of benzene and ammonia solution and crystallized from benzene–hexane. It formed large, pale yellow prisms, m. p. 81–81.5°.

Anal. Calcd. for $C_{20}H_{16}O$: C, 88.20; H, 5.92. Found: C, 88.04; H, 5.99.

Oxidation of 200 mg. as above gave 59 mg. of crude acid, m. p. 240–250°. Crystallized from alcohol, the sample melted at 251–252.5° and did not depress the m. p. of authentic 1-acenaphthoic acid.

***o*-Bromophenylacetic Acid.**[12]—The diazomethane formed by dropping 55 cc. of nitrosomethylurethan in 55 cc. of ether into 60 cc. of a warm saturated solution of potassium hydroxide in absolute alcohol covered with ether (20 cc.) was distilled through a vertical coil condenser and absorbed in cold absolute ether. After dilution to 800 cc. with cold ether, 21.4 g. of *o*-bromobenzoyl chloride (b. p. 103–104° at 5 mm.) was added in ether with mechanical stirring at 0° during one hour. After five hours at room temperature a fluffy precipitate was removed by filtration and the ether evaporated in vacuum, leaving 22.8 g. of a brownish, oily, lachrymatory product, m. p. 36–41°. Crystallized by concentrating an ether–hexane solution of

(11) All final melting points are corrected.

(12) Following the procedure of Litvan and Robinson, *J. Chem. Soc.*, 1997 (1938).

the product in vacuum and cooling, this gave 14.6 g. (66.5%) of yellow and not appreciably oily **diazomethyl-*o*-bromophenyl ketone**, m. p. 42–43° (gas evolution). The mother liquor material was largely oily (6.2 g.). A solution of the crystallized diazo ketone (14.6 g.) in technical dioxane was added in one-half hour with stirring to a suspension of 16 g. of silver oxide in 800 cc. of water containing 24 g. of sodium thiosulfate at 60–65°. After one-half hour more the evolution of gas had practically ceased and the mixture was made alkaline with 25 cc. of 10% sodium hydroxide and filtered. The filtrate was washed with benzene, acidified with dilute nitric acid, and extracted with ether. On concentrating the extract and adding hexane the product separated as an oil. By slowly acidifying a solution of the acid in dilute alkali, 11.4 g. (81.7% from the diazo ketone) of *o*-bromophenylacetic acid[13] was obtained as an odorless, pale yellow, crystalline powder, m. p. 103–105°. Treatment with Norit in an aqueous solution containing a very slight excess of sodium carbonate gave pure white acid, m. p. 103.5–105.5°, and on two crystallizations from benzene–hexane it formed clusters of jagged prisms, m. p. 105–106°.

The impure diazo ketone (6.2 g.) gave 3 g. of yellow acid, m. p. 98–102°. Crystallization failed to effect much purification, but treatment with Norit in an aqueous solution containing little excess soda and precipitation gave 1.72 g. of pure white powder, m. p. 103.5–105.5°. The total yield of satisfactory acid was 13.1 g., a 62.5% over-all yield from the acid chloride (prepared from *o*-bromobenzoic acid in 98% yield with thionyl chloride).

Acenaphthene and *o*-Bromophenylacetic Acid.—The condensation of 1.43 g. of the hydrocarbon with 2 g. of the acid in hydrogen fluoride (85 g.), conducted at room temperature for one and one-half hours, gave 3.05 g. of neutral, light yellow powder, m. p. 85–102°. Little separation was effected by crystallization as such or through the oxime, but crystallization as the picrate and dissociation of alumina afforded small amounts of a white powder, m. p. 128–129.5°, and of tiny white needles, m. p. 122–123°, from the less and more soluble fractions, respectively. Another portion processed through the trinitrobenzene derivatives gave light yellow prisms, m. p. 128–129.5°, and light yellow needles, m. p. 110.5–112.5°. Since none of these substances was obtained in practical quantity they were not characterized further.

1-Acetoacenaphthene was prepared in the pressure vessel as described by Fieser and Hershberg.[2b] The crude product from two 80-g. batches of commercial "95%" acenaphthene was collected on a Büchner funnel (cold room) and then ground in a mortar three times with water, the material each time being collected on a funnel and pressed well to force out as much oil as possible. Two similar washings were made with sodium carbonate solution, and after a final washing with water the product was dried partially by exposure to air and then fully dried by adding benzene and distilling. Distillation gave 143.4 g. of ketone mixture boiling largely at 181–183° (3 mm.), m. p. 80–95°, and there was about 10 g. of tarry residue. Crystallization at room temperature from 400 cc. of methanol and then from 750 cc. of this solvent[3] yielded 87.1 g. of the 1-isomer, m. p. 103–105°, and 5 g. of equally good material was obtained by working the second mother liquor; total yield 45% (calculated for pure acenaphthene).

1-Acenaphthylacetic Acid (VII). (a) **Arndt–Eistert Reaction.**—1-Acenaphthoic acid and its chloride were prepared according to Fieser and Cason[3] with closely agreeing results. Nitrosomethylurethan (24.3 cc.) in absolute ether (198 cc.) was dropped into 42 cc. of a solution prepared from 3 g. of sodium and 50 g. of glycol at 50°[14] and the distillate collected in a flask cooled in ice. After flushing the apparatus with ether the solution was diluted to about 275 cc. with absolute ether and a solution of 7.59 g. of 1-acenaphthoyl chloride (m. p. 108–110.5°) in absolute ether (87 cc.) and purified dioxane (44 cc.) was added during 50 minutes while stirring and cooling in ice. After stirring for two and one-quarter hours longer at room temperature, the precipitated light yellow **diazo ketone** was collected (4.01 g., m. p. 141–142° dec.) and the filtrate was concentrated to about 4 cc. and cooled, giving 3.24 g. of orange–yellow material, m. p. 137–141° (crude yield 93%). The combined product was taken up in 70 cc. of technical dioxane and the solution, filtered from a slight residue (0.1 g.), was added dropwise in one hour to a stirred suspension at 60–70° of 8.2 g. of silver oxide in 435 cc. of water containing 21.4 g. of sodium thiosulfate. After stirring for one and one-half hours longer 0.5 g. of Norit was added and the mixture was cooled and filtered and the filtrate acidified with dilute acetic acid (hydrochloric or nitric acid caused darkening of the precipitate). The precipitated 1-acenaphthylacetic acid (5.96 g.) softened at 150° and melted at 157–165°. Crystallization from methanol (15 cc.) gave pale yellow needles, m. p. 155.5–160°; yield 4.74 g. (63.5% from the acid chloride). After crystallization of the potassium salt from absolute alcohol the recovered acid melted at 158–159.5°, and repeated crystallization from benzene–hexane gave fine white needles, m. p. 163.5–164.4°.

Anal. Calcd. for $C_{14}H_{12}O_2$: C, 79.22; H, 5.70. Found: C, 78.87; H, 5.46.

(b) **Willgerodt Reaction.**—When 1-acetoacenaphthene was submitted to the reaction under the conditions specified by Willgerodt and Merk[6] (five to six hours at 200–220°) the material was badly decomposed and little amide could be isolated. After a number of variations had been tried the best results were obtained as follows. A solution of 1 g. of sulfur in 10 g. of a solution of ammonium sulfide prepared by saturating concentrated ammonia solution with hydrogen sulfide was sealed in a tube with 2 g. of 1-acetoacenaphthene and 8 cc. of purified dioxane and the mixture was heated at 160° for twelve hours. The dark solid product (m. p. 185–205°, a few yellow plates present melted at 205°) was collected and refluxed for four hours with 50 cc. of 15% sodium hydroxide. Water (50 cc.) and Norit (0.25 g.) were added and the solution was filtered hot and treated with dilute hydrochloric acid until just weakly alkaline, when a small amount of sludge separated and could be removed by filtration. Acidification of the filtrate gave 1.37 g. of 1-acenaphthylacetic acid, m. p. 159–162°. A further quantity was recovered from the ammonium sulfide filtrate. After acidifying and collecting the coagulated sulfur the filtrate was concentrated and a little gummy solid

(13) Jackson and White, *Am. Chem. J.*, **2**, 316 (1880).

(14) Meerwein and Burneleit, *Ber.*, **61**, 1845 (1928).

obtained. Extraction of the combined gum and sulfur with bicarbonate solution gave 80 mg. of crude acid. The combined material on crystallization from dilute alcohol afforded 1.24 g. (57%) of fine, light orange needles, m. p. 163–165°. On recrystallization with liberal use of Norit the substance formed pure white needles, m. p. 167.6–168.2° (slight softening at 163°).

Anal. Calcd. for $C_{14}H_{12}O_2$: C, 79.22; H, 5.70. Found: C, 79.06; H, 5.77.

In larger runs conducted in an autoclave the reaction mixture was charged into a 500-cc. round-bottomed flask connected by means of a hemispherical ground-glass joint (which effectively prevented freezing) to a spiral made from about 60 cm. of 1-mm. capillary tubing.[15] Nitrogen (at 500–1000 lb. (33–67 atm.) pressure) was admitted, and allowed to escape, very slowly. From 19.2 g. of 1-acetoacenaphthene, 96 g. of ammonium sulfide solution, 9.6 g. of sulfur and 77 cc. of dioxane, heated for eighteen hours at 175–180°, there resulted 6.8 g. (33%) of reddish-brown, semicrystalline amide. The oily filtrate was extracted with benzene and the aqueous layer on acidification and extraction of the precipitate as above gave 426 mg. (2.1%) of yellow acid, m. p. 159–160°. The benzene solution was evaporated and the residual oil refluxed for four hours with 300 cc. of 15% sodium hydroxide, giving, on acidification of the separated aqueous phase, 358 mg. (1.7%). The combined yield of crude acid and amide was thus 36.8%. For the complete hydrolysis of as much as 20 g. of the crude amide a refluxing period of six hours was required.

The unsaponified oil after washing and drying distilled at 160–163° (6 mm.), yielding 8.3 g. (46.7%) of **1-ethylacenaphthene** as a pale yellow oil which crystallized on cooling. This was redistilled and crystallized from methanol, giving colorless needles, m. p. 34.8–35.1° (not changed by recrystallization).

Anal. Calcd. for $C_{14}H_{14}$: C, 92.26; H, 7.74. Found: C, 92.21; H, 7.89.

The **picrate**, purified to constant m. p. by crystallization from absolute alcohol–hexane, formed brilliant red needles, m. p. 104.7–105.1°. The hydrocarbon could be extracted from the picrate with hexane, and after passing the solution through an alumina tower, the recovered hydrocarbon crystallized from methanol as needles, m. p. 33.5–34.5°. For the hydrocarbon and its picrate Cook, Haslewood and Robinson[7] give the melting points 30° and 102–102.5°.

In a run conducted as above except that the temperature was kept at 170° for eighteen hours, the yield of crude amide was 22% and of ethylacenaphthene 65%. With the same reaction time but at 188–190° the corresponding yields were 29 and 43%. On increasing the amount of ammonium sulfide solution (139 g.) and dioxane (120 cc.) and heating for eighteen hours at 163–164° the yield of amide dropped to 7.5% and ethylacenaphthene was obtained in 67.5% yield.

α-(*o*-Chlorobenzal)-1-acenaphthylacetic Acid (II, R = CO_2H; X = Cl).—1-Acenaphthylacetic acid was titrated in methanol to a phenolphthalein end-point with 0.5 *N* potassium hydroxide in methanol; the solvent was evaporated completely and the residue dried at 100° in vacuum. This salt (250 mg.) was refluxed with 162 mg. of freshly distilled *o*-chlorobenzaldehyde, 1 cc. of acetic anhydride and one drop of pyridine at a bath temperature of 180° for twenty-four hours. Water (75 cc.) and excess sodium bicarbonate were added and on refluxing for about two hours only a small amount of tar remained undissolved. After extracting this with benzene, acidification gave 289 mg. of acid, m. p. 175–200°. Crystallization from dilute acetic acid (Norit) gave 145 mg. of bright yellow needles, m. p. 214–216°, and 45 mg. of slightly lower m. p. (total yield 55%). After further crystallizations from dilute alcohol, dilute acetic acid or chloroform–hexane the acid melted constantly at 221.5–223.5° with slight previous softening.

Anal. Calcd. for $C_{21}H_{15}O_2Cl$: C, 75.33; H, 4.52. Found: C, 75.20; H, 4.49.

Following Hewett's procedure,[4] cyclization was attempted by fusing the acid (0.4 g.) with 85% potassium hydroxide (3 g.) at a bath temperature of 254° (cor.) but only small amounts of starting material could be recovered. At slightly lower temperatures the reaction product gave a strong Beilstein test and at slightly higher temperatures the bulk of the product was insoluble in alkali.

α-(*o*-Nitrobenzal)-1-acenaphthylacetic Acid (VIII).—The potassium salt from 24.9 g. of 1-acenaphthylacetic acid was heated with 21.7 g. of *o*-nitrobenzaldehyde and 250 cc. of acetic anhydride for three hours at a bath temperature of 125–130° and the mixture was poured into 1200 cc. of water and allowed to stand overnight. The orange-yellow product was precipitated twice as the potassium salt from aqueous potassium carbonate, the somewhat oily salt being washed each time on the filter with half-saturated potassium carbonate solution. The liberated acid without being dried was dissolved in acetic acid, and after Norit treatment the solution was concentrated to 250 cc. and allowed to cool, when 23.8 g. (59%) of yellow, crystalline product separated, m. p. 239–241°. Recrystallized from alcohol and from acetic acid, the acid formed shiny, pale yellow needles, m. p. 244.5–244.9°, dec. (black melt).

Anal. Calcd. for $C_{21}H_{15}O_4N$: N, 4.06; neut. equiv., 345. Found: N[16] (Kjeldahl), 4.17; neut. equiv., 346.

α-(*o*-Aminobenzal)-1-acenaphthylacetic Acid (IX).—Following Cassaday and Bogert,[17] a solution of 15.8 g. of the nitro acid in 120 cc. of water and 15 cc. of ammonia solution was added during five minutes to a boiling mixture of 80 g. of ferrous sulfate crystals, 261 cc. of water and 20.4 cc. of ammonia solution. While boiling, and with the addition of a little octyl alcohol to suppress frothing, 158 cc. of ammonia solution was added during twenty minutes followed by 41 cc. in the next fifty-five minutes. After cooling, Celite was added and the cake obtained on filtration was extracted six times with boiling water containing ammonia. After treatment of the combined solutions with Norit and Celite the still dark filtrate on acidification with dilute acetic acid (avoiding an excess) deposited the acid as a gum which soon changed to a yellow solid. For crystallization the acid was dissolved in alcohol and

(15) Grosse, THIS JOURNAL, **60**, 212 (1938).

(16) Microanalysis by Lyon Southworth.

(17) Cassaday and Bogert, THIS JOURNAL, **61**, 2463 (1939).

water was gradually added at the boiling point until a considerable quantity of well formed crystals had separated. The substance was thus obtained as brownish-yellow prismatic plates, m. p. 227–229°; yield 11.0 g. (76%).

Reduction proceeded less satisfactorily when a suspension of 2 g. of the nitro acid and 25 mg. of Adams catalyst in 33 cc. of alcohol was shaken with hydrogen. After eight hours 94% of the theoretical amount of hydrogen had been absorbed. After dilution with water the product was extracted with benzene and the filtered solution extracted with bicarbonate. Acidification with dilute acetic acid gave 963 mg. (53%) of amino acid, m. p. 224–226°. Recrystallization from alcohol–water as above yielded pale yellow prisms, m. p. 229–230.5°, and further crystallizations seemed to cause slight deterioration.

Anal.[16] Calcd. for $C_{21}H_{17}O_2N$: N (Kjeldahl), 4.44. Found: N, 4.41.

Concentration of the extracted benzene solution yielded 304 mg. (18%) of a colorless, neutral substance. After repeated crystallization from dioxane and acetic acid fine white needles were obtained, m. p. 236.4–238.4° dec. (black liquid). The substance seemed resistant to hydrolysis with acid or alkali; it was characterized only by analysis[16]: C, 83.82; H, 5.54; N (Dumas), 4.85.

In another experiment a trace of another neutral by-product, m. p. 278–279.5°, was also obtained (see below).

Methyl 7-Cholanthroate.—A solution of 8 g. of the amino acid in 200 cc. of purified dioxane was treated with 1.9 cc. of sulfuric acid in 100 cc. of dioxane and the voluminous yellow solid which precipitated was brought into solution by the addition of dioxane (300 cc.) and alcohol (500 cc.) and warming gently. After cooling to room temperature 4.8 cc. of isoamyl nitrite in 10 cc. of dioxane was added with stirring in ten minutes.[17,18] No temperature rise was observed, but the solution took on a dark red color and a test sample gave an intense red coloration with alkaline β-naphthol. After stirring for one hour a solution of 26 g. of sodium hypophosphite in 26 cc. of water was added all at once, followed by the Gattermann copper paste[19] prepared from 31 g. of copper sulfate crystals and 75% of the theoretical amount of zinc. Gas was evolved at once. The mixture was stirred in a bath at 50° for one hour, the coupling test being negative after fifteen minutes. Potassium carbonate solution was added to the point of alkalinity and about 1 liter of solvent was removed under vacuum. The gum separating was brought into solution by the addition of water, and after filtration from the copper the solution was poured into 200 cc. of water and 25 cc. of concentrated hydrochloric acid. The precipitated acid was collected, dried, dissolved in 325 cc. of purified dioxane and a sediment was removed by filtration. The very dark filtrate was cooled and treated with an ethereal solution of diazomethane from 23 cc. of nitrosomethylurethane, the large excess of reagent apparently being all consumed. Evaporation of the solvent left a brown powder insoluble in alkali. This was dissolved in benzene and the solution was filtered from 1.62 g. of gelatinous material, concentrated, and passed through a tower of alumina–Celite (1:1). The first filtrate was very black and eventually was discarded. The adsorbed material was eluted with benzene containing about 10% of methanol until the filtrate no longer showed appreciable color, and after evaporation of the solvent distillation at 1 mm. yielded 1.57 g. of thick, dark oil, which was taken up in benzene. The solution, filtered from a pale yellow residue (A, 64 mg.) and concentrated to a small volume, deposited clusters of dark needles, and on recrystallization from benzene methyl 7-cholanthroate was obtained as pale yellow needles, m. p. 156–158° (293 mg.). The mother liquors afforded 67 mg. of similar material; total yield 360 mg. (4.5%). On two recrystallizations from alcohol the substance formed golden-yellow needles, m. p. 159.0–159.2°, exhibiting a dull blue-green fluorescence in benzene.

Anal. Calcd. for $C_{22}H_{16}O_2$: C, 84.59; H, 5.16. Found: C, 84.54; H, 5.30.

Material eluted from the column using higher concentrations of alcohol gave a black oil on distillation and this left a yellowish residue (B, 66 mg.) on treatment with benzene; concentration of the solution gave only tars.

The total benzene-insoluble product (A and B, m. p. 270–275°), after repeated crystallization from acetic acid–water (Norit) afforded a small amount of almost colorless needles, m. p. 280.3–281.2°, dec. (black melt), which gave no depression when mixed with the high melting by-product of the catalytic reduction of the nitro acid VIII. The substance can be dissolved in boiling alkali but after precipitation does not redissolve. The composition appears to be about the same as that of the other unidentified by-product of the hydrogenation (found[16]: C, 84.15; H, 5.01; N (Dumas), 4.75).

7-Cholanthroic Acid (X).—The pure ester (207 mg.) was refluxed for one and one-half hours with 65 cc. of 10% alcoholic potassium hydroxide solution. Most of the solvent was removed under vacuum, the residue was diluted with 200 cc. of water and the filtered solution poured into 200 cc. of water containing 15 cc. of concentrated hydrochloric acid. The precipitated acid, collected after coagulation by heating, was obtained as a pale yellow powder, m. p. about 253–256° (195 mg.). The material seemed to deteriorate slightly in acetic acid or alcohol but could be crystallized satisfactorily from a large volume of benzene. Acid so purified when heated in a sealed capillary showed a fairly constant decomposition point of 258.5–261°, after incipient sublimation at 255°.

Anal. Calcd. for $C_{21}H_{14}O_2$: C, 84.55; H, 4.73. Found: C, 84.36; H, 4.78.

When a small sample was ground with basic copper carbonate and melted in an evacuated tube, a white sublimate appeared on the upper walls and was found to melt above 200°, indicating that the pure acid is not readily decarboxylated by this method. On heating 17 mg. of slightly impure acid in high vacuum (10^{-3} mm.) at 200° for nineteen hours, 14 mg. of acid, m. p. 255–259°, sublimed leaving a dark residue.

Cholanthrene.—Following a simplified procedure, 1 g. of the amino acid was diazotized as above with isoamyl nitrite and after shaking for only about two minutes Gattermann copper was added and decomposition was conducted in a bath at 50° for twenty-five minutes. The crude acid precipitated from carbonate solution was

(18) Rüggli and Staub, *Helv. Chim. Acta*, **20**, 37 (1937).
(19) Gattermann, *Ber.*, **23**, 1219 (1890).

ground with 25 mg. of basic copper carbonate and heated under vacuum in a bath which was eventually brought to a temperature of 300°. The dark distillate (294 mg.) was extracted three times with cold absolute alcohol and the undissolved material taken up in benzene. After treatment with Norit and concentration, 65 mg. (8.1%) of light brown crystals separated. Purification by adsorption of impurities on alumina gave a yellow crystalline powder, m. p. 167.5–168.5°, which gave no depression when mixed with known cholanthrene, m. p. 166.5–168.5°. The picrate agreed in m. p. and appearance with the specimen described by Cook, Haslewood and Robinson.[7]

Summary

1-Acetoacenaphthene was converted to 1-acenaphthylacetic acid via 1-acenaphthoic acid by the Arndt–Eistert reaction and, more conveniently, by the Willgerodt process of heating the ketone with yellow ammonium sulfide. The acetic acid was condensed successfully with both *o*-chloro and *o*-nitrobenzaldehyde, but only the second of the products could be utilized for effecting a phenanthrene ring closure. Although the Pschorr reaction proceeded very poorly, the 7-carboxy derivative of cholanthrene was isolated through the ester in quantity sufficient for an investigation of its possible biological actions.

The hydrogen fluoride acylation of acenaphthene with phenylacetic acid and *o*-bromophenylacetic acid does not provide a practical route to intermediates suitable for the synthesis of cholanthrenes.

CONVERSE MEMORIAL LABORATORY
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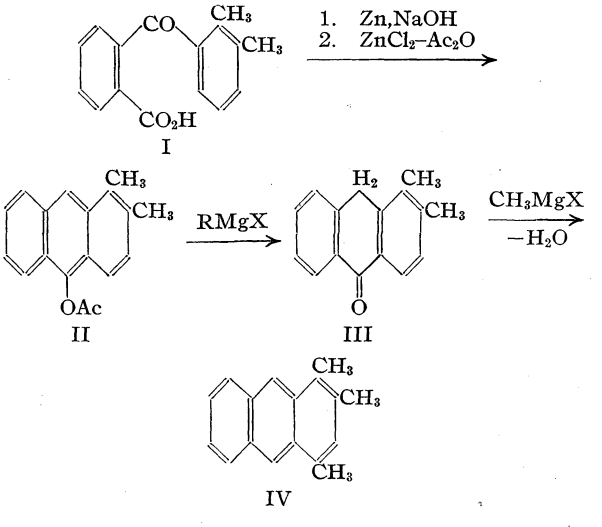
[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF HARVARD UNIVERSITY]

meso-Alkyl Anthracenes

BY LOUIS F. FIESER AND THOMAS G. WEBBER

In continuation of previous studies of model compounds structurally related to the more potently active carcinogens,[1] we sought to synthesize certain additional substituted 1,2-dialkyl anthracenes of types corresponding to known 1,2-benz derivatives of marked carcinogenic activity. The 1,2-dimethyl and 1,2-cyclopenteno derivatives of 5,10-aceanthrene were synthesized in earlier work[2] for comparison with cholanthrene, and the cyclopenteno compound was found by Shear (see ref. 1) to have definite if weak carcinogenic properties. It was hoped in the present work to obtain 1,2,10-trimethylanthracene and 1,2,9,10-tetramethylanthracene for comparison with 10-methyl-1,2-benzanthracene[3] and 9,10-dimethyl-1,2-benzanthracene,[4] respectively. The trimethyl compound was synthesized without difficulty, but the method tried for the preparation of the higher homolog proved unsatisfactory. Badger, Cook and Goulden[5] have recently reported an unsuccessful attempt to synthesize the same hydrocarbon by another method.

1,2,10-Trimethylanthracene was synthesized starting with the keto acid I[5] from *vic.*-bromo-*o*-xylene and phthalic acid. After reduction with zinc and alkali, cyclization with zinc chloride and acetic acid–anhydride[6] gave the anthranyl acetate (II), and on cleavage by the Grignard reagent the

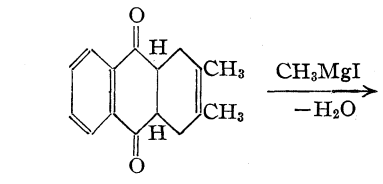


anthranol isomerized readily to the anthrone. A methyl group was then easily introduced at the 10-position. As with anthracene and a number of its derivatives,[7] the yellow trimethyl compound IV forms a colorless dimer when exposed to sunlight in solution.

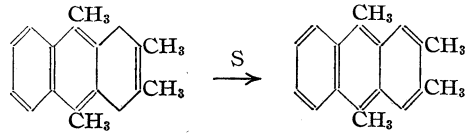
A projected synthesis of the desired tetramethyl

(1) For summary and review, see Fieser, *Am. J. Cancer*, **34**, 37 (1938).
(2) Fieser and Hershberg, THIS JOURNAL, **59**, 394 (1937).
(3) Fieser and Newman, *ibid.*, **58**, 2376 (1936).
(4) Bachmann and Chemerda, *ibid.*, **60**, 1023 (1938).
(5) Badger, Cook and Goulden, *J. Chem. Soc.*, 16 (1940).
(6) Fieser and Hershberg, THIS JOURNAL, **59**, 1028 (1937).
(7) Houben, "Das Anthracen und die Anthrachinone," Verlag Georg, Thieme, Leipzig, 1929, p. 133.

compound was tested first in a case requiring more readily available starting materials. 2,3-Dimethylbutadiene was added to α-naphthoquinone and the product (V)[8] treated with excess methylmagnesium iodide. The reaction proceeded well and a crystalline dihydroanthracene (VI) was obtained on dehydration of the crude diol. Dehydrogenation to VII was accomplished satisfactorily with the use of sulfur. The substance forms an amorphous dimer from which it can be regenerated in part by vacuum distillation.

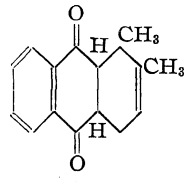


V



VI VII

3-Methylpentadiene-2,4 was then prepared according to Fisher and Chittenden[9] and found to add smoothly to α-naphthoquinone. The addition product VIII, however, behaved quite differently from the isomer in the Grignard reaction and no diol or hydrocarbon could be isolated after treatment with methylmagnesium chloride or iodide. Starting with 1,2-dimethylanthraquinone, Badger, Cook and Goulden[5] obtained a diol but found its dimethyl ether resistant to cleavage with sodium.



VIII

Experimental Part[10]

o-(2,3-Dimethylbenzoyl)-benzoic acid (I) was prepared from the Grignard reagent from 13 g. of *vic.*-bromo-*o*-xylene,[2] condensed with 30 g. of phthalic anhydride in ether–benzene. After hydrolysis and steam distillation the keto acid was precipitated from a steamed and filtered alkaline solution by pouring this into ice and hydrochloric acid. Crystallization from benzene–hexane gave 7 g. (32%) of colorless prisms, m. p. 129–131°, and after three further crystallizations the substance melted at 132–133° and remelted at 139.5–140.5°.

Anal. Calcd. for $C_{16}H_{14}O_3$: C, 75.57; H, 5.55. Found: C, 75.39; H, 5.71.

Badger, Cook and Goulden[5] used a smaller proportion of anhydride and obtained a much higher yield. They report the m. p. 126–127°.

o-(2,3-Dimethylbenzyl)-benzoic Acid.—The keto acid (3.5 g.) was refluxed in 50 cc. of 2 *N* sodium hydroxide with 3.5 g. of zinc dust for forty-seven hours, 45 cc. more alkali being added in three portions. The precipitated acid when crystallized from methanol afforded in two crops 3.1 g. (94%) of colorless prisms, m. p. 175–177°. Fully purified, the acid melted at 177.2–177.8°.

Anal. Calcd. for $C_{16}H_{16}O_2$: C, 79.97; H, 6.91. Found: C, 79.80; H, 6.89.

The **lactone of o-(2,3-dimethyl-α-hydroxybenzyl)-benzoic acid** was isolated from the reaction mixtures resulting after shorter periods of heating by extraction of the acid with soda solution. The residual material crystallized from dilute alcohol as colorless prisms, m. p. 127–128°.

Anal. Calcd. for $C_{16}H_{14}O_2$: C, 80.65; H, 5.92. Found: C, 80.47; H, 6.07.

1,2-Dimethylanthranyl-10-acetate (II).—A solution of 7.3 g. of the above acid in 45 cc. of acetic acid and 30 cc. of acetic anhydride containing 0.5 g. of anhydrous zinc chloride was refluxed for one hour and water was then added cautiously to the point of saturation. On cooling, 6.5 g. (81%) of light yellow prisms of the acetate separated, m. p. 152–154°. After four recrystallizations from dilute acetic acid the substance melted at 158.1–158.7° and had a greenish yellow tinge.

Anal. Calcd. for $C_{18}H_{16}O_2$: C, 81.79; H, 6.10. Found: C, 81.46; H, 6.12.

1,2-Dimethyl-10-anthrone (III).—The solid anthranyl acetate (6.5 g.) was added to the Grignard reagent from 3.6 g. of magnesium and excess *n*-butyl bromide and after displacement of the ether with benzene refluxing was continued for one hour. After hydrolysis, two crystallizations from benzene afforded 3 g. (55%) of the anthrone, m. p. 169–170°. The further purified material formed colorless prisms, m. p. 170.3–171.3°. The properties of the substance and its behavior in the Grignard reaction indicate the ketonic structure; the tautomeric anthranol was not encountered.

Anal. Calcd. for $C_{16}H_{14}O$: C, 86.45; H, 6.35. Found: C, 86.50; H, 6.48.

1,2,10-Trimethylanthracene.—A solution of 1.05 g. of the anthrone in 50 cc. of benzene was added to the reagent from 0.62 g. of magnesium and excess methyl bromide in ether and the mixture was refluxed for two hours before hydrolysis. The washed and dried organic layer was evaporated to dryness on the hot-plate to dehydrate the carbinol, and the residue was crystallized from hexane, giving 0.89 g. (77%) of the hydrocarbon as yellow needles, m. p. 88–90°. This was converted to the **picrate**, which crystallized from alcohol in minute dark brown needles, m. p. 138.5–139.5°. The regenerated hydrocarbon (alumina tower) was yellow and melted at 90.6–91.4°.

Anal. Calcd. for $C_{17}H_{16}$: C, 92.68; H, 7.32. Found: C, 92.60; H, 7.49.

(8) I. G. Farbenindustrie A.-G., British Patent 320,375 (1930).
(9) Fisher and Chittenden, *Ind. Eng. Chem.*, **22**, 869 (1930).
(10) All melting points are corrected.

The **trinitrobenzene derivative** formed scarlet needles, m. p. 169.6–170.2°, from alcohol.

On exposing an alcoholic solution of the hydrocarbon to the sunlight for three weeks prisms of the colorless **dimer** were deposited. Recrystallized from benzene–alcohol the substance melted at 222–226°.

Anal. Calcd. for $C_{34}H_{32}$: C, 92.68; H, 7.32. Found: C, 92.91; H, 7.28.

2,3-Dimethylbutadiene–α-Naphthoquinone (V).—A solution of 5 g. of α-naphthoquinone and 10 cc. of the diene in 20 cc. of alcohol was refluxed for three hours, and on cooling the addition product separated as fine, colorless needles. This material was collected, washed with alcohol, and dried in vacuum at 50°; m. p. 148.5–149.1°; yield, 7.25 g. (95%).

Anal. Calcd. for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 79.88; H, 6.79.

2,3,9,10 - Tetramethyl - 1,4 - dihydroanthracene (VI).—A solution of 7.2 g. of V in 50 cc. of warm benzene was added to a stirred solution of the methylmagnesium iodide from 4.2 g. of magnesium in about 70 cc. of ether–benzene and stirring was continued at room temperature for three hours. After hydrolysis and removal of the solvent the oily diol was heated to 140° to effect dehydration. On adding a little alcohol to the dark residual oil the hydrocarbon crystallized, and when collected and washed with a small volume of cold alcohol was obtained in a nearly colorless condition suitable for dehydrogenation; m. p. 165–170°, yield 3.0 g. (42%). A sample was purified by passage in benzene solution through a tower of alumina and crystallization from benzene–hexane. It formed colorless needles, m. p. 175.3–176.3°; the solutions showed intense blue fluorescence in ultraviolet light.

Anal. Calcd. for $C_{19}H_{20}$: C, 91.47; H, 8.53. Found: C, 91.42; H, 8.70.

The hydrocarbon appears to undergo ready disproportionation or other change, for further crystallized samples had higher and broader melting ranges. The **picrate** crystallized in small, dark brown needles from benzene–hexane, m. p. 149.2–149.9°. The **trinitrobenzene derivative** was obtained from benzene as scarlet needles, m. p. 150.8–151.8°.

Anal.[11] Calcd. for $C_{18}H_{20}\cdot C_6H_3O_6N_3$: N, 9.35. Found: N, 9.25.

2,3,9,10-Tetramethylanthracene.—The dihydride VI (3 g.) was heated with 0.4 g. of sulfur to 325° in one-half hour, when the evolution of gas had ceased. After heating with a pinch of zinc dust for fifteen minutes the dark residue was extracted with benzene and the solution was put through a tower of alumina. The hydrocarbon crystallized from alcohol–benzene in brownish-yellow plates, m. p. 137–139°; yield 1.65 g. (55%). On using palladium charcoal for dehydrogenation the yield dropped to 25%. The further purified hydrocarbon formed dark yellow plates, m. p. 139.4–140.2°, from benzene–hexane.

Anal. Calcd. for $C_{18}H_{18}$: C, 92.26; H, 7.74. Found: C, 92.14; H, 7.71.

Exposure of solutions of the hydrocarbon to light resulted in the separation of an amorphous, brown **dimer** which melted at about 270°. On heating this at 2 mm. pressure in a bath at 210° the monomeric form distilled and was recovered in 63% yield.

The **picrate** formed dark brown needles from benzene–hexane, m. p. 177.3–178.3°. The **trinitrobenzene derivative** separated from benzene in scarlet needles, m. p. 188.8–189.3°.

Anal.[11] Calcd. for $C_{18}H_{18}.C_6H_3O_6N_3$: N, 9.39. Found: N, 9.69.

3-Methylpentadiene–α-Naphthoquinone (VIII).—The diene (b. p. 77–80°) was prepared by the method of Fisher and Chittenden[9] in over-all yield of 2.3%. The keto alcohol resulting from the condensation of acetaldehyde with methyl ethyl ketone could not be reduced satisfactorily to the 1,3-glycol either with Adams catalyst at a low pressure or with Raney nickel in the high pressure apparatus. With a combination of the two catalysts reduction was effected at 86° and 1500 lb. (100 atm.) pressure in 75% yield, based on starting material consumed.

A solution of 10 g. of α-naphthoquinone and 6.9 g. of the diene in 20 cc. of alcohol was refluxed for three hours, and after cooling to 0° 12.3 g. (81%) of the addition product separated as fine, colorless needles, m. p. 100.2–101.4°. Recrystallization from benzene–alcohol raised the m. p. to 101–101.7°.

Anal. Calcd. for $C_{16}H_{16}O_2$: C, 79.97; H, 6.71. Found: C, 79.91; H, 6.86.

The condensation of this substance with methylmagnesium iodide or chloride was tried under various conditions but in no case could a product having the properties of a diol be isolated. In the case of the iodide a reaction occurred and two ill-defined products of lower carbon content than the starting material were encountered. One of these, amounting to nearly half the weight of starting material, formed colorless needles melting in the range 140–154° (found: C, 78.35, 78.35; H, 7.87, 7.84). With methylmagnesium chloride the only product isolated was **1,2-dimethylanthraquinone,** which was readily obtained from the addition product by air oxidation in alcohol solution to which a trace of alkali had been added. Purified by chromatographic adsorption and crystallized from benzene–hexane, the quinone melted at 157.8–158.2° (Barnett and Carlisle,[12] m. p. 156°).

Summary

1,2,10-Trimethylanthracene, desired for comparison with the carcinogenically active 10-methyl-1,2-benzanthracene, was synthesized by known methods from *vic.*-bromo-*o*-xylene and phthalic anhydride. 2,3,9,10-Tetramethylanthracene was obtained readily from the addition product of α-naphthoquinone and 2,3-dimethylbutadiene by reaction with methyl Grignard reagent, dehydration of the resulting diol, and dehydrogenation. An attempted synthesis of the 1,2,9,10-isomer by this route failed at the stage of interaction with the Grignard reagent.

CONVERSE MEMORIAL LABORATORY
CAMBRIDGE, MASSACHUSETTS RECEIVED MARCH 22, 1940

(11) Microanalysis by Herbert S. Wight.

(12) Barnett and Carlisle, *Ber.*, **64**, 535 (1931).

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

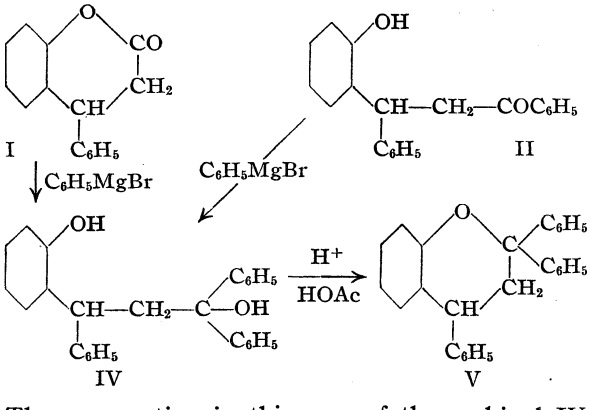
The Reaction of o-Hydroxybenzhydrylacetophenone and o-Hydroxybenzaldiacetophenone with Phenylmagnesium Bromide

BY T. A. GEISSMAN

The reactions of 4-phenyldihydrocoumarin (I) and ω-(o-hydroxybenzhydryl)-acetophenone (II) with phenylmagnesium bromide have been studied, originally in an attempt to correlate the results with the question of the mode of reaction of Grignard reagents with lactones of the dihydrocoumarin type.[1] The reaction between alkylmagnesium halides and a substance which may be either a chromanol or the corresponding hydroxyketone was first carried out by John and Schmeil.[1a] The choice of the hydroxyketone (II) used in the present study was based upon Löwenbein's[2] statement that the compound possesses neither phenolic nor ketonic properties and thus has the structure of the chromanol (III).

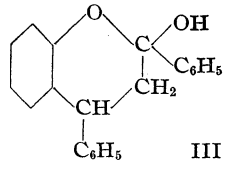
The present work has shown, however, that the properties of the compound are in agreement with its formulation as the hydroxyketone (II), a result which invalidated the original purpose of the study. The so-called chromanol is readily soluble in methanolic potassium hydroxide and forms a semicarbazone, thus showing both phenolic and ketonic characteristics.

The product of the reaction of both the dihydrocoumarin (I) and the hydroxyketone (II) was 1,1,3-triphenyl-3-(o-hydroxyphenyl)-propanol-1 (IV). The latter compound was readily dehydrated to 2,2,4-triphenylchromane (V).



The preparation in this way of the carbinol IV and chromane V constitutes, in the light of previous work[1] on the reaction between dihydrocoumarins and Grignard reagents, a proof of their structures. Consequently it became of interest to examine a report by Gomm and Hill[3] who claimed to have prepared these compounds by the reaction of phenylmagnesium bromide with o-hydroxybenzaldiacetophenone (VI). The products of this reaction have properties different from those of IV and V prepared as described above, and so the reaction of o-hydroxybenzaldiacetophenone with phenylmagnesium bromide has been reinvestigated in an attempt to elucidate the structures of the products obtained

When o-hydroxybenzaldiacetophenone is treated with phenylmagnesium bromide in boiling benzene and the reaction mixture decomposed with iced ammonium chloride, the product is an uncrystallizable oil, probably the glycol VII. This oil on treatment with a trace of sulfuric acid in acetic acid solution yields 2,2-diphenyl-4-benzhydrylidenemethylchromane (VIII). The structure of VIII was proved by its synthesis from methyl dihydrocoumarin-4-acetate (IX), the first product of the reaction between this ester and phenylmagnesium bromide being again an uncrystallizable oil, probably VII, which was converted smoothly to VIII by dehydration. Gomm and Hill obtained VIII (to which they assigned the structure of V) as the direct product of the reaction between VI and the Grignard reagent, a result which was undoubtedly due to the fact that they decomposed the reaction mixture with, and steam-distilled from, dilute acid dehydration of the glycol (VII) occurring during these operations.



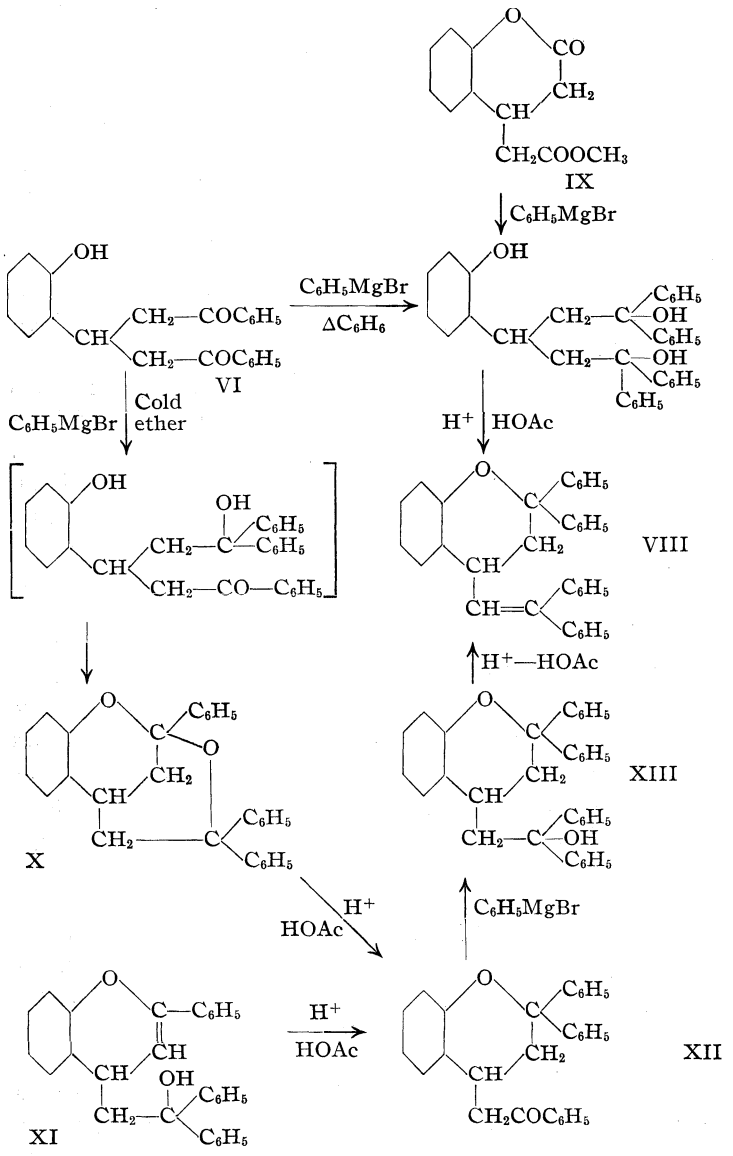
When the reaction between o-hydroxybenzaldiacetophenone and phenylmagnesium bromide was carried out in cold ether solution the product was a crystalline compound to which has been assigned the structure (X) (it is this compound to which

(1) (a) John and Schmeil, *Ber.*, **72**, 1653 (1939); (b) Smith, Ungnade and Prichard, *J. Org. Chem.*, **4**, 358 (1939); (c) Smith and Ruoff, THIS JOURNAL, **62**, 145 (1940).

(2) Löwenbein, *Ber.*, **57**, 1517 (1924).

(3) Gomm and Hill, *J. Chem. Soc.*, 1118 (1935).

Gomm and Hill assigned the structure of IV), on the basis of the following evidence. The compound does not react with carbonyl reagents in neutral or basic solution and is recovered unchanged after treatment with phenylmagnesium bromide in ether. It is isomeric with 1,1-diphenyl-2-(4-flavenyl)-ethanol-1 (XI), prepared



by the addition of phenylmagnesium bromide to 4-phenacylflavene, and upon treatment with a trace of acid in acetic acid solution both X and XI are converted to the same (isomeric) compound (XII). Structures X and XI contain groupings which are known to be unstable in acid media, and it is probable that the course of the isomerization involves attack upon these centers leading by ring-opening and subsequent closure to XII, which contains a chromane ring system and would be stable under the conditions of the reaction. The structure of XII was established by the facts that it formed a 2,4-dinitrophenylhydrazone and upon treatment with phenylmagnesium bromide was converted into a crystalline carbinol (XIII). The carbinol XIII readily underwent dehydration to yield the chromane VIII, the structure of which has been proved by its preparation as described above. The dinitrophenylhydrazone of XII can be formed directly from X or XI by treatment of these compounds with 2,4-dinitrophenylhydrazine in boiling glacial acetic acid solution.

Tricyclic structures analogous to that proposed for X have been suggested for certain chromane derivatives by Boehme and Themlitz.[4] The reactions discussed above are shown on the accompanying chart. It is probable that compound X (as the tricyclic acetal) is not produced directly, since the product obtained after careful decomposition of the reaction mixture with iced ammonium chloride is an oil which crystallizes only slowly from such solvents as ligroin or alcohol, even when seeded with crystalline material, but which rapidly deposits the compound X from glacial acetic acid solution. The direct product of the reaction is thus probably a carbinol (shown in brackets) which under the mild dehydrating action of the acetic acid is cyclized to X.

The reaction of phenylmagnesium bromide with *o*-hydroxybenzaldiacetophenone is thus seen to involve the addition of either one or two moles of the reagent to the diketone, depending upon experimental conditions, and is not a cleavage reaction as reported by Gomm and Hill.

Experimental

ω-(*o*-Hydroxybenzhydryl)-acetophenone (II).—This was prepared from *o*-hydroxybenzalacetophenone and phenyl-

(4) Boehme and Themlitz, *Arch. Pharm.*, **272**, 406 (1934).

magnesium bromide according to the directions of Löwenbein.[2] The material melted at 167–167.5° (reported, 166°). The pyrilium ferrichloride derived from it[2] melted at 167° (reported, 168°).

Semicarbazone of II.—A solution of 0.5 g. of semicarbazide hydrochloride and 1.5 g. of sodium acetate in a little water was added to a solution of 0.5 g. of the hydroxyketone (II) in 10 cc. of alcohol. The solution was heated to boiling and allowed to stand overnight. The following day water was added to cloudiness at the boiling point and the solution digested at this temperature for fifteen minutes. On cooling white prisms separated. Recrystallized from dilute alcohol the product melted at 177–178°.

Anal. Calcd. for $C_{22}H_{21}O_2N_3$: N, 11.70. Found: N, 11.57.

4-Phenyldihydrocoumarin (I).—The procedure of Liebermann and Hartmann[5] was followed. The compound was recrystallized from dilute alcohol, stout needles, m. p. 82–84° (reported, 82°).

1,1,3-Triphenyl-3-(*o*-hydroxyphenyl)-propanol-1 (IV).—(a) **From (II).**—To the Grignard reagent prepared from 6.3 g. of bromobenzene and 0.97 g. of magnesium in 40 cc. of dry ether was added 3.0 g. of the (solid) hydroxy ketone (II). The resulting solution was refluxed for thirty minutes, decomposed with iced ammonium chloride solution and the solvents removed by steam-distillation. The oily residue was extracted with ether and upon removal of the ether was obtained as a viscous oil which could not be induced to crystallize.

In a second experiment using 5.0 g. of the chromanol and equivalent amounts of the other reagents, the oil crystallized on seeding with some of the material obtained as described in (b) and yielded 4.3 g. of crystalline product after recrystallization from ligroin (b. p. 75–135°); m. p. 109–110°. Recrystallized from benzene–petroleum ether the material appeared as transparent colorless prisms containing solvent and melting indefinitely at around 85° with loss of solvent. Dried at 80° (20 mm.) or recrystallized from ligroin the compound melted at 112–113°.

(b) **From (I).**—A solution of 2.25 g. of 4-phenyldihydrocoumarin in 10 cc. of dry benzene was added to a solution of phenylmagnesium bromide prepared from 6.50 g. of bromobenzene and 1.00 g. of magnesium in 50 cc. of dry ether. The solution was refluxed for thirty minutes, decomposed with iced ammonium chloride solution and steam-distilled. The oily residue was removed with ether and after removal of the solvent was obtained as a pale yellow oil. This material could not be induced to crystallize when first obtained and 1.0 g. of it was removed for dehydration to the chromane. The remainder crystallized upon standing in ether–petroleum ether and yielded 1.5 g. of white prisms, m. p. 106–108°. Recrystallized from ligroin (b. p. 75–135°), it melted at 111–112°, showed no depression when mixed with a sample of the material obtained in (a), and caused rapid crystallization of the oil obtained in (a) when used as seed.

The compound is difficultly soluble in dilute aqueous alkali, readily soluble in methanolic potassium hydroxide, gives no color with ferric chloride and a red-orange color with concentrated sulfuric acid.

(5) Liebermann and Hartmann, *Ber.*, **24**, 2586 (1891).

Anal. Calcd. for $C_{27}H_{24}O_2$: C, 85.22; H, 6.37. Found: C, 85.20, 85.40; H, 6.54, 6.53.

2,2,4-Triphenylchromane (V).—To a hot solution of 0.50 g. of the crystalline carbinol (IV) in 5 cc. of glacial acetic acid was added two drops of concentrated sulfuric acid. Upon cooling and scratching the walls of the flask the product crystallized. There was obtained 0.47 g. of white prisms, m. p. 162–163°.

The chromane was also obtained by a similar treatment of the oily product first obtained (above, part a) as the product of the reaction between the hydroxyketone (II) and phenylmagnesium bromide. From 1.0 g. of the oily carbinol was obtained 0.9 g. of V, m. p. 161–162°, a result which indicates that the reluctance of the oil to crystallize cannot be laid to the presence of significant amounts of impurities.

The chromane gives no immediate color with concentrated sulfuric acid, but on standing a yellow color develops which gradually turns reddish. It is insoluble in methanolic potassium hydroxide and does not absorb bromine in carbon tetrachloride solution.

Anal. Calcd. for $C_{27}H_{22}O$: C, 89.45; H, 6.13. Found: C, 89.27; H, 6.16.

The Reaction between *o*-Hydroxybenzaldiacetophenone and Phenylmagnesium Bromide.—(a) In Ether: Compound (X).—A solution of phenylmagnesium bromide prepared from 57.1 g. of bromobenzene and 7.2 g. of magnesium in 150 cc. of ether was added to a well-cooled (5–10°) suspension of 35.4 g. of *o*-hydroxybenzaldiacetophenone in 150 cc. of dry ether. The initial reaction resulted in the formation of a heavy white precipitate which upon the addition of more of the reagent became semi-solid and finally formed a viscous liquid phase insoluble in the ether solution. The mixture was stirred for six hours at 5°, allowed to stand overnight and decomposed with iced ammonium chloride. After the solvents and diphenyl were removed by steam distillation, the product was isolated by taking up the residue from the steam-distillation in ether, drying the solution and evaporating the solvent. The product, a viscous oil, was dissolved in an equal volume of alcohol and allowed to stand overnight. The 3.5 g. of material which crystallized was unchanged starting material. The alcohol was removed in a stream of dry air and a further amount (3.0 g.) of starting material separated. This was removed, after dilution of the residual oil with ligroin, by filtration. The ligroin solution deposited no crystalline material, even on seeding with a sample of the expected product (obtained in a previous run). The ligroin was removed and the oil dissolved in glacial acetic acid. Crystallization began immediately and on standing a total of 10.9 g. of crystalline material separated.

Recrystallized from *n*-butanol, the product formed hard, colorless prisms, m. p. 185–186°.

Anal. Calcd. for $C_{29}H_{24}O_2$: C, 86.10; H, 6.00. Found: C, 86.39; H, 6.22.

The compound is insoluble in 10% methanolic potassium hydroxide; it instantly decolorizes bromine in chloroform solution with hydrobromic acid evolution, and reacts with bromine in acetic acid in the cold. It did not react with semicarbazide in dilute propanol solution, nor with phenylmagnesium bromide in ether solution.

The acetic acid mother liquor from the crystallization of the 185° compound was heated to boiling and several drops of sulfuric acid added. Formation of a crystalline precipitate quickly began and on cooling there was obtained 12.0 g. of compound VIII, described below (part b).

(b) **In Ether–Benzene: Compound (VIII).**—To a solution of phenylmagnesium bromide prepared from 27.5 g. of bromobenzene and 4.1 g. of magnesium in 150 cc. of ether was added a solution of 10.0 g. of *o*-hydroxybenzaldiacetophenone in 100 cc. of dry benzene. The solution was refluxed for two and one-half hours, decomposed with iced ammonium chloride solution and, after steam distillation, the product was removed with ether. Removal of the ether left 15.5 g. of a sirupy oil which could not be crystallized.

The oily material was soluble in alcoholic alkali (its solution in alcohol remained clear upon the addition of dilute alkali, but became cloudy when water was added), absorbed bromine in carbon tetrachloride solution and gave a deep red color with sulfuric acid.

When to a solution of the oily product in hot glacial acetic acid was added a trace of concentrated sulfuric acid, a crystalline precipitate formed rapidly. The material so obtained (VIII) formed soft, white needles from acetic acid, m. p. 219–220°.[6]

Anal. Calcd. for $C_{35}H_{28}O$: C, 90.48; H, 6.09. Found: C, 90.43; H, 6.24.

The compound is insoluble in 10% methanolic potassium hydroxide and is unattacked by bromine in chloroform or acetic acid solution. In contrast to its extremely difficult solubility in acetic acid, ether, alcohols and even acetic anhydride, it is readily soluble in warm benzene.

4-Phenacylflavene.—This was prepared from *o*-hydroxybenzaldiacetophenone according to the directions of Hill.[7] It was found necessary to buffer the ordinary glacial acetic acid by the addition of a small amount of sodium acetate in order to prevent the formation of large amounts of 4-phenacylideneflavene,[8] a colored impurity difficult to remove. The product formed soft, white needles, m. p. 95–96° (reported,[7] 96°).

1,1-Diphenyl-2-(4-flavenyl)-ethanol-1 (XI).—This was prepared in good yield according to the directions of Gomm and Hill.[3] The compound forms soft, white needles from *n*-butanol, m. p. 193–193.5° (reported[3] 194°).

Anal. Calcd. for $C_{29}H_{24}O_2$: C, 86.10; H, 6.00. Found: C, 86.09; H, 6.20.

The compound is insoluble in 10% methanolic potassium hydroxide and was recovered unchanged when treated with 2,4-dinitrophenylhydrazine in propyl alcohol. It decolorizes bromine in chloroform or acetic acid solution with the evolution of hydrobromic acid. A mixture of the m. p. 193° compound and compound X, m. p. 185–186°, melted at 165–170°.

4-Phenacyl-2,2-diphenylchromane (XII).—(a) **From Compound (X).**—To a solution of 1.0 g. of X, m. p. 185–186°, in 15 cc. of glacial acetic acid was added two drops of concentrated sulfuric acid. The solution was boiled for a minute, diluted slightly and cooled. The product crystallized as colorless needles weighing 0.82 g., m. p. 115–116°. Crystallized from ligroin (b. p. 75–135°) it separated as crisp white needles, m. p. 115–116°.

Anal. Calcd. for $C_{29}H_{24}O_2$: C, 86.10; H, 6.00. Found: C, 85.73; H, 6.02.

(b) **From Compound XI.**—Treatment of compound XI in the manner described in (a) resulted in the formation of the same substance, m. p. 115–116° (mixed m. p. 115–116°), as that obtained from X.

Anal. Calcd. for $C_{29}H_{24}O_2$: C, 86.10; H, 6.00. Found: C, 85.90; H, 6.04.

The compound (XII, m. p. 115–116°) is insoluble in 10% methanolic potassium hydroxide and does not react in the cold with bromine in chloroform or acetic acid; on warming with bromine in either solvent reaction occurs with evolution of hydrobromic acid.

2,4-Dinitrophenylhydrazone from X, XI, and XII.—To a solution of 0.5 g. of 2,4-dinitrophenylhydrazine in 10 cc. of glacial acetic acid was added 0.5 g. of (XII). The deep red solution was refluxed gently for five minutes; crystallization began while the solution was still boiling. On cooling there was obtained 0.66 g. of orange-red crystals which on recrystallization from chloroform–petroleum ether formed bright red-orange leaflets, m. p. 243–244° dec.

The same compound was formed when X (m. p. 185–186°) or XI (m. p. 193°) was treated with 2,4-dinitrophenylhydrazine in boiling glacial acetic acid.

Anal. Calcd. for $C_{35}H_{28}O_5N_4$: C, 71.90; H, 4.83; N, 9.50. Found: C, 71.46; H, 4.73; N, 9.51.

1,1 - Diphenyl - 2 - (2,2 - diphenyl - 4 - chromanyl)-ethanol-1 (XIII).—A solution of 2.0 g. of XII in a mixture of ether and benzene was added to an excess of phenylmagnesium bromide in ether. After one hour of refluxing the solution was decomposed with iced ammonium chloride solution and steam-distilled. The product was a viscous oil which crystallized slowly from ether–petroleum ether to form colorless prisms, m. p. 148–149°. Recrystallized from benzene–petroleum ether the compound formed colorless prisms, m. p. 149–149.5°.

Anal. Calcd. for $C_{35}H_{30}O_2$: C, 87.07; H, 6.29. Found: C, 87.06; H, 6.35.

The substance is insoluble in 10% methanolic potassium hydroxide and does not decolorize bromine in acetic acid solution.

Dehydration of XIII.—To a solution of 0.20 g. of the carbinol (XIII) in 5 cc. of warm glacial acetic acid was added a trace of concentrated sulfuric acid. Crystallization began immediately. On cooling there was obtained 0.18 g. of soft white needles of compound VIII, m. p. 219–220°.

Methyl Dihydrocoumarin-4-acetate (XII).—Dihydrocoumarin-4-acetic acid was prepared by hydrolysis of the addition product of coumarin and cyanoacetamide, according to the directions of Seshadri.[9] The acid was esterified with methanol and sulfuric acid in the usual way. The ester is a colorless, viscous oil, b. p. 208–210° (20 mm.); $n^{22}D$ 1.5369.

(6) In their experiment in which the Grignard reaction was run as just described, Gomm and Hill[3] decomposed the reaction mixture with dilute acid and obtained as the direct product a crystalline compound, m. p. 216–217°.

(7) Hill, *J. Chem. Soc.*, 1255 (1934).

(8) Feuerstein and Kostanecki, *Ber.*, **31**, 710 (1898).

(9) Seshadri, *J. Chem. Soc.*, 166 (1928).

Anal.[10] Calcd. for $C_{12}H_{12}O_4$: C, 65.42; H, 5.50. Found: C, 64.87, 65.10; H, 5.82, 5.91.

Reaction of Phenylmagnesium Bromide with Methyl Dihydrocoumarin-4-acetate.—A solution of 2.1 g. of the redistilled ester in 20 cc. of dry ether was added to an excess of phenylmagnesium bromide in ether. A vigorous reaction occurred with the formation of a white precipitate which quickly dissolved. The solution was refluxed for thirty minutes and decomposed with ice–ammonium chloride solution. The product, after steam distillation and recovery with ether, was a viscous oil which could not be induced to crystallize.

The addition of a trace of sulfuric acid to a solution of the oil in acetic acid transformed it quickly into a white crystalline material. Recrystallized from acetic anhydride this product formed soft white needles, m. p. 216–218°. Mixed with a sample of VIII, m. p. 218–219°, the melting point was 216–218°.

(10) Analysis by Dr. J. Haagen-Smit, California Institute of Technology, Pasadena, Calif.

Summary

1. It has been shown that the compounds produced by the reaction of phenylmagnesium bromide with *o*-hydroxybenzaldiacetophenone do not have the structures proposed for them by Gomm and Hill.[3]

2. The structure of one of these compounds has been established by a different method of synthesis, and a structure for the other proposed on the basis of its properties and its relationship to compounds of known structure.

LOS ANGELES, CALIFORNIA RECEIVED JANUARY 26, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF NOTRE DAME]

Chlorides and Hydrochlorides from 1-Hexyne[1]

BY G. F. HENNION AND CHARLES E. WELSH

Introduction

When 1-hexyne is chlorinated in various oxygen-containing media a complex mixture of products results, some of which contain oxygen as well as chlorine.[2] Various chlorine derivatives of 1-hexyne are thus obtained together and may be separated by fractional distillation. It was thought advisable to prepare these separately, by chlorination in inert solvents, in order to obtain pure substances for the determination of reliable physical data. It was desired also to prepare the mono and dihydrochlorides of 1-hexyne for comparison with the chlorides. During this investigation certain observations were made which may be of interest, and hence are recorded here.

Chlorination of 1-hexyne in either carbon tetrachloride or *n*-heptane containing a small amount of antimony pentachloride gave a mixture of *trans*-1,2-dichloro-1-hexene and 1,1,2,2-tetrachlorohexane only. When the antimony pentachloride was omitted the product was much less tractable and boiled over a wide range.

Direct addition of hydrogen chloride to 1-hexyne, with or without a solvent, was unsuccessful in the absence of a catalyst. Numerous metal chlorides were studied for catalytic activity. Of these bismuth chloride appeared to be best and with its use hydrogen chloride added readily to 1-hexyne to yield both 2-chloro-1-hexene and 2,2-dichlorohexane. By heating with potassium hydroxide in propyl alcohol the latter product could be reverted to the former.

Chlorination of 2-chloro-1-hexene in carbon tetrachloride containing antimony pentachloride was of particular interest because the reaction did not lead to 1,2,2-trichlorohexane, as anticipated. Instead a mixture of *cis*-1,2-dichloro-1-hexene and 1,1,2,2-tetrachlorohexane was obtained. Attempts to prepare 1,2,2-trichlorohexane by the addition of hydrogen chloride to both *cis*- and *trans*-1,2-dichloro-1-hexene likewise were unsuccessful. No reaction was observed in either case, even when bismuth chloride was present.

Physical data for the compounds prepared are given in Table I.

Experimental

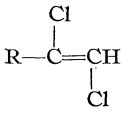
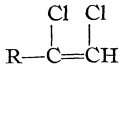
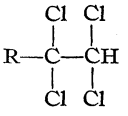
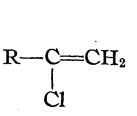
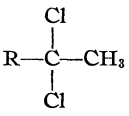
Chlorination of 1-Hexyne.—A solution of 41 g. (0.5 mole) of 1-hexyne in 200 ml. of carbon tetrachloride was placed in a one liter, three-necked flask equipped with an efficient stirrer, a reflux condenser, and a chlorine inlet tube. To the solution was added slowly, with stirring, 50 ml. of carbon tetrachloride containing 1.5 ml. of antimony pentachloride. Chlorine was then passed over the solution in a fairly rapid stream, at a temperature of 45 ± 5°, until 35.5 g. (0.5 mole) was absorbed. The solution was washed with water, dilute sodium carbonate solution, again with water, dried over calcium chloride, and fractionally distilled: yield, 15 g. (19.6%) of *trans*-1,2-dichloro-1-hexene and 39.3 g. (30.6%) of 1,1,2,2-tetrachlorohexane.

(1) Paper XXXVIII on the chemistry of substituted acetylenes and their derivatives; previous paper, THIS JOURNAL, **62**, 653 (1940).

(2) Norris, Vogt and Hennion, *ibid.*, **61**, 1460 (1939); **62**, 449 (1940).

TABLE I

PHYSICAL PROPERTIES OF CHLORIDES AND HYDROCHLORIDES OF 1-HEXYNE

Compound						
Boiling point	°C.	63–65	88	99–101	113	68
	Mm.	32	30	14	740	49
d^{25}_4		1.1167	1.0812	1.3096	0.8886	1.0150
$n^{25}D$		1.4576	1.4631	1.4888	1.4278	1.4353
Mol. wt.	Calcd.	153	153	224	119	155
	Obsd.	152	156	226	118	156
MR	Calcd.	39.2	39.2	49.4	34.3	39.8
	Obsd.	39.2	39.0	49.2	34.3	39.8
Cl, %	Calcd.	46.4	46.4	63.4	29.9	45.8
	Obsd.	46.1	46.1	63.6	29.4	46.2

Addition of Hydrogen Chloride to 1-Hexyne.—A solution of 82 g. (1.0 mole) of 1-hexyne in 350 ml. of benzene was placed in a one-liter, three-necked flask equipped with an efficient stirrer reflux condenser, and a hydrogen chloride inlet tube. To the solution was added 3 g. of bismuth chloride. Dry hydrogen chloride gas was then bubbled beneath the surface of the liquid, at a temperature of 80–85°, until no more was absorbed. The increase in weight during the addition of hydrogen chloride was 37 g. The solution was then washed twice with water, with dilute sodium carbonate solution, again with water, dried over calcium chloride, and fractionally distilled: yield, 24 g. (20%) of 2-chloro-1-hexene and 62 g. (40%) of 2,2-dichlorohexane.

Preparation of 2-Chloro-1-hexene by Desaturation.—A solution of 78 g. (0.5 mole) of 2,2-dichlorohexane in 200 ml. of *n*-propyl alcohol was placed in a 500-ml. three-necked flask equipped with an efficient stirrer, and a reflux condenser. The solution was heated to 95° and a slight excess of solid potassium hydroxide added. After heating for five hours the reflux condenser was replaced with a short Vigreux column and the contents of the flask distilled to dryness. The distillate was washed three times with water, the organic layer separated and dried over anhydrous magnesium sulfate: yield, 35 g. (60.5%) of 2-chloro-1-hexene.

Addition of Chlorine to 2-Chloro-1-hexene.—The same procedure was followed as in the chlorination of 1-hexyne, except that the temperature was maintained at 35–40°: yield, 20.3 g. (26.7%) of *cis*-1,2-dichloro-1-hexene and 28.5 g. (25.4%) of 1,1,2,2-tetrachlorohexane.

Summary

Chlorination of 1-hexyne in inert solvents in the presence of antimony pentachloride gives *trans*-1,2-dichloro-1-hexene and 1,1,2,2-tetrachlorohexane as the sole products.

Bismuth chloride is an effective catalyst for the addition of hydrogen chloride to 1-hexyne.

The reaction of chlorine with 2-chloro-1-hexene in the presence of antimony pentachloride leads to *cis*-1,2-dichloro-1-hexene and 1,1,2,2-tetrachlorohexane.

Hydrogen chloride could not be added to either *cis*- or *trans*-1,2-dichloro-1-hexene.

NOTRE DAME, INDIANA RECEIVED MARCH 15, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF NOTRE DAME]

Chlorination of the Acetylenic Alcohols Derived from Acetone[1]

BY G. F. HENNION AND G. M. WOLF

Introduction

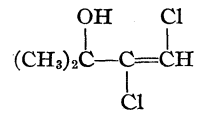
In general, chlorination of acetylenes in oxygen-containing solvents gives mixtures of chlorinated compounds.[2] Continuing these studies the action of chlorine on two acetylenic alcohols has been investigated. Dimethylethynylcarbinol (I) and 2,5-dimethyl-3-hexyne-2,5-diol (II) were selected for this work because they are easily obtainable in large quantity.[3] Carbon tetrachloride, methanol, and water were used separately as solvents. Methanol and water function also as reagents in the chlorination reactions, thus affording products not obtainable when carbon tetrachloride is used.

Chlorine added directly to (I) in carbon tetra-

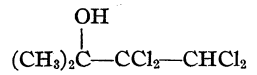
(1) Paper XXXIX on substituted acetylenes and their addition products; previous paper, THIS JOURNAL, **62**, 1367 (1940). Also paper No. 6 on halogenation in reactive solvents; *cf.* THIS JOURNAL, **62**, 449 (1940).

(2) Hennion, *et al.*, *ibid.*, **60**, 1711 (1938); **61**, 1458, 1460 (1939); **62**, 449 (1940).

(3) Froning and Hennion, *ibid.*, **62**, 653 (1940).

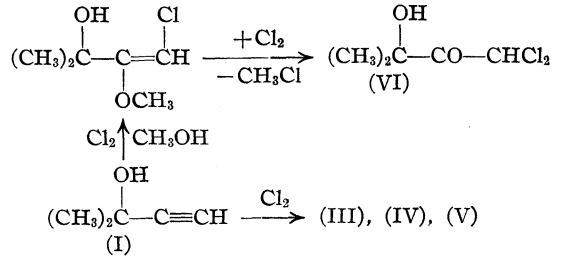


(III)



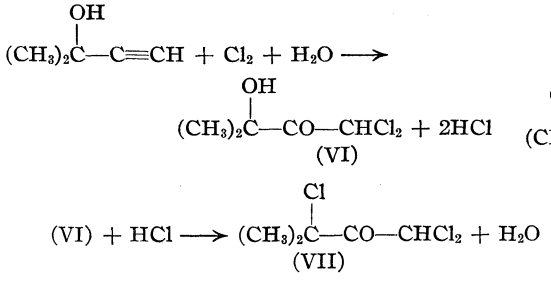
(IV)

chloride to yield only *trans*-1,2-dichloro-3-methyl-1-butene-3-ol (III) and 1,1,-2,2-tetrachloro-3-methyl-3-butanol (IV). A methanol solution of (I) reacted at 25–30° to give (III), (IV), *cis*-1,2-dichloro-3-methyl-1-butene-3-ol (V) and 1,1-dichloro-3-methyl-3-hydroxy-2-butanone (VI). These products may be explained according to the following mechanism, based on previous work.[2]

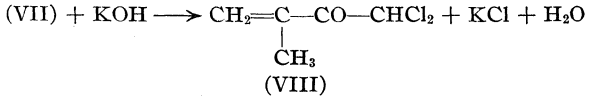


When the reaction in methanol was carried out at 60–65°, (V) was eliminated and the yield of (IV) was increased.

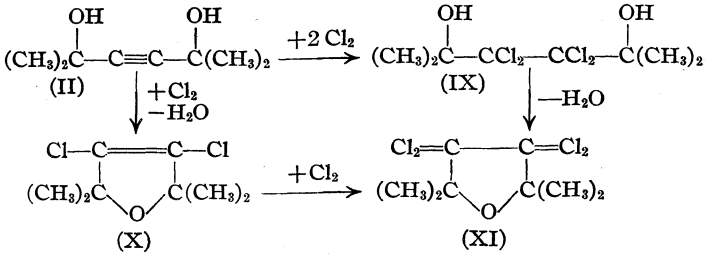
Chlorination of (I) in aqueous solution gave (V) and considerable quantities of 1,1,3-trichloro-3-methyl-2-butanone (VII). No doubt (VII) was formed by reaction of hydrogen chloride with the tertiary hydroxyl group of (VI).



Attempts to revert (VII) to (VI) by treatment with potassium hydroxide resulted in desaturation and gave 1,1-dichloro-3-methyl-3-butene-2-one (VIII).

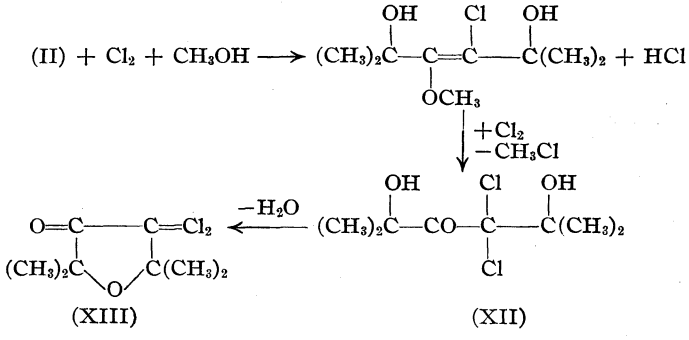


Chlorination of the acetylenic glycol (II) invariably was accompanied by considerable cyclodehydration and thus gave rise to furan derivatives as well as direct addition products. In carbon tetrachloride solution (II) gave (IX), (X) and (XI).



These results are in accord with those of Kruglov,[4] who obtained a 30% yield of 2,5-dimethyl-3,4-dibromo-3-hexenediol and nearly a 70% yield of 2,2,5,5-tetramethyl-3,4-dibromodihydrofuran by the action of bromine on a chloroform solution of (II).

Chlorination of (II) in methanol solution also gave (XI). In addition small amounts of 2,5-dimethyl-2,5-dihydroxy-3,3-dichloro-4-hexanone (XII) were obtained as well as considerable quantities of 2,2,5,5-tetramethyl-3,3-dichlorotetrahydro-4-furanone (XIII). There was evidence also for small amounts of a methoxyl-containing product, b. p. 47–49° at 6 mm., not identified for lack of sufficient material.



Aqueous solutions of (II) absorbed chlorine readily and gave preponderantly (XIII) and low yields of its precursor (XII).

Yield data for the various experiments are given in Tables I and II. Physical constants and analytical data are given in Table III. Parachor values were determined to establish structures for the products. Practically all of the compounds enumerated are unstable and darken upon standing. The dichloroketones are

(4) Kruglov, *J. Gen. Chem.* (U. S. S. R.), **6**, 925 (1936); *C. A.*, **31**, 682 (1937).

TABLE I

CHLORINATION OF ONE-MOLE LOTS OF DIMETHYLETHYNYLCARBINOL IN 500 ML. OF SOLVENT AT 25–30°

Solvent	Cl_2, g. absorbed	Yields of products, %[a] (III)	(IV)	(V)	(VI)	(VII)
CCl_4	148	22.0 (7.7)[a]	44.6 (38.5)	.....	.....	.....
CH_3OH	160	20.6 (7.2)	35.6 (32.1)	6.9 (3.1)	10.5 (4.9)	.....
H_2O	134	.....	.....	15.5 (8.0)	.....	30.0 (21.2)

[a] Values in parentheses are for purified compounds. Other values are for crude samples obtained on first distillation.

TABLE II

CHLORINATION OF HALF-MOLE LOTS OF 2,5-DIMETHYL-3-HEXYNE-2,5-DIOL IN 500 ML. OF SOLVENT AT 60–65°

Solvent	Cl_2, g. absorbed	Yields of products, %[a] (IX)	(X)	(XI)	(XII)	(XIII)
CCl_4	135	16.9 (4.6)[a]	20.5 (8.6)	45.8 (26.8)	.....	.....
CH_3OH	123	.....	.....	46.6 (30.1)	1.7 (1.5)	40.5 (14.6)
H_2O	106	.....	.....	.....	3.5 (3.2)	80.5 (57.5)

[a] Values in parentheses are for purified compounds. Other values are for crude samples obtained on first distillation.

TABLE III

ANALYTICAL AND PHYSICAL DATA

Compd.	B. p., °C. at 6 mm.	$n^{20}D$	d^{20}	Mol. wt.[a] Calcd.	Obsd.	% Cl Calcd.	Obsd.	MR Calcd.	Obsd.	[P][b] Calcd.	Obsd.
(III)	64–66	1.4778	1.213	155.0	156	45.74	45.4	36.08	36.22	312.6	304.6
(IV)	95–97	1.5086	1.488	225.9	223	62.78	62.8	46.28	45.24	398.0	389.6
(V)	76–78	1.4822	1.268	155.0	159	45.74	46.35	36.08	34.87	312.6	303.4
(VI)	58–60	1.4825	1.339	171.0	169	41.46	41.68	36.56	36.45	332.6	330.7
(VII)	61–63	1.4765	1.345	189.5	184	56.13	56.1	39.90	39.77	349.8	347.6
(VIII)	64–66	1.4752	1.261	153.0	154	46.34	46.4	34.57	34.18		
(IX)	82–84	1.5006	1.346	284.0	279	49.93	49.6	61.66	62.06	535.0	531.3
(X)	46–48	1.4638	1.125	195.1	190	36.35	37.7	47.85	47.80	403.9	404.8
(XI)	96–98	1.5110	1.354	266.0	261	53.32	53.8	58.05	58.85	489.3	481.4
(XII)	M. p. 99°			229.1	234	30.95	31.1				
(XIII)	84–86	1.4880	1.243	211.1	213	33.60	33.9	48.33	48.85	423.9	419.2

[a] Cryoscopic method in benzene. [b] Calculated from values of Sugden.

the least stable and turn almost black after several weeks.

Experimental

Reagents.—Dimethylethynylcarbinol (I) and 2,5-dimethyl-3-hexyne-2,5-diol (II) were prepared as previously described.[2] Further quantities of (II) were obtained by the method of Macullum.[5]

Chlorination of (I) in Methanol.—Into a 1-liter 3-necked flask equipped with a mechanical stirrer, reflux condenser and a gas inlet tube were introduced 500 ml. of anhydrous methanol and 84 g. (1 mole) of (I). A moderately rapid stream of chlorine was introduced below the surface of the agitated solution. The temperature was held at 25–30°, by occasional cooling, for seven hours, after which time the solution acquired a greenish-yellow color. Methanol was removed by distillation through a helix-packed total-condensation, partial take-off column. The residue separated into two layers. The upper layer was an aqueous solution of hydrogen chloride. The lower layer (165 g.) was fractionally distilled, *in vacuo*, and successive small fractions collected in 15-ml. vials. Fractions were recombined on the basis of boiling range and refractive index and refractionated.

Chlorination of (I) in Water.—After chlorination as described above the reaction mixture separated into two layers. The organic material was removed, washed with water, twice with 10% sodium bicarbonate solution, again with water, and dried over calcium chloride. Fractional distillation at 6 mm. gave (V) and (VII).

Haloform Reaction with (VI).—Ten grams of (VI) and 20 g. of bleaching powder were mixed with 100 ml. of distilled water, refluxed for thirty minutes and steam distilled. The distillate contained 3 g. of chloroform, b. p. 59–60°; d^{20} 1.485; $n^{20}D$ 1.4443.

Desaturation of (VII) to (VIII).—To 14 g. of (VII) in 30 ml. of methanol was added 10 ml. of 50% potassium hydroxide solution. There was an immediate exothermic reaction. The potassium chloride was removed by filtration and methanol distilled from the filtrate. The residue was dried and fractionated to obtain (VIII). The yield was 60% of the theoretical.

Chlorination of (II) in Methanol.—Seventy-one grams (0.5 mole) of (II) was dissolved in 500 ml. of methanol and chlorinated as described above. Temperature was held at 60–65°. After the chlorination reaction, methanol was distilled directly from the product. The organic layer was removed from the residue and fractionally distilled at 6 mm. Fractions boiling between 85–95° (6 mm.) deposited fine white crystals on standing. These fractions were filtered and the solid crystallized from petroleum ether to yield (XII), m. p. 99°. In addition (XI) and (XIII) were obtained as shown in Table II.

Other Chlorinations.—The above procedures were followed for the six chlorination reactions studied. Since

(5) Macullum, U. S. Patent 2,162,676 (1939).

mixtures of products were obtained in all cases, it was necessary to fractionate repeatedly so as to obtain compounds sufficiently pure for analysis. All distillations were carried out at 6 mm., through suitable fractionating columns, and small fractions collected in 15-ml. vials. The yields of crude products were estimated from the first distillation. Ordinarily 10 to 20 fractions were collected. These were recombined for subsequent distillations on the basis of boiling range, refractive index, and chlorine content.

Summary

Dimethylethynylcarbinol and 2,5-dimethyl-3-hexyne-2,5-diol have been chlorinated, each in three solvents: carbon tetrachloride, methanol, and water. The products have been identified and characterized.

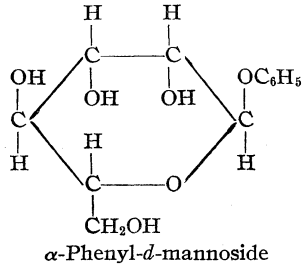
NOTRE DAME, INDIANA RECEIVED MARCH 2, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY, LEIPZIG, GERMANY]

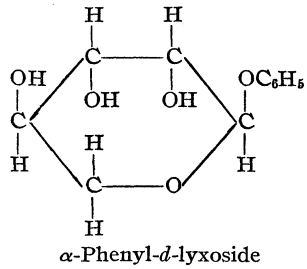
The Action of Almond Emulsin on α-Phenyl-d-lyxoside

BY WILLIAM WARD PIGMAN[1]

The occurrence in almond emulsin of enzymes which hydrolyze glycosides is well known. However, with very few exceptions, the previous work with these enzymes has been confined to glycosides of naturally occurring sugars. In an earlier paper,[2] the results of a study of the action of almond emulsin on a number of methyl glycosides of synthetic sugars were reported and in no instance was an hydrolysis observed which was larger than the experimental error. In general, the phenyl glycosides are much better materials for such studies since, when they are hydrolyzable, the rate of hydrolysis is much greater than that of the corresponding methyl glycosides. Also, a very sensitive method for the measurement of the degree of hydrolysis of the phenyl glycosides is available.[3] The negative results reported for α-methyl-d-lyxoside in the previous work[2] were somewhat surprising since α-phenyl-d-mannoside is known to be hydrolyzed by the enzymes in almond emulsin and as illustrated in the following formulas the pyranose rings of the phenyl-d-mannosides and lyxosides are identical except for the groups attached to the fifth carbon atom.



α-Phenyl-d-mannoside



α-Phenyl-d-lyxoside

In order to settle this question definitely α-phenyl-d-lyxoside was prepared according to the general method of Helferich and Schmitz-Hillebrecht.[4] The new substance which most probably has a pyranose structure and which has the expected rotation for the alpha isomer was found to be hydrolyzed by almond emulsin (the "Rohferment" of Helferich[5]). The rates of hydrolysis of β-phenyl-d-glucoside and α-phenyl-d-mannoside also were determined under the same conditions. The results are summarized in Table I.

TABLE I

Glycoside	$k \times 10^3$	Enzyme efficiency (Wertigkeit)
α-Phenyl-d-lyxoside	0.088[a]	9.4×10^{-4}
α-Phenyl-d-mannoside	3.5	0.15[b]
β-Phenyl-d-glucoside	7.3	.31[b]

[a] The enzyme concentration was four times as great for the lyxoside experiments as for the other experiments.

[b] The substrate concentrations were more dilute than those normally used but the values found are substantially the same as those reported by Helferich and Winkler.[6]

The value of 9.4×10^{-4} found for the α-phenyl-d-lyxoside is the smallest value reported for a hydrolyzable phenyl glycoside and compares with a value of 20×10^{-4} for β-phenyl-d-xyloside and a value of 3000×10^{-4} for β-phenyl-d-glucoside.

(1) This work was made possible by a grant from the Lalor Foundation of Wilmington, Del. The present address of the author is National Bureau of Standards, Washington, D. C.

(2) B. Helferich, W. W. Pigman and H. S. Isbell, *Z. physiol. Chem.*, **261**, 55 (1939).

(3) B. Helferich, H. Appel and R. Gootz, *ibid.*, **215**, 282 (1933).

(4) B. Helferich and E. Schmitz-Hillebrecht, *Ber.*, **66**, 378 (1933).

(5) B. Helferich, S. Winkler, R. Gootz, O. Peters and E. Günther, *Z. physiol. Chem.*, **208**, 91 (1932).

(6) B. Helferich and S. Winkler, *ibid.*, **209**, 269 (1932).

Almond emulsin contains a number of enzymes and it was considered important to determine which of these is responsible for the hydrolysis of the α-phenyl-*d*-lyxoside. The similarity of the pyranose rings of mannose and lyxose made it seem probable that the enzyme in question was α-mannosidase. This was easily tested since α-mannosidase is more stable to heating than the other important enzymes found in almond emulsin.[7] Therefore, a solution of emulsin was heated and its action on α-phenyl-*d*-lyxoside, α-phenyl-*d*-mannoside, and β-phenyl-*d*-glucoside determined. The results are summarized in Table II. As seen

TABLE II

Glycoside	Enzyme	$k \times 10^3$	$\frac{k(\text{heated})}{k(\text{unheated})}$
α-Phenyl-*d*-lyxoside	Heated	0.071	0.81
α-Phenyl-*d*-lyxoside	Unheated	0.088	
α-Phenyl-*d*-mannoside	Heated	3.1	.89
α-Phenyl-*d*-mannoside	Unheated	3.5	
β-Phenyl-*d*-glucoside	Heated	3.9	.53
β-Phenyl-*d*-glucoside	Unheated	7.3	

from the table, the enzyme responsible for the hydrolysis of the α-phenyl-*d*-lyxoside is quite resistant to heat and is, therefore, most probably α-mannosidase.

The action of almond emulsin on the phenyl-*d*-xylosides and *l*-arabinosides has been studied previously.[8] The β-phenyl-*d*-glucoside, which except for a group substituted on the fifth carbon atom has the same pyranose ring as β-phenyl-*d*-xyloside, is hydrolyzed 126 to 165 times as fast as the xyloside. The enzyme responsible for the hydrolysis of the *d*-xylosides is most probably β-glucosidase or a special β-*d*-xylosidase. The presence of a special *d*-xylosidase, *i. e.*, an enzyme cleaving *only* *d*-xylosides, in a natural enzyme mixture would not be unexpected since the sugar *d*-xylose is a constituent of natural products. However, the *d*-lyxosides are derived from a sugar which is not found in naturally occurring materials and therefore the existence of a special *d*-lyxosidase seems improbable. The relative rates of hydrolysis of α-phenyl-*d*-mannoside and lyxoside (160:1) are approximately the same as those for β-phenyl-*d*-glucoside and xyloside (125–165:1). This approximate agreement of the relative rates when considered with the reasons given for ascribing the hydrolysis of α-phenyl-*d*-lyxoside to α-mannosidase, indicates that the postulation of a special *d*-xylosidase is not necessary and that the *d*-xylosides are hydrolyzed by β-glucosidase. On the other hand, β-phenyl-*d*-galactoside, which in the configuration of its pyranose ring closely resembles phenyl-*l*-arabinoside,[9] is hydrolyzed only 2.2 times more rapidly than the arabinoside. This small difference may be due to the presence of a special arabinosidase in the emulsin or to a closer configurational relationship between the galactosides and arabinosides than that between the glucosides and xylosides or the mannosides and lyxosides.

In the heptose series of sugars, there are found synthetic sugars with ring configurations similar to the naturally occuring hexose sugars. From the results reported in this paper, it is possible to indicate which of the glycosides of these sugars should be hydrolyzed by the enzymes of almond emulsin. It seems probable that the heptosides which have ring configurations similar to hydrolyzable hexosides also should be hydrolyzed. Thus, the β-*l*-β-galaheptosides (*d*-glucose ring) the α-*l*-α-galaheptosides (*d*-mannose ring) and the β-*d*-α-mannoheptosides (*d*-galactose ring) should be cleaved by β-glucosidase, α-mannosidase and β-galactosidase, respectively. In all of these cases, however, it is to be expected that the heptosides will be hydrolyzed at a slower rate than the corresponding hexosides since it is known that an increase in the size of the atom or group attached to the fifth carbon atom decreases the rate of hydrolysis.[10] Experiments to verify these predictions are now in progress in the laboratories of the National Bureau of Standards.

The prediction given above, as to the action to be expected of the enzymes of almond emulsin on the synthetic heptosides, may be extended to describe the specificity to be anticipated for the enzymes of this general type. In general it seems most probable in light of the existing information *that special enzymes are required to split each of sixteen fundamental hexose types,*[11] *(eight "d" and eight "l" isomeric aldohexopyranosides) as well as each of the alpha-beta isomers.* It is anticipated, however, that *naturally occurring enzymes are only such which will hydrolyze glycosides with pyranose rings identical (except for groups substituted on the*

(7) B. Helferich and U. Lampert, *Ber.*, **67**, 1667 (1934); B. Helferich, H. Heyne and R. Gootz, *Z. physiol. Chem.*, **214**, 139 (1933).

(8) B. Helferich and U. Lampert, *Ber.*, **68**, 1266 (1935); **67**, 1667 (1934); B. Helferich, E. Günther and W. Pigman, *ibid.*, **72**, 1953 (1939).

(9) This compound would be called "β" by Isbell and "α" by Hudson.

(10) B. Helferich, S. Grünler and A. Gnüchtel, *Z. physiol. Chem.*, **248**, 85 (1937).

(11) H. S. Isbell and W. Pigman, *J. Research Bur. Standards*, **18**, 141 (1937); H. S. Isbell, *ibid.*, **18**, 505 (1937).

fifth carbon atom) with those of naturally occurring glycosides. Enzymes hydrolyzing furanosides have been omitted from this classification since only one of this type, fructofuranosidase, is known. Disaccharides apparently fit into this scheme when considered as glycosides[12] although there is some objection to this.[13] According to this generalization, it may be expected that enzymes which split hexosides also will cause a cleavage of the pentosides, heptosides and higher homologs which have similar ring configurations. It seems probable that special pentosidases may exist which hydrolyze particular pentosides but the action of which on the hexosides is very weak. The generalizations here outlined are extensions of those proposed by Weidenhagen[12] and by Lettré.[14] Previous work, principally by Helferich and his coworkers,[15] also makes it possible to generalize as to the effect of structural changes of the substrate on the action of the enzyme. Thus it can be said that the substitution of the hydroxyls attached to carbons 2, 3, and 4 of "hydrolyzable" glycosides by other groups causes the substituted glycoside to be unhydrolyzable. Changes in the groups attached to carbons 1 and 5 cause only a change in the rate of hydrolysis. As shown above, configurational changes of the carbons forming the pyranose ring produce new hexose types each of which requires a special enzyme. It is possible that hexose types differing in configuration only at carbon 4 may be hydrolyzed by the same enzyme but as yet this problem is not settled since there is some doubt as to whether β-glucosidase and β-galactosidase are identical.

Experimental

A. Preparation of α-Phenyl-*d*-lyxoside.—A mixture of 7.4 g. of *d*-lyxose tetraacetate ($[\alpha]^{20}D$ +26.0, $CHCl_3$) and 9.5 g. of phenol was heated on a water-bath until melting occurred and after 2.5 g. of freshly fused zinc chloride had been added, the heating was continued for fifteen minutes. After the mixture had cooled, 50 cc. of benzene and 100 cc. of water were added and the sirupy phase was brought into solution. The layers were separated and the benzene solution was washed several times with water, then several times with *N* sodium hydroxide solution and again with water. The benzene was removed by vacuum distillation and the residue dried by dissolving it in absolute alcohol and then evaporating the solvent *in vacuo*. The residue was dissolved in 35 cc. of absolute methyl alcohol, 2 cc. of 0.1 *N* barium methylate was added and the solution was refluxed for ten minutes. When the solution had cooled, crystallization occurred, yield, 1.6 g. An additional 1.2 g. was obtained by evaporating the mother liquors. The material was recrystallized from a boiling mixture of equal amounts of alcohol and water. The new substance, after three crystallizations, melted at 178–181°. In aqueous solution, the phenyl lyxoside had a rotation of $[\alpha]^{20}D$ 123 (*c*, 0.6; 0.0307 g. substance; 5 cc. of solution; 2 dm.). The solubility in water at 20° is approximately 0.5 g. per 100 cc.

Anal. Calcd. for $C_{11}H_{14}O_5$: C, 58.40; H, 6.24. Found: C, 58.54; H, 6.31.

B. Action of Almond Emulsin on α-Phenyl-*d*-lyxoside

1. Preparation of Enzyme Solution.—Two and one-half grams of almond emulsin ("Rohferment" of Helferich[5]) was rubbed up in a mortar with 100 cc. of water, and after standing for two hours at 0° the solution was centrifuged until clear. Ten cc. of the solution when dried to constant weight in a vacuum desiccator over calcium chloride yielded a residue of 0.1886 g. The beta-glucoside-value (β-Gl.-V. or β-Gl.-W.[16]) of the solution was 0.85.

2. Method of Making Measurements.[3]—To 5 cc. of a solution of 0.0423 g. of α-phenyl-*d*-lyxoside in approx. 0.1 *N* acetate buffer[17] (*p*H 5.0 at 18°) was added 2.5 cc. of the enzyme solution. The reacting solution after several drops of toluene had been added was kept a measured time in a thermostat set at 30.0°. The reaction was then stopped by adding the solution to a mixture of 2.5% potassium carbonate solution and 50 cc. of 0.1 *N* iodine–potassium iodide solution. After fifteen minutes of standing the solution was acidified by the addition of 30 cc. of 2 *N* sulfuric acid solution and the excess iodine determined by titration with 0.1 *N* sodium thiosulfate solution.

Blank experiments also were made in a similar manner, in one experiment by replacing the substrate solution with water and in a second experiment by replacing the enzyme solution with water. These solutions were kept at 30° for 3780 minutes. The experimental results and calculations are given in Table III.

TABLE III

ACTION OF ALMOND EMULSIN ON α-PHENYL-*d*-LYXOSIDE

Time, min.	0.1 *N* I_2 used, cc. Total	Corrected[a]	% Hydrolysis	$k^b \times 10^6$	E. E.[c] $\times 10^4$
3780	9.74	8.04	53.7	88.5	9.4
5280	11.50	9.80	65.5	87.5	9.3
		(14.96)[d]	Average	88.0	9.4
5280[e]	10.20	8.65	57.8	71.0	

[a] The enzyme solution alone required 1.70 cc. of 0.1 *N* iodine solution. The heated solution used 1.55 cc. [b] Expressed in Briggs logarithms. [c] E. E. (enzyme efficiency or "wertigkeit") is calculated from:

$$\text{E. E.} = \text{Log}\frac{100}{100 - \%\text{ hydrolysis}}\frac{1}{tg\ (\log 2)} = \frac{k}{g(\log 2)}$$

where "*t*" is the time in minutes and "*g*" the weight of the enzyme in 50 cc. of the reaction solution. [d] Calculated value. [e] Heat treated emulsin used.

(12) R. Weidenhagen, *Ergebn. Enzymforsch.*, **1**, 168 (1932).

(13) J. Leibowitz and S. Hestrin, *Science*, **143**, 333 (1939); **141**, 552 (1938).

(14) H. Lettré, *Angew. Chem.*, **50**, 581 (1937).

(15) B. Helferich, *Ergebn. Enzymforsch.*, **7**, 83 (1938).

(16) R. Weidenhagen, *Z. Ver. deut. Zucker-ind.*, **79**, 591 (1929).

(17) The solutions were supersaturated but did not crystallize while the experiments were in progress. Since the solubility of the substrate is quite low, a lower concentration than usual was used.

C. Comparison of Rate of Splitting of the Phenyl Glycosides of Lyxose, Mannose and Glucose

1. Preparation of Enzyme Solutions.—Two solutions were used for this work. The one, called "unheated," was the same as that used in the above work. The second, called "heated," was prepared by heating the first solution in a soft glass bottle for thirty-six hours at 50° and then centrifuging. Some evaporation occurred during this process. The dry residue determined in the same manner as for the "unheated" solution was 0.1765 g. in 10 cc.

2. Preparation of Substrate Solutions.—Equivalent solutions were prepared by dissolving the following amounts in 25 cc. of 0.1 *N* acetate buffer (*p*H 5.0): 0.240 g. α-phenyl-*d*-mannoside, 0.273 g. β-phenyl-*d*-glucoside-$2H_2O$ and 0.212 g. α-phenyl-*d*-lyxoside.

3. Method of Making Measurements.—To 1 cc. of the enzyme solutions, diluted 1:4 for the mannoside and glucoside experiments, there was added 2 cc. of the substrate solution and after the reaction was allowed to take place at 30° for the required time, it was stopped by the addition of 20 mg. of potassium carbonate. The optical rotation (D line of sodium) was then measured in 2-dm. tubes at 20° and the degree of hydrolysis calculated from the observed value and the known specific rotations of the unhydrolyzed glycosides and the corresponding sugars. The results are given in Table IV. The measurements on the lyxoside were carried out as described for the hydrolysis experiments reported in Table III and are given in that table.

TABLE IV

Enzyme solution	Time, min.	α_t	% Hydrolysis	$k \times 10^3$
β-Phenyl-*d*-glucoside, $\alpha_0 = -0.94$; $\alpha_\infty = +0.48$				
Heated	30.5	−0.60	23.9	3.90
Heated	80.0	− .22	50.7	3.84
Unheated	33.4	− .33	43.0	7.30
α-Phenyl-*d*-mannoside, $\alpha_0 = 1.39$; $\alpha_\infty = 0.12$				
Heated	33.0	1.10	22.8	3.41
Heated	79.8	0.87	40.9	2.87
Unheated	78.7	.79	47.2	3.53

Acknowledgment.—The writer wishes to express his appreciation of the coöperation, assistance and advice given by Professor B. F. Helferich during the progress of this investigation. The assistance given by the Lalor Foundation of Wilmington, Del., is also gratefully acknowledged.

Summary

The preparation of α-phenyl-*d*-lyxoside is reported. This substance is hydrolyzed by almond emulsin. The rate is the slowest reported for a hydrolyzable phenyl glycoside. The enzyme responsible for the hydrolysis is shown to be α-mannosidase. A prediction is made of the specificity to be expected of the enzymes found in almond emulsin and of other similar enzymes.

RECEIVED JANUARY 23, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

A Laccase from the Wild Mushroom, *Russula Foetens*

BY DONALD C. GREGG[1] AND WILBUR H. MILLER

Much of the early information regarding the enzyme, laccase, resulted from the researches of Bertrand and his students.[1a] Bertrand reported that laccase, the enzyme responsible for the blackening of lac tree juices, could be distinguished from tyrosinase by its ability to catalyze the oxidation of polyphenols such as hydroquinone, pyrogallol and guaiacol. In recent years, the enzymatic oxidation of these substrates, and in addition *p*-phenylenediamine, has become a criterion of laccase activity.[2–5] Most of this work has been concerned with an enzyme prepared from lac tree juices. In 1939, Graubard[5] reported limited studies on an enzyme that he obtained from the wild mushroom, *Russula foetens*. This enzyme was called laccase because of its ability to catalyze the aerobic oxidation of hydroquinone and *p*-phenylenediamine. In view of the present limited knowledge regarding the action of the plant oxidases, a more extensive study on the laccase from *Russula foetens* seemed desirable.

The enzyme preparations were obtained by the general method used in these laboratories for the preparation of oxidases from mushrooms. In a typical preparation, 100 g. of dried mushroom powder was suspended in 500 cc. of water in a refrigerator for seventy-two hours. To the resulting crude extract, solid ammonium sulfate was added to make the solution 0.5 saturated. The dark colored, gummy precipitate was triturated with a small quantity of disodium phosphate and dissolved in water. For each volume of solution, two volumes of acetone were added. At room temperature, the acetone not only precipitates the

(1) Geo. W. Ellis Fellow, 1939–1940.
(1a) G. Bertrand, *Compt. rend.*, **118**, 1215 (1894).
(2) K. Suminokura, *Biochem. Z.*, **224**, 292 (1930).
(3) G. Books, *La Nature*, No. 3011, 359–363 (1937).
(4) D. Keilin and T. Mann, *Nature*, **143**, 23 (1939).
(5) M. Graubard, *Enzymologia*, *V*, 332 (1939).

laccase, but apparently inactivates the tyrosinase. Three or more adsorptions to alumina, each followed by elution and subsequent dialysis, removed much inert protein and all color. Such preparations had a dry weight of about 5 units (defined below) per mg. which corresponds to a Q_{O_2} of about 3000. Because of a very limited supply of this wild mushroom, it was not practical to further concentrate and purify the enzyme. For the same reason, no extensive attempt was made to correlate the copper content with enzyme activity. These laccase preparations were found to be unstable to heat treatment and were markedly inhibited in their action by cyanide.

The activity of the laccase preparations was determined by measuring the rate of oxygen uptake during the enzymatic oxidation of hydroquinone. This substrate was chosen since its oxidation by laccase is not measurably affected by the presence of other common plant oxidases. The measurements were made in Warburg respirometer flasks of 30 cc. capacity.[6] The rate of shaking was 120 complete oscillations per minute, and the temperature was maintained at 25°. The reaction mixture consisted of 1 cc. of an aqueous solution of hydroquinone (10 mg.) added from the side arm at zero time, 3 cc. of (0.2 *M*) citrate–(0.4 *M*) phosphate buffer (*p*H, 6.1), 1 cc. of an aqueous solution containing 5 mg. of gelatin, enzyme solution and sufficient water to make a total volume of 8 cc. The amount of enzyme causing an oxygen uptake of 10 cu. mm. per minute is defined as one "hydroquinone" unit. Under these conditions, the rate of oxygen uptake is directly proportional to the amount of laccase used provided the amount of enzyme in the flask is not much in excess of two "hydroquinone" units. Furthermore, the rate of oxygen uptake remains constant for periods of at least thirty minutes.

As previously mentioned, the rate of oxidation of hydroquinone by laccase is not significantly affected by the presence of other plant oxidases. This has been demonstrated by the introduction of varying quantities of other oxidases into the reaction mixture containing a fixed amount of laccase (0.90 "hydroquinone" units). The introduction of tyrosinase (*campestris*) preparations with catecholase activity varying from 10 to 60 units and cresolase activity ranging from 1 to 33 units[7] caused less than a 5% variation in the rate of oxidation of hydroquinone by the laccase. Ascorbic acid oxidase also was found to have very little effect, 142 units[5] causing a variation of less than 8%. These experiments were performed according to the procedure for measuring hydroquinone units of laccase except that the additional enzyme solutions replaced part of the water in the flask.

Since tyrosinase is without effect on the oxidation of hydroquinone by laccase, it cannot be detected by this procedure. However, with the catechol–hydroquinone mixture used for measuring catecholase activity,[7] the activity of these two enzymes appears to be additive. Thus, in a typical experiment, 0.68 "hydroquinone" units of laccase gave an oxygen uptake of 6.8 cu. mm. per minute with the catechol–hydroquinone mixture. 0.80 tyrosinase catecholase unit gave no measurable activity toward hydroquinone alone, but did cause an oxygen uptake of 8 cu. mm. per minute with the substrate mixture. Upon mixing the 0.68 laccase unit and 0.80 tyrosinase (*campestris*) catecholase unit, an oxygen uptake of 14.7 cu. mm. per minute was observed with the catechol–hydroquinone mixture. Therefore, if tyrosinase is present in the laccase preparations, the rate with the catechol–hydroquinone mixture should be greater than with hydroquinone alone. No such differences were observed with the laccase preparations used in this paper.

The marked stability of this enzyme to changes in *p*H over a wide range (*p*H, 2 to 9.5) is of considerable interest. In comparison with other oxidases of this type it appears to be more stable, the contrast in stability being especially marked in the lower *p*H regions. This is illustrated by the data in Table I in which tyrosinase has been used for comparison.

TABLE I[a]

SHOWING THE DIFFERENCE IN RESISTANCE OF LACCASE AND TYROSINASE PREPARATIONS TO *p*H INACTIVATION

Enzyme	Prep. no.	Units[a] cc. at start	*p*H	Exposed to indicated *p*H	Activity remaining, %
Laccase	Crude juice	0.18	2.20	20 days	70
Laccase	L-64	.40	1.95	13 days	65
Laccase	L-64	.20	1.50	13 days	17
Laccase	L-64	.20	1.10	30 min.	15
Tyrosinase	C-7-25-10	1.50	2.50	3 min.	2.2
Tyrosinase	C-7-25-10	2.25	2.20	1 min.	3.5
Tyrosinase	C-7-25-10	0.92	2.00	1 min.	0.0

[a] The tyrosinase units in the table are catecholase units.[7] All activities were measured at *p*H 6.10. Low *p*H values were obtained by using citric acid and acetic acid, the latter being used for all values below *p*H 2.0.

(6) M. Dixon, "Manometric Methods," Univ. Press, Cambridge, 1934.

(7) M. H. Adams and J. M. Nelson, THIS JOURNAL, **60**, 2479 (1938).

When laccase activities of equal quantities of the same enzyme preparation were determined at different *p*H values over a range of *p*H 2.6 to 8.1, a marked *p*H optimum was observed in the vicinity of *p*H 6.1 (Fig. 1, Curve I). With other substrates such as catechol the same *p*H optimum effect was observed (Curve II, Fig. 1). The apparent decrease in laccase activity observed on both sides of the *p*H optimum is a reversible effect. This was demonstrated by bringing the *p*H to 6.10 after a fifteen to twenty minute reaction period at the indicated *p*H. In all cases the optimum rate of oxidation was observed within experimental error. The reason for measuring laccase activity at a *p*H 6.10 is now apparent.

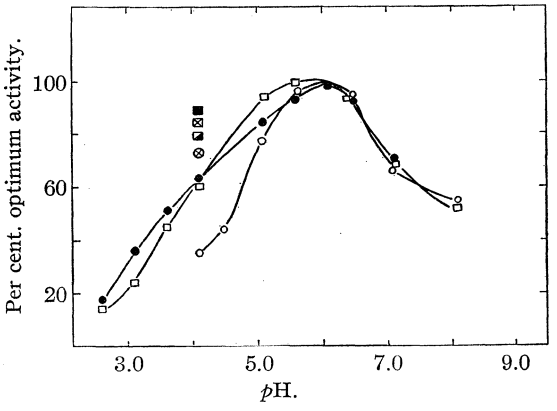


Fig. 1.—Showing the combined effect of *p*H and substrate concentration on the percentage optimum activity of laccase based on the maximum obtainable rate at *p*H 6.10. Oxygen uptake determined by means of Warburg respirometer (Barcroft differential manometers used for *p*H 7.1 and 8.1), temperature 25°. Citrate–phosphate buffers were used in all cases. ○, Curve I, reaction mixture: 3 cc. buffer, 1 cc. gelatin solution (5 mg.), 1 cc. hydroquinone solution (10 mg.) (added from side arm at zero time), 1 cc. laccase preparation containing 1 unit, and sufficient water to make final volume in reaction vessel 8.0 cc. ●, Curve II, reaction mixture same as for Curve I except 1 cc. catechol solution (25 mg.) in place of hydroquinone. □, Curve III, reaction mixture same as for Curve I, 1 cc. hydroquinone solution containing 25 mg. instead of 10 mg. The additional data noted at *p*H 4.10 were obtained using the same reaction mixture as for Curve I except for the following substrate concentrations: ■, IV, 75 mg. catechol; ⊗, V, 1.5 cc. hydroquinone solution (75 mg.); ◭, VI, 50 mg. catechol; ⊗, VII, 40 mg. hydroquinone.

The activity of laccase (*Russula foetens*) is dependent on substrate concentration as well as hydrogen-ion concentration. Thus, for each substrate, a concentration has been observed above which further increase in substrate caused no appreciable increase in the rate of oxidation. This value of concentration varies considerably with the choice of substrate (Fig. 2). After a consideration of the results shown in Fig. 2, 10 mg. of hydroquinone was chosen as a suitable concentration for the measurement of laccase units. For the measurement of maximum activity on catechol, 25 mg. has been used.

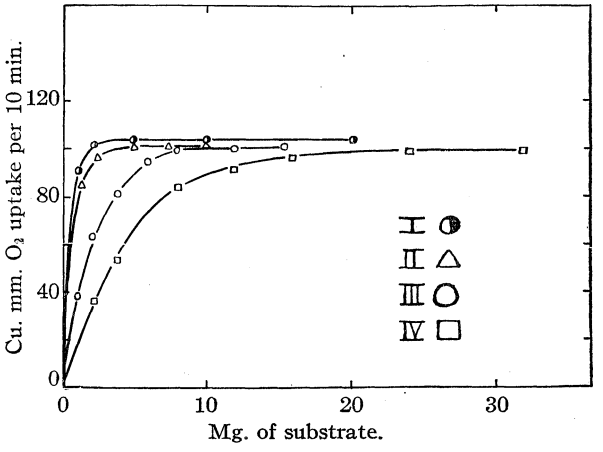


Fig. 2.—The effect of concentration of substrate on laccase activity, using four different substrates at *p*H 6.10. The rate of oxidation was determined by means of Warburg respirometers; temperature 25°. ◑, Curve I, reaction vessels contained: 1 cc. enzyme solution (1.0 unit), buffer, gelatin, aqueous *p*-phenylenediamine solutions to give indicated concentrations, and sufficient water to make the final volume 8.0 cc. △, Curve II, reaction mixtures same as for Curve I except dimethyl catechol was used as substrate. ○, Curve III, same as for Curve I, hydroquinone as substrate. □, Curve IV, same as for Curve I, catechol as substrate.

Curve III, Fig. 1, represents the results of a *p*H optimum study of laccase using 25 mg. of hydroquinone. It will be noted that this curve is similar to that obtained using 25 mg. of catechol (Curve II, Fig. 1). A comparison of Curve III with Curve I (dataf rom 10 mg. hydroquinone) demonstrates that the effect of substrate concentration is more pronounced at *p*H values below the optimum. Additional data obtained at *p*H 4.10 have been included in Fig. 1 to emphasize this point. The maximum rate obtainable at *p*H 4.10 is that obtained using 75 mg. of catechol or hydroquinone. It is interesting to note that this rate does not equal that obtained at the optimum *p*H (6.10), using much smaller concentrations of substrate (Fig. 2). In the case of catechol at *p*H 4.10, an increase in substrate from 25 mg. to 75 mg. caused about a 25% increase in rate, yet this rate was less than the optimum value at *p*H 6.10 by about 12%. A similar

increase in rate was observed with hydroquinone, the maximum rate being about 18% less than the optimum rate. Due to the fact that on the alkaline side of the *p*H optimum, both hydroquinone and catechol show an increasing tendency to undergo autoxidation, enzymatic studies become less reliable in this region. This is especially true with substrate concentrations larger than those used to obtain maximum activity at *p*H 6.10 (Fig. 2). For this reason, the alkaline side of the *p*H optimum has not been studied as extensively as in the acid regions. Regardless of this fact, the data in Fig. 1 clearly support the contention that laccase exhibits a *p*H optimum, and the nature of the *p*H effect is dependent on the substrate concentration used during the study.

Laccase preparations from *Russula foetens* are unusual in their ability to catalyze the aerobic oxidation of a wide variety of substrates. Because of this ability it is probable that these activities will be confused with those of other plant oxidases. This has been the case with laccase preparations reported from other sources. Before this confusion in classification can be eliminated, careful comparisons of these activities must be made. For future study of the relative abilities of these enzymes to react with various substrates, it is the writers' contention that unless the maximum activity of the enzyme toward the substrate at any given *p*H is obtained the results are of little comparative value. Comparable studies of the catalytic effect of these laccase preparations on the oxidation of certain common substrates follow.

Hydroquinone.—The aerobic oxidation of hydroquinone by laccase involves one atom of oxygen per molecule of substrate (Table II), the oxidation of the product *p*-quinone being immeasurably small. The effect of substrate concentration on the rate has been discussed. No appreciable inactivation was noted under normal conditions over periods of one to two hours. Chlorohydroquinone was similar in its behavior (Table II).

***p*-Phenylenediamine.**—This substrate has been used for the measurement of laccase activity by other investigators.[4] Since *p*-phenylenediamine is not as water soluble, is more easily autoxidized, and apparently has a more complex reaction mechanism than hydroquinone, it is felt that the latter substrate is a better choice for the measurement of laccase activity. While the rate with *p*-phenylenediamine approximates that of hydroquinone and remains constant over a concentration range of 2 to 20 mg. of substrate (Fig. 2), the total oxygen uptake is indefinite (Table II).

TABLE II

SHOWING THE TOTAL OXYGEN UPTAKE CORRESPONDING TO THE TOTAL OXIDATION OF 1 MG. OF SUBSTRATE BY TWO UNITS OF LACCASE FOR FIVE DIFFERENT SUBSTRATES AT *p*H 6.10

Substrate	Total uptake in cu. mm. corresponding to 1 atom oxygen per mg. substrate	Total observed oxygen uptake in cu. mm. using 1 mg. of substrate	No. of atoms of oxygen per molecule of substrate
Hydroquinone	102	106	1
Chlorohydroquinone	77	80	1
p-Phenylenediamine	104	145+	1.4+
Catechol	102	207	2
Dimethylcatechol	81	83	1

Catechol.—The enzymatic oxidation of catechol by laccase (*Russula foetens*) occurs at nearly the same rate as *p*-phenylenediamine and hydroquinone (Fig. 2). Some laccase preparations described in the literature,[4] however, are reported to oxidize *p*-phenylenediamine twice as rapidly as catechol. No substrate concentrations were given and so no conclusion concerning the similarity or dissimilarity of the laccase preparations may be made. The aerobic oxidation of catechol by our laccase preparations involves two atoms of oxygen per molecule of substrate (Table II). This behavior is similar to that of tyrosinase.[8] However, the apparent absence of inactivation of laccase in the oxidation of catechol in contrast to the marked inactivation experienced by tyrosinase (*campestris*) indicates the dissimilarity of the two oxidases. According to Ludwig and Nelson[9] one unit of purified *campestris* tyrosinase is completely inactivated after an oxygen uptake of approximately 100 cu. mm. According to their definition of a catecholase unit, this means that one unit of tyrosinase remains active with catechol for only about ten minutes. The writers have found that one unit of laccase with 24 mg. of catechol caused an oxygen uptake of 3100 cu. mm. during a period of eight hours. During this eight hour period the gradual drop in rate of oxidation was little more than that to be expected due to the constantly decreasing concentration of catechol. In other words, there appeared to be little inactivation of the laccase during this long period of oxidation.

Dimethylcatechol.—The behavior of dimethylcatechol with laccase contrasted to that of the

(8) H. Wagreich and J. Nelson, THIS JOURNAL, **60**, 1545 (1938).
(9) B. Ludwig and J. Nelson, *ibid.*, **61**, 2601 (1939).

closely related substrate catechol is of interest from two viewpoints. First, the mode of oxidation differs from that of catechol in that the reaction proceeds rapidly to an oxygen uptake of one atom per molecule (Table II). Further oxidation is very slow. Second, the same rate of oxidation was observed over a concentration range of 2 to 10 mg. of substrate (Curve II, Fig. 2).

Potassium Ferrocyanide.—Laccase preparations (*Russula foetens*) have been found to have the ability to catalyze the oxidation of potassium ferrocyanide. This enzymatic oxidation of an inorganic salt is rather unusual. In measuring the activity of the enzyme on this substrate, Barcroft differential manometers[6] were used to avoid any possible errors due to autoxidation of the salt. One "hydroquinone" unit of laccase with 5 mg. of potassium ferrocyanide resulted in an oxygen uptake of 10 cu. mm. per ten minutes. With this concentration of potassium ferrocyanide, the enzyme appeared to have very little catalytic effect. However, when the concentration of this substrate was increased to 100 mg., one "hydroquinone" unit of laccase caused an oxygen uptake of 70 cu. mm. per ten minutes. This rate of oxidation did not appear to be further increased by larger concentrations of substrate. From these results, potassium ferrocyanide seems to compare favorably with certain organic substrates.

Less detailed studies have been made on some other substrates. More work on these is being carried out along the lines of the above discussion.

Discussion

Measurement of Laccase Activity.—A practical method for the measurement of enzyme activity should be specific, reproducible, and convenient. The method that has been proposed herein for the measurement of laccase activity meets these requirements. The convenience of using the Warburg respirometer in following oxidase activity is well established. The high reproducibility of the method is a result of the fact that during the laccase-catalyzed oxidation of hydroquinone, the rate of oxygen uptake remains constant over periods of a half hour to an hour, thus allowing several observations on the rate to be made. The specificity of the method is demonstrated by the fact that relatively large concentrations of other plant oxidases have no appreciable effect on the measurement of laccase activity.

Effect of *p*H.—In defining the experimental conditions for the measurement of laccase activity, it was stated that the reaction mixture should be buffered to about *p*H 6. This is necessary since it was found experimentally that the same quantity of enzyme caused lower rates of oxygen uptake at higher and lower *p*H values than the one indicated. The fact that this *p*H optimum effect is reversible shows that the enzyme is not inactivated. This *p*H optimum effect is partially offset by increasing the substrate concentration. The marked stability of laccase over a wide *p*H range, and especially at the low *p*H values, is in contrast to the behavior of many plant oxidases, in particular tyrosinase with which it has been compared.

Substrate Concentration Effects.—The apparent activity of a fixed quantity of laccase varies with the substrate concentration up to a certain value above which further increase in substrate concentration causes no greater rate of oxygen uptake. It has been shown that this optimum substrate concentration varies with different substrates. Likewise, different enzymes which act on the same substrate show a difference in the amount of that substrate needed for optimum activity. Because of these facts, the substrate concentrations used have been fixed to ensure maximum activity at a definite *p*H. It is felt that this general procedure of fixing conditions of substrate concentrations and *p*H relative to a definite quantity of enzyme for maximum activity is necessary in all cases where a differentiation between the laccase preparations and other oxidase preparations is to be made.

Substrate and Enzyme Behavior.—The reproducibility of measuring laccase units has been found to result largely from the stability of the enzyme during the oxidation of hydroquinone. This stability has been observed with other substrates, especially catechol. In contrast to tyrosinase, which is completely inactivated by catechol after a short period of time, laccase does not appear to be inactivated to any appreciable extent even after a long reaction period. The oxidation of substrates considered here appears to proceed in a manner similar to that with other enzymes, except for the extent of enzyme inactivation.

Acknowledgment.—The authors wish to express their appreciation to Professor J. M. Nelson for his interest and friendly advice during this investigation. They are grateful to Dr. C. R.

Dawson for his help and constructive criticism in preparing the material for publication.

Summary

1. A method is described for the preparation of the enzyme, laccase, from the wild mushroom, *Russula foetens*. A typical preparation has a Q_{O_2} of 3000.

2. A measurement of units using hydroquinone as the substrate is outlined. Common plant oxidases do not appear to interfere in this procedure.

3. The unusual stability of the laccase preparations over a wide *p*H range is demonstrated.

4. The optimum *p*H for measurement of laccase activity is shown to be in the vicinity of *p*H 6.0.

5. The enzymatic oxidation of hydroquinone, *p*-phenylenediamine, catechol, dimethylcatechol, and potassium ferrocyanide has been described.

6. The behavior of the laccase preparations is contrasted when possible with tyrosinase (*campestris*).

7. The importance of substrate concentration in studying the behavior of the enzyme has been emphasized.

NEW YORK, N. Y. RECEIVED MARCH 4, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF WASHINGTON]

The Ionization Constant of Monoethanolammonium Hydroxide at 25° from Electrical Conductance Measurements

BY V. SIVERTZ, R. E. REITMEIER AND H. V. TARTAR

In this investigation use has been made of the work of several investigators[1-5] who have shown that accurate conductance measurements of solutions of weak electrolytes are adequate for the determination of limiting equivalent conductance and of thermodynamic ionization constants. The method finally developed is based upon the solution of three simultaneous equations. The first is

$$K = \frac{Cx^2f_{\pm}^2}{1-x} = K'f_{\pm}^2$$

where K and K' are the thermodynamic and stoichiometric ionization constants, respectively, x is the degree of dissociation, C is the concentration of base in equivalents per liter of solution and $f_{\pm}$ is the mean activity coefficient of the ions. The activity coefficient of the undissociated base is assumed to be unity. The second equation is

$$-\log f_{\pm} = a\sqrt{Cx}$$

where a is the Debye and Huckel coefficient. Lastly

$$x = \frac{\Lambda}{\Lambda_0}\left[1 + \frac{(\alpha\Lambda_0 + \beta)}{\Lambda_0}\sqrt{Cx}\right]$$

where α and β are the Onsager coefficients.

The authors have determined the electrical conductance at 25° of aqueous solutions of monoethanolammonium hydroxide. Since we were unable to obtain from the literature an accurate value for the equivalent conductance of the hydroxyl ion, the conductances of sodium and potassium hydroxide solutions have also been measured over a limited range of concentrations.

Experimental

Apparatus and Technique.—A Leeds and Northrup conductivity bridge[6,7] was used. The conductance cell, used with nitrogen, was similar in design to a cell described by Shedlovsky[8] and made of Pyrex glass. The electrode chamber met the specifications given by Jones and Bollinger.[9] Because of the magnified effects due to adsorption at very dilute concentrations, platinization was limited to the minimum value to prevent polarization. The electrodes were given a light gray coating, using the procedure suggested by Jones and Bollinger.[9] The cell constant at 25° was of the order of 0.26228 and was determined by comparison with a cell which had been calibrated with 0.01 demal potassium chloride, the specific conductance of which was taken from the recent work of Jones and Prendergast.[10] The cell was cleaned before each run with redistilled alcohol and ether and dried under nitrogen. This procedure produced no undesirable effects either on the character of the platinized electrodes or in the operation of the cell.

The current was supplied to the bridge by a Leeds and Northrup a. c. oscillator, the frequency of which could be varied in steps over a range of 500 to 2000 cycles. Several trials in each series of measurements showed that the conductance was essentially independent of the frequency. A Leeds and Northrup two-stage amplifier and telephone formed the detector circuit.

(1) MacInnes and Shedlovsky, THIS JOURNAL, **54**, 1429 (1932).
(2) Fuoss and Kraus, *ibid.*, **55**, 476 (1933).
(3) Shedlovsky and Uhlig, *J. Gen. Physiol.*, **17**, 549 (1934).
(4) Fuoss, THIS JOURNAL, **57**, 488 (1935).
(5) Shedlovsky, *J. Franklin Inst.*, **255**, 739 (1938).
(6) Dike, *Rev. Sci. Instruments*, **2**, 379 (1931).
(7) Jones and Josephs, THIS JOURNAL, **50**, 1049 (1928).
(8) Shedlovsky, *ibid.*, **54**, 1411 (1932).
(9) Jones and Bollinger, *ibid.*, **53**, 411 (1931).
(10) Jones and Prendergast, *ibid.*, **59**, 731 (1937).

The temperature of the oil thermostat, controlled to ±0.001° by a Thyratron relay, was established by a thermometer certified by the Bureau of Standards.

All solutions were made up by weight. An analytical balance accurate to 0.1 mg. was used for the more accurate weighings, and a large balance which was read to 1 mg. was used for weighing the water and solutions. The weights were calibrated against a set standardized by the Bureau of Standards.

Materials.—The water used in the preparation and dilution of solutions had a specific conductance of 5.0 (10^{-7}) mho. Since the measurements were made on alkaline solutions, it was necessary to know the carbon dioxide content of the water used. The conductivity water was drawn into a weight pipet, paraffined with material which had been specially purified, and nitrogen, free from carbon dioxide, was passed through for sixty minutes. This procedure gave water with a constant specific conductance which was assumed to be due to the presence of residual carbon dioxide and the specific conductance of pure water. The water correction was made accordingly, using the method suggested by Kolthoff,[11] and by Jeffery and Vogel.[12]

The monoethanolamine was from two sources and, after fractional crystallization and distillation, had a boiling point of 171.1° at 760 mm. pressure and a melting point of 11.52°. The density was found to be 1.0117 at 25° and the refractive index measured with an Abbé refractometer was 1.4539 at 20°. As a check on its purity, the monoethanolamine was analyzed by potentiometric titration against hydrochloric acid and by weight titration using methyl orange indicator. Several titrations gave the purity as 99.97% by the potentiometric titration and 99.96% by the weight titration. The standard hydrochloric acid used was a carefully prepared constant boiling mixture using the data of Foulk and Hollingsworth.[13] As a check on its standardization, the chloride content was determined by precipitation as silver chloride.

Paraffin was purified by shaking the melted material with hot concentrated sodium hydroxide. It was then leached thoroughly with conductivity water until the conductance of the wash water reached that of the original.

The solutions of monoethanolammonium hydroxide were prepared from monoethanolamine that was freshly distilled under nitrogen, care being taken that it did not come in contact with carbon dioxide at any time.

The stock solutions of sodium hydroxide were prepared by two methods. One solution was prepared by permitting pure metallic sodium to react with carbon dioxide-free conductivity water in a paraffined flask. The metallic sodium was cut under benzene, transferred under an atmosphere of nitrogen to the paraffined flask and the reaction permitted to take place under nitrogen. A second stock solution was prepared from sodium amalgam prepared by the electrolysis of a solution of C. P. sodium chloride over pure mercury. The stock solution of potassium hydroxide was prepared in a similar manner from C. P. potassium chloride. All solutions were stored in Pyrex bottles lined with specially purified paraffin and were maintained carbon dioxide-free. These stock solutions were standardized by titrating potentiometrically against hydrochloric acid and by weight titration using methyl red indicator.

The monoethanolammonium chloride solutions were prepared by neutralizing standard hydrochloric acid (to *p*H of 7.5) with monoethanolammonium hydroxide. It was necessary to know the *p*H of these solutions in order to make the proper correction for the trace of excess monoethanolammonium hydroxide, a procedure adopted to control hydrolysis.[8] The measurement was made electrometrically using a Leeds and Northrup *p*H meter that had been checked against standard *p*H buffers over the range used.

Results

Table I gives the data for monoethanolammonium hydroxide. The columns are, respectively, the concentration in equivalents per liter,

TABLE I

EQUIVALENT CONDUCTANCE AND IONIZATION CONSTANT OF MONOETHANOLAMMONIUM HYDROXIDE AT 25°, $\Lambda_0 = 239.79$

Concn. $C \times 10^3$	Λ	x	$f_\pm$	$K' \times 10^5$	$K \times 10^5$
0.22761	74.874	0.31351	0.9902	3.259	3.195
.26771	70.087	.29351	.9897	3.265	3.198
.38478	60.123	.25190	.9886	3.264	3.190
.49003	54.142	.22693	.9878	3.264	3.185
.77751	44.163	.18523	.9861	3.274	3.184
1.0182	39.072	.16395	.9851	3.274	3.177
1.2754	35.104	.14735	.9842	3.248	3.146
2.2535	26.995	.11344	.9815	3.271	3.152
2.6870	24.931	.10481	.9806	3.297	3.171
3.6628	21.550	.09065	.9790	3.310	3.173
3.9557	20.680	.08701	.9786	3.280	3.141
5.3468	17.947	.075564	.9768	3.303	3.152
6.4121	16.462	.069341	.9757	3.313	3.154
6.5739	16.204	.068261	.9756	3.288	3.129
7.5866	15.170	.063929	.9747	3.313	3.147
7.6417	15.122	.063729	.9746	3.315	3.149
9.0240	13.918	.058681	.9735	3.301	3.139
9.2932	13.705	.057787	.9734	3.294	3.121
13.546	11.438	.048282	.9706	3.318	3.126
14.334	11.132	.046999	.9702	3.323	3.127
16.759	10.279	.043419	.9690	3.303	3.102
26.015	8.297	.035100	.9654	3.322	3.096
26.063	8.326	.035223	.9653	3.352	3.123
30.603	7.667	.032455	.9639	3.332	3.096
33.872	7.310	.030956	.9626	3.350	3.106
36.033	7.062	.029911	.9625	3.323	3.079
45.308	6.335	.026858	.9602	3.359	3.097
57.955	5.586	.023707	.9577	3.337	3.060
60.745	5.472	.023229	.9572	3.356	3.074
81.261	4.7250	.020084	.9540	3.345	3.045
89.213	4.4990	.019132	.9530	3.329	3.024
89.486	4.4999	.019135	.9529	3.341	3.034
109.014	4.0642	.017300	.9506	3.321	3.001
122.92	3.8096	.016225	.9493	3.290	2.964
162.97	3.2949	.014055	.9457	3.265	2.921
198.47	2.9453	.012576	.9434	3.179	2.830
199.75	2.9453	.012577	.9432	3.200	2.847
326.83	2.2577	.009668	.9366	3.085	2.706

(11) Kolthoff, *Rec. Trav. Chim.*, **48**, 664 (1929).
(12) Jeffery and Vogel, *Phil. Mag.*, **15**, 395 (1933).
(13) Foulk and Hollingsworth, THIS JOURNAL, **45**, 1220 (1923).

the equivalent conductance, the degree of dissociation, the mean activity coefficient of the ions, the stoichiometric ionization constant and the thermodynamic ionization constant. This table is based on a Λ_0 value obtained from the conductance of the strong electrolytes, sodium and potassium hydroxides, by the additive method.

Equivalent conductances of sodium and potassium hydroxides and monoethanolammonium chloride over a limited concentration range are given in Tables II, III and IV, respectively.

TABLE II

EQUIVALENT CONDUCTANCE OF SODIUM HYDROXIDE AT 25°

Concn. $C \times 10^3$	Λ	Concn. $C \times 10^3$	Λ
0.25339	246.34	1.0034	244.94
.26417	246.14	1.7954	243.58
.29973[a]	246.11	2.7419	242.67
.31230	246.11	3.2893	242.27
.57934[a]	245.04	3.8729	241.65
.75295	244.83	5.8921[a]	240.12
.77058	244.92	8.5340	238.82
.80892[a]	245.00	10.211	237.93
.81373[a]	245.22	10.513	237.85

$\Lambda_0 = 247.83$

[a] The values from conductance measurements made on the stock solution prepared from sodium amalgam.

TABLE III

EQUIVALENT CONDUCTANCE OF POTASSIUM HYDROXIDE AT 25°

Concn. $C \times 10^3$	Λ	Concn. $C \times 10^3$	Λ
0.15581	269.60	1.2503	267.60
.17545	269.51	1.4395	267.44
.19920	269.34	2.3630	266.32
.23780	269.68	3.5242	265.41
.32192	269.18	4.4166	264.48
.34780	268.90	5.9956	263.57
.58624	268.67	9.3414	261.68
.79877	268.22	11.165	260.90
1.0525	267.84		

$\Lambda_0 = 270.94$

TABLE IV

EQUIVALENT CONDUCTANCE OF MONOETHANOLAMMONIUM CHLORIDE AT 25°

Concn. $C \times 10^3$	Λ	Concn. $C \times 10^3$	Λ
0.28495	117.55	7.7008	111.34
.77892	116.44	7.7412	112.11
.88910	116.38	12.492	109.97
1.0842	116.03	13.068	109.98
1.4052	115.51	19.821	107.84
2.1825	114.83	22.726	106.73
2.6130	114.55	62.597	101.21
3.0936	114.52	109.010	97.21
3.7512	113.56	112.110	96.90
4.3850	113.38	116.120	96.46
6.7983	112.54		

$\Lambda_0 = 118.58$

The limiting conductance values of potassium and sodium hydroxides and monoethanolammonium chloride were determined by using Shedlovsky's method of extrapolation in which $1/\Lambda$ is plotted against $\sqrt{C}$. This gives $\Lambda_0 = 247.83$ for sodium hydroxide, $\Lambda_0 = 270.94$ for potassium hydroxide and $\Lambda_0 = 118.58$ for monoethanolammonium chloride. These values, combined with limiting conductance for the Na^+, K^+ and Cl^- as determined by MacInnes, Shedlovsky and Longsworth[14] (corrected to the Jones and Prendergast basis[11]), give the Λ_0 value for monoethanolammonium hydroxide which was used in Table I, as well as 197.71 and 197.41 for the limiting conductance of the hydroxyl ion, obtained from sodium hydroxide and potassium hydroxide, respectively.

The mean of the values of K in the concentration range below 0.0015 N gives 3.19×10^{-5}. Other weak electrolytes show a constant value of K below this concentration.[15,16] The values of K in this range show a variation to be expected with a weak base. It is improbable that this variation is due to the solution of glass, since we were able to confirm the findings of Jeffery and Vogel[12] and Wynne-Jones[17] that the change in conductance of the more concentrated solutions (0.005–0.01 N) was inappreciable over the period of time required for a series of measurements. It is more likely that this variation results from fluctuations in the carbon dioxide content of the water used in preparing solutions, *i. e.*, a failure to comply strictly with the assumption made earlier in this paper regarding constancy of carbon dioxide content of the water.

Table I also shows a tendency for the constant, K, to decrease as the concentration of the monoethanolammonium hydroxide increases. This decrease is expected due to the assumption made that the activity of the undissociated base is unity.

Summary

1. Conductances of sodium and potassium hydroxides, of monoethanolammonium chloride and of monoethanolammonium hydroxide have been measured over a limited range of concentrations at 25°.

2. A new value for the limiting conductance of hydroxyl ion is reported.

3. From these measurements the thermody-

(14) MacInnes, Shedlovsky and Longsworth, THIS JOURNAL, **54**, 2758 (1932).

(15) Shedlovsky, *ibid.*, **54**, 1429 (1932).

(16) Martin and Tartar, *ibid.*, **59**, 2672 (1937).

(17) Wynne-Jones, *J. Chem. Soc.*, 630 (1926).

namic ionization constant of monoethanolammonium hydroxide has been calculated and found to be 3.19×10^{-5} at 25°.

SEATTLE, WASHINGTON RECEIVED MARCH 5, 1940

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF THE GENERAL ELECTRIC COMPANY]

Vapor Pressures of Nickel and of Nickel Oxide

BY H. L. JOHNSTON* AND A. L. MARSHALL

Vapor pressures of copper and of iron, determined by measuring the rates of evaporation from metal rings heated inductively in a vacuum, were recently published from this Laboratory.[1] We have completed a similar investigation with nickel between the temperatures of 1300 and 1600°K., and have also determined vapor pressures of nickel oxide, by measuring rates of nickel and of oxygen loss from nickel rings coated with a thin film of the oxide. From these data, and thermodynamic and quantum-statistical data on both the solid and gaseous forms of nickel and of nickel oxide, we have computed their heats of sublimation and have derived vapor pressure formulas.

Vapor pressures, p, are computed from the measured rates of evaporation, m, by use of the relationship[1,2]

$$\log p + \log \alpha = \log m - {}^1/_2 \log M + {}^1/_2 \log T - 1.647 \quad (1)$$

where p is in atmospheres; m is in grams per square centimeter per second; M is the molecular weight in the vapor phase; T the absolute temperature; and α, termed the *accommodation coefficient*, is a measure of the efficiency with which molecules that strike the equilibrium surface from the vapor phase are condensed. The accommodation coefficient is unity if condensation results at every collision.

As with copper and with iron, the results with nickel establish this coefficient as unity and support the general validity of the Langmuir method in its application to metals. Vapor pressures, and the accommodation coefficient, could not be determined for the oxide with the same accuracy as for the metal, but the accommodation coefficient appears to be unity within the limits of experimental error.

Nickel

Experimental.—Apparatus and procedure were described previously.[1] Except as noted below the same description applies here.

The nickel used, in all but one of the runs, was electrolytic in origin and had been vacuum melted in an alundum crucible. Spectrographic analysis indicated the absence of any impurity, in significant amount, other than cobalt. The latter was present to the extent of 0.64% in the original specimen and, within limits of a colorimetric method employed for the analysis, this percentage remained unchanged in the evaporated film.[3] The results obtained in a single (subsequent) run[4] with a ring turned from pure carbonyl nickel[5] were undistinguishable from those obtained with the electrolytic nickel.

Dimensions of the nickel ring turned from the vacuum ingot were: outer diameter, 2.23 cm.; inner diameter, 1.13 cm.; thickness, 0.63 cm.; total surface, 12.46 sq. cm. Correction for condensation of atoms which strike the inner surface of the ring reduces the effective surface area to 11.74 sq. cm.

Evaporation losses were determined by weighing the approximate 16 g. ring on a sensitive balance. Weighings were reproducible to within 0.02 milligram.

Temperatures were determined by setting the filament of the optical pyrometer on two holes, 1.2 mm. in diameter, drilled vertically into the face of the specimen to a depth of about four millimeters. Measurements on a specimen drilled with holes of 0.6 mm., 1.2 mm. and 1.8 mm. diameter proved that the emissivity from the 1.2 mm. hole was indistinguishable from that from the 0.6 mm. hole to the highest temperature to which measurements were carried, 1600°K., and was therefore the equivalent of black body radiation. On the other hand, the emissivity from the 1.8 mm. hole was definitely less than black body at 1100° and yielded brightness temperatures more than twenty degrees in error at 1600°.

Temperatures determined as described above were normally reproducible within limits of approximately three degrees (each determination the average of five to ten successive observations). This corresponds to limits of approximately 10% on individual vapor pressure determinations. Temperatures were taken continuously during

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(1) Marshall, Dornte and Norton, THIS JOURNAL, **59**, 1161 (1937).

(2) Langmuir, *Phys. Rev.*, **2**, 329 (1913).

(3) The influence of this amount of cobalt on the measurements of the evaporation of nickel must lie well within the accuracy of the latter. The observation that the composition of the evaporated metal is identical with that of the original specimen within limits of the analytical error indicates that vapor pressures of cobalt and of nickel are nearly equal, which is in agreement with the data of Ruff and Bormann (*Z. anorg. Chem.*, **88**, 386, 397 (1914)) on liquid nickel and cobalt.

(4) Run *M* in the tables. This run was made by Dr. F. J. Norton and Dr. R. W. Dornte.

(5) The metal for this ring was furnished through the courtesy of the International Nickel Co. Its composition was stated to be: 99.89% nickel, 0.048% iron, 0.035% carbon, 0.014% copper and 0.008% sulfur.

TABLE I

VAPOR PRESSURES OF NICKEL

Run	Temp., °K.	Time, seconds	Effective time, seconds	Wt. loss, g.	m g./sq. cm./sec.	p, atm.
4	1307	67,680	68,942	0.00457	5.65×10^{-9}	6.00×10^{-10}
7	1308	2,580	1,948	(.00012)[7]	(5.3×10^{-9})	(5.6×10^{-10})
6	1387	19,620	19,600	.01196	5.20×10^{-8}	5.70×10^{-9}
10	1397	20,640	19,632	.01517	6.58×10^{-8}	7.24×10^{-9}
11	1397	(11,100)[8]	(11,272)	.00980	(7.41×10^{-8})	(8.16×10^{-9})
5	1415	11,040	9,856	.01142	9.87×10^{-8}	1.09×10^{-8}
2	1465	3,480	3,325	.0129	3.30×10^{-7}	3.72×10^{-8}
9	1466	10,740	10,152	.04570	3.83×10^{-7}	4.33×10^{-8}
1	1507	1,980	1,872	.0191	8.69×10^{-7}	9.92×10^{-8}
8	1576	1,680	1,882	.08539	3.87×10^{-6}	4.52×10^{-7}
3	1578	1,550	1,481	.06774	3.89×10^{-6}	4.55×10^{-7}
M	1583	2,362	1,972	.0808	3.98×10^{-6}	4.63×10^{-7}

short runs and at frequent intervals during longer runs. Corrections were applied for evaporation losses during a preliminary period of degassing the nickel and during the period that the sample was coming up to temperature. Corrections were also made for small temperature fluctuations that sometimes resulted from variations in operating conditions during the period of the run. It was found convenient to make these corrections graphically by plotting relative evaporation rates (obtained as a function of the temperature) against time and to apply them to yield an "effective" length of run at constant rate of evaporation. The magnitudes of these corrections may be judged by comparison of the third and fourth columns of Table I.

The pyrometer used in this work was the one previously employed by Marshall, Dornte and Norton,[1] and calibrated by them against a standard tungsten ribbon filament lamp (designated as Standard Lamp W 91) supplied and calibrated by Forsythe.[6] The pyrometer calibration has been rechecked by Dr. R. W. Dornte subsequent to the work reported in this paper, and found not to deviate from the earlier calibration.

Window corrections which normally amounted to about 12 degrees, were determined by calibrations *in situ*.

Data.—The experimental results are recorded in Table I. All of our runs are included although 7 and 11 are entitled to less weight than the others. Runs 1 to 7 inclusive were made with a preliminary 600–700° bakeout in vacuum. In runs 8 to 11 hydrogen was present during the bakeout. There was no significant difference in results.

Thermodynamic Treatment.—The reliability of vapor pressure data is best confirmed by establishing the constancy of ΔH_0° in the thermodynamic relationship

$$R \ln p \text{ (atmospheres)} = \left(\frac{F^\circ - H^\circ}{T}\right)_{\text{condensate}} - \left(\frac{F^\circ - H_0^\circ}{T}\right)_{\text{vapor}} - \frac{\Delta H_0^\circ}{T} \quad (2)$$

applied to the individual data. Here $F^\circ - H_0^\circ/T$ for a solid is calculable from its heat capacity by the equation

$$\left(\frac{F^\circ - H_0^\circ}{T}\right)_{\text{solid}} = \frac{1}{T}\int_0^T C_p dT - \int_0^T C_p d \ln T \quad (3)$$

and $(F^\circ - H_0^\circ/T)_{\text{vapor}}$ can be evaluated accurately by statistical methods which depend partly on information gained from the spectrum.[9] ΔH_0° has the significance of the heat of sublimation to ideal gas at the absolute zero.

Kelley[10] has reviewed the experimental data on solid nickel published prior to 1934, and has computed and tabulated the free energy function on the basis of these data. More recent work[11] indicates that the heat capacity curve in the high temperature region should run somewhat under the values adopted by Kelley. We have accordingly recalculated the thermodynamic functions for solid nickel to conform with the newer data. The results, which differ from Kelley's tables by amounts sufficient to make a difference of about 0.3 of a unit in the free energy function at 1500°, are entered in Table II, together with the free energy function for nickel vapor computed by Overstreet[12] and quoted by Kelley.[10] The last column is the change in the standard free energy function, in the evaporation of nickel.

(6) Forsythe, *J. Optical Soc. Am.*, **4**, 305 (1920).

(7) This figure is the smoothed average of the weight determination (0.00014 g.) and of a colorimetric determination of nickel in a nitric acid solution of the deposit formed on the walls of the cell (0.000104 g.). Colorimetric determinations on deposits from other runs differed from the more accurate weight determinations by amounts which were generally under 5% but doubled this percentage in one or two instances.

(8) There is an uncertainty of approximately eleven minutes in the duration of Run 11 due to the fact that the power went off unexpectedly during a period when the apparatus was not under continuous observation. This is equivalent to a 6% uncertainty in evaporation rate and in pressure.

(9) W. F. Giauque, THIS JOURNAL, **52**, 4808 (1930).

(10) K. K. Kelley, *Bureau of Mines Bulletin*, **350**, 34 (1932); *ibid.*, **371**, 36 (1934); *ibid.*, **383**, 73 (1935).

(11) Grew, *Proc. Roy. Soc.* (London), **A145**, 509 (1934); Ahrens, *Ann. Physik*, **21**, 169 (1934); Clusius and Goldmann, *Z. physik. Chem.*, **B31**, 256 (1936); Rosenblum and Jaeger, *Proc. Acad. Sci. Amsterdam*, **39**, 366 (1936); Ewert, *ibid.*, **39**, 833 (1936); Bronson, Hewson and Wilson, *Can. J. Research*, **14A**, 181, 194 (1936); Steinwehr and Schulz, *Phys. Z.*, **37**, 753 (1936); Moser, *ibid.*, **37**, 737 (1936).

(12) R. Overstreet, Master's Thesis, University of California, 1930.

TABLE II

THERMODYNAMIC FUNCTIONS OF NICKEL AND CHANGE OF THE STANDARD FREE ENERGY FUNCTION IN THE EVAPORATION

T, °K.	$H^\circ - H^\circ$	$(H^\circ - H_0^\circ)/T$	S°	$\left(\frac{F^\circ - H_0^\circ}{T}\right)_{\text{solid}}$	$\left(\frac{F - H_0^\circ}{T}\right)_{\text{vapor}}$	$\Delta\left(\frac{F - H_0^\circ}{T}\right)_{\text{evap.}}$
298.1	1142	3.83	7.02	− 3.19	−38.058	−34.87
400	1800	4.50	8.92	− 4.42	−39.672	−35.25
500	2507	5.01	10.46	− 5.44	−40.908	−35.47
600	3286	5.48	11.88	− 6.40	−41.929	−35.53
700	4068	5.81	13.09	− 7.28	−42.796	−35.52
800	4801	6.00	14.07	− 8.07	−43.557	−35.49
900	5538	6.15	14.93	− 8.78	−44.231	−35.45
1000	6283	6.28	15.72	− 9.44	−44.831	−35.39
1100	7038	6.40	16.44	−10.04	−45.382	−35.34
1200	7802	6.50	17.10	−10.60	−45.885	−35.28
1300	8574	6.60	17.72	−11.13	−46.348	−35.22
1400	9354	6.68	18.30	−11.62	−46.777	−35.16
1500	10141	6.76	18.84	−12.08	−47.174	−35.10
1600	10936	6.84	19.35	−12.51	−47.548	−35.04
1700	11739	6.91	19.84	−12.93	−47.901	−34.97

Our values are based principally on the data of Keesom and Clark[13] for temperatures below 10°K.; on those of Clusius and Goldmann[11] for the interval 10 to 26°; those of Eucken and Werth[14] and of Rodebush and Michalek[15] for the interval 25 to 200° and on the recent careful work of Moser[11] for the interval 300 to 1000°K. Above 1000°K. we have extrapolated the curve of Moser by continuing it parallel to that of Ewert.[11] There may be an uncertainty of 100 calories in the enthalpy at 1600° in this extrapolation, but this will be almost fully compensated in the entropy term. The work of Moser on pure carbonyl nickel, with a carefully controlled adiabatic calorimeter, appears to justify this weighting to the exclusion of earlier data. The enthalpy values secured from Moser's data are in good agreement with the total heats between room temperature and about 800°K., determined by Bronson, Hewson and Wilson who estimate their limits of error at 0.2 of 1%. The entropy of the magnetic transformation was obtained by dividing Moser's heat input for the interval 600 to 673° by 641°, the "center of gravity" of this input, determined from the C_p *vs.* log T plot.

TABLE III

ΔH_0° FOR THE EVAPORATION OF SOLID NICKEL

Run	T, °K.	$4.575 \log_{10} p$	$\Delta\left(\frac{F^\circ - H^\circ}{T}\right)_{\text{evap.}}$	ΔH_0°
4	1307	−42.19	35.21	101,162
7	1308	(−42.31)	35.21	(101,403)
6	1387	−37.72	35.17	101,098
10	1397	−37.24	35.16	101,143
11	1397	(−37.01)	35.16	(100,815)
5	1415	−36.42	35.15	101,272
2	1465	−33.99	35.12	101,246
9	1466	−33.69	35.12	100,875
1	1507	−32.04	35.10	101,172
8	1576	−29.03	35.05	100,990
3	1578	−29.02	35.05	101,102
M	1583	−28.98	35.05	101,359

Average ΔH_0° (Runs 7 and 11 not included), 101,141 ± 150 cal.

Table III gives the values of the sublimation heat at 0°K., obtained by combination of the data of Table II with the experimental vapor pressures recorded in Table I.

Substitution of the average ΔH_0° into equation (2), with a linear expansion of $\Delta(F^\circ - H_0/T)$ as a function of T (Table II), leads to the vapor pressure equation

$$\log p \text{ (atmospheres)} = -\frac{22{,}107}{T} - 1.31 \times 10^{-4} T + 7.869 \quad (4)$$

which we believe accurate to within 5% of the pressure. The fit with our experimental data is shown graphically in Fig. 1. The curve in this graph is constructed from equation (4), and the radii of the circles drawn to correspond to the uncertainty in the individual measurements (±3° in all runs except Nos. 7 and 11).

The Accommodation Coefficient.—The good agreement of ΔH_0° among runs, and the absence of any temperature trend, establish the accommodation coefficient as unity within sensible limits of error. This depends on the fact that, for α other than unity, the entries in the third column of Table III would be in error by the amount 4.575 log α, and those in the fifth column by the

(13) W. H. Keesom and C. W. Clark, *Physica*, **2**, 513 (1935).
(14) A. Eucken and H. Werth, *Z. anorg. Chem.*, **188**, 152 (1930).
(15) W. H. Rodebush and J. C. Michalek, THIS JOURNAL, **47**, 2117 (1925).

amounts 4.575 T log α. The values of the *supposed* ΔH_0° would thus vary with the temperature at a rate proportional to the magnitude of α (except in the fortuitous case that log α vary in exact inverse proportion to T). The absence of any sensible variation in the ΔH_0°'s computed from the nickel data thus makes it reasonably certain that the accommodation coefficient for nickel is unity. The data would not preclude an α intermediate between 0.75 and 1.00, however.[16]

This conclusion receives qualitative confirmation from: (1) the absence of condensation in the re-entrant portions of the quartz cell[17]; and (2) the observation that, within limits of error, the loss in weight per unit time is no different for a nickel cylinder perforated with many deep, narrow drill holes than for a non-perforated cylinder of equal external dimensions.[18]

Comparison with other Investigators.—Rates of evaporation from nickel surfaces have been reported previously by Jones, Langmuir and Mackay[19] and by Bryce.[20] These data are entered in Table IV and Fig. 1, and ΔH_0°'s likewise computed.

Both Langmuir and co-workers and Bryce measured evaporation losses from nickel filaments. The ring evaporation method possesses the advantage of being free from the following sources of error, which are difficult to avoid in filament evaporation: the considerable variation in evaporation rate in the course of each run due to decrease in the dimensions of the filament; the effect of superheating at thin spots in the filament; the difficulty of obtaining good pyrometer settings on a thin wire and of properly correcting for temperature gradients along the wire and the necessity of making corrections for surface emissivity.[21]

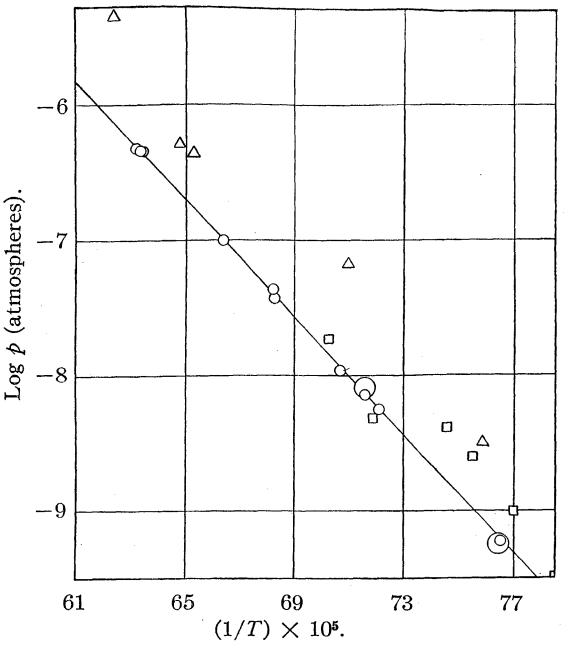


Fig. 1.—Vapor pressures of nickel: ○, this research; △, Jones, Langmuir and Mackay; □, Bryce. The dimensions of the circles, representing this research, are drawn in scale to represent error limits. The curve is constructed from equation (4).

TABLE IV

VAPOR PRESSURES OF NICKEL REPORTED BY OTHER OBSERVERS

T, °K.	p (atm.)	ΔH_0°	Observer
1252	1.29×10^{-10}	100,460	Bryce
1273	3.22×10^{-10}	99,808	Bryce
1299	9.88×10^{-10}	98,932	Bryce
1318	3.20×10^{-9}	97,276	J., L. & M.
1324	1.38×10^{-9}	99,922	Bryce
1341	1.45×10^{-9}	100,119	Bryce
1391	4.85×10^{-9}	101,432	Bryce
1409	6.67×10^{-8}	95,375	J., L. & M.
1423	1.84×10^{-8}	99,952	Bryce
1532	4.34×10^{-7}	97,827	J., L. & M.
1544	5.06×10^{-7}	98,107	J., L. & M.
1602	4.38×10^{-6}	97,925	J., L. & M.

Nickel Oxide

Experimental.—The rings used to determine evaporation rates of nickel oxide were of approximately the same

(16) If one out of every four atoms fails to condense on the *hot* surface at equilibrium (an accommodation coefficient of 0.75) there would result an apparent increase in ΔH_0° of 180 calories, between 1300° and 1600°. This is just under the precision of our measurements (±300 calories on individual points from an estimated limit of 3° in temperature). Actually, our deviations from the mean ΔH_0° lie within 150 calories with two exceptions.

(17) This relates directly to the accommodation coefficient on a *cold* surface while the calculation of vapor pressures from evaporation rates requires a knowledge of the accommodation coefficient on the *hot* equilibrium surface. We may ordinarily expect the accommodation coefficient to be unity on both hot and cold surfaces if unity on either but this is not a necessary consequence and is apparently not true in the case of graphite (which we expect to discuss in a subsequent communication).

(18) This is evidence that atoms evaporated from the walls of the drill holes are recondensed before they reach the surface. The data obtained with the nickel cylinders will be included in a subsequent paper on the evaporation of graphite.

(19) H. A. Jones, I. Langmuir, and G. M. J. Mackay, *Phys. Rev.*, **30**, 20 (1927).

(20) Bryce, *J. Chem. Soc.*, 1517 (1936). Dr. Bryce kindly communicated the numerical values of the data which he shows graphically in his paper, in correspondence with Dr. H. A. Liebhafsky of this Laboratory, and has consented to their use. The pressures attributed by us to Bryce, in our Table IV, and the corresponding values of ΔH_0°, were computed by us from Bryce's evaporation rates, with the aid of our equations (1) and (2).

(21) In conjunction with our own work we obtained a value of 0.41 for the emissivity of nickel at $\lambda = 0.665\ \mu$. This is slightly higher than the value employed by Jones, Langmuir and Mackay, but of the wrong sign and wrong magnitude to account for the approximately 50° discrepancy between their data and ours. Our own temperature scale in no wise depends on the value adopted for the emissivity of nickel since we obtained the equivalent of "black body" radiation.

dimensions as the one employed with nickel and were corrected in the same manner for condensation on the inner surface of the ring. Results obtained with rings turned from electrolytic nickel (0.64% cobalt) were indistinguishable from those obtained with a ring of carbonyl nickel.[5]

The rings were oxide coated prior to each run by oxidation in air for several minutes at about 900° and were partially degassed prior to evaporation by a preliminary bakeout in vacuum at about 400°. Uniform, adhering films of olive-green oxide were produced. Approximate calculations indicate that the film thicknesses varied from 10,000 to about 50,000 NiO layers. Lengths of runs were ordinarily chosen so that only 4 or 5% of the oxide coating was evaporated. One run (1566°K.) in which 35% of the oxide was evaporated yielded data in good agreement with the lesser removals of film.

The measurements were complicated by the fact that evaporation losses were made up in large part of pure nickel which escaped through the film. It was thus necessary to distinguish between total losses in weight and the weight loss of oxygen. The latter was obtained, by difference, through determination of the residual oxygen which remained on the ring. This determination was made by reducing the ring in an atmosphere of hydrogen at 800°. The reduction was repeated, for ten or twenty minute reduction periods, until the ring came to constant weight. This result was usually attained (within an accuracy of 0.01 or 0.02 mg.) with two reductions. The final weighing was corrected (a correction of 0.08 mg.)[22] for hydrogen dissolved in the nickel at 800°.

Temperatures were determined by pyrometer settings on 1.2-mm. holes drilled into the surface of the specimen.[23] Corrections for fluctuations in temperature and for preliminary heating periods were applied in the manner described for nickel.

No deposit was formed in the re-entrant portions of the cell. On the basis of this observation the accommodation coefficient was taken to be unity.

Data.—Data from a typical run are shown in Table V. Summaries from all of the runs are entered in Table VI.

Thermodynamic Treatment.—The integral $\int_{296}^{T} C_p dT$, for solid nickel oxide, has been measured by Kapustinsky and Novoseltsev[24] for various upper limits of the integral to 1396°K. They employed a high temperature calorimeter of new design.[25] Heat capacities between 68° and 298°K. have been measured with a vacuum calorimeter, by Seltz, DeWitt and McDonald,[26] who extrapolate their data to 0°K. by means of a combination of Debye and Einstein terms in accordance with the formula

$$C_p = D\left(\frac{404}{T}\right) + E\left(\frac{620}{T}\right) \qquad (5)^{27}$$

They further find that their own data at 298° and the integrals $\int_{298}^{T} C_p dT$ determined by Kapustinsky and Novoseltsev can be represented by the equation

$$C_p = 13.69 + 0.83 \times 10^{-3}T - 2.915 \times 10^{5}T^{-2} \quad (6)$$

up to the highest limits of Kapustinsky's measurements (1396°K.). This represents an improvement over the equation published by Kapustinsky and Novoseltsev,[24] which fails to reproduce the heat capacity at low temperatures. The fact that the data can be so represented excludes the possibility of a transition below 1400°.

From the values[27] for $(H^\circ_{298.1} - H^\circ_0)$ and for $S^\circ_{298.1}$ obtained from Seltz' data and from the integration of equation (6) between 298.1 and T we obtain, for the free energy function of solid nickel oxide, the relationship (*cf.* eq. 3)

TABLE V

DATA FROM RUN 4

Temperature, 1511°K. Effective time, 609 seconds

Initial wt. before oxidation, g.	15.46038
Wt. after oxidation, g.	15.46955
Wt. after evaporation, g.	15.46490
Wt. after H_2 reduction (corrected for dissolved hydrogen), g.	15.45613
By difference:	
Oxygen initially added, g.	0.00917
Evaporation loss (NiO + Ni), g.	.00465
Residual oxygen, g.	.00877
Oxygen evaporated (as NiO), g.	.00040
NiO evaporated, g.	.00187
Free nickel evaporated, g.	.00278
m (g./sq. cm./sec.) for NiO	2.62×10^{-7}
p (atm.)	2.66×10^{-8}

(22) This correction was determined experimentally by collecting, and measuring, the gas liberated from the ring of electrolytic nickel subsequent to one of the 800° reductions. To accomplish this the bare nickel ring was sealed into the quartz apparatus[2] and heated by means of high frequency to approximately 1000°. By means of a mercury diffusion pump the evolving hydrogen was pumped into a separate vessel of known volume and the final pressure was determined on a McLeod gage.

As the correction was not large, and care was taken always to reproduce the approximate 800° temperature and other experimental conditions under which reduction was brought about, it was considered justifiable to apply this same correction in all of the runs.

(23) The holes were clearly visible at temperatures above about 900°. We obtained an average value of 0.86 (for $\lambda = 0.665\ \mu$) for the emissivity of the oxide coated surface. This value is higher than that we have obtained for a specimen of graphite (0.53) and is a reasonable value. Consequently we may conclude that no significant temperature gradient exists between the oxide film and the metal.

(24) Kapustinsky and Novoseltsev, *J. Phys. Chem.* (U. S. S. R.), **11**, 61 (1938).

(25) Kapustinsky and Veselovsky, *ibid.*, **11**, 68 (1938).

(26) Seltz, DeWitt and McDonald, THIS JOURNAL, **62**, 88 (1940).

(27) The extrapolation below 68° contributes only 33 calories to $(H - H_0)$ and 0.65 E. U. to the entropy. We obtain $H^\circ_{298.1} - H^\circ_0 = 1630$ calories by graphical integration of Seltz's data, which was kindly furnished us in advance of its publication. Dr. Seltz (personal communication) informs us of an error in the published value of the entropy. The correct value is $S_{298.1^\circ} = 9.22$ E. U. We have used this corrected value in the subsequent calculations.

TABLE VI

VAPOR PRESSURES OF NICKEL OXIDE

Run	T, °K.	Effective time, sec.	Initial O_2, g.	Evap. loss, total g.	Residual O_2, g.	NiO evap., g.	Pressure, atm.
6	1438	6930	0.01424	0.01732	0.01381	0.00200	2.43×10^{-9}
5	1441	7001	.00759	.01160	.00722	.00173	2.09×10^{-9}
7	1495	2286	.01840	.01803	.01770	.00327	1.23×10^{-8}
4	1511	609	.00917	.00465	.00877	.00187	2.66×10^{-8}
Run 3 was lost through an accident							
2	1529	1340	.00921	.01139	.00837	.00392	2.72×10^{-8}
1	1566	759	.0044	.01893	.00289	.0070	8.51×10^{-8}

$$\left(\frac{F^\circ - H_0^\circ}{T}\right)_{\text{NiO solid}} = 84.360 - 0.415 \times 10^{-3}T - 31.523 \log T - (3465/T) + (1.46 \times 10^5/T^2) \quad (7)$$

For gaseous NiO we have used the equation

$$\left(\frac{F^\circ - H_0^\circ}{T}\right)_{\text{NiO gas}} = 3.5\,R - 3.5\,R \ln T - 1.5\,R \ln M - R \ln \mu - 2\,R \ln r_0 - 175.38 - R \ln q + R \ln (1 - e^{-ch\nu/kT}) \quad (8)^{28}$$

with ν set equal to 700 wave numbers,[29] r_0 set equal to 1.65×10^{-8} cm.,[30] and q set equal to 3.[31]

(28) The first term in this equation is the contribution to $(H^\circ - H_0^\circ/T)$ arising from translation and rotation; the succeeding five terms constitute the sum of translational and rotational entropies for a rigid rotator of molecular weight M, reduced mass μ and internuclear distance r_0 [Sackur, *Ann. Phys.*, **36**, 958 (1911); Tetrode, *ibid.*, **38**, 434 (1921); Ehrenfest and Trkal, *Proc. Acad. Sci. Amsterdam*, **23**, 162 (1920)] the seventh term is the electronic contribution to $(F^\circ - H_0^\circ)/T$ from the multiplicity of the ground state; and the final term is the contribution from an harmonic oscillator with the fundamental frequency ν (expressed in wave numbers). R, c, h and k have their usual meaning.

(29) Our estimate of 700 cm.$^{-1}$ for the fundamental frequency of NiO is an interpolation within the group of transition elements of which nickel is a member. In order of increasing atomic number the series runs: TiO, 1007; VO, 1011; CrO, 896; MnO, 840; FeO, —; CoO, —; NiO, (700 est.); CuO, 620 cm.$^{-1}$ [*cf.* Herzberg, "Molecular Spectra," I, Table 36, Prentice–Hall, New York, N. Y., 1939]. Among the monochlorides and the hydrides nickel fits regularly into position: (a) TiCl, 456; VCl, —; CrCl, —; MnCl, —; FeCl, 406; CoCl, 420; NiCl, 418; CuCl, 417; ZnCl, 390; (b) MnH, 1580; FeH, —; CoH, 1890; NiH, 1926; CuH, 1940. (In some instances—*e. g.*, FeCl—these frequencies may not represent the ground electronic state.)

(30) Our estimate of 1.65 Å. for the covalent bond in NiO vapor is based on values for the atomic radius of nickel in various of its covalent compounds. We further assume the bond to be double (*cf.* ref. 31).

Pauling ["The Nature of the Chemical Bond," The Cornell University Press, 1939, p. 232] makes an estimate of about 1.22 Å. for the covalent single bond radius of nickel. A recent reliable determination of r_0 in the vapor of NiH [Heimer, Dissertation, Stockholm, 1937; *cf.* Herzberg, *loc. cit.*] yields 1.487 Å. for the Ni-H bond. Taking the H covalent radius to be 0.30 ± 0.03 Å. (Pauling, *loc. cit.*, p. 158) this gives 1.19 ± 0.03 Å. for the nickel single bond radius, in good agreement with the X-ray measurements. Use of the factor 0.915 for the double bond–single bond ratio (Pauling, *loc. cit.*, p. 154) yields 1.09 Å. for the double bond radius of nickel, and 1.66 Å. for r_0 in NiO vapor. This lies within the limits imposed by the results of electron diffraction measurements on the vapor of $Ni(CO)_4$ [Brockway and Cross, *J. Chem. Phys.*, **3**, 828 (1935); *cf.* also Pauling, *loc. cit.*, p. 232, *et seq.*]. These yield 1.82 Å. for the Ni–C bond, which resonates between single bond and double bond character, and result in extremes of 1.53 Å. and 1.72 Å. for the Ni–O double bond, with the most probable value near the upper limit.

(31) Professor R. S. Mulliken (private communication) expresses the opinion that the ground state of NiO is probably $^3\Sigma^-$, resulting from either the configuration Ni $d\sigma d\pi^3 d\delta^4 s\sigma^2$; O $p\sigma\ p\pi^3$ or Ni $d\sigma^2 d\pi^3\ d\delta^4\ s\sigma$; O $p\sigma\ p\pi^3$, or a mixture, and that the Ni–O bond would be expected to exhibit properties similar to the double bond in molecular oxygen. The multiplicity (q) of the $^3\Sigma$ state would be 3. It is possible, though less likely that $^1\Sigma^+$ (with $q = 1$) would be more stable than $^3\Sigma^-$ (analogy to the possible situation in Se_2 and Te_2). Less probable multiplicities are 2, 5, 6 or 10.

The first two of these constants are necessarily estimates since no band spectra have been observed for nickel oxide. However, they are probably reliable to within 50 cm.$^{-1}$ in ν and to within 0.1 Å. in r_0. Combined errors of 50 cm.$^{-1}$ and 0.1 Å., respectively, would influence our calculations of ΔH_0° (Table VIII) by less than 600 calories in an absolute sense and would introduce a temperature trend into the supposed values of ΔH_0° of only 50 calories over the 130° experimental range. These are well within the limits of

TABLE VII

STANDARD FREE ENERGY FUNCTIONS OF NICKEL OXIDE (NiO) IN SOLID PHASE AND IN THE VAPOR (BASED ON THE SUPPOSITION THAT THE GROUND ELECTRONIC STATE OF NiO VAPOR IS $^3\Sigma$). CHANGE OF THE STANDARD FREE ENERGY FUNCTION IN EVAPORATION

T	$\left(\frac{F^\circ - H_0^\circ}{T}\right)_{\text{solid}}$	$\left(\frac{F^\circ - H_0^\circ}{T}\right)_{\text{vapor}}$	$\Delta\left(\frac{F^\circ - H_0^\circ}{T}\right)_{\text{evap.}}$
1000	−13.942	−57.420	−43.478
1100	−14.998	−58.195	−43.197
1200	−15.988	−58.907	−42.919
1300	−16.918	−59.567	−42.649
1400	−17.795	−60.183	−42.388
1500	−18.626	−60.763	−42.137
1600	−19.414	−61.306	−41.892
1700	−20.165	−61.815	−41.650
1800	−20.881	−62.292	−41.411
1900	−21.566	−62.745	−41.179
2000	−22.223	−63.182	−40.959

TABLE VIII

ΔH_0° FOR THE SUBLIMATION OF NICKEL OXIDE (NiO)

Run	T, °K.	$4.575 \log_{10} p$	ΔH_0° ($q = 3$)	ΔH_0° ($q = 1$)	ΔH° ($q = 10$)
6	1438	−39.41	117,489	*114,350*	*120,929*
5	1441	−39.71	118,156	*115,011*	*121,604*
7	1495	−36.16	117,070	*113,807*	*120,647*
4	1511	−34.66	115,997	*112,699*	*119,612*
2	1529	−34.61	117,233	*113,895*	*120,890*
1	1566	−32.35	116,386	*112,968*	*119,913*
Average ΔH_0° (±1000 cal.)			117,055	*113,789*	*120,635*

error imposed by the measurements of sublimation rates of nickel oxide, and would not alter their interpretation.

Values of the free energy function, computed by equation (7) for solid nickel oxide and by equation (8) for the vapor, are given in Table VII, together with $\Delta(F^\circ - H_0^\circ)/T$ for the sublimation process. The latter is well represented, empirically, by the equation

$$\left(\frac{F^\circ - H_0^\circ}{T}\right)_{\text{NiO (gas)}} - \left(\frac{F^\circ - H_0^\circ}{T}\right)_{\text{NiO (solid)}} = -46.656 + 3.508 \times 10^{-3}T - 3.30 \times 10^{-7}T^2 \quad (9)$$

Values for the sublimation heat at the absolute zero, based on $^3\Sigma^-$ as the probable ground state of nickel oxide vapor, are given in the fourth column of Table VIII. These are computed by combination of equations (2) and (9) with the experimental pressures recorded in Table VI.

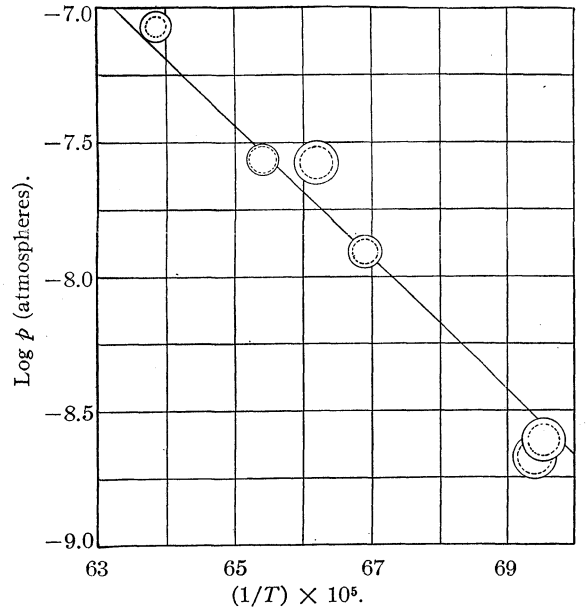


Fig. 2.—Vapor pressures of nickel oxide. The dimensions of the outer (solid line) circles are drawn to scale to represent approximate error limits. The inner (broken line) circles represent probable errors. The curve is constructed from equation (10).

Substitution of the average value for ΔH_0° (117,055) into equation (2), in combination with equation (9), leads to the vapor pressure equation

$$\log p \text{ (atmospheres)} = -\frac{25{,}586}{T} - 7.67 \times 10^{-4}T + 7.21 \times 10^{-8}T^2 + 10.198 \quad (10)$$

The fit with the individual experimental data is shown graphically in Fig. 2, in which the curve is constructed from equation (10). Approximate error *limits* of the individual data are represented by the dimensions of the outer (full line) circles and their *probable* errors by the inner (broken line) circles.[32]

Although 3 is the most likely value for q in equation (8) extreme limits of 1 and of 10 are not definitely excluded (*cf.* ref. 31). Accordingly, we include in Table VIII columns (italics) based on these extreme assignments. When allowance is made for the added small uncertainties from r_0 and from ν and from an experimental uncertainty of 1000 calories in the average of ΔH_0° for a single column, it is seen that the total uncertainty in ΔH_0° may attain 4 to 5 kilocalories as a limit. A "best" straight line drawn among the experimental points, as in graphic treatment by the Clausius-Clapeyron equation, yields about 127 kilocalories for ΔH_{1500°, which is equivalent to about 132 kilocalories for ΔH_0°. However, the slope of this line may be varied, within the limits of error of the data, by an amount that corresponds to nearly ±15 kilocalories in ΔH_0°. Hence, even with the possibility of a four kilocalorie error in the estimates of r_0, ν and of q the thermodynamic treatment represented in equations (2), (7) and (8) is markedly superior to treatment by the Clapeyron equation, for the purpose of smoothing up vapor pressure data, or of computing ΔH_0°.

Evidence against the Presence of Dissociation.—The preceding kinetic and thermodynamic treatment for nickel oxide is based on the supposition that sublimation as nickel oxide represents the only mechanism by which oxygen escapes from the oxide film during the process of evaporation. The good agreement of ΔH_0° among the several runs (Table VIII) substantiates this treatment. However, in view of the conflicting values reported in the literature for nickel oxide dissociation pressures[33] (some being higher, at 1500°,

(32) The error limits for NiO are considerably greater than for nickel (Fig. 1) due to the small evaporation losses of oxygen (on which the evaporation losses of NiO are based) and to the fact that these must be computed as differences between four weighings (each uncertain to ±0.02 mg. (*cf.* Table V). The error *limits* were arrived at by combining arithmetically the error from ±3° uncertainty in temperature with a 0.05 mg. probable error from accumulation of four weighing errors. The *probable* errors of the plotted points are computed from the usual probable error formula for addition or subtraction of chance errors, namely, P. E. = $\sqrt{\Sigma e^2}$, and make allowance for the chance that temperature and weighing errors may be of opposite sign.

(33) Foote and Smith, THIS JOURNAL, **30**, 1344 (1908); Pease and Cook, *ibid.*, **48**, 1199 (1926); Wohler and Balz, *Z. Elektrochem.*, **27**, 406 (1931); Skapsky and Dabrowsky, *ibid.*, **38**, 365 (1932); Kapustinsky and Shamovsky, *Z. anorg. allgem. Chem.*, **216**, 10 (1933). *Cf.* also Emmett and Schultz, THIS JOURNAL, **52**, 4268 (1930). Our own observation that free nickel readily passes through the oxide films (*cf.* Tables V and X) raises serious doubt as to the validity of the experimental method employed by Kapustinsky and Shamovsky.

TABLE IX
DISSOCIATION PRESSURES OF NiO

T, °K.	1440	1495	1511	1529	1566
p (mm. of O_2)	5.9×10^{-7}	2.5×10^{-6}	3.8×10^{-6}	5.6×10^{-6}	1.4×10^{-8}

than the residual gas pressure in our apparatus) we have given special consideration to the alternative mechanism of nickel oxide decomposition into nickel and free oxygen.

Direct evidence that dissociation was not taking place was provided by a micro-determination[34] of the gases pumped off continuously and collected, during one of the runs. No measurable trace of oxygen was present. Had decomposition into nickel and free oxygen been the evaporation mechanism the order of 0.5 cc. of oxygen (N. T. P.) would have been liberated. While some of this would unquestionably react with the fresh nickel film which formed on the walls of the cell (*cf. seq.*), it does not appear plausible that no trace would reach the pump, out of such a relatively large sample.

The conclusion to be drawn from this evidence is also confirmed by a calculation of dissociation pressures which can now be made from the thermodynamic data for nickel (Table II), for nickel oxide (Table VII), and that for oxygen[35] in conjunction with Roth's[36] thermochemical value of -58.9 kilocalories for the standard ΔH of formation of solid nickel oxide from its elements at 25°. These data yield the following oxygen pressures (Table IV) for dissociation at the respective temperatures of our runs.

Consideration of the ($O_2 = 2\,O$) equilibrium[35] at these temperatures and O_2 pressures yields the result that the partial pressures of monatomic oxygen are negligible in comparison.

The pressures in Table IX lie below the residual pressure of gas in our apparatus, with the possible exception of the 1566° run. Therefore, we can definitely eliminate dissociation for any of the runs in the lower range of temperature. Furthermore, if dissociation occurred at significant rate in either the 1566 or 1529° runs, these runs would have been attended with an abnormally high loss of oxygen and we would have computed correspondingly low values for ΔH_0°. Actually, no significant variation was observed among the values for ΔH_0° (*cf.* Table VIII). Thus we may conclude that dissociaton cannot have occurred with any of the runs by amounts that can be regarded as significant in the data.

Evaporation of Nickel.—It is interesting to observe that the evaporation of free nickel is almost as great as it would be in the absence of the oxide film and that there is little correlation between nickel evaporation and the film thickness. This is brought out in Table X. In general, it does appear that very thick films of oxide permit more rapid escape of nickel than do thin films. This may be the result of mechanical breakage of the film in the process of heating up the coated rings or in the escape of dissolved oxygen during evacuation.

TABLE X
EVAPORATION OF NICKEL THROUGH A FILM OF NiO

Run	T, °K.	Film thickness, Å.	Nickel evaporation, g. Calcd. for pure Ni	Obsd.	% of calcd.
6	1438	70,000	0.0149	0.0153	100 (+)
5	1441	38,000	.0161	.0099	61
7	1495	92,000	.0191	.0148	78
4	1511	46,000	.0072	.0028	39
2	1529	50,000	.0218	.0075	35
1	1566	21,000	.0265	.0119	45

Summary

Rates of evaporation of solid nickel have been measured between approximately 1300 and 1600°K., and the data employed to compute vapor pressures of the metal. The results obtained are in good agreement with thermodynamic requirements for the free energy of evaporation and yield 101,141 (±150) calories for the heat of sublimation at the absolute zero. The data yield the accurate vapor pressure equation, for solid nickel

$$\log p \text{ (atmospheres)} = -\frac{22{,}107}{T} - 1.31 \times 10^{-4} T + 7.869$$

Comparisons are made with earlier data by Jones, Langmuir and Mackay, and by Bryce, who measured evaporation rates from thin nickel filaments.

The accommodation coefficient for the condensation of nickel vapor on the equilibrium surface is unity within the experimental limits of accuracy and cannot lie below 0.75 as a lower limit.

Vapor pressures of nickel oxide (NiO) also have been determined, for the temperature interval 1440 to 1566°K., by measurement of the evapora-

(34) F. J. Norton and A. L. Marshall, *Trans. Am. Inst. Mining Met. Eng.*, **102**, 287 (1932); Langmuir, THIS JOURNAL, **35**, 105 (1913).

(35) H. L. Johnston and M. K. Walker, *ibid.*, **55**, 172, 187 (1933); *ibid.*, **57**, 682 (1935).

(36) Roth, *Z. angew. Chem.*, **42**, 981 (1929).

tion losses from oxide films coated on nickel rings. While less accurate than the data for nickel, the results are in agreement with the thermodynamic requirements for evaporation of nickel oxide, and yield 117,055 (±1000) calories for the heat of sublimation at the absolute zero. Allowance for some uncertainty in the ground state multiplicity of NiO vapor, and in molecular constants, increases the possible error limit by three to four kilocalories. The data yield the vapor pressure equation

$$\log p \text{ (atmospheres)} = -\frac{25{,}506}{T} - 7.67 \times 10^{-4}T + 7.21 \times 10^{-8}T^2 + 10.198$$

Absence of oxygen in the gases pumped from the sample during evaporation, and a comparison of the residual gas pressures in our apparatus with the dissociation pressures of NiO within the temperature range of our measurements, exclude any significant influence from NiO dissociation.

Evaporation of free nickel was little retarded by the presence of the oxide coatings ranging from 20,000 to 90,000 Å. in thickness.

Recent data on the heat capacity of nickel have been reviewed and values for the heat content, entropy and free energy function have been computed and tabulated. Tables of the free energy functions of NiO (solid) and NiO (vapor) are also included.

RECEIVED FEBRUARY 21, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, PURDUE UNIVERSITY]

The Vapor Pressures of Salt Solutions[1]

BY MAX F. BECHTOLD[2] AND ROY F. NEWTON

A convenient and accurate method for measuring the activities of water in salt solutions is very desirable in those cases in which it is difficult or impossible to obtain satisfactory measurements of the activities of the solute by electromotive force measurements. The method of Washburn and Heuse[3] modified by Gibson and Adams[4] and by Newton and Tippetts[5] appears to be quite promising, and has been further modified to increase both its accuracy and its convenience. Essentially the method consists of passing a gas successively through saturators containing pure water, an absorber, saturators containing the solution, and finally through a second absorber. Passing the same gas through both the pure water and the solution eliminates the need of measuring the gas. The vapor pressure of the solution can then be expressed simply in terms of the vapor pressure of pure water, the total pressure at each saturator, and the gain in weight of each absorber. In the older apparatus the pressure at the saturators varied, and it was necessary to read the pressures at frequent intervals during long runs in order to obtain reliable averages. The adaptation of relays for controlling the discharge pressure and the rate of passage of gas through the apparatus has made necessary only a single reading of each pressure. Slight condensation in the tubes connecting the saturators with the absorbers may produce serious uncertainties in the results, which has been obviated by enclosing the absorbers and connecting tubes in an air-bath just above the water-bath, maintained about five degrees higher than the latter, and at high humidity, thus preventing cooling due to evaporation at the point where the connecting tubes leave the water-bath. During preliminary adjustments the air-bath must be removed, and condensation may then occur in the connecting tubes. To avoid error due to collecting this condensate in the absorbers, a pair of "dummy" absorbers is connected in parallel with the weighed ones, and the gas is passed through them for about an hour after the air-bath has been adjusted. The establishment of steady flow conditions before the collection of water in the weighed absorbers also ensures that the same quantity of gas passes through both absorbers.

Apparatus and Materials

Measurements were made on solutions of barium chloride and of calcium chloride. The barium chloride solutions were prepared and analyzed as reported by Newton and Tippetts.[5] A sample of Mallinckrodt Analytical

(1) Based upon a thesis submitted by Max F. Bechtold to the Faculty of Purdue University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1939. Presented at the Boston meeting of the American Chemical Society, September, 1939.

(2) Present address: du Pont Experimental Station, Wilmington, Delaware.

(3) Washburn and Heuse, THIS JOURNAL, **37**, 309 (1915).

(4) Gibson and Adams, *ibid.*, **55**, 2679 (1933).

(5) Newton and Tippetts, *ibid.*, **58**, 280 (1936).

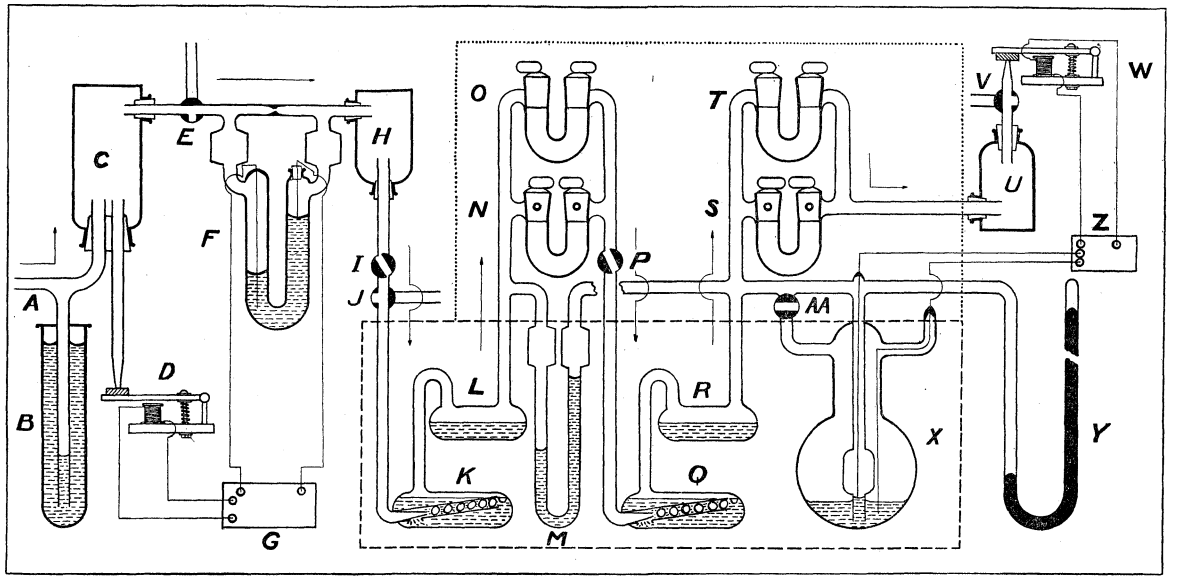


Fig. 1.

Reagent calcium chloride was found to contain only 0.12% of magnesium and alkali metal salts expressed as sulfates, and was judged sufficiently pure without recrystallization. The calcium chloride in the solutions was determined by adding a slight excess of sulfuric acid, evaporating, igniting, and weighing.

The final apparatus is shown diagrammatically in Fig. 1. The portion from A to J is a system for supplying the saturators with a stream of air at a uniform rate independent of atmospheric pressure and supply pressure. Air enters A at a rate in excess of that desired through the saturators. B acts as a safety valve which prevents the attainment of excessive pressures in case of accidental stoppage of the air stream. Flowmeter F maintains a constant rate through the saturators by controlling the action of magnetic valve D through the vacuum tube relay G. Dibutyl phthalate saturated with mercuric iodide is used as the manometer liquid in F because of its low density, negligible volatility and satisfactory electrical conductivity. Bottles C and H serve to smooth out pressure pulsations. The remainder of the apparatus is for the saturation of the air stream at a controlled temperature and pressure and for the absorption of water from it. The air stream passes into saturators K and L containing pure water, to absorber N or O, into saturators Q and R containing the solution being investigated, then through absorber S or T and out to the atmosphere. Throttling stopcocks I and P are necessary for satisfactory bubbling in the saturators. K and Q each represent a series of five similar saturators. It is necessary to place water in the first of the series Q because concentrated solutions crystallize in the jet of the bubbler and cause stoppage. The total pressures at L and R must be known in order to calculate the vapor pressure of the solution. The pressure at R is maintained constant within the accuracy of reading the barometer Y, by means of the regulator X which actuates the exhaust valve W through the relay Z. The conducting liquid used in X is the same as in F. The manometer M, which is filled with dibutyl phthalate, measures the difference in pressure between L and R. Previously it had been necessary to read M hourly because of change of porosity of the drying agent. This change is eliminated by using barium perchlorate in the left arm of each absorber and magnesium perchlorate in the right arm. The absorbers are completely refilled when the barium perchlorate is visibly wetted. The absence of clogging of the absorbers and the constant rate of gas flow make it unnecessary to read M more than once during a measurement. Only one reading of the barometer Y is required, whereas the hourly reading of a barometer and two manometers previously was necessary. The apparatus within the broken line is in a water-bath kept at 25, 35, or 45 ± 0.01°, while that within the dotted line is in an air-bath directly over the water surface. By the use of a small fan and a light bulb the air-bath was maintained about five degrees above the water-bath temperature and at about 85% humidity. These conditions prevent cooling the tubes which protrude from the water-bath. The stirring was such that no temperature difference between the bath around the upper saturators (K–L) and that around the lower ones (Q–R) could be detected by a Beckmann thermometer.

In places where flexibility is required, ends of glass tubing are joined by being butted together with neoprene tubing. Tests on these joints show no appreciable permeability to water vapor.

Procedure.—Assuming that the predetermined rate of flow has been set by adjusting the electrode in the right arm of F, air is started through A, and E is turned to connect C and F. The cocks of the "dummy" absorbers are opened, J is turned to connect H and K, and cock V is closed. When the pressure at R reaches a value not likely to be exceeded by the atmosphere, AA is closed and V is turned to connect U with the discharge tip controlled by W. After operating for some time, the air stream is diverted from the absorbers N and S to the

TABLE I

ACTIVITY OF WATER IN SOLUTIONS OF BARIUM CHLORIDE AND OF CALCIUM CHLORIDE

Molality	Activity at 25°	Probable error	Trials	Activity at 35°	Probable error	Trials	Activity at 45°	Probable error	Trials
				Barium chloride					
0.01017	0.99975	0.00009	7	.....	.....	...	.....	.....	..
.09505	.99608	.00004	5	.....	.....	...	.....	.....	..
.19087	.99151	.00006	4	0.99134	0.00012	4	0.99166	0.00008	5
.47231	.97866	.00007	12	.97830	.00005	4	.97834	.00011	7
.87460	.95774	.00008	4	.95831	.00010	6	.95874	.00016	10
1.23237	.93746	.00006	4	.93757	.00012	7	.93793	.00012	8
1.60010	.91483	.00011	5	.91460	.00008	4	.91493	.00006	7
				Calcium chloride					
0.3043	0.98633	0.00005	7	.....	.....	...	0.98705	0.00005	4
3.0335	.74583	.00010	6	0.74893	0.00006	6	.75256	.00029	5
7.0310	.30964	.00013	4	.32512	.00007	4	.34060	.00012	4

weighed absorbers O and T. The run is stopped by reversing all of the above operations.

Results

Measurements were made at 25, 35, and 45°, most of them on barium chloride, since comparison could be made with the activity calculated by the equations previously derived from electromotive force data.[5,6] The results are expressed in terms of the activity of water, assuming that

$$a_1 = p_1/p_0 \qquad (1)$$

and calculating p_1/p_0 by the equation

$$\frac{p_0 - p_1}{p_1} = \frac{m_0(B_0 - p_0) - m_1(B_1 - p_0)}{m_1 B_1} \qquad (2)$$

in which p_0 and p_1 are the vapor pressures of pure water and solution, m_0 and m_1 are the weights of water evaporated from pure water and from solution, and B_0 and B_1 are the total pressures at the ends of the saturators filled with pure water and with solution, respectively. Equations (1) and (2) will be strictly true only if the gaseous mixture is a perfect gas, but as previously pointed out[5] the activity calculated by (1) and (2) is much less sensitive to imperfection of the gas than is either (1) or (2) itself, and the a_1 so calculated is almost free of error due to imperfection of the gas.

As a check on the apparatus, $(p_0 - p_1)/p_1$ was determined with pure water in both sets of saturators. The average of ten runs, some performed at each temperature, is +0.00014, with a probable error of the mean of 0.00008.

The number of runs under each set of conditions was varied according to the agreement of the results. When they were very consistent, as few as four runs were made, but when the consistency was not so good, runs were continued until it was judged that the mean was reliable. The "probable error" of the mean is given merely as a crude measure of the consistency of the results, since for so few cases the usual formulas give only the order of magnitude of the probable error. On very dry days difficulty was experienced in getting reproducible weighings of the glass absorbers, and in spite of the precautions taken to obtain reproducible conditions on the glass surfaces, it is believed that a large part of the chance error is due to error in weighing. It may be noted in Table II that all the differences are positive, which seems to indicate a systematic difference of about 0.02% between the two sets of measurements. In the vapor pressure measurements, the gas always passed first through the pure water. Some slight imperfections in the apparatus may lead to a small systematic error which could undoubtedly be reduced by carrying out half of the measurements with the solution in the first set of saturators.

(6) A typographical error is present in each of equations (5) and (6) of reference (5). In equation (5) the term beginning 0.34444 should begin with 0.034444, and in equation (6) the term 0.1349 m should be 0.01349 m.

TABLE II

COMPARISON OF ACTIVITIES IN BARIUM CHLORIDE AT 25° BY INDEPENDENT METHODS

Molality	Activity from vapor pressure	Activity from e. m. f.	Difference
0.01017	0.99975	0.99950	0.00025
.09505	.99608	.99573	.00035
.19087	.99151	.99148	.00003
.47231	.97866	.97831	.00035
.87460	.95774	.95764	.00010
1.23237	.93746	.93739	.00007
1.60010	.91483	.91466	.00017

Summary

An automatically controlled apparatus has been constructed for the precise measurement of vapor pressures of solutions by the dynamic method,

and measurements have been made on aqueous solutions of barium chloride and of calcium chloride at 25, 35, and 45°. The activity of water in the barium chloride solutions changes only very slightly with temperature. The activity of water by vapor pressure measurement is in very good agreement with that calculated from electromotive force data, the maximum difference being 0.035%.

LAFAYETTE, INDIANA RECEIVED FEBRUARY 16, 1940

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

The Hydrogenation of Ethylene at Surfaces of Certain Oxides. I. Zinc Oxide and Zinc Chromite

BY JOHN F. WOODMAN AND HUGH S. TAYLOR

The measurement of the activity of oxides as catalysts for the hydrogenation of ethylene was originally undertaken in the expectation of checking the results of Vaughen and Lazier[1] on zinc oxide. These authors had reported negligible amounts of ethane resulting from the passage of hydrogen and ethylene over zinc oxide and other oxides at 400°. It was hoped that this absence of activity would be confirmed by a few preliminary runs, after which it was planned to investigate possible activity of zinc oxide for deuterium substitution, with a view to developing a convenient method for the production of deutero-ethylenes free from overwhelming amounts of the ethanes.

Unfortunately for this program, the preliminary runs showed that the ability of zinc oxide to catalyze the hydrogenation of the double bond in ethylene is far from negligible, even at temperatures much below those used by Vaughen and Lazier. Since the latter authors had made their results the basis of a rather inclusive hypothesis regarding the specificity of oxide catalysts for the hydrogenation of organic compounds, it seemed worth while to investigate the discrepancy more closely, and, if possible, to determine the factors responsible for it.

Lazier and Vaughen[2] themselves soon discovered the high activity of chromium oxide for the hydrogenation of the alkene bond and stated that this property set chromium oxide apart from other oxides. Turkevich[3] showed that ethylene introduced to a mixed manganese–chromium oxide catalyst at temperatures of 184° and above, underwent activated adsorption accompanied by decomposition, the products pumped off at higher temperatures being largely saturated hydrocarbons. This indicated activity for hydrogenation at lower temperatures than had previously been reported for chromium oxide catalysts. As a consequence of his observations, Turkevich pointed out that the specificity of oxide catalysts must be regarded as a matter of degree.

The discovery of the activity of zinc oxide and its thorough study led to test of the activity of zinc chromite. In a later paper[4] we report work on compounds of molybdenum, chosen because of the well-known industrial applications of the oxides and sulfides of this element in hydrogenation and cracking of oils and tars.

Experimental Details

Apparatus.—The apparatus used consisted of the following units: (a) a catalyst tube, at controlled temperature, isolated from the system by a trap kept at −78° to keep out mercury vapor; (b) a mercury manometer; (c) a pump system for evacuation; (d) burets for gas mixing and measurement; (e) purification trains for the gases.

Catalysts.—Zinc oxide was prepared from the oxalate by the method of Taylor and Sickman,[5] zinc chromite according to the method of Taylor and Strother.[6]

Gases.—Electrolytic hydrogen and tank ethylene, carefully purified, were employed.

Procedure.—Originally the gaseous mixtures were circulated by means of a Toepler pump over the catalyst in a closed cycle. The later determinations were made in a static system of conventional design with the catalyst at the bottom of a Pyrex cylinder of 35 mm. diameter and 250 cc. capacity.

Experimental Results

Zinc Chromite.—A mixture of 357 mm. of hydrogen and 198 mm. ethylene was admitted to 5.5 g. of catalyst at 21° and slowly raised in temperature to 215°, with frequent gas circulation.

(1) Vaughen and Lazier, THIS JOURNAL, **53**, 3719 (1931).
(2) Lazier and Vaughen, *ibid.*, **54**, 3080 (1932).
(3) Turkevich and Taylor, *ibid.*, **56**, 2254 (1934).
(4) Woodman, Taylor and Turkevich, *ibid.*, **62**, 1397 (1940).
(5) Taylor and Sickman, *ibid.*, **54**, 602 (1932).
(6) Taylor and Strother, *ibid.*, **56**, 586 (1934).

After thirty hours at 215° a decrease in pressure of 183 mm. was recorded. The final gas contained 53% C_2H_6, 44% H_2 and 2.2% olefins. A mixture of 222 mm. of H_2 and 403 mm. of C_2H_4 showed a slow pressure decrease at room temperature. After sixty hours at 250°, the gas contained 58% C_2H_6, 34.9% olefin and 7% H_2.

Zinc Oxide.—Qualitatively this catalyst behaved in the cyclic system at 200 and 300° like zinc chromite but was more active. With 333 mm. of H_2: 266 mm. of C_2H_4 at 200°, a pressure decrease of 256 mm. occurred in 2.5 hours, the product showing 77.2% C_2H_6, 20.4% H_2 and 2.2% olefin.

Static experiments showed that with evacuation at 450° of the air-ignited oxide the catalyst, weighing approximately 1 g., showed activity in the temperature range 0–80° with 56.5° (acetone vapor-bath) as a convenient working temperature. In successive experiments at 56.5°, with evacuation between experiments for intervals of two to twenty-one hours at the same temperature, a progressive decrease in velocity of reaction occurs, as shown by the following data for the period of half reaction, t_{50} = 19, 24, 35, 49, 68 minutes. In the succeeding experiment, after evacuation at 450° for twenty-nine hours, t_{50} fell once more to twenty minutes. Evacuation at 218° was not adequate to eliminate this progressive deterioration, as is shown by the following data for t_{50} at 56.6°, with intermediate evacuation at 218° for three hours: t_{50} = 74, 90, 100, 120, 140, 150 minutes.

Air activation of the surface by heating in a static system of air between each experiment to 450° for seventy-five minutes after evacuation of the catalyst for a few minutes at 56.5°, followed by a final three-hour evacuation at 450° immediately decreased the half-period of reaction of such deteriorated catalysts, as the following data with an initially inactive surface reveal: t_{50} = 170, 25, 23, 16, 19, 33, 44, 35, 29, 44, 44.

The decrease in reaction rate indicated by the final figures in the data just cited led to investigation of this secondary loss of activity. Since it would not appear to be due to inefficiency of removal of the primary agent of deterioration or its oxidation products, a test was made to ascertain whether the decrease might be due to strong adsorption of one of the components of the activating gas, most probably oxygen. This effect was tested thus: in a series of runs, activation with air for brief intervals at successively lower temperatures was tried, the conditions of evacuation, three hours at 450°, being maintained unchanged. The following data show that greater activity is obtained by using a shorter activation time. Further, lowering the activation temperature as far as 150° does not decrease the effectiveness of the activation. Activation with air at 56° is less effective.

TABLE I

INFLUENCE OF ACTIVATION CONDITIONS AT REACTION TEMPERATURE 56.5°

Activ. temp., °C.	450	450	400	345	305	250	200	150	56
Activ. time, min.	75	18	20	18	18	18	18	18	18
t_{50} min.	44	21	26	21	23	24	20	25	31

The increase in activity on decreasing the time and temperature of activation signifies that, with long activation, the primary effect of cleaning the surface, by removal of a deposit formed during reaction, is being partially nullified by a second effect, presumably oxygen adsorption, the resulting adsorbed layer not being completely removed by the evacuation procedure. To test this view, it was shown that admission of air, at 450°, for forty-five minutes to a surface of standard activity (t_{50} = 14–17 min.) followed by the standard evacuation at 450° for three hours gave a surface of lower activity, t_{50} = 29 minutes. The secondary film produced by air treatment is more tenaciously held than the primary poison, since evacuation at 250° of surfaces activated for eighteen minutes in air at 250° gave very slow reaction, t_{50} = 85 minutes. Evacuation, even at 450°, for less than twelve hours, does not clean an air activated surface completely. The highest and most reproducible activity was obtained by treating the catalyst with air at 250° for five to twenty minutes, then evacuating at 450° for twelve hours or longer.

Evacuation at 450° without activation with air was found to be undesirable practice since reduction of the catalyst by reactants may occur during the temperature rise after an experiment. Experiments at 218°, followed by evacuation at 450°, caused reduction of the surface and sublimation of metallic zinc. This does not occur after reaction at 56.5° if the system is thoroughly evacuated at 56° prior to raising the temperature to 450°.

The kinetics of the reaction on such surfaces, where the variability is great and not easily controlled, is difficult to study. A variation in the

H_2:C_2H_4 ratio from 5:1 to 3:1 ($p_{C_2H_4}$ = 50 mm.) gave no change in t_{50}. For H_2:C_2H_4 varying from 3:1 to 1:1 (for p_{H_2} = 160 mm.) the half-life varied from twenty-two to seventy-one minutes, and calculation from the initial slopes of the rate curves results in a dependence on the 0.1 power of the ethylene pressure. For equimolar mixtures with total pressures of 320 and 120 mm. the half-lives were seventy-one and forty minutes. Addition of 26 mm. of ethane to a 3:1 H_2:C_2H_4 mixture, $P_{C_2H_4}$ = 52 mm., did not change the half-life. Within these limits the reaction velocity appears to be independent of the reactant pressures.[7] The order of magnitude of the apparent activation energy of the reaction was determined, from two pairs of runs at 39 and 56°, as ~ 18 kcal.

To study the influence of water vapor, experiments were carried out at 56 and at 400°, the latter being the temperature used by Vaughen and Lazier. Water vapor is known to be a strong reversible poison for zinc oxide catalysts[5,8] and its effect on the hydrogenation of ethylene is of interest because the experiments of Vaughen and Lazier, which failed to detect any activity in this reaction, were carried out with moist gases stored over salt solution. At 56° a hydrogen–ethylene mixture containing 3% water vapor or 7×10^{-5} moles per gram of catalyst, required a half period of reaction equal to seventy-five minutes, or threefold the rate for dry gases. When the catalyst at 56° was equilibrated with water vapor from ice at 0° for two hours, the standard 3 hydrogen:1 ethylene mixture showed only a change of 1 mm. pressure in fifteen minutes. The catalyst was completely inactive.

At 400°, after the standard air activation and evacuation, the % reaction in fifteen minutes of a $3H_2$:$1C_2H_4$ mixture was negligible with 3.7 and 2% of water vapor in the gas, whereas the dry gas showed 72% reaction in the same interval. The 2% of water vapor present in the experiment corresponds to about 1.9 cc. at N. T. P. on the gram of catalyst used. Vaughen and Lazier used twenty grams of catalyst over which they several times passed samples of six to seven liters of gas stored over saturated salt solution. Thus, after the passage of 2.5 liters of gas, their catalyst would have been in contact with water vapor sufficient to stop reaction on our catalyst even if their technique had eliminated water vapor from the catalyst surface initially. Their failure to detect significant activity is thus completely explained. The greater effect of adsorbed water vapor at 400° compared to that at 56° is consistent with the known high temperature activated adsorption of water vapor on zinc oxide.[5]

Hydrogenation at 218° produced much more rapid decreases in velocity in successive runs; after three runs the velocity became almost negligible. Subsequent evacuation at 450° brought a tremendous increase in activity, to such an extent that diffusion became the rate-determining step, with t_{50} at 218° of the order of three minutes.

The evacuation process following reaction at 218° caused a grayish film of metal to appear on the cold walls of the reaction vessel, the deposit increasing with successive evacuations following later runs at 218°. The deposit could be sublimed. When the tube was heated after admission of air the color of the film changed to white. The film was evidently metallic zinc formed by reduction of the oxide surface by the reaction mixture at 218° or during the evacuation. Evacuation at 450° before access of the hydrogen–ethylene mixture produced no such deposit. The zinc was therefore not formed by thermal dissociation.

Pretreatment with 25 mm. of hydrogen for thirty minutes at 56° caused the adsorption of about 0.1 cc. at S. T. P. A mixture of hydrogen and ethylene added to make the total ratio a $3H_2$:$1C_2H_4$ mixture reacted slightly more slowly than normal. Exposure to hydrogen at 80° and 1 atm. pressure for five hours, with evacuation at 56° for fifteen minutes before the experiment, gave a retardation of the same order. Treatment with hydrogen at 218° turned the catalyst gray and the succeeding run at 56° after evacuation for fifteen minutes at 56° was very much slower. The change in color is a definite indication of reduction.

An atmosphere of hydrogen in contact with the catalyst at 218° for five hours changed the color to gray. After fifteen minutes of evacuation at 56° a run at this latter temperature showed very great retardation. Reduction of bulk zinc oxide by hydrogen has been shown not to occur below about 310°.[9] Reduction of active zinc oxide catalysts by hydrogen at lower temperatures has frequently been observed in this Laboratory[5,8,10]

(7) *Cf.* Pease and Stewart, THIS JOURNAL, **47**, 2763 (1925).
(8) Burwell and Taylor, *ibid.*, **58**, 1753 (1936).
(9) St. John, *J. Phys. Chem.*, **33**, 1438 (1929); Schacherl, *Gazz. chim. ital.*, **62**, 839 (1932).
(10) Taylor and Kistiakowsky, THIS JOURNAL, **49**, 2468 (1927).

and the effect seems to be enhanced by hydrocarbons.[11]

Ethylene at a pressure of 320 mm. in contact with 5 g. of catalyst at 218° gave a pressure decrease of 53 mm. in one hundred hours. The gaseous product was completely condensable in liquid air, indicating that polymerization had taken place with no significant formation of hydrogen or methane. At 445°, 600 mm. of ethylene on the same catalyst gave first a rapid absorption of gas to 474 mm. in two hours followed by a slow pressure increase to 504 mm. in ninety hours. From 77 cc. of ethylene initially present, 11 cc. of hydrogen and 11 cc. of methane were recovered. Polymeric products also were formed. The ability of zinc oxide slowly to attack both C–H and C–C bonds at 445° is thus demonstrated.

General Discussion

Lazier and Vaughen[2] assumed a specific capacity in chromium oxide for the activation of alkenes leading to their hydrogenation, and the absence of such capacity in other difficultly reducible oxides. The accumulated chain of evidence, of which this article furnishes the latest link, shows definitely that this assumption is not in agreement with the facts now available.

Howard[12] observed that on chromium oxide at 218°, adsorbed hydrogen reacted readily with ethylene. Turkevich[3] found ethylene activated by adsorption on manganese–chromium oxides at 184°, and recoverable largely as ethane. The present work shows that, already at 56°, zinc oxide is activating ethylene for hydrogenation, and moreover suggests that, even at this temperature, there is activation of specific bonds leading to the formation of a hydrocarbon deposit which poisons the active centers. That this deposit is actually of hydrocarbon origin, and is not merely adsorbed hydrogen, is attested by its accumulation in successive runs, contrary to what one would expect from the known behavior of hydrogen, and by the failure to detect an inhibitory effect of hydrogen present in the reaction mixture.

With rising temperature, the parallelism in the cases of chromium oxide, manganese–chromium oxides, and zinc oxide is complete. On the last catalyst, hydrogenation is rapid at 218°, and activation of specific bonds is clearly established by the disappearance of ethylene alone in contact with the catalyst, forming probably $(C_2H_4)_n$, but no permanent gases. At higher temperatures, both C–C and C–H bonds are broken, with formation of methane and hydrogen, and deposition of carbon. These results for zinc oxide over the range from room temperature to 444° are entirely analogous, at the higher temperatures, to the behavior of chromium oxide,[12] and manganese–chromium oxides,[3] no attempt having been made, on these catalysts, to test the possibility of hydrogenation at lower temperatures. It is even more interesting that the behavior of zinc oxide parallels that shown by Morikawa, Trenner and Taylor[13] to be characteristic of nickel in the temperature range from −78° to about +130°.

(11) Smith and Taylor, THIS JOURNAL, **60**, 362 (1938).

(12) Howard and Taylor, *ibid.*, **56**, 2259 (1934).

(13) Morikawa, Trenner and Taylor, *ibid.*, **59**, 1103 (1937).

Summary

1. Zinc oxide and zinc chromite have been shown to act as catalysts for the hydrogenation of ethylene with measurable velocity at and above room temperature. At 56° the reaction velocity on zinc oxide has been shown to be independent of hydrogen, ethylene and ethane partial pressures within a range of variation of these quantities.

2. On zinc oxide at 56° the number of active centers decreases because of the deposition of some substance probably arising from very slow polymerization or decomposition of ethylene at the surface. This poison can be oxidized by air at 150° and above, and the products removed by long pumping at 450°.

3. There is some evidence that oxygen is strongly adsorbed on the active centers of zinc oxide at 150° and above.

4. Reduction of zinc oxide to metallic zinc by the reaction mixture does not take place at 56°, but does so at 218° and above. The reducing effect of hydrogen alone at 218° has been confirmed.

5. Ethylene has been shown to polymerize slowly on zinc oxide at 218°, without appreciable formation of permanent gases. At 445°, polymerization is rapid, but accompanied by the formation of considerable amounts of hydrogen and methane.

6. Small amounts of water vapor have been shown to poison the surface of zinc oxide completely at 56° and even at 400°. This effect is responsible for the failure of Vaughen and Lazier[1] to observe the activity of this catalyst with their experimental procedure.

PRINCETON, NEW JERSEY RECEIVED MARCH 6, 1940

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

The Hydrogenation of Ethylene at Surfaces of Certain Oxides. II. Molybdenum Oxide Compounds

BY JOHN F. WOODMAN, HUGH S. TAYLOR AND JOHN TURKEVICH

Following the study of the activity of zinc oxide and zinc chromite surfaces described in the preceding paper,[1] a series of experiments was carried out to test the activity of some molybdenum compounds, in view of the well-known industrial applications of the oxides and sulfides of this element in hydrogenation and cracking of oils and tars. Catalytic masses were prepared by decomposition and reduction of ammonium phosphomolybdate, ammonium paramolybdate, and ammonium nickel molybdate. Suspicion of the presence of metallic nickel in extremely active catalysts produced by reduction of the nickel compounds suggested tests of the efficiency of hydrogen sulfide as a poison for these surfaces and measurements of the magnetic susceptibilities of the materials.

Experimental Details

Apparatus and Procedure.—The catalytic system was the same as that used in the static experiments on zinc oxide.[1]

The magnetic susceptibilities were determined by the method of Gouy.[2] Measurements were carried out with magnetic fields up to about 4800 gausses, the magnet current being increased from zero to 12 amp. in steps of about 2 amp., then reduced again to zero in the same manner, with the change in weight of the sample determined at each step. For purposes of calculation, the results were plotted against current and values taken from the smooth curve at intervals of 2 amp. The relationship between current and field strength was established by calibration with Mohr salt, for which χ, the specific susceptibility, was taken as 32.1×10^{-6} cgsm. unit at 22°.[3]

The finely divided samples were contained in uniform 5 mm. Pyrex tubes, each filled to a depth of 12.2 cm. Reduced samples were filled into the tubes under vacuum and sealed off without access to air. Measurements were corrected for the small diamagnetic effect of the tubes.

During measurements the sample tube hung freely in a Pyrex jacket through which dry nitrogen gas had been passed for one-half to one hour.

Only the measurements at room temperature are reported; others at 0, −80 and −190° gave similar results.

Materials.—Ammonium phosphomolybdate, $3(NH_4)_2O \cdot P_2O_5 \cdot 24MoO_3 \cdot 6H_2O$, was prepared following the analytical procedure.[4] The yellow product was dried at 120°.

Molybdenum oxide was prepared by heating ammonium paramolybdate to 300° in a current of air until the off-gas gave no test for ammonia.

Ammonium nickel molybdate was prepared by dissolving 145 g. of ammonium paramolybdate in one liter of water, and adding the filtered solution to a solution of 27 g. of nickel nitrate hexahydrate in 100 cc. of water. The whole was heated to boiling, with mechanical stirring, while precipitation took place. Next, the solution was diluted with water to three liters, cooled, and allowed to settle. The slightly greenish supernatant liquid was decanted, and the precipitate stirred once with three liters of water containing 25 g. of ammonium nitrate. It was then filtered with suction, and washed with 100 cc. of water. The bluish, finely crystalline product was dried overnight at 125°. From this product all the catalysts containing nickel were prepared as subsequently noted. The most probable formula for the preparation, according to Barbieri,[5] is $(NH_4)_4H_6[Ni(MoO_4)_6] \cdot 5H_2O$.

Hydrogen sulfide was synthesized from hydrogen and molten sulfur at 350°.

Results and Discussion

Phosphomolybdate and Molybdenum Oxide Catalysts.—A catalyst from 1.5 g. of ammonium phosphomolybdate (B), heated for eight hours in a current of dry air, evacuated for thirty-six hours (BI) and then treated with hydrogen for nineteen hours, followed by a further evacuation, all at 300°, changed progressively from mustard yellow, through light green to black, after reduction. The preparation (BII) failed to show significant activity in catalyzing the reaction of a 3:1 mixture of hydrogen and ethylene below 256°.

A preparation ignited in an air stream at 475° for six hours, then reduced with hydrogen at 450–475° for eight hours, was similarly inactive at 256°, the half-life value, t_{50}, being about two and a half hours. A preparation of this nature has been shown by Kingman[6] to be an excellent catalyst for the reduction of phenol at 280–350°.

Ammonium paramolybdate decomposed at 300°, evacuated at 450° and reduced for eight hours at 300° gave on evacuation a black catalyst mass. It showed no activity for ethylene hydrogenation at 256° nor was its activity increased by further reduction at 450°.

Nickel Molybdate Catalysts.—A 1.5-g. sample of ammonium nickel molybdate (A) was heated

(1) Woodman and Taylor, THIS JOURNAL, **62**, 1393 (1940).

(2) Gouy, *Compt. rend.*, **109**, 935 (1889); see also Klemm, "Magnetochemie," Leipzig, 1936, pp. 50–52.

(3) Jackson, *Phil. Trans. Roy. Soc.* (London), **A224**, 1 (1923).

(4) Treadwell and Hall, "Analytical Chemistry," 7th ed., Vol. II, p. 382.

(5) Barbieri, *Atti accad. Lincei*, [5] **23**, II, 357 (1914).

(6) Kingman, *Trans. Faraday Soc.*, **33**, 784 (1937).

slowly in a dry air stream to 300° and kept there for nine hours while ammonia was evolved. The tube was then cooled, evacuated, and the air stream replaced by pure hydrogen for four hours. During the succeeding twenty hours a stationary hydrogen atmosphere caused further reduction. The catalyst was then evacuated for six and a half hours at 350°, further reduced at 305° for fifteen hours, and then thoroughly evacuated at 350°. The product (AII) was black. Its activity was very high, a half-life of three minutes being recorded at −80° for a $3H_2$:$1C_2H_4$ mixture. The rate was not increased by raising the temperature; the observed rate of change of pressure was determined by diffusion processes.

Catalyst masses (AI) prepared as above but without the hydrogen reduction were olive-green to gray in color. Evacuation at 350° for thirteen hours caused a color change to blue, evidently with formation of a lower oxide of molybdenum. This material showed no hydrogenation activity at 0, 100, 156 and 218°, even though before each run the surface was left in contact with hydrogen for eight hours at a temperature five to ten degrees higher than the operating temperature. Treatment with hydrogen at 270° for six hours caused water formation and the catalyst became black. Its activity was then similar to that of the reduced catalyst already discussed. The reduction of a component of the catalyst, occurring at 270–300°, is thus essential to its activity in ethylene hydrogenation.

That the high activity of the reduced nickel–molybdenum oxide catalysts was due to the presence of metallic nickel highly dispersed through the molybdenum oxide was indicated by three different lines of approach. Measurements of the magnetic susceptibility, discussed in the next section, gave an estimate of the amount of nickel present. This estimate was in agreement with measurements of the hydrogen sulfide required to poison the catalysts completely for hydrogenation. The inactivity of the other molybdenum oxide preparations not containing reducible metals discussed above, afforded indirectly a third corroboration.

Magnetic Measurements.—Values of χ, the specific susceptibility, calculated for samples of the nickel–molybdenum oxide compounds (A) which had undergone the various treatments described, are contained in Table I. For comparison, values for some preparations from ammonium phosphomolybdate (B) are included.

The striking feature of this table is the decrease in susceptibility with increasing field strength which occurs in the case of the reduced samples prepared from ammonium nickel molybdate. This behavior is characteristic of ferromagnetic substances. Its occurrence in the present instance can only indicate that under the conditions of preparation of these samples, some of the nickel present became reduced to the metal.

If we make the plausible assumption that the susceptibilities of the various phases present are additive, it is possible to calculate approximately the percentage of the total nickel present as metal after the various treatments. The additive relationship is

$$(m_1 + m_2)\,\chi = m_1\chi_1 + m_2\chi_2 \qquad (1)$$

where m_1 is the mass of the ferromagnetic material, χ_1 its specific susceptibility, m_2 and χ_2 are the corresponding quantities for the remaining, non-ferromagnetic material, and χ is the observed susceptibility of the sample. For χ_1, we may take the values for pure metallic nickel at room temperature,[7] and we know $(m_1 + m_2)$ and χ from the measurement at the same temperature. It is then possible to set up an equation of the form of (1) for each field strength. Solution of these equations simultaneously gives the approximate weight of nickel present in each sample.

Assuming the composition of the decomposed and reduced samples to be closely represented by the formula $2NiO{\cdot}6Mo_2O_3$, the calculated percentage of the total nickel present which has been reduced to the metal is shown in the last column of Table I. These values are of course to be considered as indicative only of order of magnitude, and as such are not significantly changed by selection of other formulas.

Poisoning with Hydrogen Sulfide.—Two catalysts corresponding to AII of Table I were tested for resistance to hydrogen sulfide by adding increasing amounts of this gas to the reaction mixtures in successive runs. In each case a reproducible minimum of hydrogen sulfide was found to be required in any single run to cause complete cessation of reaction at −80°. The poison was apparently completely removed by evacuation at 350° between runs, and the series of runs with increasing amounts of the sulfur compound could be repeated, with no observable retardation until the critical amount was present. We attribute this unusual behavior on poisoning to the fact that

(7) "International Critical Tables," Vol. VI. p. 403.

TABLE I

MAGNETIC SUSCEPTIBILITIES OF MOLYBDENUM OXIDE COMPOUNDS

Material[a]	T, °C.	Magnet current, amp.	$\chi \times 10^6$ obsd.	% Ni reduced[b]
A	27	2–12	(4.3)[c]	0
AI	23	2	367	
		4	209	
		6	147	~10
		8	119	
		10	102	
		12	93	
AII	21	2–12	(5.9)[c]	0
AIII	24	2	1523	
		4	750	>30
		6	549	
		8	424	
B	26	2–12	(0 ± 1)[d]	
BI	24	2–12	(~0.1)[d]	
BII	26	2–12	(~0.2)[d]	

[a] Catalyst A, ammonium nickel molybdate; B, ammonium phosphomolybdate. I, decomposed at 300°; II, decomposed at 300°, reduced at 300°; III, decomposed at 475°, reduced at 475° for twelve hours. [b] % total Ni present as metal. [c] These figures represent the mean of measurements at each field strength, the values differing by <5%, and showing no trend. [d] These susceptibilities were too low for accurate measurement with our apparatus.

reaction was immeasurably rapid at −80° when *any* metallic nickel was present.

Table II compares the results of the hydrogen sulfide poisoning with those of the magnetic measurements, on corresponding samples.

TABLE II

METALLIC Ni IN NICKEL–MOLYBDENUM OXIDE CATALYST REDUCED AT 300°, BY MAGNETIC MEASUREMENTS AND H_2S POISONING

Catalyst	*a*	*b*
Wt., g.	1.25	0.64
Total moles Ni, calcd.	11×10^{-4}	5×10^{-4}
Moles Ni metal, from χ	11×10^{-5}	5×10^{-5}
Moles H_2S to poison	12×10^{-5}	4×10^{-5}

Ogden[8] has measured the adsorption of hydrogen by material prepared in essentially the same way as that described in this section and found it to differ entirely from the adsorption characteristic of metallic nickel. The preparation showed no observable hydrogen adsorption from −78 to +110°, whereas nickel shows its maximum adsorptive capacity at 0°. His failure to detect adsorption characteristic of nickel is doubtless due to the very small amount of the metal present.

It is apparent from the results noted above that the activity of these nickel–molybdenum oxide structures is a function of their content of metallic nickel; and that, lacking reduction sufficient to produce the metal, such materials resemble other molybdenum oxide structures not containing nickel or any reducible metal, in being ineffective as catalysts for ethylene hydrogenation below 250°. It is striking that these molybdenum compounds fail to show activity comparable to that of zinc oxide, which hitherto had not been classed among the surfaces on which hydrocarbon reactions might be secured.

Summary

1. A catalyst prepared by decomposition and reduction of ammonium nickel molybdate at 300° is active at −80° in the hydrogenation of ethylene. Magnetic susceptibility measurements, together with poisoning experiments using hydrogen sulfide, have suggested that this activity is due to metallic nickel, very highly dispersed.

2. Catalysts prepared from ammonium phosphomolybdate and ammonium paramolybdate have shown negligible activity for ethylene hydrogenation below 256°.

PRINCETON, NEW JERSEY RECEIVED MARCH 6, 1940

(8) G. Ogden, Master's Thesis, Manchester, 1932.

[CONTRIBUTION FROM THE RESEARCH DEPARTMENT, CALCO CHEMICAL DIVISION, AMERICAN CYANAMID COMPANY]

Chemical Constitution and Reactivity. I. Phenyldiazonium Chloride and its Mono Substituted Derivatives

BY M. L. CROSSLEY, R. H. KIENLE AND C. H. BENBROOK

In this investigation an attempt has been made to throw some light on the relationship between chemical constitution and reactivity by making an exhaustive study of the reactions which occur when aromatic diazo compounds decompose in aqueous solutions. As a first step an accurate, simple and automatic apparatus was designed for measuring and recording evolved nitrogen.[1] By use of this apparatus, aqueous solutions of phenyldiazonium chloride,[2] and twenty-four of its mono substituted derivatives have been investigated.

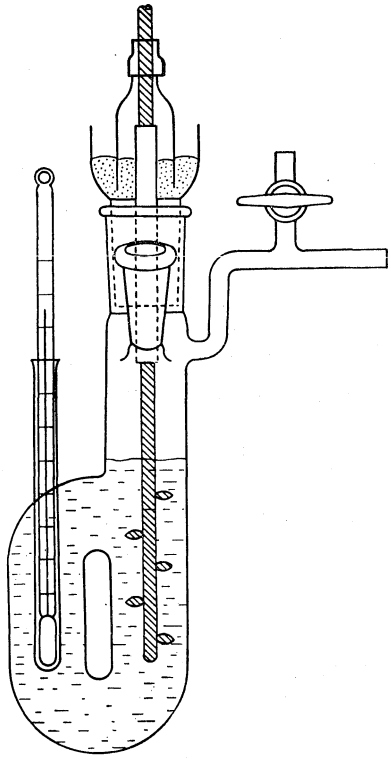


Fig. 1.—Reaction cell.

The experiments were carried out at constant temperature, within ±0.05°, in the dark in an 80-cc. glass cell of special construction, Fig. 1, equipped with an efficient stirrer to prevent supersaturation of the solution with nitrogen. The volume of the gas evolved from the reaction cell was continuously measured and recorded by means of the previously described apparatus.[1]

Effect of Temperature.—Freshly distilled aniline was diazotized at 0° in aqueous solution, using 2.2 molar equivalents of hydrochloric acid and 1.0 molar equivalent of sodium nitrite. The solution was diluted to 0.1 molar concentration with ice water, immediately added to the reaction cell and brought to the experimental temperature. The rate of decomposition was determined over a wide temperature range. The values of the reaction velocity constants are given in Table I. The accuracy of the method of measurement has been described previously.[1]

TABLE I

EFFECT OF TEMPERATURE ON THE REACTION VELOCITY OF DECOMPOSITION OF PHENYLDIAZONIUM CHLORIDE SOLUTION OF CONCN. 0.1 MOLAR AND *p*H 1.6–1.8

Temp., °C.	k (sec.$^{-1}$) × 10^5
5	0.15
25	4.10
35.2	20.0
50	140.0

The data in Table I are linear when plotted as ln k *vs.* $1/T$, thus satisfying the Arrhenius equation

$$\ln k = \ln Z - (E/RT) \qquad (1)$$

The heat of activation for the reaction has been calculated from these data and found to be 27,200 cal./g. mole.

Effect of Concentration.—The effect of concentration on the reaction velocity was studied over a very wide range. In this series the solutions were prepared from crystalline phenyldiazonium chloride, synthesized as follows.

Aniline hydrochloride, 6.475 g., was suspended in 25 cc. of glacial acetic acid and cooled in an ice-bath to 10°; 10 cc. of octyl nitrite was added rapidly and the solution simultaneously cooled externally to about 5°. The solution was carefully examined for any undissolved and unreacted particles of aniline hydrochloride and these were broken up carefully. The solution was spotted against 5% sodium carbonate solution, and octyl nitrite was added dropwise as long as the spot test was red. As much as 15 cc. of octyl nitrite was necessary in some preparations. When the diazotization was complete, 125 cc. of ether was added in a steady stream, whereupon the product precipitated out as an oil. This was allowed to settle for two minutes and the excess ether decanted until there remained a volume of ether approximately equal to that of the oily precipitate. Then, 200 cc. of acetone was added as rapidly as possible and the solution stirred vigorously, whereupon the product came out as a thick slurry of

(1) Crossley, Kienle and Benbrook, *Ind. Eng. Chem., Anal. Ed.*, **12**, 216 (1940).

(2) In this paper, the term "phenyldiazonium chloride" will be used rather than phenyldiazochloride, although it is recognized that the nitrogens may be tri-valent under some of the conditions imposed.

coarse crystals. The product was filtered, washed by resuspension twice in acetone and twice in ether. It was dried in air until free of ether and then in a desiccator until free of moisture. The yield was 3.5 g. All reasonable safety precautions were taken because of the highly explosive nature of the product.

The product was stored in a desiccator. In the dry state, no measurable decomposition occurred. The evolved nitrogen per gram remained constant. Each aliquot was weighed out and dissolved immediately prior to use.

In order to justify the comparison of data obtained by use of crystalline diazonium chloride with those obtained by use of diazonium chloride solutions prepared by direct diazotization, two decomposition experiments, identical except as regards the method of preparation, were run. No difference in the rate data was found.

Separate experiments were carried out at concentrations ranging from a water–diazo ratio of 1280:1 (moles) to an extremely concentrated solution wherein the ratio was 2.36:1 (moles). It was observed that for all concentration ratios the reaction followed the first order law. Data showing both the mono- and bimolecular treatments of the most concentrated solution investigated illustrate this point (Fig. 2). The reaction, therefore, appears to be truly monomolecular.

The principal reaction products in the decomposition of phenyldiazonium chloride in water are usually considered to be phenol, nitrogen and hydrochloric acid. By analysis of the residues in the concentration series of experiments, it was found however, that the percentage yield of phenol is a function of the dilution. In the most concentrated experiments carried out, where the water–diazo ratio was 2.36:1 (moles), the percentage yield of phenol was 24.3%. On the other hand, in the most dilute experiment, the corresponding yield of phenol was 95.2%.

The reaction velocity constants and phenol yield obtained for the various concentrations studied are given in Table II.

An attempt was made to determine qualitatively what products other than phenol are present after decomposition has occurred. In the concentrated solutions monochlorobenzene, benzene, and biphenyl were identified, monochlorobenzene appearing in greatest quantity. The formation of monochlorobenzene has been observed by Hantzsch.[3]

TABLE II

EFFECT OF CONCENTRATION ON THE REACTION VELOCITY CONSTANT AND YIELD OF PHENOL IN DECOMPOSITION OF PHENYLDIAZONIUM CHLORIDE SOLUTIONS, TEMP. 35°

Moles H_2O/moles diazo	k (sec.$^{-1}$) $\times 10^5$	% yield of phenol
2.36	26.2	24.3
3.11	26.8	30.0
3.54	25.6	27.1
3.94	26.7	31.4
7.93	..	37.0
11.89	25.3	40.0
23.80	24.5	48.7
31.70	23.9	58.5
47.58	23.4	59.3
79.30	21.9	78.0
158.60	21.2	88.0
317.20	..	90.8
634.40	..	94.6
1268.00	19.2	95.2

Deuterium Oxide as Solvent.—Two runs were made under identical conditions except that in the first run the diazonium chloride was dissolved in water, whereas in the second run the solvent was deuterium oxide. The reaction velocity constants were essentially the same, *i. e.*, 0.00025 sec.$^{-1}$ and 0.00024 sec.$^{-1}$, respectively.

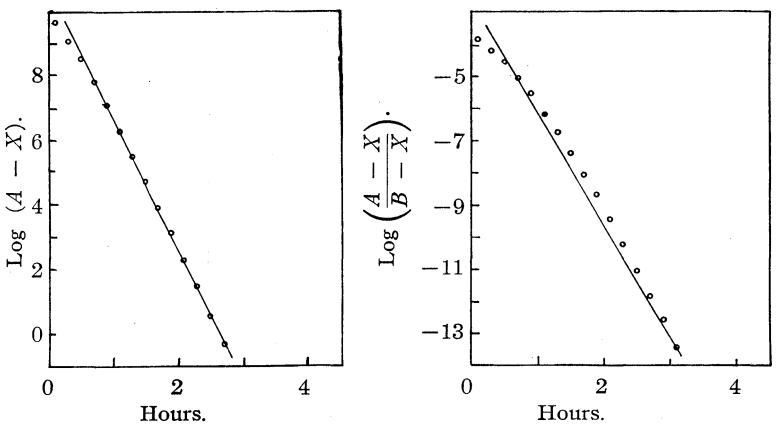


Fig. 2.—Comparison of unimolecular and bimolecular plots. Ratio of diazo to water 1:2.36 moles.

Effect of *p*H on the Reaction.—A series of experiments was run in which phenyldiazonium chloride was dissolved in different strengths of concentrated hydrochloric acid. In changing the normality of the hydrochloric acid from 0.1 to 12 *N*, only a slight change in the value of the reaction velocity constant is noticed (see Table III). It is interesting to note that the change in

(3) Hantzsch, *Ber.*, **33**, 2534 (1900).

reaction velocity is small even though Hantzsch[3] has found that in concentrated hydrochloric acid solution the yield of monochlorobenzene increases to 60%.

TABLE III

EFFECT OF ACID CONCENTRATION ON THE REACTION VELOCITY CONSTANT IN DECOMPOSITION OF PHENYLDIAZONIUM CHLORIDE SOLUTION, 0.1 MOLAR, TEMP. 35°

HCl concn., N	k (sec.$^{-1}$) $\times 10^5$
0.1	20.0
5.0	23.5
10.0	24.1
12.0	22.6

Several solutions of phenyldiazonium chloride were brought to different pH values by the addition of sodium hydroxide solution. Each sample was held at a temperature of 35°. When the pH was brought to a value of 11.2 (Fig. 3), it dropped within a period of forty minutes to a pH of 2.

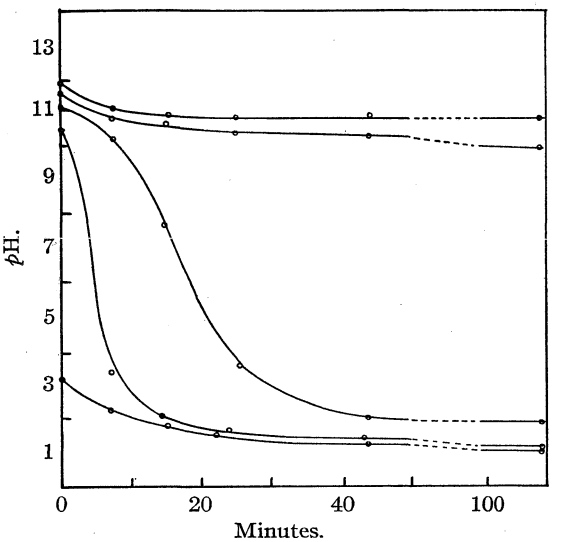


Fig. 3.—pH *vs.* time plot, phenyl diazo chloride solution, T = 35°, concn. = 0.1 molar.

However, when the original pH was 11.6 or more, the pH value remained above 10. This series was followed by another in which buffered samples were studied at various pH's to cover the range 3 to 11.8. The data obtained showing the percentage nitrogen evolved, together with the pH changes which occur in spite of the buffering, are given in Fig. 4.

Mono-substituted Derivatives of Phenyldiazonium Chloride.—A temperature study was made on the ortho, meta, and para methyl, methoxy, phenyl, hydroxy, chloro, carboxy, sulfo, and nitro phenyldiazonium chlorides. The amines from which the diazonium salts were prepared were Eastman Kodak Co. C. P. chemicals, except for *m*-aminobiphenyl, which was synthesized by the method of Fichter and Sulzberger.[4] The Eastman samples were further purified in our laboratory.

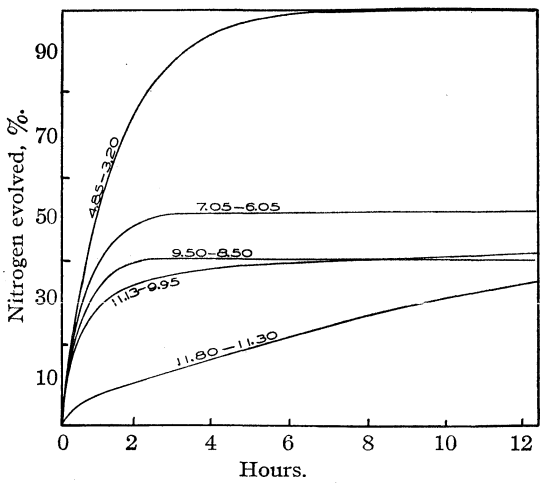


Fig. 4.—Per cent. nitrogen evolved *versus* time at pH values indicated, T = 35°, 0.1 M solution.

The amines were dissolved in water by the use of 2.20 molar equivalents of hydrochloric acid, iced to zero and diazotized by use of a normal solution of sodium nitrite and then diluted to 0.1 molar concentration of diazonium chloride and 0.02 molar concentration of hydrochloric acid. In general, the completely diazotized solutions were perfectly clear, but whenever a cloudiness occurred as a result of the formation of diazoamino compound, the cold solution was filtered before use. Prior to the decomposition experiments, the pH of each solution was checked with the glass electrode and used if between 1.60 and 1.80.

Rate of Decomposition.—On the basis of preliminary experiments, two or more temperatures were selected at which virtually 100% decomposition could be reached for each diazo within a reasonable time (three to thirty-six hours). Each experiment was then carried to completion and the unimolecular reaction velocity constants calculated, careful correction having been made for all such factors as slight changes in room temperature and/or barometric pressure. A linear relationship between log concentration and time was found over 95–96% of the entire reaction for every diazo in the present series, except for the diazo derived from *o*-anisidine. The latter com-

(4) Fichter and Sulzberger, *Ber.*, **37**, 878 (1904).

pound does not decompose according to the simple unimolecular law but rather with an autocatalytic trend with the production of an "S" curve. This has been found to be characteristic of several other less common mono-substituted derivatives of phenyldiazonium chloride as well as a large number of poly-substituted derivatives. These exceptions will be treated in a subsequent communication.

TABLE IV

VALUES OF k IN DUPLICATE EXPERIMENTS, SUBSTITUTED PHENYLDIAZONIUM CHLORIDE, CONCN. 0.1 M, pH 1.6–1.8

Diazo from	Temp., °C.	k (sec.$^{-1}$) × 10^5
o-Aminophenol	69.7	20.6
	69.7	20.7
o-Toluidine	35.0	96.0
	35.4	95.6
p-Nitroaniline	60.0	3.29
	60.0	3.30
p-Chloroaniline	59.3	1.72
	59.7	1.79

Duplicate experiments check closely as shown in Table IV.

A further test of the accuracy of the present investigation was obtained when experiments on the same diazo were run at more than two temperatures. From the values of ln k at two temperatures, E and ln Z were calculated by equation (1), after which ln k values at other temperatures were calculated. The calculated values of ln k were compared with the experimental values and agreements of the order of magnitude shown in Table V obtained.

All of the individually determined values of k, for simplicity, are given graphically in Fig. 5. The values of E and ln Z calculated by use of equation (1) are shown in Table VI.

It will be observed that the stabilities as measured by k vary greatly, although the values of E are surprisingly of the same order. Insofar as the latter are not equal, however, crossing of lines occurs when the data for each compound are plotted as ln k *vs.* $1/T$. Consequently, when the diazos are listed according to increasing or decreasing stability, one order is obtained at one temperature and a slightly different order may be obtained at another temperature.

TABLE V

COMPARISON OF OBSERVED VALUES OF ln k WITH VALUES CALCULATED FROM E AND ln Z IN TABLE VI. SUBSTITUTED PHENYLDIAZONIUM CHLORIDES; 0.1 M SOLN., pH 1.6–1.8

Substituent	Temp., °C.	ln k Obsd.	ln k Calcd.
o-Cl	82.7	−10.46	−10.48
p-C_6H_5	40.0	−10.98	−10.98
o-C_6H_5	30.0	− 9.01	− 8.98
-H	25.0	−10.10	−10.12
-H	35.2	− 8.52	− 8.59

The authors wish to acknowledge the assistance of a former associate, Dr. E. G. Kelley, during the early stages of the investigation.

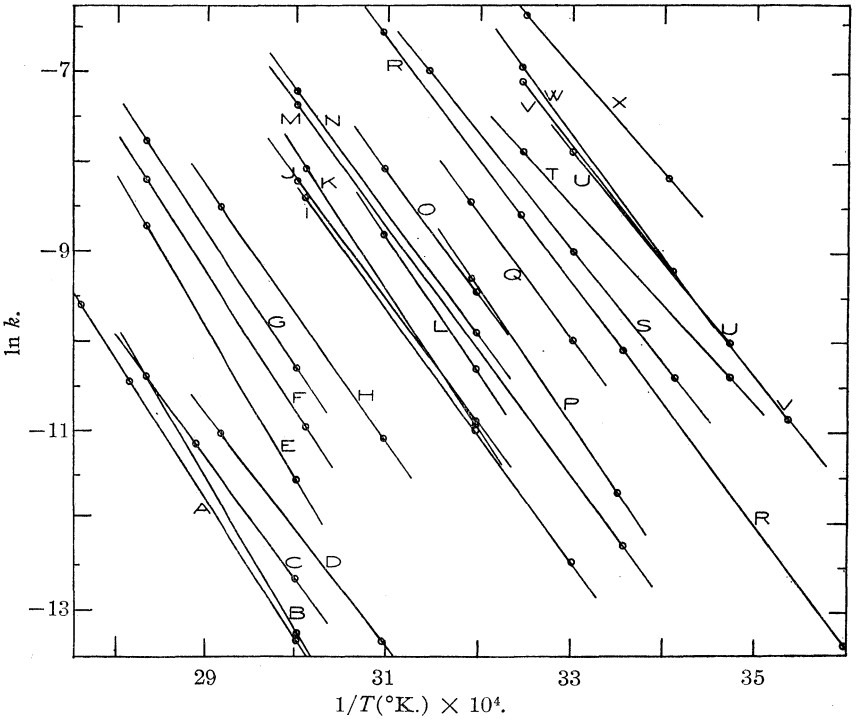


Fig. 5.—ln k *vs.* $1/T$ plots, substituted phenyldiazonium chlorides, 0.1 M solution, pH 1.6–1.8: A, *o*-chloroaniline; B, *p*-anisidine; C, *o*-nitroaniline; D, *p*-aminophenol; E, *m*-nitroaniline; F, *p*-chloroaniline; G, *p*-nitroaniline; H, *o*-aminophenol; I, *p*-aminobiphenyl; J, *p*-aminobenzene sulfonic acid; K, *m*-chloroaniline; L, *o*-aminobenzene sulfonic acid; M, *p*-toluidine; N, *p*-aminobenzoic acid; O, *m*-aminobenzene sulfonic acid; P, *o*-aminobenzoic acid; Q, *m*-aminobenzoic acid; R, aniline; S, *o*-aminobiphenyl; T, *m*-aminobiphenyl; U, *m*-anisidine; V, *m*-toluidine; W, *o*-toluidine; X, *m*-aminophenol.

TABLE VI

VALUES OF E AND ln Z FOR THE DECOMPOSITION OF PHENYLDIAZONIUM CHLORIDE AND A NUMBER OF ITS MONO-SUBSTITUTED DERIVATIVES; 0.1 M SOLUTION, pH 1.6–1.8

Diazo compound from	Substituent	E Ortho	E Meta	E Para	ln Z Ortho	ln Z Meta	ln Z Para
Aminophenol	—OH	30,400	26,000	25,600	36.5	36.3	26.5
Anisidine	—OCH_3	....	24,600	32,500	..	33.0	35.9
Aminobiphenyl	—C_6H_5	25,500	22,800	27,600	33.4	29.3	33.5
Toluidine	—CH_3	26,200	25,700	27,500	35.8	34.8	34.2
Chloroaniline	—Cl	30,800	30,200	31,600	33.2	37.6	36.9
Aminobenzoic acid	—COOH	29,400	27,100	27,700	37.8	35.1	34.6
Aminobenzene sulfonic	—SO_3H	30,300	28,000	27,400	38.9	35.6	33.3
Nitroaniline	—NO_2	26,500	33,200	29,800	27.1	38.8	34.7
Aniline	—H	27,200			35.8		

Summary

1. Rate measurements over 96% of the reaction indicate that the decomposition of phenyldiazonium chloride in dilute hydrochloric acid, pH 1.75, is a first order reaction. This is true over the entire range of concentrations studied, *i. e.*, 1280 moles of water:1 mole of diazo to 2.36 moles of water:1 mole of diazo.

2. The heat of activation of the reaction was found to be 27,200 cal./g. mole.

3. The nature of the decomposition products and the reaction velocity are functions of the concentration of the diazonium chloride solution. In very concentrated solution, the phenol yield falls to 24%. Other products formed under these conditions are monochlorobenzene, benzene and biphenyl.

4. The reaction velocity appears to increase very slightly as the concentration of hydrochloric acid is increased, but decreases again above 10 N hydrochloric acid.

5. In deuterium oxide solution the reaction velocity is substantially the same as in water.

6. At initial pH's below 11.2 the pH of the decomposing solution drops slowly to about 2. At initial pH's above 11.6 the pH drops only to about 10.

7. In buffered solutions the percentage of the total nitrogen which is evolved as a gas varies with the pH.

8. Rate measurements of the decomposition of 24 monosubstituted derivatives of phenyldiazonium chloride indicate that with the exception of the *o*-methoxy derivative, the reactions are of the first order. The diazos studied are the ortho, meta and para methyl, methoxy, phenyl, hydroxy, chloro, carboxy, sulfo and nitro phenyldiazonium chloride.

9. The stability of the parent compound, phenyldiazonium chloride, was decreased by *m*-hydroxy, *o*- or *m*-methyl, *m*-methoxy or *o*- or *m*-phenyl substitution. In all other cases studied, the stability was increased.

10. The values of E vary from 22,800 cal./g. mole for *m*-aminobiphenyl diazo to 33,200 for *m*-nitroaniline. The values of ln Z vary from 26.5 for *p*-aminophenol diazo to 38.9 for orthanilic acid diazo.

BOUND BROOK, NEW JERSEY

RECEIVED SEPTEMBER 12, 1939

[CONTRIBUTION FROM THE DEPARTMENT OF MEDICINE, COLLEGE OF PHYSICIANS AND SURGEONS, COLUMBIA UNIVERSITY, AND THE PRESBYTERIAN HOSPITAL]

The Viscosity–Fluidity Relations of Proteins[1]

BY HENRY P. TREFFERS

In the course of an investigation on the properties of antibody solutions, comparison has been made with the viscosities of related constituents in normal animal sera. Numerous empirical equations have been proposed[2] to account for the variation of the viscosity with protein concentration but singularly enough, in spite of its wide application elsewhere,[3] little or no serious use of the fluidity function has been made in protein chemistry. As this relation, in addition to its advantages of simplicity and ease of application, fits the available data quite well, it would seem to deserve further mention.

If the relative viscosity of a solution be expressed by η/η_0, where η is the viscosity of the solution and η_0 the viscosity of the solvent, the relative fluidity $\varphi_{rel.}$ is defined by the reciprocal

$$\varphi_{rel.} = \eta_0/\eta \qquad (1)$$

The fluidity is thus obtained directly from the experimental measurements with no more calculation than is required for the relative viscosity.

In Fig. 1 data on two proteins of rather widely different viscosity–concentration relations, egg albumin,[4] and a horse serum globulin, PII,[2c] have been plotted according to three representative equations. Curves 1 and 2 represent the fluidities, as in equation (1), curves 3 and 6 the logarithms of η/η_0 (Arrhenius relation[2a]), as plotted against the protein concentration. Curves 4 and 5 are a modification of the Einstein equation in which $\eta/\eta_0 - 1$ has been plotted against the quantity KVC, in which K is a constant, V the partial volume, and C the concentration.[2c,5] The abscissas have all been set equal, which necessitates, however, that curve 5 be shorter than curve 4.[6]

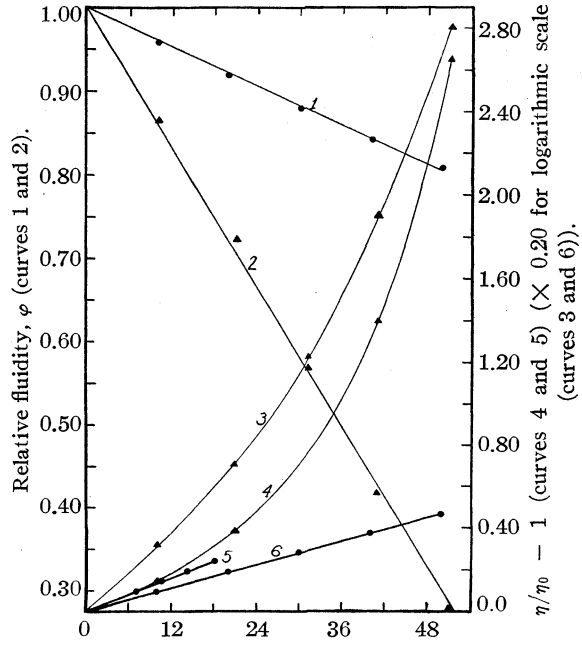


Fig. 1.—Viscosity and fluidity of egg albumin and horse serum globulin using three different equations: Curve (1) fluidity of egg albumin; (2) fluidity of serum globulin; (3) log η/η_0, globulin; (4) $\eta/\eta_0 - 1$, globulin; (5) $\eta/\eta_0 - 1$, egg albumin; (6) log η/η_0, egg albumin.

The utility of the fluidity function is seen from the fact that practically all protein solutions for which data are available in the literature yield a satisfactory linear plot for the relative fluidity φ against the protein concentration expressed in grams per liter of solution. The examples presented in Fig. 2 were selected for their representative slopes rather than for their agreement with the relation presented; nevertheless, the average deviation of all points from their respective "least square" lines is only 0.54%. In this calculation a deviation of the experimental fluidity 0.805 from the calculated 0.809 is taken as 0.5%.

Unfortunately only a few measurements are available at relatively high protein concentrations. Several of these, over their linear range, are given in Fig. 3. At sufficiently high concentrations of some proteins the measured fluidities lie above the line drawn through the lower points, but a comparison of the figures shows that the linearity

(1) The work reported in this communication was presented before the Division of Biological Chemistry at the Boston meeting, September, 1939, and was carried out under the Harkness Research Fund of the Presbyterian Hospital.

(2) Literature reviewed in (a) Cohn, *Physiol. Rev.*, **5**, 423 (1925); (b) Bredée and de Booys, *Kolloid-Z.*, **79**, 31 (1937); (c) Fahey and Green, THIS JOURNAL, **60**, 3039 (1938); (d) Greenberg, in "Chemistry of the Amino Acids and Proteins," ed. Schmidt, C. C. Thomas, Springfield, Ill., 1938, p. 452.

(3) Bingham, "Fluidity and Plasticity," McGraw-Hill Book Co., Inc., New York, N. Y., 1923.

(4) Polson, *Kolloid-Z.*, **88**, 51 (1939).

(5) Daniel and Cohn, THIS JOURNAL, **58**, 415 (1936).

(6) (a) Cohn and Prentiss, *J. Gen. Physiol.*, **8**, 622 (1925–1928); (b) Kunitz, Anson and Northrop, *ibid.*, **17**, 365 (1934); (c) Achard, Boutaric and Thevenet, *Compt. rend.*, **204**, 928 (1937).

covers a useful working range which compares favorably with that provided by other relations. Deviations at very high concentrations may represent a failure of the relation, or perhaps a departure of the behavior of the solution itself from that of true viscous flow. For some reason which is not clear, the data on casein solutions do not pass through the origin. Tobacco mosaic virus protein solutions give a linear relation for six out of the seven points given by Lauffer,[7] *i. e.*, up to 1.0 mg. of protein per cc.[8]

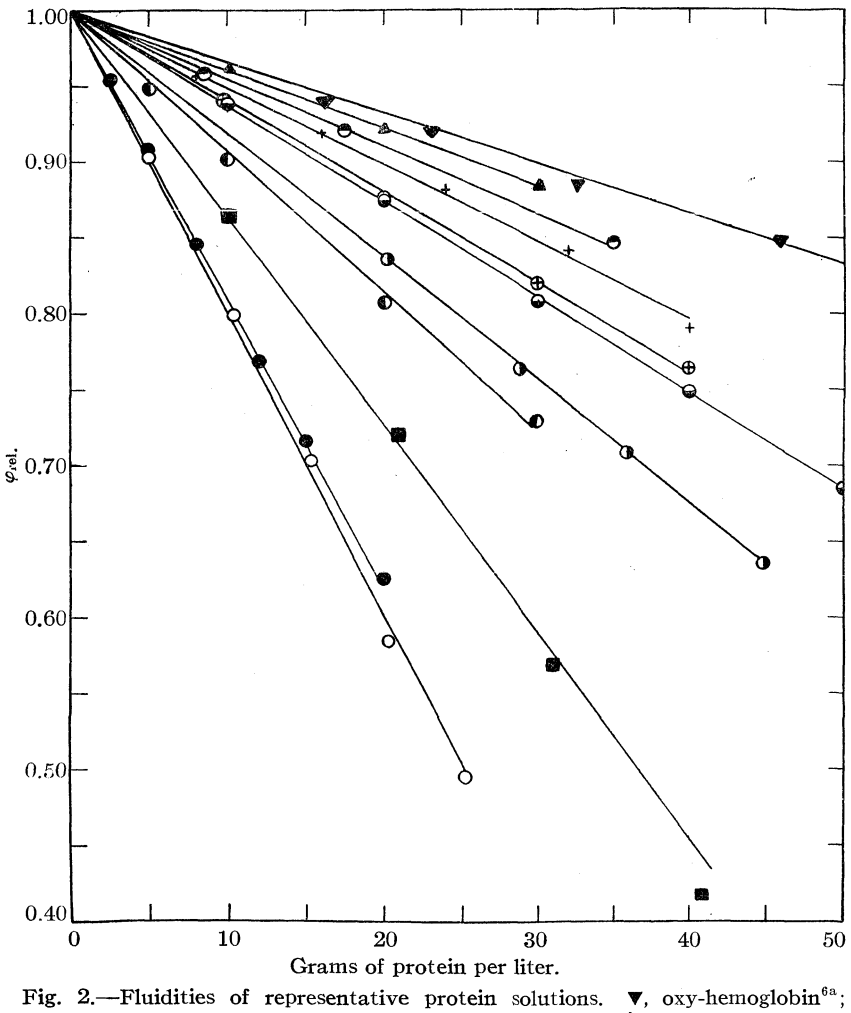


Fig. 2.—Fluidities of representative protein solutions. ▼, oxy-hemoglobin[6a]; ▲, CO-hemoglobin[4]; ◓, homarus hemocyanin[4]; +, trypsin[6b]; ⊕, octopus hemocyanin[4]; ◒, thyroglobulin[4]; ◑, horse pseudoglobulin, ■, PII, ○, PIII (horse globulin fractions)[2c]; ◐, gliadin[4]; ●, beef globulin.[6c]

The concentration of protein has been expressed in all cases in grams per liter rather than as the volume fraction, since the necessary density data were not always available. The volume fraction is probably the more general function on both theoretical and experimental grounds,[3] but since the concentration in grams per liter is proportional to it, it may be used in practice, provided that the partial specific volume of the protein remains constant. This constancy may be verified by plotting the specific volume against the weight fraction, which should yield a linear plot.[9]

Since the origin is always unity, each line may be determined in principle by a single accurate measurement, permitting the fluidity or, if desired, its reciprocal the viscosity, to be determined easily for any other concentration. However, two or more additional points are desirable to ensure greater accuracy and to establish the validity of the linear relation over the range in question.

That the linear relation holds for denatured as well as for native proteins, in spite of the change in absolute values, is seen when the viscosity data of Neurath and Saum[10] are converted to the corresponding fluidities. The resulting family of lines represents the behavior of horse serum albumin dissolved in urea solutions, a denaturing solvent (Fig. 4).

The relation holds as well for a protein which has been modified by the introduction of new chemical groupings, in this case a phosphorylated egg albumin[11] (Fig. 5).

In addition to providing a convenient interpolation formula, the fluidity method appears to offer a convenient tool in studying protein mixtures.

Experimental

Globulin prepared by half-saturation of diluted normal rabbit serum with ammonium sulfate was dialyzed for several days against frequent changes of distilled water.

(7) Lauffer, *Science*, **87**, 469 (1938).

(8) Loeb, *J. Gen. Physiol.*, **4**, 73 (1921–1922).

(9) Lewis and Randall, "Thermodynamics," McGraw-Hill Book Co., Inc., New York, N. Y., 1923, pp. 38–40.

(10) Neurath and Saum, *J. Biol. Chem.*, **128**, 347 (1939).

(11) Heidelberger, Davis and Treffers, in press.

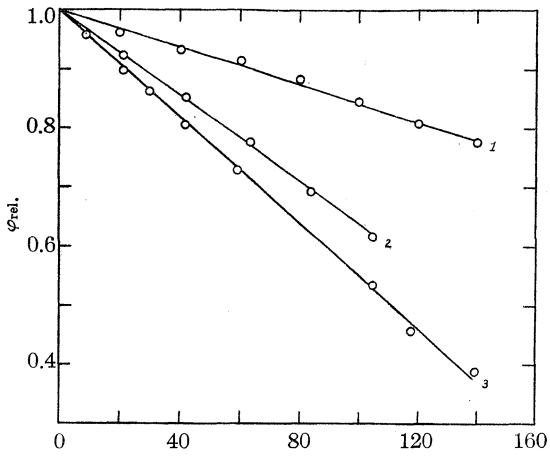


Fig. 3.—Fluidities at higher protein concentrations: Curve 1, egg albumin[8]; curve 2, CO-hemoglobin[6b]; curve 3, serum albumin.[20]

The portion which precipitated is designated euglobulin, the soluble material as pseudoglobulin. In order to avoid effects due to variation in the *p*H and salt concentration, both fractions were arbitrarily made up in solutions at *p*H 5.70 and 0.15 *M* potassium chloride. Several mixtures of the two solutions were made and the observed fluidities, compared with the calculated values from the fluidities of the separate components, are given in Table I.

As an albumin–globulin system was desired, a rather weak immune horse serum was centrifuged clear of lipid at 0° and an equal volume of half-saturated ammonium

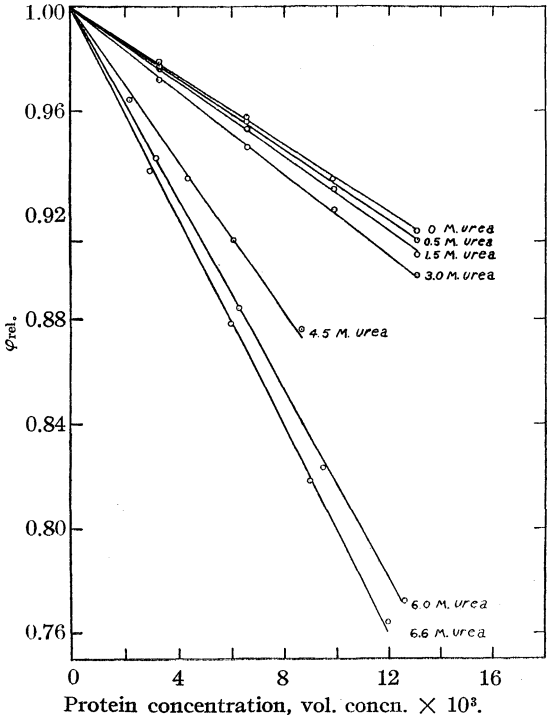


Fig. 4.—Fluidity of horse serum albumin in various urea solutions (Neurath and Saum[10]).

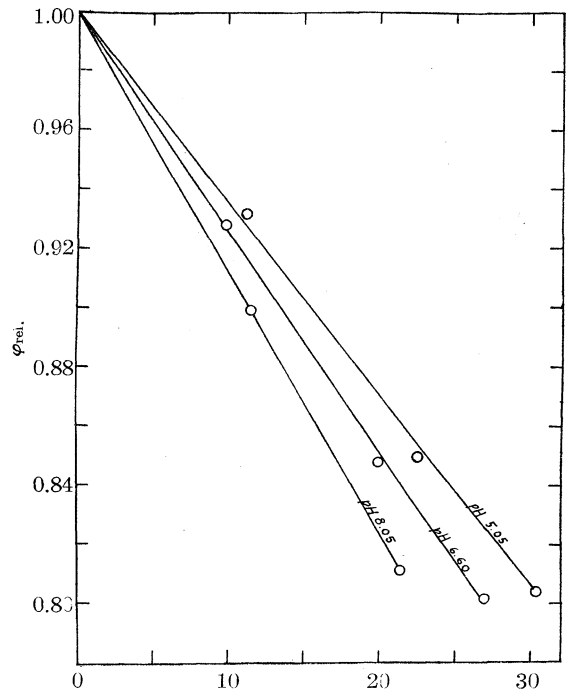


Fig. 5.—Fluidity of phosphorylated egg albumin at various hydrogen-ion concentrations.[11]

TABLE I

FLUIDITIES OF RABBIT PSEUDO- AND EUGLOBULIN MIXTURES AT 25.0°

Pseudoglobulin stock solution, 2.89 mg. of N/ml., rel. density 1.004. Euglobulin stock solution, 3.07 mg. of N/ml., rel. density 1.004.

Ratio pseudo/euglobulin solutions	Fluidity found	Fluidity calcd. eq. (4)
100 : 0	0.883	...
80 : 20	.862	0.867
64 : 36	.858	.855
53.3 : 46.7	.848	.847
43 : 57	.842	.838
0 : 100	.807	...

sulfate solution added. The supernatant albumin solution and the redissolved total globulin precipitate were dialyzed separately against 0.15 *M* potassium chloride until free of sulfate, and then adjusted to *p*H 5.70. Two series of mixtures were made, one from a concentrated albumin solution A and the globulin solution C, and the other from a more dilute albumin solution B with the same globulin solution C (Fig. 6). As Bingham has pointed out,[3] the fluidities of an ideal mixture do not in general lie exactly along a line joining the fluidities of the two separate components because of the difference between weight and volume concentrations. When the densities of the two component solutions are very close, however, the correction may be quite negligible, as is the case here.

Discussion

From the linear relation presented, the fluidity

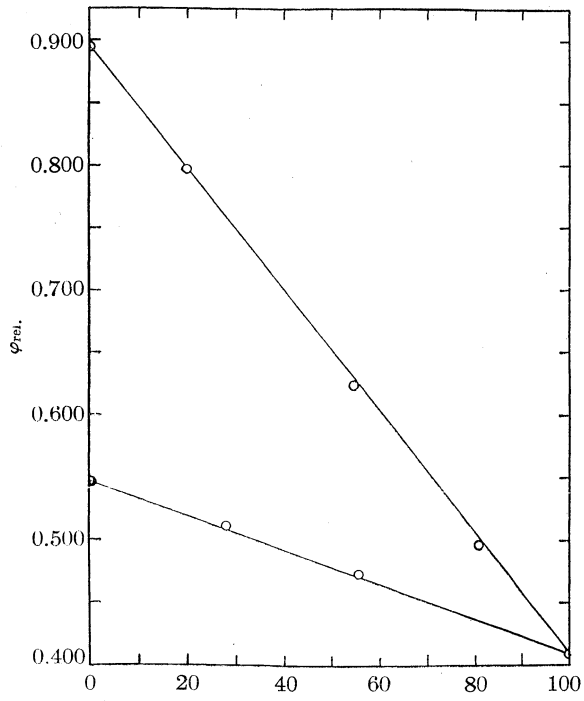


Fig. 6.—Fluidities of mixtures of a horse globulin solution with a horse albumin solution of two different concentrations.

of solutions of the water soluble globulin of concentration C_1 may be expressed as

$$\varphi_1 = 1 - k_1C_1 \qquad (2)$$

and that of the water insoluble euglobulin as

$$\varphi_2 = 1 - k_2C_2 \qquad (3)$$

where the k's are the respective slopes.

In the absence of any specific interaction between the two proteins the fluidity of a mixture of the two is therefore given by

$$\varphi_{mix.} = 1 - k_1C_1 - k_2C_2 \qquad (4)$$

Alternatively, for mixtures of protein solutions which do not differ greatly in density, the fluidities may be represented directly by a graphical method, as in Fig. 6.

Nugent and Towle[12] have outlined a method for the determination of albumin/globulin ratios—a quantity of some clinical importance—by the comparison of the viscosity at known total protein concentrations with that of standard curves for known mixtures. The modification employing fluidities, as shown here, should be somewhat more direct in application since an implicit value for the ratio is given by solving eq. (4) for the ratio C_1/C_2, which gives

$$\frac{C_1}{C_2} = r = \frac{A}{1 - A} \qquad (5)$$

where

$$A = \frac{\dfrac{1 - \varphi_{mix.}}{C_{total}} - k_2}{k_1 - k_2}$$

The ratio is thus given directly from the fluidity of the mixture, and the total protein concentration when the slopes of the fluidity lines of the separate components are known. For simplicity only two components have been assumed but there is nothing in the treatment to limit extension to systems of three or even more components.

Although no completely satisfactory theoretical justification is available at present for the use of the fluidity rather than the viscosity, comparison of the figures indicates the marked regularities which obtain with the fluidity. The graphical expression of experimental data is thus much easier, especially if it is desired to calculate a least square fit.[13]

It is not without interest that this single, simple relation should hold for such a diversity of protein solutions, and up to concentrations as high as 14% in some cases. The examples presented in Figs. 2 and 3 cover an important range of molecular weights, from that of gliadin 27,400, to that of octopus hemocyanin 2,785,000. The molecular shape factor, as given by the axial ratio, likewise varies from a value of 3.84 for egg albumin to 10.64 for gliadin.[4] Some of the solvents represented are half-saturated magnesium sulfate (trypsin), 0.85 M sodium chloride (beef globulin), and 61 vol. % alcohol (gliadin). Other examples, not given here, show that the same protein solution may give linear fluidity curves at several temperatures and, as indicated in Fig. 5, at various hydrogen-ion concentrations.

The ultimate dependence of the viscosity on the volume occupied by the protein molecules has been pointed out by numerous authors.[3,4] Furthermore, Kuhn, Polson and others have demonstrated that there is a close connection between the axial ratio and the viscosity.[14] It might be expected therefore that if a compound were to be

(12) Nugent and Towle, *Proc. Soc. Expll. Biol. Med.*, **33**, 374 (1935).

(13) For this special case, in which the line passes through the origin, the least square slope is given by the expression

$$\text{slope} = [\Sigma(C\varphi) - \Sigma(C)]/\Sigma(C^2)$$

in which each term denotes the summation of the corresponding column of data.

(14) A preliminary study indicates that, like the Polson relation for a viscosity function, the relation between the *slope* of the fluidity line and the square of the axial ratio may be a linear one for most proteins.

formed between two proteins, or a change in the state of aggregation were to occur, the volume fraction, or more especially the effective shape of the protein components, would be changed with a consequent deviation of the fluidity from that predicted on an additive basis (*cf.* Chap. V, ref. 3). The data in Table I and in Fig. 6 do not indicate such deviation, within the experimental error (*cf.* also ref. 2a). Nor do density determinations on beef albumin–globulin mixtures show any variation from strict additivity.[15] Even such a complicated mixture as serum yields a constant average partial specific volume, over the entire range, if one plots the density data of Chick and Lubrzynska.[16] A fair linear fluidity curve up to and including physiological concentrations of protein may also be obtained for this system.

Further discussion of this question, especially as to its bearing on the interesting effects observed in the ultracentrifuge by McFarlane[17] and by Pedersen[18] must await more accurate fluidity data, particularly on protein containing systems in which known compound formation and dissociation occur.

The author wishes to express his appreciation to Dr. Michael Heidelberger for his aid in the preparation of this paper.

(15) Nugent and Towle, *J. Biol. Chem.*, **104**, 395 (1934).
(16) Chick and Lubrzynska, *Biochem. J.*, **8**, 59 (1914).
(17) McFarlane, *ibid.*, **29**, 407 (1935).
(18) Pedersen, *Compt. rend. trav. lab. Carlsberg*, **22**, 427 (1937).

Summary

1. It has been found that the fluidity, or reciprocal of the relative viscosity, is linear with the protein concentration over a wide range of proteins and concentrations.

2. The fluidity provides a convenient interpolation formula for converting the fluidity or viscosity obtained at one concentration to that at any other.

3. It is shown that the fluidity is additive for mixtures of rabbit eu- and pseudoglobulin, and for horse albumin and globulin fractions.

4. The relation of additive fluidities to the presence of compounds in mixtures of proteins is discussed.

NEW YORK, N. Y. RECEIVED FEBRUARY 29, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, COLUMBIA UNIVERSITY]

Ascorbic Acid Oxidase from Summer Crook-neck Squash (C. pepo condensa)

BY P. L. LOVETT-JANISON AND J. M. NELSON

In 1928 Szent Györgyi[1] observed that certain plant tissues catalyzed the aerobic oxidation of ascorbic acid, and in 1930[2] he postulated the existence of a specific enzyme in cabbage leaves. Since then, other investigators[3,4,5,6,7] have reached the same conclusion working with different plant sources, such as apples, Hubbard squash, Drumstick, cauliflower, bananas, cabbage, carrots, cucumbers, potatoes and string beans.

Barron, DeMeio and Klemperer[8] were among the first to show that the aerobic oxidation of ascorbic acid was catalyzed by ionic copper, and in a later paper[9] they questioned the enzymic nature of ascorbic acid oxidase. Stotz, Harrer and King,[10] working upon this problem, were inclined to attribute the catalytic activity of squash juice to copper in combination with protein material, rather than to a specific oxidase. On the other hand, Spruyt and Vogelsang[11] working with fruit juices concluded that, "ascorbic acid oxidation and copper do not go hand in hand and that this oxidation is certainly not exclusively to be ascribed to the presence of copper."

From the above, it is obvious therefore that some confusion arises. It is the object of this paper to show that ascorbic acid oxidase is indeed a true enzyme, consisting of a copper-protein, similar in type to tyrosinase (polyphenol oxidase), which has been recognized as a true enzyme.

Purification of Enzyme from Summer Squash.—After experimenting with cucumber, cauliflower, summer squash, apples, parsnips, carrots, spinach, string beans, cabbage,

(1) A. Szent Györgyi, *Biochem. J.*, **22**, 1387 (1928).
(2) A. Szent Györgyi, *Science*, **72**, 125 (1930).
(3) S. S. Zilva, *Biochem. J.*, **28**, 663 (1934).
(4) H. Tauber, I. S. Kleiner and D. Mishkind, *J. Biol. Chem.*, **110**, 211 (1935).
(5) M. Srinivasan, *Biochem. J.*, **30**, 2077 (1936).
(6) F. G. Hopkins and E. J. Morgan, *ibid.*, **30**, 1446 (1936).
(7) W. Stone, *ibid.*, **31**, 508 (1937).
(8) E. S. G. Barron, R. H. DeMeio and F. Klemperer, *J. Biol. Chem.*, **112**, 625 (1935–1936).
(9) E. S. G. Barron, A. G. Barron and F. Klemperer, *ibid.*, **116**, 563 (1936).
(10) E. Stotz, C. J. Harrer and C. G. King, *ibid.*, **119**, 511 (1937).
(11) J. P. Spruyt and G. M. D. Vogelsang, *Arch. Néerland Physiol.*, **23**, 423 (1938).

oranges and green peppers, we have found the best source of ascorbic acid oxidase to be that from summer crook-neck squash (*C. pepo condensa*).

Ebihara[12] has shown, in the cases of certain plants, that the enzyme is most abundant in the external layers. We have confirmed this in the case of summer crook-neck squash. Consequently, the rinds of squash were minced to a fine pulp, then subjected to hydraulic pressure in order to remove all juice. Determinations upon various crude juice preparations gave values ranging from 0.52 to 0.73 unit per mg. dry weight (for definition of unit see next section). This was followed by treatment with *M* barium acetate (20 cc. to 1 liter of juice), which removed a considerable amount of color and extraneous protein without appreciable loss of activity. After filtering, the juice was brownish-yellow in color. Excess barium ion was now removed as barium sulfate by the addition of 0.05 saturated ammonium sulfate solution and filtering. By the addition of ammonium sulfate to 0.6 saturated, the enzyme was precipitated. After filtering, the precipitate was washed with saturated ammonium sulfate solution until the filtrate was colorless. Addition of *M*/15 secondary sodium phosphate dissolved the precipitate which, after filtering, now contained about 85% of the original enzyme. The solution of the enzyme was then made 0.9 saturated with magnesium sulfate, which precipitated about two-thirds of the enzyme (Part I). After filtering the filtrate was now saturated with magnesium sulfate and the remaining third precipitated (Part II). After dialysis, these two parts, I and II, contained 70 and 144 units per mg. dry weight, respectively. Since on further treatment Part I failed to give preparations of low dry weight comparable with those obtained later from Part II, it was eventually discarded. The remaining steps in the purification apply, therefore, to Part II only.

Part II of the enzyme was now adsorbed to 10% alumina[12a] at *p*H 6.5, eluted with secondary phosphate and dialyzed in distilled water at *p*H 8.0. It was then fractionated with 0.1 saturated lead acetate and acetone (cooled with dry-ice) in the following manner. To the whole, lead acetate (14 drops per 100 cc. enzyme solution) was added, followed by the addition of 10% of the total volume of acetone and the precipitate centrifuged. The supernatant liquid was again treated with the same reagents (10 drops of lead acetate per 100 cc. of enzyme solution, followed by acetone up to 25% of the total volume), and the resulting precipitate again centrifuged. This procedure was repeated twice. The precipitates obtained were taken up in secondary phosphate, filtered and dialyzed in redistilled water at *p*H 8.0. Adsorption to 20% alumina followed by elution and dialysis yielded a fraction of 557 units per mg. dry weight. Further fractionations of this fraction with lead acetate and acetone, followed by treatments with alumina, yielded fractions of 600 to 631 units per mg. dry weight. Further treatments have, so far, failed to improve upon these values.

These purifications removed all the brownish-yellow pigment and it is interesting to note that while at dilutions of about 500 units per cc. the enzyme solution was colorless, at high concentrations of about 4000 units per cc. the solution was green and at intermediate dilutions the color was pale blue or greenish-blue.

Definition of Unit and Determination of Activity of Enzyme Preparations.—In these Laboratories one unit of ascorbic acid oxidase is that quantity which in the presence of its substrate, ascorbic acid, catalyzes a reaction involving an oxygen uptake of 10 c. mm. per minute.

The determinations were carried out in the Warburg respirometer at 25°. In the vessels were 2 cc. of 0.2 *M* phosphate–citrate buffer of *p*H 5.6, 1 cc. of gelatin (5 mg. per cc.), 1 cc. of *l*-ascorbic acid (2.5 mg. per cc.), the diluted enzyme solution and distilled water to make the total volume 8 cc. At all times one of the flasks contained no enzyme, being used as a control. Readings were usually taken every two minutes.

Adams and Nelson[13] have shown in the case of tyrosinase preparations that the addition of gelatin furnishes protection to the enzyme against inactivation. Similarly with ascorbic acid oxidase we have found that the addition of 3.0 mg. of gelatin helps by stabilization of the enzyme when in a highly purified state.

Determination of Copper.—The method used for the determination was that devised by Warburg[14] and is based upon the oxidation of cysteine by copper in the presence of sodium pyrophosphate, which inhibits the action of any iron or manganese which may be present.

The operation was carried out in a Warburg respirometer at *p*H 7.6. A typical run is shown in Table I.

TABLE I

Flask	1	2	3	4	5	6
0.2 *M* pyrophosphate, *p*H 7.75, cc.	2	2	2	2	2	2
(1) Copper soln. 0.1 γ/0.1 cc., cc.	0.1	0.2	...	...	...	...
(2) 0.2 *M* hydrochloric acid, cc.	.1	.1	0.1	0.1	0.1	0.1
(3) Enzyme solution, cc.	.1	.1	...	.1	.2	.3
(4) Cysteine hydrochloride 6 mg./ 0.2 cc., cc.	.2	.2	.2	.2	.2	.2
Water, cc.	.1	...	.3	.2	.1	...

The reagents (1), (2), (3), (4) were placed in the side arm and added to the buffer solution and water, contained in the reaction flask, when the temperature was constant at 25°. Flask 3 contained no enzyme, and served as a control, by being a blank on all the reagents used. The total volume in each flask was 2.6 cc., and the *p*H after mixing was 7.6. Readings were taken at five-minute intervals. It is obvious that when the manometer readings were converted to c. mm. of oxygen, then subtraction of the value for flask 4 from those of flasks 1 and 2 gave the values of the uptakes due to 0.1 γ and 0.2 γ of copper, while subtraction of the value for flask 4 from flasks 5 and 6 gave the values of the uptakes due to 0.1 cc. and 0.2 cc. of enzyme solution. In such a way two determinations of copper and enzyme uptakes were obtained in each run. In all cases at least two runs were performed. Dividing the uptake due to 0.1 cc. of enzyme solution by that due to 0.1 cc. of copper solution gave the concentration of copper in the enzyme solution. Knowing also the activity of enzyme in units per cc. enabled one to obtain the activity of enzyme in units of enzyme per γ of copper. The results of copper estimations carried out on different enzyme prepa-

(12) T. Ebihara, *J. Biochem. (Japan)*, **28**, 415 (1938).

(12a) Suspension 15 g. of alumina per liter.

(13) M. H. Adams and J. M. Nelson, THIS JOURNAL, **60**, 2472 (1938).

(14) O. Warburg, *Biochem. Z.*, **187**, 255 (1927).

rations have been found to give a constant value of 432 ± 30 units per γ of copper.

Table II shows that the percentage of copper increased with rise of enzyme activity until it reached the value of 0.15%. In spite of further attempts at purification, this was the highest purity reached to date. The figures given are those obtained only after a more or less constant value for the activity of the enzyme (in units per γ Cu) had been reached. This proportionality between the copper contents and enzyme activities (column 2) is, we think, strong evidence for the conclusion that the active group of ascorbic acid oxidase contains copper.

TABLE II

Prepn.	Concn. enzyme in sample (units/cc.)	Activity, units/γ Cu	% Cu	Activity, units/mg.
1	1412	488	0.029	142
2	161	400	.040	144
3	1287	390	.047	183
4	2248	480	.060	286
5	496	400	.10	379
6	730	415	.12	480
7	3480	431	.12	512
8	530	452	.12	525
9	786	405	.14	586
10	5640	429	.15	600
11	531	406	.15	612
12	516	490	.15	631
		432 ± 30		

Further purification failed to alter this value for copper, which represented about 5% of the total copper present in the original squash juice. It was only by successive stages of purification that the copper which did not belong to the ascorbic acid oxidase was gradually eliminated, together with other impurities.

On comparing the activity of copper in units per γ with those of Stotz, Harrer and King,[10] who used solutions of copper only, copper–gelatin, and copper–albumin mixtures, and the juices of cauliflower and squash (somewhat purified), we find that our purified enzyme is 1100 times more active than copper alone, 13,000 times more active than the copper–albumin mixture, 4100 times more active than the copper–gelatin mixture, and 3800 and 1700 times, respectively, more active than the juices taken from cauliflower and squash and used by these investigators. This very great activity or increased specificity shown by our purified enzyme constitutes, we consider, a strong argument in favor of our purified squash juice containing a true enzyme. This is in line with the copper content of other enzymes such as tyrosinase (polyphenol oxidase).

Dry Weight Determinations.—For details of the method by which these determinations were performed, refer to the work of Lutz and Nelson[15] in 1934.

Determination of Manganese.—Theorell,[16] working upon dihydroxymaleic acid oxidase, has offered evidence to show that manganese is the activator for this enzyme. Since the configurations of dihydroxymaleic and ascorbic acids show similarity, it was thought at one time in this Laboratory that manganese might play some part as activator for ascorbic acid oxidase. With this end in view, the direct microdetermination of manganese, as outlined by Wiese and Johnson,[17] was carried out upon samples of ascorbic acid oxidase from squash, in which the samples varied from crude juice to purified preparations. It was found that the quantity of manganese in the samples was very small and bore no relation to enzyme activity. With each stage of purification, the value for manganese slowly diminished, even when the enzyme concentration was increased. From this work we must conclude that manganese seems to play no part in the catalytic function of ascorbic acid oxidase. This seems to be in agreement with the work of Barron, DeMeio and Klemperer,[8] who found that of the metals, manganese, iron, copper, nickel, cobalt and calcium, copper was the only metal to catalyze the oxidation of ascorbic acid.

Determination of Peroxidase.—Several investigators[5,18,19] have shown that ascorbic acid oxidase preparations contain peroxidase. We also have found this to be the case in crude or partially purified samples.

The method used by us for the determination of peroxidase was that of Balls and Hale,[20] a method which we used on samples of ascorbic acid oxidase varying from crude juice to our purest preparations. Determinations conducted through the various stages of purification indicated that considerable amounts of peroxidase were being removed as the purification proceeded. In the filtered crude squash juice the concentration of peroxidase was found to be 0.0022 unit of peroxidase per unit of ascorbic acid oxidase, while in the purest preparation (Prepn. 10 (see table) containing 600 units of ascorbic acid oxidase per mg. dry weight) this ratio was 0.0000078. This indicated that 99.65% of the peroxidase had been removed during purification, and for all practical purposes it may be considered as a peroxidase-free preparation. This should be of interest to other workers in this field, because of the importance that has been attributed to peroxidase in the respiration of plants by investigators such as Szent Györgyi,[21] St. Huszák,[18] and Robězieks.[22]

Behavior of Ascorbic Acid Oxidase toward Catechol, *p*-Cresol and Hydroquinone.—Since

(15) G. J. Lutz and J. M. Nelson, *J. Biol. Chem.*, **107**, 169 (1934).
(16) H. Theorell and B. Swedin, *Naturwissenschaften*, **27**, 95 (1939).
(17) A. C. Wiese and B. C. Johnson, *J. Biol. Chem.*, **127**, 203 (1939).
(18) St. Huszák, *Z. physiol. Chem.*, **247**, 239 (1937).
(19) T. Ebihara, *J. Biochem. (Japan)*, **29**, 217 (1939).
(20) A. K. Balls and W. S. Hale, *J. Assoc. Off. Agr. Chem.*, **16**, 445 (1933).
(21) A. Szent-Györgyi, *Bull. soc. chim. biol.*, **20**, 846 (1938).
(22) I. Robězieks, *Z. physiol. Chem.*, **255**, 255 (1938).

we have shown that ascorbic acid oxidase is a copper–protein enzyme similar to tyrosinase (polyphenol oxidase), we thought it of interest to try its effect upon the above substrates, although some investigators[4,5] already have shown that the enzyme does not catalyze the oxidation of phenols. Using one of our preparations of highest purity (600 units per mg.) we found that it was about 520 times more active toward ascorbic acid than toward catechol and about 335 times more active toward its own substrate than toward hydroquinone. No activity toward *p*-cresol was obtained when an amount of ascorbic acid oxidase as high as 846 units was used. These activities are extremely small and to all intents and purposes it may be concluded that the enzyme does not catalyze the oxidation of these substances except at high concentrations.

Summary

1. A method has been described for the preparation of a highly purified ascorbic acid oxidase having an activity of 600 to 630 units per mg. dry weight.

2. At high concentrations the enzyme was green, at lower concentrations blue or bluish-green.

3. The ascorbic acid oxidase was found to be a copper-protein compound, containing 0.15% of copper.

4. The purest enzyme preparations obtained had an activity of 432 units per γ of copper.

5. Manganese seems to play no part as activator for this enzyme.

6. The purest enzyme preparation was found to have lost 99.65% of the peroxidase accompanying the enzyme in the crude juice and may be considered practically free of this enzyme.

7. Ascorbic acid oxidase has no action toward *p*-cresol and only shows a slight action toward catechol and hydroquinone at comparatively high concentrations.

NEW YORK, N. Y. RECEIVED MARCH 27, 1940

[CONTRIBUTION FROM THE DIVISION OF INDUSTRIAL AND CELLULOSE CHEMISTRY, MCGILL UNIVERSITY]

Studies on Lignin and Related Compounds. XLVII. The Synthesis of Xylosides Related to Lignin Plant Constituents

BY J. H. FISHER, W. LINCOLN HAWKINS AND HAROLD HIBBERT

The question of whether lignin is in chemical combination with a carbohydrate constituent in the plant has been a matter of speculation for many years. Some workers[1] believe that lignin is present as an incrustant in the cell wall and is not in chemical union with any other product. Evidence[1] from a study of X-ray patterns of pure cotton cellulose and cellulose from wood appears to indicate the absence of a chemical union. However, the possibility of the existence of a lignin-hemicellulose complex as suggested by Harris, Sherrard and Mitchell[2] and later supported by Norman and Shrikhande[3] is not excluded.

Recent studies on the enzymatic degradation of wood by Ploetz[4] provide further evidence for the presence of a lignin carbohydrate complex. Bailey[5] in work dealing with lignin extracted by the use of butyl alcohol obtains evidence indicating a chemical combination of part of the lignin with cellulose in certain woods. Norman[6] and also Hägglund[7] have presented comprehensive reviews concerning the relationship between lignin and cellulose in the cell wall.

Possible Mode of Combination.—The two principal carbohydrate constituents of the cell wall, cellulose and xylan, may be combined with the lignin through ether, ester or glycosidic bonds, that of the last-named occurring most frequently in natural products. To obtain further information on the nature of the lignin union in wood, a number of glycosides have been synthesized from products presumably closely related to lignin.

Although the structure of "protolignin" is unknown, recent studies on the ethanolysis of wood[8] and the hydrogenation of certain isolated lignins[9]

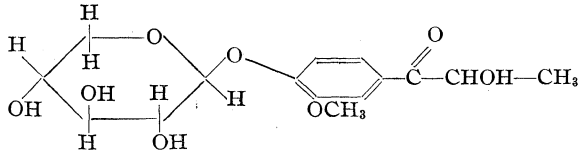
(1) Freudenberg, *J. Chem. Education*, **9**, 1171 (1932).
(2) Harris, Sherrard and Mitchell, THIS JOURNAL, **56**, 889 (1934).
(3) Norman and Shrikhande, *Biochem. J.*, **29**, 2259 (1935).
(4) Ploetz, *Ber.*, **73**, 57, 61, 74 (1940).
(5) Bailey, *Paper Trade J.*, **110**, No. 1, 29 (1940).
(6) Norman, "Biochemistry of Cellulose, Polyuronides, Lignin," Clarendon Press, Oxford, 1937, pp. 59–62.
(7) Hägglund, "Holzchemie," Akademische Verlagsgesellschaft, Leipzig, 1939, pp. 206–212.
(8) Cramer, Hunter and Hibbert, THIS JOURNAL, **61**, 509 (1939); Hunter, Cramer and Hibbert, *ibid.*, **61**, 516 (1939).
(9) Harris, D'Ianni and Adkins, *ibid.*, **60**, 1467 (1938).

have indicated the fundamental building units are C_6-C_3 derivatives. Ethanolysis experiments have been highly informative in that, contrary to those carried out on high pressure hydrogenation, the functional groups of the aromatic nuclei as well as those of the aliphatic side chains remain intact. Thus it has been possible to isolate such C_6-C_3 lignin building units as α-ethoxypropiovanillone and α-ethoxypropiosyringone. These compounds are considered to be derived from etherification of the corresponding α-hydroxy compounds, their dismutation isomers or their ene-diol forms[10] during ethanolysis. Recently Brickman, Hawkins and Hibbert[11] have isolated the corresponding diketones, vanilloyl and syringoyl methyl ketones, from the ethanolysis products of wood.

The manner in which the building units may be combined in protolignin has been dealt with in a previous communication,[10] in which it has been shown that, in such polymers, there may be primary, secondary or tertiary aliphatic and phenolic hydroxyl groups present so that the carbohydrate material of the cell wall may be combined through any or all of these hydroxyls.

Degradation of lignin sulfonic acids has yielded other aromatic compounds containing the guaiacyl and syringyl nuclei, such as guaiacol,[12] acetovanillone,[13] acetosyringone,[14] and pyrogallol 1,3-dimethyl ether.[15]

In view of the isolation of these derivatives as part of the lignin complex, the synthesis of the following xylosides was undertaken as the first stage in a study of possible glycosidic linkages in protolignin: (1) α-hydroxypropiovanillone β-*d*-xyloside:



(2) α-hydroxypropiosyringone β-*d*-xyloside, (3) guaiacol β-*d*-xyloside, and (4) acetovanillone β-*d*-xyloside.

An extensive investigation of the properties of these xylosides, including a quantitative determination of their stability under a variety of conditions, is in progress. The acidity of the phenolic hydroxyl groups of the phenols in question is to be determined and the stability of the xylosides correlated with these values. The results of this investigation, and the conclusions which may be drawn therefrom regarding the plausibility of a phenolic glycosidic link between lignin and carbohydrate will be presented in a subsequent communication. Such results may possibly have a marked bearing on the mechanism of sulfite pulp manufacture.

Syntheses of Acetylated Xylosides.—The acetylated forms of the above xylosides were synthesized by condensation of acetobromoxylose with the phenol by a modification of Helferich's process.[16] Attempted synthesis of the acetylated xylosides of α-acetoxypropiovanillone and α-acetoxypropiosyringone by his method resulted in very low yields (13%), even when a large excess of acetobromoxylose was used. By (1) substitution of the potassium for the sodium salt of the phenol, (2) operating at 0° throughout the reaction, and (3) carefully controlling the *p*H of the reaction medium during addition of the reagents, it was possible to double the yield, an important point in view of the difficulties involved in the preparation of the phenolic products.

In the Helferich reaction the salt of the phenol used and the water present in the reaction mixture, both react with acetobromoxylose. Since the phenol reacts only in the form of its salt, the yield of the xyloside depends on the proportion of this salt present throughout the reaction. In Helferich's method the aqueous solution of the sodium salt of the phenol is mixed with an acetone solution of the acetobromoxylose and allowed to stand at room temperature. Part of the acetobromoxylose reacts with the water present producing hydrogen bromide which in turn liberates the phenol from its salt, resulting in an increasing amount of the free phenol. By adding alkali throughout the reaction this is prevented and a maximum amount of phenol available for condensation is obtained, thus ensuring maximum utilization of the acetobromoxylose. Excess of alkali is to be avoided in order to prevent decomposition of the acetobromoxylose and deacetylation of the xyloside as well as fission of the newly formed xylosidic union. Sufficient alkali is added to keep 90% of the phenol in the form of its potassium salt. The exact proportion of phenol as

(10) Hibbert, THIS JOURNAL, **61**, 725 (1939).
(11) Brickman, Hawkins and Hibbert, *ibid.*, **62**, 986 (1940).
(12) Leger and Hibbert, *Can. J. Research*, **B16**, 68 (1938).
(13) Buckland, Tomlinson and Hibbert, *ibid.*, **B16**, 54 (1938).
(14) Leger and Hibbert, THIS JOURNAL, **60**, 565 (1938).
(15) Leger and Hibbert, *Can. J. Research*, **B16**, 151 (1938).
(16) Helferich, *Ann.*, **520**, 156 (1936).

potassium salt required to give a maximum yield will depend on the acidity of the phenolic group and the stability of the resulting xylosidic bond.

α-Acetoxypropiovanillone and α-acetoxypropiosyringone contain asymmetric carbon centers. Condensation of these racemic compounds with optically active acetobromo-*d*-xylose should give rise to isomers of slightly different properties. The difficulties encountered in the purification of the acetylated xylosides of the above two phenols, especially the latter, would indicate that this is the case.

Deacetyla ion of Acetylated Xylosides.—The Zemplén method[17] proved to be the most satisfactory process for deacetylation. Guaiacol triacetyl β-*d*-xyloside and acetovanillone triacetyl β-*d*-xyloside were successfully deacetylated by Mauthner's aqueous ammonia method[18] with yields of 85–90%. The former xyloside also was deacetylated by the anhydrous methanolic ammonia method.[19] However, the triacetyl xylosides of α-acetoxypropiovanillone and of α-acetoxypropiosyringone are unstable under both these conditions. The β-*d*-xyloside of α-hydroxypropiosyringone proved to be remarkably unstable. Mere solution in pure hydroxylic solvents, such as ethanol, acetone, dioxane or water, at 45° resulted in decomposition as indicated by a marked decrease in the melting point.

Experimental

α-Acetoxypropiovanillone.—α-Bromopropiovanillone[20] (24 g.), glacial acetic acid (144 cc.) and anhydrous potassium acetate (62 g.) were heated together on the steam-bath at 100° for six hours. The solution was poured into cold water (1152 cc.) with stirring, and the product allowed to crystallize at 0° for thirty-six hours. It was recrystallized from carbon tetrachloride in the form of fine needles; yield, 13.3 g. (60%); m. p. 105–106°. *Anal.* Calcd. for $C_{12}H_{14}O_5$: C, 60.48; H, 5.93; OCH_3, 13.0. Found: C, 60.45; H, 6.02; OCH_3, 13.0.

Triacetyl β-*d*-Xyloside of α-Acetoxypropiovanillone.—This was obtained by a *p*H controlled modification of the Helferich method.[16] The *p*H of an aqueous acetone solution of α-acetoxypropiovanillone containing 90% of an equivalent amount of potassium hydroxide was found to be approximately 9.0. The reaction was carried out under nitrogen at 0°.

A trace of phenolphthalein and 2.38 g. of α-acetoxypropiovanillone (0.01 mole) were dissolved at room temperature in a mixture of 8 cc. of acetone and 13.85 cc. of 0.724 *N* aqueous potassium hydroxide (0.01 mole). Acetobromoxylose (6.80 g., 0.02 mole) in 32 cc. of anhydrous acetone was then added to the above solution, and the flask shaken to ensure rapid admixture of the two solutions. In a few moments the *p*H of the resulting solution dropped below 9.0, as indicated by the color change. The dropwise addition of potassium hydroxide was begun at a rate sufficient to maintain the *p*H at 9.0. When 13.85 cc. of potassium hydroxide (0.724 *N*) had been added (twenty minutes) the reaction mixture was set aside for three hours, when the *p*H was approximately 7.0. The mixture was extracted thoroughly with benzene (150 cc.), the benzene extract shaken quickly with two 200-cc. portions of sodium carbonate (2%) at 5°, washed with water and dried for a few minutes with calcium chloride. The solution was evaporated at 40° under reduced pressure. Recrystallization of the residue twice from 50% aqueous ethanol (127 cc.) yielded 1.08 g. (25%) of fine needle-shaped crystals: m. p. 149.4–149.7°. *Anal.* Calcd. for $C_{23}H_{28}O_{12}$: C, 55.62; H, 5.69; OCH_3, 6.26; $COCH_3$, 34.7. Found: C, 55.50; H, 5.76; OCH_3, 6.20; $COCH_3$, 35.5.[21]

In the above reaction only 0.48 g. of α-acetoxypropiovanillone could be recovered unchanged.

α-Acetoxypropiosyringone.—This was synthesized by the method of Hunter, Cramer and Hibbert.[8] One of the steps in this synthesis involves the dehydration of 3,4,5-trimethoxyphenyldiethylcarbinol to the corresponding pentene. It was found convenient to effect this dehydration by heating with a trace of iodine at 100° for one hour.[22] This method gives a purer pentene derivative and an increase in yield to 60% of 3,4,5-trimethoxypropiophenone on ozonization.

Triacetyl β-*d*-Xyloside of α-Acetoxypropiosyringone.—This was synthesized by the same procedure as used with α-acetoxypropiovanillone. The crude product (m. p. 100°) was very difficult to purify, and this was effected by recrystallization from 33% aqueous ethanol. Six recrystallizations were necessary before a product in the form of small flaky crystals and of constant melting point (128.6–128.8°) was obtained, yield 25%. *Anal.* Calcd. for $C_{24}H_{30}O_{13}$: C, 54.73; H, 5.74; OCH_3, 11.78; $COCH_3$, 32.7. Found: C, 54.70; H, 5.75; OCH_3, 11.8; $COCH_3$, 34.1.[21]

Guaiacol Triacetyl β-*d*-Xyloside.—This was prepared, as above, by using equimolecular quantities of acetobromoxylose and potassium guaiacolate and omitting *p*H control of the reaction mixture. The xyloside crystallized from 50% aqueous ethanol in large rhombic crystals; yield 43%; m. p. 139.8–140.0°. *Anal.* Calcd. for $C_{18}H_{22}O_9$: C, 56.51; H, 5.81; OCH_3, 8.1; $COCH_3$, 33.8. Found: C, 56.50; H, 5.82; OCH_3, 8.0; $COCH_3$, 33.9.

Acetovanillone Triacetyl β-*d*-Xyloside.—A similar procedure was employed using a 50% excess of acetovanillone; yield 58%. It crystallized from aqueous acetone in large monoclinic crystals; m. p. 133.3–133.6°. *Anal.* Calcd. for $C_{20}H_{24}O_{10}$: C, 56.58; H, 5.71; OCH_3, 7.31; $COCH_3$, 30.4. Found: C, 56.50; H, 5.83; OCH_3, 7.29; $COCH_3$, 31.5.[21]

β-*d*-Xyloside of α-Hydroxypropiovanillone.—The deacetylation of the acetylated xyloside was carried out by the Zemplén method.[17] The reaction was allowed to pro-

(17) Zemplén, *Ber.*, **62**, 1613 (1929).
(18) Mauthner, *J. prakt. Chem.*, **124**, 313 (1930).
(19) Lucas, *Bull. soc. chim.*, (5) **2**, 1605 (1935).
(20) Cramer and Hibbert, THIS JOURNAL, **61**, 2205 (1939).
(21) High acetyl values were found to be due to production of volatile acids other than those from the acetyl groups.
(22) Hibbert, THIS JOURNAL, **37**, 1748 (1915).

ceed for four hours at 20°, the sodium methylate neutralized by addition of an equivalent amount of acetic acid, and the solvent evaporated at 20° under reduced pressure. The residue crystallized from a mixture of anhydrous methanol and ether (1:1) as dense rhombic crystals; yield 76%; m. p. 193–194.5°, with slight decomposition. *Anal.* Calcd. for $C_{15}H_{20}O_8$: C, 54.85; H, 6.14; OCH_3, 9.45. Found: C, 54.90; H, 6.30; OCH_3, 9.40.

β-d-Xyloside of α-Hydroxypropiosyringone.—Deacetylation was effected as described for the β-d-xyloside of α-hydroxypropiovanillone. The residue obtained after evaporation of the methanol from the reaction mixture had to be purified with utmost care, otherwise decomposition resulted. This was effected by dissolving in a minimum amount of anhydrous methanol at 20° and cooling to −10° when the xyloside crystallized in the form of fine needles; yield 73%; m. p. 149.4–150.0°. *Anal.* Calcd. for $C_{16}H_{22}O_9$: C, 53.60; H, 6.18; OCH_3, 17.32. Found: C, 53.51; H, 6.35; OCH_3, 17.28.

Guaiacol β-d-Xyloside.—This was prepared by deacetylation of the acetylated xyloside by the Zemplén method.[17] The xyloside crystallized from ethyl acetate in rod-shaped crystals, yield 85%, m. p. 175.3–176.0°. *Anal.* Calcd. for $C_{12}H_{16}O_6$: C, 56.23; H, 6.29; OCH_3, 12.10. Found: C, 56.20; H, 6.43; OCH_3, 12.05.

Acetovanillone β-d-Xyloside.—The conditions of deacetylation were as described by Zemplén.[17] The xyloside was recrystallized, first from ethyl acetate, and then from 50% anhydrous methanol–ether, and obtained in the form of very fine hair-like crystals; yield 85%; m. p. 145.2–145.7°. *Anal.* Calcd. for $C_{14}H_{18}O_7$: C, 56.25; H, 6.08; OCH_3, 10.40. Found: C, 56.20; H, 6.41; OCH_3, 10.30.

Acknowledgment.—The authors wish to thank the National Research Council of Canada for the financial assistance given to one of them (J. H. F.).

Summary

Methods are given for the synthesis of the β-d-xylosides of α-hydroxypropiovanillone, α-hydroxypropiosyringone, guaiacol and acetovanillone, and their corresponding fully acetylated derivatives.

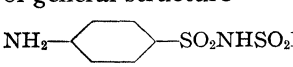
MONTREAL, CANADA RECEIVED MARCH 28, 1940

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE CALCO CHEMICAL DIVISION OF THE AMERICAN CYANAMID COMPANY]

Sulfanilamide Derivatives. VII. N¹-Alkanesulfonylsulfanilamides and Related Compounds[1]

BY M. L. CROSSLEY, E. H. NORTHEY AND MARTIN E. HULTQUIST

We were led to further investigation of sulfanilamide derivatives containing a disulfonamide linkage, $-SO_2NHSO_2-$, by the preliminary pharmacological results on disulfanilamide.[2] Long chain N¹-alkanesulfonylsulfanilamides analogous to the N¹-acylsulfanilamides[3] were of most interest, but a series of compounds was synthesized of general structure



$NH_2-C_6H_4-SO_2NHSO_2R$, where R was alkane (from 2 to 12 carbons), cycloalkane, and aralkane.

The synthesis of the intermediate sulfonyl chlorides followed the procedure of Treat B. Johnson.[4]

These were treated with N⁴-acetylsulfanilamide in aqueous solution and the resulting N⁴-acetyl-N¹-alkanesulfonylsulfanilamides were hydrolyzed by boiling with sodium hydroxide to remove the N⁴-acetyl group. The resulting N¹-alkanesulfonylsulfanilamides were highly water soluble for the lower members of the series, but became increasingly water insoluble in the higher members. All were strongly acidic and formed neutral sodium salts.

Chemotherapeutic Properties.[5]—Preliminary results in mice against beta-haemolytic streptococci indicate that these compounds as a class are of low chemotherapeutic activity. A complete evaluation of them awaits the final results of the chemotherapeutic study.

Experimental Part

N¹-Butanesulfonylsulfanilamide.—78.3 grams (0.5 mole) of 1-butanesulfonylchloride was added to a slurry of 214 g. (1 mole) of N⁴-acetylsulfanilamide and 400 cc. of water; 50% sodium hydroxide solution was added gradually to maintain a pink spot test on benzoazurine paper (*p*H 11–12) while holding the temperature at 35–40° by addition of ice. The time of adding sodium hydroxide was thirty minutes. When no more sodium hydroxide was consumed after stirring for thirty minutes, the reaction was considered

(1) Presented in part before the Division of Medicinal Chemistry, A. C. S. Meeting, Cincinnati, Ohio, April, 1940.

(2) Crossley, Northey and Hultquist, THIS JOURNAL, **60**, 2222 (1938).

(3) Crossley, Northey and Hultquist, *ibid.*, **61**, 2950 (1939).

(4) Johnson and Sprague, *ibid.*, **58**, 1348 (1936); Sprague and Johnson, *ibid.*, **59**, 1837 (1937); Johnson and Douglass, *ibid.*, **61**, 2549 (1939); U. S. Patent 2,147,346, Feb. 14, 1939.

(5) This phase of the work was carried out under the direction of W. H. Feinstone and will be reported elsewhere.

TABLE I

N^1-ALKANESULFONYLSULFANILAMIDES

Alkanesulfonyl group	Appearance	Melting range, °C.	Assay by $NaNO_2$	Assay by NaOH
Ethanesulfonyl-	Short prisms	206.5–207.5	101.0	101.0
1-Butanesulfonyl-	Plates	209.0–210.5	100.1	100.8
1-Pentanesulfonyl-	Plates	183.0–184.5	99.6	98.5
2-Ethyl-1-hexanesulfonyl-	Plates	189.0–191.0	100.5	100.0
1-Dodecanesulfonyl-	Plates	188.8–189.9	...	99.4
Cyclohexanesulfonyl-	Leaflets	230 dec.	100.0	100.3
10-*dl*-Camphorsulfonyl-	Leaflets	213.0–214.5	100.8	100.2
Phenylmethanesulfonyl-	Plates	242.0–243.5	99.8	99.4

to be complete. Dilute hydrochloric acid was added to bring the *p*H to 8–9 and the mixture was cooled to 15°. The excess N^4-acetylsulfanilamide was filtered and washed well with cold water. The mother liquor was acidified to *p*H 1 with hydrochloric acid. A sticky precipitate formed which soon crystallized to white, sandy crystals of N^4-acetyl-N^1-(1-butanesulfonyl)-sulfanilamide. A portion of the crude product was saved and purified by solution as the sodium salt, treatment with activated charcoal and reprecipitation. On attempting to recrystallize from water, partial hydrolysis of the N^4-acetyl group resulted.

The balance of the crude product was hydrolyzed with sodium hydroxide by the same procedure used for N^1-acylsulfanilamides.[3] The hydrolyzate on cooling and standing deposited coarse crystals of sodium N^1-(1-butanesulfonyl)-sulfanilamide which were salted out of solution by the excess sodium hydroxide present. The salt was twice recrystallized from concentrated aqueous solutions. Recoveries from the sodium salt mother liquors were made by acidifying to *p*H 4.0–4.5 and filtering off the free compound. This was recrystallized from water.

The other compounds listed in Table I were similarly prepared. All were assayed by the same procedures used for the N^1-acylsulfanilamides.[3] N^1-1-Dodecanesulfonylsulfanilamide was too insoluble in mineral acids to be analyzed by diazotization.

Summary

1. Sulfanilamide derivatives of the general formula, $NH_2(4)C_6H_4SO_2NHSO_2R$, were synthesized where R was alkane (2 to 12 carbons), cycloalkane and aralkane.

2. Preliminary studies in mice indicated low effectiveness of these compounds against beta-haemolytic streptococci.

BOUND BROOK, N. J. RECEIVED APRIL 9, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF MOUNT HOLYOKE COLLEGE]

Differences Observed in the Behavior of Unsaturated Hydantoins under the Action of Bromine

BY MARGARET J. MCLEAN AND DORIS R. SEEGER[1]

Reactions involving the addition of bromine to hydantoins possessing unsaturated side chains in the C-5-position have been reported as leading to the formation of quite different classes of compounds, the character of which seems to depend upon the conditions of the experiment. For example, unsaturated hydantoins in which a bromine atom was found to have replaced a hydrogen atom in the side chain invariably were formed when benzalhydantoin, anisalhydantoin and many similar compounds,[2] dissolved in glacial acetic acid, were treated with molecular quantities of bromine

(a) $HNCONHCOC{=}CHC_6H_5 \xrightarrow{+\ Br_2} NHCONHCOC{=}CBrC_6H_5 + HBr$

In other cases[3] where reactions were carried out in chloroform or carbon tetrachloride and these solvents subsequently displaced by alcohol, saturated ethoxy-monobromo derivatives of the hydantoins were formed.

(b) $CH_3NCON(CH_3)COC{=}CHC_6H_5 \xrightarrow[+\ C_2H_5OH]{+\ Br_2} CH_3NCON(CH_3)COC(OC_2H_5)CHBrC_6H_5 + HBr$

The question naturally arises as to whether these differences are due to the nature of the unsaturated hydantoins involved, or solely to experimental conditions. In the latter case *all*

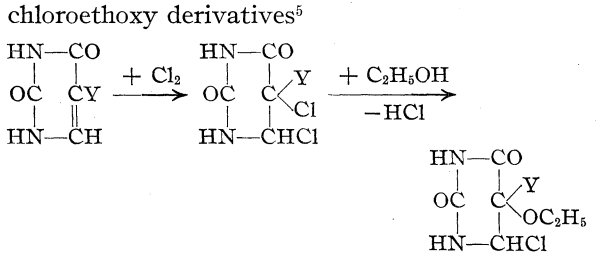
(1) Acknowledgment must be made to Dr. Dorothy A. Hahn for suggesting and coöperating in this research.

(2) Wheeler, Hoffman and Johnson, *J. Biol. Chem.*, **10**, 154 (1911); Wheeler and Hoffman, *Am. Chem. J.*, **45**, 376 (1911); Johnson and Wrenshall, THIS JOURNAL, **37**, 2133 (1915); Johnson and Davidson, *ibid.*, **47**, 563 (1925).

(3) Litzinger, *ibid.*, **56**, 676 (1934); Hahn, McLean and Murphy, *ibid.*, **60**, 1927 (1938).

classes of unsaturated hydantoins,[4] as represented for example by benzalhydantoin, its N-3-methyl and its N-1-N-3-dimethyl derivatives, might be assumed to be capable respectively of undergoing both types of transformation (a and b). This has now been shown to be the case.

That in each instance the final product results from a secondary reaction appears obvious because of the fact that the bromine is decolorized as rapidly as added and the reaction, which is usually complete within five minutes, is not accompanied by any apparent evolution of hydrobromic acid. Recently reactions similar to those indicated as (b) have been reported as taking place when the 2,4-diketotetrahydropyrimidines were treated first with chlorine in chloroform solution and subsequently with alcohol. In the case of unsaturated compounds of this type it was possible, moreover, to isolate primary dichloro addition products and then later under the direct action of alcohol to transform them into secondary chloroethoxy derivatives[5]



In the case of the unsaturated hydantoins under investigation the problem of isolating similar primary dibromo addition products presented serious technical difficulties because of the fact that they were extremely unstable. Nevertheless a single compound belonging to this class, namely, N - 3 - methyl - C - 5,5 - bromo - bromobenzyl-hydantoin, finally was obtained in the form of fine white needles which possessed a well-defined melting point and which was sufficiently stable to allow of a fairly satisfactory analysis. That the latter was not completely satisfactory was due to the fact that the substance is so unstable that even in solid condition it loses hydrobromic acid slowly at ordinary temperatures and on long standing passes quantitatively into the corresponding *unsaturated* mono-bromo derivative. It is insoluble in cold alcohol but, when warmed slightly, passes instantly into the corresponding *saturated* ethoxybromo derivative with the evolution of heat and hydrobromic acid. The corresponding dibromo addition product of benzalhydantoin was also separated in solid crystalline form but never in a sufficiently pure condition to justify an analysis. In the case of dimethylbenzalhydantoin all of the compounds involved in the bromination were so extremely soluble as to preclude any possibility of separating them.

That the final products formed in the transformations (a) and (b) belong to unsaturated and saturated classes of hydantoins, respectively, was confirmed by a spectrographic study, the results of which are presented in Fig. 1.[6] The pronounced differences between these two classes of hydantoin derivatives both as to intensity and region of absorption already have been established[7] and the present results agree closely with earlier reports.

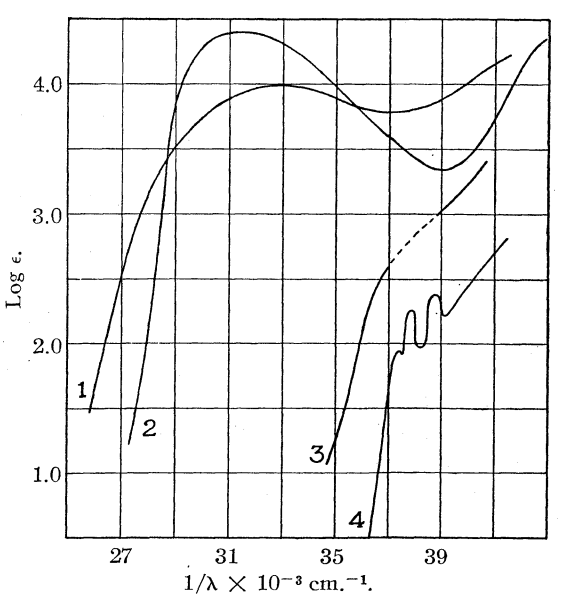


Fig. 1.—(1) Bromobenzalhydantoin; (2) benzalhydantoin; (3) C-5,5-ethoxy-bromobenzyl-hydantoin; (4) benzylhydantoin.

It may be noted in passing that the bromo-ethoxy addition products are compounds of phar-

(4) Compare Seikel, THIS JOURNAL, **59**, 436 (1937).

(5) Johnson and Sprague, *ibid.*, **59**, 2436–2439 (1937). It is interesting to note that ethylene linkages in both pyrimidines and hydantoins react under analogous conditions to form similar types of halogen-alkoxy addition products. This is perhaps remarkable in view of the fact that the double bond is incorporated in the ring structure in one case and in the side chain in the other. It should be added however that the kinetics of reactions of this kind have not as yet been completely elucidated [Bartlett and Tarbell, *ibid.*, **58**, 466 (1936)].

(6) Grateful acknowledgment is due Dr. Hildegard Stücklen for directing this work. The curves were plotted by Doris R. Seeger in partial fulfilment of the requirements for a B.A. degree with honors, June, 1939. In the case of 3 it may be added that a dotted line is used to indicate narrow bands due to the presence of the phenyl group although the exact positions could not be measured because of the diffuseness of the bands.

(7) Hahn and Evans, THIS JOURNAL, **50**, 809 (1928); Hahn and Dyer, *ibid.*, **52**, 2505 (1930); Hahn, McLean and Murphy, *ibid.*, **60**, 1928 (1938).

macological interest because of their relation as 5,5-disubstituted hydantoins to sodium diphenylhydantoin[8] and C-5,5-phenyl-ethylhydantoin.[9] The latter, due to their anticonvulsant and other therapeutic effects, are, as is well known, finding application in medicine in the treatment of epilepsy and related disorders. In this connection attention may be called to the marked decrease in toxicity that results from the substitution of methyl for hydrogen in the N-3- and N-1-N-3 positions in the hydantoin ring, as shown in the table,[10] where the figures represent the minimum lethal dose administered orally to mice:

$HN\overline{CONHCOC}(OC_2H_5)CHBrC_6H_5$	3.0 mg./M.
$HN\overline{CON(CH_3)COC}(OC_2H_5)CHBrC_6H_5$	80.0 mg./M.
$CH_3N\overline{CON(CH_3)COC}(OC_2H_5)CHBrC_6H_5$	120.0 mg./M.

These figures are especially significant in view of the fact that 12.0 mg./M. represents the minimum lethal dose of sodium diphenylhydantoin. None of the other possible physiological effects of the above bromoethoxyhydantoins have as yet been investigated.

Experimental

The N-3-methyl-C-5-benzalhydantoin[11] and N-1,N-3-dimethyl-C-5 benzalhydantoin[12] used in all of the following experiments were obtained by methods previously developed in this Laboratory. In preparing the corresponding unsaturated bromo derivatives the method used in the case of benzalhydantoin as reported by Wheeler, Hoffman and Johnson,[2] was followed.

N-3-Methyl-C-5-bromobenzalhydantoin, m. p. 173–173.5°, was obtained by adding bromine (4.5 g.) slowly to a suspension of N-3-methyl-benzalhydantoin (5.0 g.) in glacial acetic acid (25 cc.). The bromine was decolorized as rapidly as added and, on heating, copious fumes of hydrobromic acid were evolved. The clear solution, when evaporated to 15 cc. over a steam-bath and then set aside to crystallize, deposited 4.28 g. of a product, m. p. 160–166°, which was purified by recrystallization from alcohol.

Anal. Calcd. for $C_{11}H_9O_2N_2Br$: C, 46.99; H, 3.23; N, 9.97; Br, 28.43. Found: C, 46.79; H, 3.29; N, 10.00; Br, 28.50.

The substance is only slightly soluble in cold (1.0 g. in 100 cc.) but more soluble in boiling alcohol (10.0 g. in 100 cc.). Treated with hydrogen iodide and red phosphorus, it passed quantitatively into N-3-methylbenzylhydantoin which was identified by comparision with an analyzed specimen, m. p. 140–141°.[13]

N-1,N-3-dimethyl-C-5-bromobenzalhydantoin, m. p. 122–123°, was obtained and purified in a manner analogous to that described above.[14]

Anal. Calcd. for $C_{12}H_{11}O_2N_2Br$: C, 48.81; H, 3.76; N, 9.50; Br, 27.08. Found: C, 48.82; H, 3.94; N, 9.57; Br, 27.45.

The compound is very soluble in acetic acid and alcohol. Treated with hydrogen iodide and red phosphorus, it was transformed into N-1,N-3-dimethylbenzylhydantoin which was identified by comparison with an analyzed specimen, m. p. 86.5–87°.[11]

The method previously reported by Hahn, McLean and Murphy[3] was again applied in the preparation of C-5,5-ethoxy-bromobenzylhydantoin and of the corresponding N-3-methyl derivative although, due to the relative insolubility in carbon tetrachloride of the compounds taking part in both of these reactions, certain experimental difficulties were encountered. However, when care was taken to avoid the formation of any least trace of hydrobromic acid prior to the introduction into the reaction mixture of a relatively large volume of absolute alcohol, yields of more than 90% of each of the above products were obtained.

$N\overline{HCONHCOC}(OC_2H_5)CHBrC_6H_5$, **C-5,5-Ethoxy-bromobenzyl-hydantoin,** m. p. 202.5–203°, was prepared by adding a molecular quantity of bromine (17.2 g. diluted to 25 cc.) at 0° and under constant stirring, to benzalhydantoin, m. p. 218–219°, suspended in carbon tetrachloride (20.0 g. in 300 cc.). The reaction, which was complete in a few minutes, was accompanied by the transformation of the yellow crystals of benzalhydantoin into a precipitate of fine white crystals, the bromine being decolorized rapidly with no perceptible formation of hydrobromic acid. When, however, 300 cc. of absolute alcohol was added to the mixture and heat applied, hydrobromic acid was evolved in large quantities and a perfectly clear colorless solution was formed.[15] The latter was then alternately concentrated and treated with additional quantities of absolute alcohol until the carbon tetrachloride and last traces of hydrobromic acid had been largely eliminated, when upon cooling a white crystalline compound was deposited. Successive precipitates obtained from filtrates, all melting between 199 and 202°, were combined (31.9 g.) and purified by recrystallization from boiling absolute alcohol.[16]

(8) Merritt and Putnam, *Arch. Neurol. Psychiatry,* **42,** 1053 (1939).

(9) Pilcher and Gerstenberger, *Am. J. Diseases Children,* **40,** 1239 (1930).

(10) The biochemical investigation of ten gram specimens of these compounds, which were prepared in this Laboratory, was very kindly undertaken by Dr. Oliver Kamm, of the Research and Biological Laboratories of Parke, Davis and Company.

(11) Litzinger, THIS JOURNAL, **56,** 673 (1934).

(12) Hahn and Evans. *ibid.*, **50,** 817 (1928).

(13) For the electrolytic dissociation constant of this compound, compare Pickett and McLean, *ibid.*, **61,** 424 (1939).

(14) It is significant that the unsaturated monobromo derivatives can be recrystallized unchanged from alcohol and even from alcoholic solutions of hydrogen bromide. Great care must nevertheless be exercised in their preparation to avoid the presence of any trace of alcohol since otherwise mixtures are obtained which are very difficult to separate.

(15) In cases where hydrobromic acid was given off *before* the alcohol had been added, the product was found to be contaminated by the presence of a considerable quantity of bromobenzalhydantoin. Since the latter can be separated only with the greatest difficulty, care must be taken to avoid its formation which is always attended by the evolution of hydrogen bromide.

(16) The solubilities of the ethoxybromo derivatives of (a) benzal- and (b) methylbenzal-hydantoins in 100 cc. of absolute alcohol are respectively (a) 2.84 g. at 20° and 13.64 g. at the temperature of the boiling solvent; (b) 0.64 g. and 5.73 g. under the same conditions.

Anal. Calcd. for $C_{12}H_{13}O_3N_2Br$: C, 46.02; H, 4.18; Br, 25.52. Found: C, 46.09; H, 4.28; Br, 26.31.

$\overline{NHCON(CH_3)COC(OC_2H_5)CHBrC_6H_5}$, **N-3-Methyl-C-5,5-ethoxy-bromobenzyl-hydantoin,** m. p. 179–180°, was prepared under exactly the same conditions as those described above and obtained in approximately the same percentage yields. It was, however, also prepared by treating N-3-methyl-C-5,5-bromo-bromobenzyl-hydantoin directly with absolute alcohol, a reaction which will be described in more detail later. In both cases the product was purified by recrystallization from boiling absolute alcohol.[16]

Anal. Calcd. for $C_{13}H_{15}O_3N_2Br$: C, 47.71; H, 4.62; N, 8.57; Br, 24.42. Found: C, 47.71, 47.80; H, 4.62, 4.55; N, 8.59; Br, 24.37.

It will have been noted that the addition of bromine to both benzalhydantoin and N-3-methylbenzalhydantoin was accompanied by the formation of a voluminous white crystalline precipitate. This was thought to represent a primary dibromo addition product, but the fact that in each case it was practically as insoluble in carbon tetrachloride as the unsaturated hydantoin from which it was formed, made its separation from small unacted-upon quantities of the latter extremely difficult. In the case of benzalhydantoin this addition product was never obtained in a sufficiently pure condition to justify its analysis although a white crystalline compound was finally separated mechanically. The latter melted at 178–182° with an evolution of gas, formed a colorless solid on cooling and melted again at about 235°. This is interesting in view of the fact that bromobenzalhydantoin was reported by Wheeler, Hoffman and Johnson[2] as melting at 239–240°.

$\overline{NHCON(CH_3)COCBrCHBrC_6H_5}$, **N-3-Methyl-C-5,5-bromo-bromobenzyl-hydantoin,** m. p. 153–154° to a clear liquid prior to the evolution of gas, was prepared by treating 20 g. of N-3-methylbenzalhydantoin suspended in 300 cc. of boiling carbon tetrachloride with one equivalent of bromine. Within a few minutes the color had become pale orange and there was a heavy precipitate of very fine white needles which was filtered and washed free from bromine (27.0 g.). The precipitate was then suspended in cold carbon tetrachloride, and unchanged methylbenzalhydantoin which floated on the surface was removed by repeated decantations.

Anal. Calcd. for $C_{11}H_{10}O_2N_2Br_2$: C, 36.50; H, 2.78; Br, 44.15. Found: C, 36.82; H, 2.82; Br, 41.75. The same specimen analyzed two months later was found to have sustained a further loss of hydrobromic acid that made the amount practically quantitative.

Anal. Calcd. for $C_{11}H_9O_2N_2Br$: Br, 28.43. Found: Br, 28.67.

The compound is in fact so unstable that it loses hydrobromic acid slowly at room temperature, and when heated in an oven at 105° it passes quantitatively into N-3-methyl-C-5-bromobenzalhydantoin, m. p. 173–173.5°. It is almost insoluble in cold absolute alcohol but dissolves on warming to form a pale yellow solution. The latter suffers an almost immediate discharge of color accompanied by the evolution of hydrobromic acid and the separation of N-3-methyl-C-5,5-ethoxy-bromobenzyl-hydantoin, m. p. 179–180°.

Spectrographic measurements were made by the method developed by Stücklen[17] for use with a hydrogen lamp as the light source. Each compound was dissolved in absolute alcohol which had been especially purified for spectrographic use. A Hilger quartz spectrograph (E 36) was employed, and photographs were made on Eastman no. 40 plates. Although curves were plotted for the corresponding derivatives of both benzal- and methylbenzal-hydantoins, the latter corresponded so closely with the former that it has not been thought necessary to reproduce them.

Summary

The preparation under the action of bromine of C-5,5-bromoethoxy derivatives of both benzal- and N-3-methylbenzalhydantoins has been described and certain of their biochemical properties noted. In the case of N-3-methylbenzalhydantoin interest centers in the fact that a primary dibromo addition product was isolated which when warmed with absolute alcohol decomposed to give the corresponding bromo-ethoxy derivative but which when heated alone, passed quantitatively into N-3-methyl-C-5-bromobenzalhydantoin.

SOUTH HADLEY, MASS. RECEIVED APRIL 12, 1940

(17) Stücklen *J. Opt. Soc. Am.*, **29**, 37 (1939).

[CONTRIBUTION FROM ALLERGEN INVESTIGATIONS, BUREAU OF AGRICULTURAL CHEMISTRY AND ENGINEERING, U. S. DEPARTMENT OF AGRICULTURE, AND THE ALLERGY CLINIC OF PROVIDENCE HOSPITAL]

The Chemistry of Allergens. II. Isolation and Properties of an Active Protein Component of Cottonseed[1]

BY JOSEPH R. SPIES, E. J. COULSON, HARRY S. BERNTON AND HENRY STEVENS

The human allergic response provides the only available criterion for recognizing allergens, the substances in the diet or environment that act as specific incitants of a distinct group of human disease reactions called allergies. For the most part, allergens are considered to be either complete or partial antigens and, by virtue of this classification, closely related to the native proteins. To isolate and characterize as chemical entities the allergens of cottonseed is the objective of this investigation.

The isolation of a potent allergenic fraction CS-1[1a] from cottonseed recently has been described.[2] The previously characterized proteins of cottonseed were also shown to possess no important degree of inherent allergenic activity.[3]

The chemical procedures used in isolating CS-1 included alcohol precipitations, boiling in aqueous solution, precipitation of impurities with basic lead acetate, and removal of lead with hydrogen sulfide. These procedures are more drastic than are usually employed in the isolation of a biologically active substance. However, each step leading to the separation of CS-1 resulted in demonstrable increase in specific activity.

The literature concerning the immunological specificity of native plant proteins and protein split products is extensive.[4] As recently as 1936 Landsteiner stated, "The most important studies on the specificity of plant proteins were made by Wells and Osborne." The active protein constituent of CS-1 corresponds essentially in chemical and physiological properties with the "so-called proteoses" separated from seeds by Wells and Osborne.[5] Their proteoses were apparently chemically distinct from the other reserve proteins of seeds, possessed strong anaphylactogenic activity and were stable to heating at 100°. Earlier, Schloss[6] had demonstrated that the proteoses from almonds and oatmeal were more active than the other proteins in producing local skin reactions on a boy hypersensitive to these foods.

Clinically important allergenic constituents of cottonseed have been concentrated in CS-1. This paper describes the isolation from CS-1 of a protein-like substance possessing an unusual combination of chemical and physiological properties.

CS-1 formed a picrate having allergenic activity equal to that of CS-1. Retention of activity by the yellow picrate (CS-3) suggested chromatographic adsorption for further purification, characterization, and evaluation of homogeneity. The active constituents of CS-3 were quantitatively adsorbed by activated aluminum oxide in a sharply defined yellow layer which was resolvable into two layers by development with the solvent.

Diagram I shows the results of a typical chromatographic analysis of the picrate.

The major allergenic fraction, CS-5, appeared to be chromatographically homogeneous or composed of chemical entities too closely related to allow fractionation by this technique. Fractions CS-5 and CS-6 exhibited no appreciable differences in clinical activity. Both gave specific cutaneous reactions on cottonseed-sensitive patients in threshold dilutions ranging from $1:10^5$ to $1:10^6$ and could not be differentiated by im-

(1) Not subject to copyright.

(1a) For convenience in reference a system of symbols has been adopted to designate fractions.

(2) Spies, Bernton and Stevens, *J. Allergy*, **10**, 113 (1939).

(3) Jones and Csonka, *J. Biol. Chem.*, **64**, 673 (1925), in their study of the proteins of cottonseed observed that a significant portion of the total nitrogen in sodium chloride extracts of cottonseed was lost during dialysis of the heat uncoagulable fraction. This fraction was precipitable by tungstic acid but was not isolated or further characterized. This non-coagulable, diffusible fraction is apparently contained in CS-1.

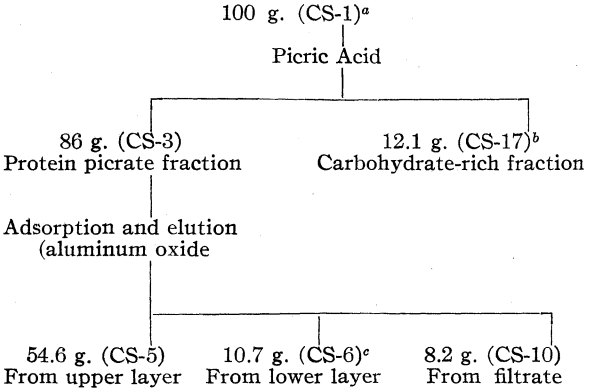
(4) For comprehensive reviews on these subjects see: H. Gideon Wells, "The Chemical Aspects of Immunity," The Chemical Catalog Co., N. Y., 1929; K. Landsteiner, "The Specificity of Serological Reactions," Charles C. Thomas, Baltimore, 1936; H. Zinsser, J. F. Enders and L. D. Fothergill, "Immunity—Principles and Applications in Medicine and Public Health," The Macmillan Co., New York, N. Y., 1939.

(5) Wells and Osborne, *J. Infectious Diseases*, **17**, 259 (1915), stated, "In their anaphylactic power these 'natural proteoses' differ sharply from proteoses obtained from animal proteins by digestion with enzymes or by chemical hydrolysis, such artificial products being almost if not entirely non-anaphylactogenic. Furthermore, those products of hydrolysis which result from heating vegetable proteins with acids, with water under pressure, or by peptic digestion, have, so far as we have tested them, no anaphylactogenic properties. From these facts it would seem that the vegetable 'proteoses' belong to a group of proteins which are chemically different from any heretofore recognized. They resemble highly soluble native proteins in their anaphylactogenic capacity and are probably quite as complex in their chemical constitution. Their designation as 'proteoses' is consequently improper." *Cf.* Fink, *J. Infectious Diseases*, **25**, 97 (1919).

(6) O. M. Schloss, *Am. J. Diseases Children*, **3**, 341 (1912).

DIAGRAM I

CHROMATOGRAPHIC ANALYSIS OF ALLERGENIC PROTEIN PICRATE FROM COTTONSEED



[a] Contained 5.1% water. [b] CS-17 was obtained from the filtrate, after removal of the picrate, by precipitation with 75% alcohol. Purification involving further precipitations with alcohol yielded a colorless substance containing 8.7% nitrogen. CS-17 does not reduce Benedict's reagent, but after acid hydrolysis has strong reducing properties, indicating its polysaccharidic nature. CS-17 possessed lower allergenic activity than CS-5, but evidence obtained in preliminary hydrolysis studies which are in progress indicates that this activity is inherent and not due to incomplete separation from the active portion of CS-5. [c] A chromatographic analysis of CS-6 with prolonged development failed to cause sufficient partitioning to indicate separation of chemically different components.

munological tests.[7] CS-10 obtained from the filtrate of the adsorption showed no allergenic activity and no antigenic properties.

CS-5 was demonstrated to be immunologically identical with antigen present in the unheated aqueous extract of cottonseed embryo. Intramuscular injection of 0.5 mg. of CS-5 in one arm produced wheals (15–40 mm. in diameter) in sites on the opposite arm passively sensitized with 0.05 ml. of serum from cottonseed-sensitive patients.[8]

A picric acid-free, nitrogenous compound (CS-13) was recovered from CS-5. CS-13 exhibited allergenic activity greater than CS-5 and was also immunologically identified with antigen present in the unheated aqueous extract of cottonseed embryo.

The method originally developed for the isolation of CS-1 has been modified and adapted to a larger scale process. The use of hydrogen sulfide in removing excess lead was eliminated to avoid possible introduction of sulfur into the product, CS-1A. CS-1A yielded an active picrate from which the picric acid-free compound CS-13A could be obtained analogously to CS-13. CS-13 and CS-13A gave the usual protein color and precipitation tests. The Molisch test was positive but the amount of carbohydrate present in these fractions was insufficient to reduce Benedict reagent even after acid hydrolysis. CS-13A contained 2.06% sulfur. Intramuscular injection of 0.01 mg. of CS-13A in one arm produced wheals (15–25 mm.) in sites on the opposite arm passively sensitized with 0.05 ml. of serum from cottonseed-sensitive patients.[9]

Available evidence indicates that the allergenic fractions CS-13 and CS-13A are protein in nature and native to the cottonseed.[10] The possibility is recognized, however, that these fractions may represent the allergenic group of some larger protein molecule, native to cottonseed. Further study would be required to reach a definite conclusion as to which hypothesis is correct. Designation of this type of substance as native protein is not provided for in existing protein classification systems. It is suggested, therefore, that the term natural proteose be adopted to describe them.

(7) The anaphylactic reaction of the guinea pig was used to demonstrate antigenicity. A detailed account describing the immunological reactions of allergenic constituents of cottonseed will be reported elsewhere.

(8) Thereafter, all sensitized sites failed to respond to a second similar injection of CS-5. However, a subsequent injection of 0.5 ml. of an unfractionated water extract of cottonseed (1:11) produced moderate wheals of less than one-half the size induced by the initial injection of CS-5. These results showed that CS-5 contained the principal allergenic constituent of cottonseed. Also demonstrated was the fact that the unfractionated extract contained more than one allergen capable of inducing positive reactions in sites passively sensitized with serum from cottonseed-sensitive subjects. Clinical observations have previously prompted the hypothesis that foods or pollens contain multiple allergens. For the first time the validity of this hypothesis has been experimentally demonstrated by actual isolation of one of the allergenic components. Clinical significance of these observations will be presented elsewhere. *Cf.* Lippard and Schmidt, *Am. J. Diseases Children*, **54**, 288 (1937).

(9) This was the threshold dilution, as 0.001 mg. of CS-13A produced slight reaction only in some cases.

(10) In chemical properties CS-13 corresponds to the proteoses except, however, that it does not give a precipitate with nitric acid and is more diffusible. The best evidence available, however, for regarding CS-13 as a complete or native protein is based on immunological data. While the subject is somewhat controversial, weight of opinion supports the view that complete proteins are required for antigenicity. P. Hartley, "A System of Bacteriology," vol. 6, His Majesty's Stationery Office, London, 1931, page 231, states, "The results which have been obtained in carefully conducted experiments in which due regard has been paid to chemical changes produced by hydrolysis and to the properties of the materials used led to the conclusion that antigenic function, so characteristic a property of native proteins, is lost when the large protein molecule is broken down into smaller fragments. At what stage in the breakdown of the proteins the property is lost is unknown but all available evidence supports the view that this occurs very early and before substances known as proteoses have been formed." Zinsser and Bayne-Jones, "Textbook of Bacteriology," 8th edition, 1939, p. 166, state, "The antigenic substance of proteins is easily destroyed by cleavage. Even the higher cleavage products, polypeptides and proteoses, no longer show antigenic properties."

Experimental[11]

Isolation of Active Fraction (CS-1A).—The fat was removed from choice quality, ground cottonseed embryo by extraction with benzene at temperatures not exceeding 25°.[12]

Three kilograms of benzene-extracted cottonseed was mechanically stirred for at least two hours with 18 liters of distilled water. The cake was separated by centrifuging and discarded. The extract was filtered through cheesecloth and heated to 100° in 12-liter flasks in an autoclave. After cooling, the coagulum was filtered off on cheesecloth. The filtrate was concentrated under reduced pressure (water pump) so that the volume of the combined extracts from 6 kg. of cottonseed was reduced to 5 liters. During this concentration the extract was allowed to flow into a 12-liter, three-necked distilling flask heated at 92–95° on a water-bath at a rate slow enough to prevent excessive foaming. It was also necessary to occasionally remove the concentrate from the distilling flask to facilitate evaporation.

Ethanol[13] was added slowly to the concentrated extract (5 l.) with stirring to 75%. The sticky brown coagulum which formed was collected and the brown solution was decanted and discarded. The coagulum was dissolved in 5 liters of distilled water by mechanical stirring and warming with a glass steam coil. When solution and uniform suspension was complete, ethanol was added to 25%. To this suspension was added 2.5 liters of 10% basic lead acetate (of the type used for sugar analysis) dissolved in 25% ethanol solution. The precipitated lead salts were separated by centrifuging and discarded. Colloidal lead salts suspended in the solution were further removed by passing through a Sharples super-centrifuge at 50,000 r. p. m. To the slightly turbid solution ethanol was again added with stirring to 70% concentration. The resulting suspension was allowed to settle at −7° overnight. The clear supernatant liquid was decanted and discarded. The solid was freed from most of the ethanol by suction on a Büchner funnel. When dried in a vacuum desiccator over phosphorus pentoxide and ground, 100 to 130 g. of a brown powder was obtained. The next step can be carried out directly, however, without drying the solid. The brown solid obtained from 6 kg. of cottonseed was dissolved and suspended in 1200 ml. of distilled water by vigorous mechanical stirring for two hours. The suspension was centrifuged in 250-ml. lots in the batch bowl of the Sharples super-centrifuge for twenty minutes at 45,000 r. p. m. A viscous, brownish, slightly turbid solution was obtained. To the centrifuged solution 60 ml. of 10% sodium carbonate solution was added. The suspended lead carbonate was removed by centrifuging in the batch bowl of the Sharples super-centrifuge at 45,000 r. p. m. for thirty minutes. The slightly turbid solution was then filtered with pressure through a no. 7 Seitz clarifying pad. The average *p*H of the solutions thus obtained was 9.5.[14] The *p*H was adjusted to 6.1–6.3 with 50% acetic acid solution. This solution was poured slowly with stirring into five volumes of cold ethanol. The suspension was adjusted to *p*H 6.1–6.3 with 20% sodium hydroxide and cooled overnight at −7°. The supernatant solution, which should be clear, was siphoned off and the solid was obtained by centrifuging. The solid (CS-1A) was dried in a vacuum over phosphorus pentoxide and powdered. The average yield from twelve 6-kg. lots of cottonseed was 68.4 g. A dried sample of CS-1A equilibrated with air contained 10.7% total nitrogen and 3.6% water. Clinical comparison of CS-1 and CS-1A showed that they possessed equal activity. CS-1A did not reduce Benedict reagent but gave strong reduction after acid hydrolysis. Preparations of CS-1 contained 14.7 to 15.8% nitrogen and undoubtedly the lower nitrogen content of CS-1A was due to a greater proportion of polysaccharide.

Preparation of Allergenic Protein Picrate (CS-3).—To the solution of 50 g. of CS-1 in 800 ml. of water there was added with stirring 1 liter of a saturated aqueous solution of picric acid (25°). The picrate suspension was cooled overnight at 5° and the yellow precipitate was separated by centrifuging. The picrate precipitate was washed by stirring with 500 ml. of water and recentrifuged. The resulting solid (CS-3) was dried in a vacuum over phosphorus pentoxide; yield, 42.5 g.

Chromatographic Adsorption of Allergenic Picrate.—Approximately 20-g. lots of finely ground CS-3 were dissolved in 5 liters of 50% ethanol by warming (50–60°) and stirring. The clear filtered solution was allowed to flow slowly through a 44 × 188 mm. column of activated aluminum oxide[15] (Brockmann).

A sharply defined yellow layer formed at the top of the column. Development with 500 to 1500 ml. of 50% ethanol resolved the original layer with formation of two layers.

Elution of Picrate.—Ninety-one grams of the aluminum oxide–picrate adsorption compound from the upper layer (from 20 g. of CS-3) was stirred for ten minutes with 500 ml. of 0.05 *N* sodium hydroxide. The solid was separated by centrifuging and eluted with three more 400-ml. portions of 0.05 *N* alkali. To the combined alkaline extracts there was added with stirring an equal volume of a saturated aqueous solution of picric acid (excess). The precipitated picrate was separated by centrifuging and washed by stirring with 500 ml. of water. The picrate (CS-5) was dried in a vacuum over phosphorus pentoxide. The average yield of eluted picrate from this layer was 64%. CS-5 contained 18% total nitrogen, was insoluble in water and organic solvents, moderately soluble in 50% aqueous ethanol, and very soluble in 50% dioxane.

Recovery of Active Protein from the Picrate.—To a solution containing 15 g. of eluted picrate dissolved in 1150 ml. of 0.05 *N* sodium hydroxide an equal volume of ethanol was added with vigorous mechanical stirring.

(11) Microanalyses were carried out by Thomas H. Harris and Ernest J. Umberger. Dorris C. Chambers assisted in the clinical studies.

(12) A modification of the extractor described by Drake and Spies, *Ind. Eng. Chem., Anal. Ed.*, **5**, 284 (1933), was used which permitted extraction of 25-pound (11-kg.) lots with solvent cooled to room temperature.

(13) Throughout this work commercial absolute ethanol was used and concentrations are expressed as volume per cent.

(14) The *p*H of aqueous solutions was usually determined with a Beckman *p*H meter. The *p*H of alcoholic suspensions, later referred to, was determined colorimetrically on a spot plate using brom cresol purple indicator.

(15) Obtained from Merck & Company, Rahway, N. J. Celite (Johns Manville Co.) adsorbs CS-5 weakly. Commercial silica gel does not adsorb it at all from 50% ethanol solution.

The *p*H of the clear solution was adjusted to 6.3 with 50% acetic acid. A second 1150 ml. volume of ethanol was then added and the suspension was allowed to stand at 5° overnight. The separated solid was centrifuged off and extracted with 400 ml. of water. The insoluble portion was separated and discarded. The solution was brought to *p*H 6.3 and, after stirring with decolorizing carbon, was filtered through a Seitz sterilizing pad. The clear solution was poured into 3 volumes of cold ethanol. The *p*H was adjusted to the coagulation point and the solution was allowed to stand at 5°. The coagulation point in 75% ethanol lies between *p*H 6.1 and 6.3 and is very sharp. The solid was separated and redissolved in 500 ml. of water. The solution was boiled with activated carbon, filtered, and reprecipitated with ethanol as before. The solid, CS-13, was centrifuged off and dried in a vacuum over phosphorus pentoxide; yield, 2.9 g. *Anal.* Found: N, 17.9.

CS-13 was soluble in water but insoluble in organic solvents. Results of color tests were: pinkish biuret, deep blue ninhydrin, positive Millon, negative Hopkins–Cole, faintly positive Molisch, no reduction of Benedict reagent after acid hydrolysis. Results of precipitation tests were: precipitates with phosphotungstic acid, picric acid and 2.5% trichloroacetic acid after boiling and cooling. No precipitates with basic lead acetate nor mercuric acetate. All tests were conducted on a 1% aqueous solution of CS-13. CS-13 diluted $1:10^6$ gave strong cutaneous reactions on cottonseed-sensitive patients.

CS-13A.—In an electrophoretic system the picric acid precipitable fraction of CS-1 and CS-1A migrated toward the negative electrode. In an electrophoretic fractionation of CS-1A (which will be described separately) the active substance in the cell containing the negative electrode was precipitated as the picrate. From this fraction the picric acid-free protein was isolated as follows: 2.9 grams of picrate was dissolved in 230 ml. of 0.05 *N* sodium hydroxide and 230 ml. of ethanol was added. The *p*H of the clear solution was adjusted to 6.3 with 10% acetic acid. To the suspension was added 460 ml. of cold ethanol and the *p*H again carefully adjusted to the coagulation point (6.1–6.3). The suspension was cooled overnight at −5°. The precipitated solid was centrifuged off. The gummy solid was dissolved in 75 ml. of warm water and the solution was boiled with carbon, cooled, centrifuged, and filtered through a Seitz sterilizing pad. The filtrate was poured into 300 ml. of cold ethanol. If coagulation does not occur, adjustment of *p*H to 6.3 is necessary. The suspension was cooled at −5° overnight. A yield of 1.47 g. was obtained by centrifuging and drying the solid over phosphorus pentoxide.

Further purification consisted of again reprecipitating with picric acid and recovering the picric acid-free solid (1.0 g.) as described before. This solid was dissolved in 50 ml. of water and the solution was boiled with carbon, cooled, and centrifuged. The solution was filtered through a fritted glass filter and poured into 190 ml. of cold ethanol. Coagulation occurred without *p*H adjustment. The suspension was cooled to −5°, centrifuged and the solid dried in a vacuum over phosphorus pentoxide. A yield of 0.79 g. of white solid (CS-13A) was obtained. A 1% solution of CS-13A gave the same reactions as those obtained with CS-13. A dried sample of CS-13A equilibrated with air was used for analysis. *Anal.* Found: C, 43.4; H, 6.78; ash, 0.51; N, 18.1 (micro Kjeldahl); S, 2.04, 2.09 (micro); H_2O, 9.4; P, neg. CS-13A diluted $1:10^6$ gave strong cutaneous reaction on cottonseed-sensitive patients.

Summary

1. The active component of the protein picrate obtained from a concentrate of allergenic constituents from cottonseed embryo was adsorbed quantitatively on aluminum oxide.

2. The adsorbed picrate fractions were eluted and recovered without loss of allergenic activity.

3. A protein possessing an unusual combination of chemical and physiological properties was recovered from the active picrate. The term natural proteose is suggested to designate proteins of this class.

4. Unfractionated aqueous extracts of cottonseed contain a substance or substances other than those present in CS-5 capable of inducing positive reactions in sites passively sensitized with serum from cottonseed-sensitive patients.

WASHINGTON, D. C. RECEIVED JANUARY 5, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF MCGILL UNIVERSITY]

The Reduction of α-Bromo-ketones by Aluminum Isopropylate with a Note on the Isomeric Amino-alcohols of the Ephedrine Series

BY PHILIP G. STEVENS, OWEN C. W. ALLENBY AND ADRIAN S. DUBOIS

In an earlier communication we[1] reported the reduction of α-bromo-ketones with aluminum isopropylate. Thus α-bromopropiophenone yielded the bromohydrin and halogen-free products. The former with methylamine gave a mixture of isomeric amino-alcohols, one of which was *dl*-pseudo-ephedrine. No *dl*-ephedrine was isolated.[2] The other isomeric amino-alcohol has now been found to be the *dl*-isoephedrine of Emde and Runne.[3] Inasmuch as this substance and *dl*-pseudo-ephedrine yield the same oxide, according to the boiling points recorded by Rabe and Hallensleben,[4] very likely it has the pseudo configuration, and so should be called *dl*-pseudo-isoephedrine.

In view of the discovery of Winstein and Lucas[5] that replacement by bromine of the hydroxyl group of certain bromohydrins involves a cyclic intermediate, with net retention of configuration, we believe that a similar series of reactions takes place here, rather than direct replacement with inversion. This would mean that both isomeric amino-alcohols are derived from the *threo*-bromohydrin through the *erythro*-oxide. We have no satisfactory explanation for the failure to obtain *dl*-ephedrine, unless the bromohydrin was principally the *threo*- form, or the *threo*-oxide gave complex products instead of the expected *dl*-ephedrine.[6] Work on this problem is now in progress.

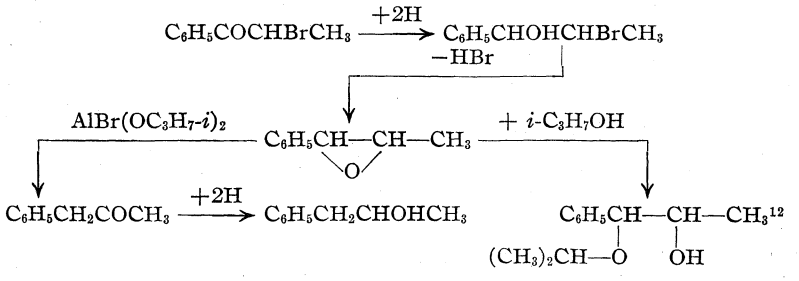
The secondary reduction products of the bromo-ketone are lower boiling, and bromine-free. The higher boiling of these turned out to be a mixture of carbinols, one of which was methylbenzylcarbinol. This carbinol undoubtedly arises from further action of aluminum isopropylate on the bromohydrin for, actually, purified bromohydrin yields appreciable amounts of the carbinol when treated separately with the alcoholate. Probably this transformation involves the oxide as an intermediate, which then must rearrange to phenylacetone,[7] followed by further reduction. It was puzzling, however, to understand how this could occur so easily in an aluminum isopropylate solution, until we found that part of the hydrobromic acid removed from the reaction products appeared as isopropyl bromide. The acid could not then be completely neutralized, and was still available, possibly in the form of $AlBr(OC_3H_7\text{-}i)_2$, for either reactions with alcohols, or isomerization of the oxide.

To test this, we treated the oxide with the isopropylate containing aluminum bromide. Rearrangement and simultaneous reduction occurred readily, and the products appeared to be the same mixture of carbinols with methylbenzylcarbinol predominating. We therefore prefer this oxide-rearrangement mechanism in this case, to that suggested by Winstein,[8] which would involve disproportionation of the bromo-ketone to propiophenone and the dibromo-ketone, because this should yield ethylphenylcarbinol and not methylphenylcarbinol. While it is possible that such disproportionation occurred, yet it must have been to a very small extent only, since Kröhnke[9] has shown that the equilibrium between dibromopropiophenone and propiophenone in the presence of hydrobromic acid is almost completely on the side of the monobromo ketone.

The carbinol fraction obtained both from reduction of the bromo-ketone and the oxide boiled over a wide range. This was not due to the other possible rearrangement reduction product of the oxide, hydratropic alcohol,[10] but to another non-isomeric hydroxy compound. This substance was obtained almost exclusively from the oxide and aluminum isopropylate without any aluminum bromide. Its composition corresponded to $C_{12}H_{18}O_2$, and it formed a *p*-nitrobenzoate and phenylurethan melting[11] at 100 and 95.5°, re-

(1) Stevens, THIS JOURNAL, **60**, 3089 (1938).
(2) Compare Fourneau, *J. Pharm. Chim.*, [6] **20**, 481 (1904).
(3) Emde and Runne, *Arch. Pharm.*, **249**, 369 (1911).
(4) Rabe and Hallensleben, *Ber.*, **43**, 2622 (1910).
(5) Winstein and Lucas, THIS JOURNAL, **61**, 2845 (1939).
(6) Compare Schmidt, *Arch. Pharm.*, **253**, 60 (1915).
(7) Compare Fourneau and Tiffeneau, *Compt. rend.*, **141**, 663 (1905); also Lévy and Dvoleitzka-Gombinska, *Bull. soc. chim.*, [4] **49**, 1765 (1931).
(8) After our first paper appeared, Winstein [THIS JOURNAL, **61**, 1610 (1939)] reported the reduction of α-bromocyclohexanone with aluminum isopropylate to about equal amounts of bromohydrin and cyclohexanol.
(9) Kröhnke, *Ber.*, **69**, 921 (1936).
(10) Compare Ref. 7.
(11) The *p*-nitrobenzoate of hydratropic alcohol melts at 65° (Cohen, Marshall and Woodman, *J. Chem. Soc.*, **107**, 887 (1915)).

spectively. The substance is possibly a mixture of mono isopropyl ethers of α-phenylpropylene glycol, formed by the addition of isopropyl alcohol to the oxide. The reduction reaction can then be represented as follows:



The lower boiling secondary product has not yet been identified. From its odor it cannot be the intermediate oxide. Because of the poor yields, we turned to α-bromoisobutyrophenone. As expected, reduction in the usual way gave products of very low bromine content (3–7%), and from these could be separated similar bromine-free products in much better yields. The higher boiling of these was a carbinol, $C_{10}H_{14}O$, not yet identified. By analogy it was a mixture of alcohols formed from the oxide.[13]

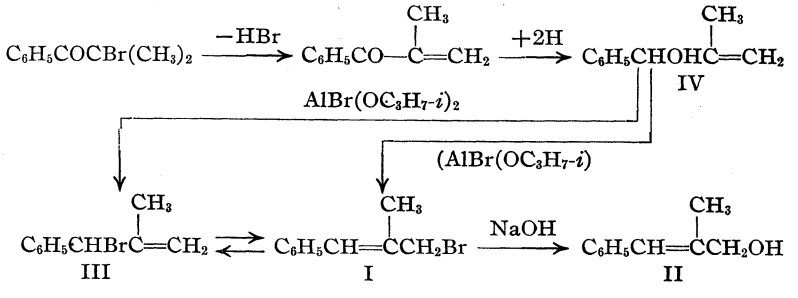
The lower boiling substance again was not the oxide. Its composition corresponded to $C_{13}H_{20}O$, and so it might be an isopropyl ether of some carbinol. Work on both alcohol and ether fractions is now in progress.

The most interesting development with α-bromoisobutyrophenone lay in its reduction with aluminum isopropylate at 33° *in vacuo*. Here the reduction took an entirely different course. In place of the usual products, the main product contained 37.2% bromine, with the composition $C_{10}H_{11}Br$. Oxidation with chromic acid yielding benzoic acid, and hydrolysis with sodium hydroxide to 2-methylcinnamyl alcohol II, indicated that the substance was 2-methylcinnamyl bromide I, or its isomer 1-phenylmethallyl bromide III. The bromide however had a higher boiling point (117°, 8 mm.) than 1-phenylmethallyl alcohol (100°, 8 mm.), strong evidence for the primary structure, as Claisen and co-workers[14] first pointed out with the isoprenyl bromides. Furthermore, the exaltation of the molecular refractivity was in good agreement with the primary structure:

	MR calcd.	MR found	Me
$C_6H_5CH{=}C(CH_3)CH_2OH$	45.84	46.94	+1.10
$C_6H_5CHOH{-}C(CH_3){=}CH_2$	45.84	45.70	−0.14
$C_6H_5CH{=}C(CH_3)CH_2Br$	52.08	52.72	+0.64

There is therefore little doubt but that the bromide is mainly the primary one. The original crude bromide, however, may well be an equilibrium mixture of both allylic isomers.

The formation of this primary bromide shows that at 33° reduction is very slow, and the aluminum isopropylate acts first to withdraw halogen acid. At 80–85°, however, it acts mainly to reduce the carbonyl group, the bromohydrin formed then undergoing secondary reactions. The steps in the former case can be written thus



This mechanism was tested by treating the carbinol IV with aqueous hydrobromic acid. The bromide formed, on hydrolysis with sodium hydroxide, yielded the isomeric primary alcohol II. Attempts to duplicate these reactions with α-bromopropiophenone at 33° were unsuccessful, for little if any reaction occurred. However, it is likely that both types of reaction occur whenever α-bromo-ketones with β-hydrogen are treated with aluminum isopropylate, the main course of the reaction depending on the conditions of the experiment, and the structure of the bromo-ketone.

We have also tried the reduction of a cyclic ketone[8] with secondary α-bromine. With 2-bromocholestanone, the more stable of the two α-bromocholestanones, according to Butenandt and Wolff,[15] reduction certainly occurred, but apparently no bromohydrin (if formed) survived.

Experimental Part

Reduction of α-Bromopropiophenone.—126 grams of the bromo-ketone, b. p. 127–129.5° (10 mm.), was added to a

(12) And/or its isomer, the β-ether.

(13) Lévy and Tabart, *Bull. soc. chim.*, [4] **49**, 1776 (1931).

(14) Claisen, Kremers, Roth and Tietze, *J. prakt. Chem.*, **105**, 65 (1922).

(15) Butenandt and Wolff, *Ber.*, **68**, 2091 (1935).

solution of 33.0 g. of aluminum as isopropylate in 1200 cc. of isopropyl alcohol, and the solution boiled under a reflux distilling column for nine hours. The acetone was removed by fractional distillation. The combined distillate on treatment with alcoholic silver nitrate gave a precipitate of silver bromide equivalent to approximately 8% of the total bromine, indicating the presence of isopropyl bromide. Propylene was also present as evidenced by rapid reduction by aqueous permanganate. Most of the isopropyl alcohol was removed *in vacuo*, and the residual pasty mass poured onto ice and dilute sulfuric acid, extracted with ether, washed with dilute acid, water, potassium carbonate, sodium hydroxide, water, dried over anhydrous potassium carbonate and distilled: first fraction up to 75° (0.1 mm.), second fraction, 44 g., b. p. 75–95° (0.1 mm.). The black tarry residue weighed 42.7 g. Redistillation of the second fraction yielded the bromohydrin, a somewhat viscous yellow-brown oil, b. p. 73–75° (0.1 mm.), $n^{25}D$ 1.5611. *Anal.* Calcd. for $C_9H_{11}OBr$: Br, 37.2. Found: Br, 34.8.

Another reduction was made using 60 g. of bromoketone, 26 g. of aluminum and 1730 ml. of isopropyl alcohol, the solution being approximately one-half as concentrated as above. The solution was boiled for nine hours. Very little isopropyl bromide was formed. The reaction product was worked up as before, and yielded 45 g. of a distillate passing at 70–73° (0.03 mm.). This was not homogeneous, however, and redistillation at 0.02 mm. of 69.5 g. gave the following fractions: (1) 5 g., 45–57°; (2) 7.8 g., 57–58°; (3) 20.8 g., 58–62°; (4), 25 g., 62–68°. The first two fractions were mainly the carbinols, etc., and the last was fairly pure bromohydrin, $n^{25}D$ 1.5643; d^{25}_4 1.429; MR calcd., 49.45; found, 48.96. *Anal.* Calcd. for $C_9H_{11}OBr$: C, 50.2; H, 5.1; Br, 37.2. Found: C, 49.9; H, 5.1; Br, 38.0. The bromohydrin was not very stable, redistillation always yielding considerable tarry residue. Freshly distilled bromohydrin was yellowish, but turned dark green on standing.

The Reduction Side-Reaction Products.—The more volatile material from the reduction of 126 g. of bromoketone boiled from 73–98° (8 mm.) of which the carbinol fraction boiled at 104–111° (16 mm.). This was redistilled taking the fraction b. p. 106–108° (16 mm.). Treatment with phenyl isocyanate yielded the phenylurethan of methylbenzylcarbinol, crystallizing from Skelly Solve B in fine silky needles, m. p. 87.0–87.5° (mixed m. p., 87–88°). The lower boiling substance was not investigated further.

Synthesis of Methylbenzylcarbinol.—This carbinol, b. p. 102–103° (16 mm.), $n^{25}D$ 1.5191, was prepared from phenylacetaldehyde and methylmagnesium iodide. The yield was poor, due to the formation of condensation products. The phenylurethan crystallized as fine needles from Skelly Solve B, m. p. 87–88°.[16]

One of the condensation products crystallized from ether and Skelly Solve A as fine long needles, m. p. 126.5–127.0°. *Anal.* Calcd. for $C_{17}H_{20}O_2$: C, 79.7; H, 7.8. Found: C, 79.8; H, 7.6. Its composition and reactions indicated a glycol structure. Oxidation with chromic acid yielded a yellow-brown oil which gave a deep wine color with ferric chloride, but no copper derivative with copper acetate. Very likely the substance is the aldol condensation product of phenylacetaldehyde which has reacted with methylmagnesium iodide, with the structure $C_6H_5CH_2CHOHCH—CHOHCH_3$, with C_6H_5 on the CH.

Action of Methylamine on the Bromohydrin.—27.2 grams of bromohydrin (34.8% Br) was treated with 40 g. of methylamine dissolved in absolute methanol. After twenty-eight days in the dark at 20–25°, the excess amine was removed *in vacuo*. The entire mass, now solid, was shaken with ether and water, and then extracted four times with dilute hydrochloric acid. The acid solution was extracted twice with ether, and then neutralized with cold concentrated sodium hydroxide. The liberated amine, partially crystalline, was extracted thrice with ether, dried over anhydrous potassium carbonate and the ether evaporated, thus yielding crystals. These were washed with cold Skelly Solve A, weight 7.7 g., yield 33%. After four recrystallizations from Skelly Solve B, the silky crystals melted 116.5–117° with preliminary sintering. A mixed melting point with an authentic sample of *dl*-pseudoephedrine (prepared from *dl*-ephedrine by heating with 25% hydrochloric acid, and recrystallized from Skelly Solve B, m. p. 116.5–117.2°) was 116.5–117°. Recrystallized from water, the melting point was 117–117.7°. The hydrochloride crystallized from alcohol and ether as needles, m. p. 162–163°.

The filtrate from the *dl*-pseudoephedrine was evaporated, yielding 10 g. of a red oil, 43% yield. This was taken up in ether, extracted with dilute hydrochloric acid, neutralized to a faint acid reaction using congo red, and evaporated in a current of air, then over potassium hydroxide *in vacuo*, yielding 13 g. of a dry salt. This salt was crystallized from isopropyl alcohol from which after 6–8 recrystallizations it separated as hexagonal plates, m. p. 188–190.5°. It was much more soluble than *dl*-ephedrine hydrochloride. *Anal.* Calcd. for $C_{10}H_{15}ON$: C, 59.6; H, 7.9. Found: C, 59.8; H, 8.1. A mixed melting point with an authentic specimen[17] of *dl*-pseudoisoephedrine hydrochloride (m. p. 188–190°) was 188–190°. A mixed melting point with *dl*-ephedrine hydrochloride, m. p. 184–185°, was 155–175°. The mother liquors contained in substantial amounts the basic complex products, which did not lend themselves to purification, and so were not further investigated.

Action of Aluminum Isopropylate on the Bromohydrin.—A solution of 10.75 g. of bromohydrin, b. p. 62–68° (0.02 mm.) in 150 cc. of isopropyl alcohol containing 4 g. of aluminum was boiled for fifteen hours. At first the distillate gave a heavy silver bromide precipitate with silver nitrate, and a copious test for acetone. At the end of the reaction these tests were faint. The products were worked up as usual and distilled at 16 mm., yielding 2.8 g. of a liquid, b. p. 66–120°, and much tar; redistillation at 16 mm., first fraction 0.7 g., b. p. 68–100° (mostly 72–74°); second, 1.1 g., 100–109°. This fraction formed a phenylurethan, m. p. 86–87° (mixed m. p. 86.5–88.0°).

α-Methyl-β-phenylethylene Oxide.—21.5 grams of α-phenylpropylene (prepared by the method of Gauthier[18]

(16) Emde and Runne reported 88–89° (ref. 3).

(17) Prepared according to the direction of Emde and Runne, ref. 3.

(18) Gauthier and Gauthier, *Bull. soc. chim.*, [4] **53**, 323 (1933).

and Gauthier) b. p. 79–82° (20 mm.) was added to 37 g. of perphthalic acid (prepared following the directions of Böhme[19]), dissolved in one liter of ether. After twenty-four hours at −1°, and four days at 20–25°, the ether solution was decanted from the phthalic acid, washed thoroughly with aqueous sodium carbonate and water, dried over anhydrous potassium carbonate, and distilled. The oxide fraction, b. p. 74–75° (9 mm.) weighed 15 g., 61% yield. Several batches of oxide were combined and redistilled, b. p. 77–78.8° (10 mm.), $n^{20}D$ 1.5207, $n^{25}D$ 1.5189.

Action of Aluminum Isopropylate on the Oxide. (a) **Without Aluminum Bromide.**—Fifteen grams of the oxide was added to a 1 molar solution of aluminum isopropylate (9 g. of aluminum), and the solution boiled under a reflux column for twelve hours. Fractions were removed at intervals. The reaction of the oxide was very slow, as evidenced by the slow formation of acetone. After eight hours, no more acetone could be detected. The products were worked up as usual. There was no odor of any remaining oxide. Distillation at 16 mm.: first fraction, 1 g., b. p. 118–121°; second, 14 g., 121–124°, viscous residue 1–2 g. Obviously there was very little if any methylbenzylcarbinol, b. p. 102–103° (16 mm.), or hydratropic alcohol, b. p. 111–112° (16 mm.). Redistillation at 11 mm.: b. p. 114–116°, $n^{25}D$ 1.4924, d^{25}_4 0.9877; MR calcd. 57.18; found 57.05. *Anal.* Calcd. for $C_{12}H_{18}O_2$: C, 74.2; H, 9.3. Found: C, 73.4; H, 9.1. The substance contained a hydroxyl group, as it formed a *p*-nitrobenzoate, crystallizing from ethyl alcohol, m. p. 99.5–100°. *Anal.* Calcd. for $C_{19}H_{21}O_5N$: N, 4.1. Found: N, 4.2. The phenylurethan crystallized from Skelly Solve A as feathery needles, m. p. 94.5–95.5°. *Anal.* Calcd. for $C_{19}H_{23}O_3N$: N, 4.5. Found: N, 4.6. The ease of formation of these derivatives suggests the α-ether structure rather than the β.

(b) **With Aluminum Bromide.**—The same quantities were used here as in (a), adding 4.5 g. of aluminum bromide. The isomerization and reduction were quite rapid, as acetone was evolved readily. After thirteen hours of boiling, the products were worked up in the same way and distilled at 16 mm., first fraction, 0.2 g., b. p. 85–107; second fraction, 9.35 g., b. p. 107–118°, third fraction, 3.85 g., b. p. 118–124°. There was very little residue. Obviously here the product was essentially a mixture of methylbenzylcarbinol, and the higher boiling so-called glycol ether. Fraction 2 was converted to the phenylurethan, m. p. 87–88° (mixed m. p. 87–88°).

Reduction of α-Bromoisobutyrophenone. (a) **At 80–85°.**—This bromo-ketone is easily prepared from isobutyrophenone by simple bromination. In spite of its tertiary bromine atom it reacts extremely slowly with alcoholic silver nitrate, a faint opalescence appearing only after fifteen to twenty minutes at 20–25°. This inactivity, it appears, is quite normal for α-bromo-ketones, for α-bromopropiophenone and α-bromopentamethylacetone likewise react very slowly. Unlike the former, but similar to the latter, α-bromoisobutyrophenone has almost no lachrymatory power. It boils about 10° lower than α-bromopropiophenone, b. p. 119–120° (10 mm.), $n^{25}D$ 1.5550, d^{25}_4 1.3663.

Sixty-eight grams of bromo-ketone was reduced by boiling with 27.5 g. of aluminum as isopropylate in 1000 cc. of isopropyl alcohol for seven hours. The amount of isopropyl bromide formed was approximately 30%. The products were worked up as usual, and distilled, b. p. 25–75° (0.03 mm.). This product was separated by repeated distillation into two fractions, (1) b. p. 81–87° (9 mm.) and (2) b. p. 100–103.5° (9 mm.). The first was refractionated through a reflux column packed with glass helices, and so yielded a substance with an odor somewhat reminiscent of geraniol, b. p. 83.8–84.5° (9 mm.),[20] $n^{25}D$ 1.4756, d^{25}_4 0.8985. It gave no precipitate with hot alcoholic silver nitrate, but reduced aqueous permanganate to some extent. *Anal.* Calcd. for $C_{13}H_{20}O$: C, 81.2; H, 10.4. Found: C, 81.0; H, 10.3.

The carbinol fraction contained about 5% bromine, and so was purified through the phthalate. It still boiled over the range 100–104° (9 mm.) but was bromine-free. The fraction of b. p. 101–103° (9 mm.) was possibly a mixture of carbinols. *Anal.* Calcd. for $C_{10}H_{14}O$: C, 80.0; H, 9.3. Found: C, 80.2; H, 9.5.

(b) **At 33°** *in vacuo*.—Thirty-four grams of bromo-ketone was added to a solution of 13.8 g. of aluminum in 865 cc. of isopropyl alcohol, and distilled through a reflux column at 63–65 mm. The bath temperature was 33–34°. The distillation was continued for about fifteen hours, and the reaction products stood two nights at 20–25°. Finally the test for acetone in the distillate was very faint. Very little if any isopropyl bromide could be detected. The product was worked up as usual and distilled, yielding 28.5 g. of an oil, b. p. 65–85° (0.02 mm.). The residue was only 1.7 g. Redistillation in a modified Claisen flask at 0.04 mm. yielded the following fractions, (1) 2.0 g., b. p. 30–64°; (2) 4.6 g., b. p. 64–73°; (3) 18.9 g., b. p. 73–74°. This last was redistilled at 8 mm. taking the following fractions (1) b. p. 80–107°, (2) b. p. 107–115°, (3) b. p. 115–117°. The third fraction represented 70% of the total, $n^{25}D$ 1.5921, d^{25}_4 1.323, MR calcd. 52.08, found 52.72. The bromohydrocarbon, a mild lachrymator, reacts instantly with alcoholic silver nitrate, and reduces permanganate rapidly. It did not absorb bromine in carbon tetrachloride, but did so slowly in acetic acid. *Anal.* Calcd. for $C_{10}H_{11}Br$: C, 56.9; H, 5.2; Br, 37.9. Found: C, 56.9; H, 5.1; Br, 37.2. Oxidation with chromic acid in hot acetic acid was rapid, and a lachrymator was evolved. The acid fraction was isolated in the usual way, yielding copious amounts of benzoic acid, m. p. 121–122°.

Hydrolysis of the Unsaturated Bromide.—One gram of the bromide was boiled for several hours with dilute aqueous sodium hydroxide, the oil extracted with ether, dried, the ether evaporated, and the residual oil distilled *in vacuo*. The distillate was colorless, bromine-free, and had a fine odor. It reduced permanganate instantly, and absorbed bromine in carbon tetrachloride rapidly. The dibromide crystallized from Skelly Solve B as needles, m. p. 86–87° (mixed m. p., 86–87°). The phenylurethan crystallized in long needles from Skelly Solve B, m. p. 78.2–78.8° (mixed m. p. 78.2–78.8°).

2-Methylcinnamic Aldehyde.—This aldehyde was prepared from propionaldehyde and benzaldehyde according to the directions of Miller and Kinkelin[21] with only slight

(19) Böhme, *Ber.*, **70**, 379 (1937).

(20) α,α-Dimethyl-β-phenylethylene oxide boils at 74° (10 mm.).

(21) Miller and Kinkelin, *Ber.*, **19**, 526 (1886).

modifications. The aldehyde, purified through the semicarbazone, m. p. 206–208°, boiled at 113° (12 mm.).

2-Methylcinnamyl Alcohol.—Reduction of the above aldehyde was carried out with aluminum isopropylate. The unsaturated alcohol boiled at 124–124.3° (8 mm.), $n^{25}D$ 1.5697, d^{25}_4 1.034, MR calcd. 45.84, found 46.94. On cooling it solidified, m. p. 19–21°. *Anal.* Calcd. for $C_{10}H_{12}O$: C, 81.1; H, 8.1. Found: C, 80.9; H, 8.1. The dibromide crystallized from Skelly Solve A as needles, m. p. 86.0–87.0°. *Anal.* Calcd. for $C_{10}H_{12}OBr_2$: Br, 51.9. Found: Br, 51.8. The phenylurethan crystallized from Skelly Solve B, m. p. 78.5–79.3°. *Anal.* Calcd. for $C_{17}H_{17}O_2N$: N, 5.6. Found: N, 5.5.

1-Phenylmethallyl Alcohol.—This isomeric alcohol was prepared from α-methylacrolein and phenylmagnesium bromide in the usual way, b. p. 99.8–100.0° (8 mm.), $n^{25}D$ 1.5361, d^{25}_4 1.010, MR calcd. 45.84, found 45.70. *Anal.* Calcd. for $C_{10}H_{12}O$: C, 81.1; H, 8.1. Found: C, 81.2; H, 8.3.

The dibromide was an oil. The phenylurethan crystallized from Skelly Solve B, m. p. 79.5–79.9° (mixed m. p. with the phenylurethan of its isomer above (m. p. 78.5–79.3°) was 57–65°). *Anal.* Calcd. for $C_{17}H_{17}O_2N$: N, 5.6. Found: N, 5.6.

Action of Hydrobromic Acid on 1-Phenylmethallyl Alcohol.—Fifteen grams of the alcohol was treated with 30 ml. of constant boiling hydrobromic acid for one hour, with frequent shaking. The alcohol layer became olive-green. The upper layer was separated, washed with cold sodium bicarbonate, dried over sodium sulfate and distilled, b. p. 165–165.5° (30–26 mm.), 10.3 g. The bromide was now boiled with dilute aqueous sodium hydroxide for four hours, and then worked up as usual. The unsaturated alcohol was distilled, b. p. 147–150° (33 mm.), and converted to the phenylurethan, m. p. 78.0–78.5° (mixed m. p. with the phenylurethan of 2-methylcinnamyl alcohol (m. p. 78.5–79.3°) 78.5–79.0°).

Reduction of 2-Bromocholestanone.—One-half gram of the bromo-ketone, m. p. 169–170°, prepared according to the directions of Butenandt and Wolff[15] was treated with 55 ml. of a 0.2 molal aluminum isopropylate solution. The ketone did not appear to dissolve even after four and one-half hours boiling. The product, recovered in the usual way, was a gum, which gave only a faint opalescence with boiling alcoholic silver nitrate. It was not investigated further.

Summary

1. Reduction of α-bromopropiophenone yielded the bromohydrin and halogen-free products, one of which was methylbenzylcarbinol.

2. The bromohydrin with methylamine gave *dl*-pseudo-ephedrine and *dl*-pseudo-isoephedrine. No *dl*-ephedrine was isolated.

3. Reduction of α-bromoisobutyrophenone at 80–85° yielded principally bromine-free compounds.

4. Reduction of α-bromoisobutyrophenone at 33° *in vacuo* yielded 2-methylcinnamyl bromide, the result of a loss of hydrogen bromide, reduction and replacement by halogen accompanied by an allylic rearrangement.

5. Reduction of 2-bromocholestanone occurred with complete removal of bromine.

MONTREAL, CANADA RECEIVED MARCH 27, 1940

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, NO. 222]

Intermediate Complexes in the Friedel and Crafts Reaction

BY JAMES F. NORRIS AND JOHN EDWARD WOOD, III[1]

In a former paper[2] a number of complexes were described which contained aluminum halides, aromatic hydrocarbons and hydrogen halides. The complexes differed in stability when submitted to diminished pressure. When the one having the composition $Al_2Br_6 \cdot 2C_6H_5(C_2H_5)_3 \cdot HBr$ was held at 0.002 mm. pressure until constant weight was obtained, one-half of the hydrocarbon was lost. We accordingly attempted to prepare directly a complex which contained its components in molecular ratio of $1Al_2Br_6$ to 1 *s*-$C_6H_3(C_2H_5)_3$. When a mixture of these compounds in the above ratio was treated with hydrogen bromide, a compound was formed which was shown by analysis to have the composition represented by the formula $Al_2Br_6 \cdot s\text{-}C_6H_3(C_2H_5)_3 \cdot HBr$. A compound of similar composition containing aluminum bromide, mesitylene and hydrogen bromide also was prepared.

The previous work of Norris and Ingraham indicated that a complex could be formed in which ethyl bromide replaced the hydrogen bromide. We have isolated complexes which have the formulas $Al_2Br_6 \cdot s\text{-}C_6H_3(C_2H_5)_3$, C_2H_5Br and $Al_2Br_6 \cdot s\text{-}C_6H_3(CH_3)_3 \cdot C_2H_5Br$. We were unsuccessful in attempts to prepare complexes of definite composition containing only aluminum halides and

(1) From the thesis of John Edward Wood, III, presented in partial fulfillment of the requirements for the degree of Doctor of Philosophy, 1939.

(2) Norris and Ingraham, THIS JOURNAL, **62**, 1298 (1940).

hydrocarbons. As far as the work has progressed it appears that a third component is necessary.

The complex which contained ethyl bromide was stable for several days. When it was heated or treated with additional ethyl bromide, hydrogen bromide was eliminated and the hydrocarbon was ethylated. This fact furnishes an explanation of the observation previously reported[3] that when methyl chloride was passed into a mixture of *m*-xylene and aluminum chloride at the temperature of a steam-bath no hydrogen chloride was evolved until about two-thirds of the methyl chloride had been added. It is probable that a ternary complex was first formed and later decomposed with the formation of alkylated benzenes or that the hydrogen chloride formed combined with the hydrocarbon and aluminum chloride to form a ternary complex.

The action of carbon dioxide on several complexes was studied since it has been shown[4] that when a mixture of benzene and aluminum chloride is treated under pressure with carbon dioxide, benzoic acid is formed. When the complex $Al_2Br_6 \cdot s\text{-}C_6H_3(C_2H_5)_3 \cdot HBr$ was allowed to stand with carbon dioxide at about 60 atmospheres pressure for fifty hours, no reaction took place. Under the same conditions the complex which contained two moles of triethylbenzene gave very small yields of what appeared to be the corresponding acid and ketone. When aluminum bromide and mesitylene without hydrogen bromide were used, 26% of the hydrocarbon was converted into *s*-trimethylbenzoic acid and 47% into the ketone. It was evident that the presence of hydrogen bromide in the complex interfered with the carbonation reaction. It is possible that the intermediate in this case contains aluminum bromide, hydrocarbon and carbon dioxide. If this is the case the hydrogen bromide must be removed before reaction takes place.

In order to gain information which might be of value in the interpretation of the structural relationships of the complexes, the compound having the formula $Al_2Br_6 \cdot s\text{-}C_6H_3(C_2H_5)_3 \cdot HBr$ was subjected to electrolysis. Wohl and Wertyporoch[5] have reported on the electrolysis of a compound to which they assign the formula $[Al(C_2H_5Br)n(C_6Et_6)_4]^{+++}3(AlBr_4)^-$.

In a preliminary experiment the conductivities were measured of a solution of aluminum bromide in toluene and of a similar solution after hydrogen bromide had been passed into it to form a complex. The conductivity of the latter was over 1000 times as great as that of the simple solution.

The complex $Al_2Br_6 \cdot s\text{-}C_6H_3(C_2H_5)_3 \cdot HBr$ was electrolyzed in a cell containing a porous cup. When the voltage between the anode and cathode was 18 volts and the current 0.1 ampere, gases were formed at both electrodes. After nine hours the material around the cathode and that around the anode were analyzed. Pure triethylbenzene separated at the cathode only. Analyses of the heavy oils in the two compartments of the cell for hydrocarbon, aluminum and bromine showed that a part of the aluminum bromide had been transferred from the catholyte to the anolyte. The oil from the latter yielded an organic product which consisted of *s*-triethylbenzene and higher boiling substances which contained bromine.

The results indicate that the complex studied is an ionized compound, that the positive ion contains hydrocarbon, and the negative ion aluminum and bromine, that the negative ion is transferred more rapidly than the positive ion, and that the reaction at the anode involves bromination. Whether or not a part of the aluminum bromide is present in the positive ion can be determined only by additional work which is to be done. The simplest formula which could be assigned to the complex with the present knowledge is $[C_6H_3(C_2H_5)_3H]^+Al_2Br_7^-$.

In the paper by Norris and Ingraham it was stated that when the complexes which contained aluminum bromide were treated with hydrogen chloride the bromine of the bromide was replaced by chlorine and a complex containing aluminum chloride was formed. It was of interest to find out whether a similar replacement took place when the aluminum halide was combined with other organic molecules. We have shown that similar replacements take place when the complex contains benzene or toluene. When hydrogen bromide was passed into the complex $AlCl_3 \cdot C_6H_5NO_2$ the chlorine was replaced by bromine, and the complex so formed was converted into the one containing aluminum chloride when it was heated with hydrogen chloride. A small amount of a by-product was formed. When hydrogen iodide was used some triiodoaniline was isolated.

The complexes containing aluminum halides and nitrobenzene are oxidizing agents. It should be noted the complex $2AlCl_3 \cdot C_6H_5NO_2$ must be

(3) Norris and Rubinstein, THIS JOURNAL, **61**, 1169 (1939).
(4) British Patent 307,223.
(5) Wohl and Wertyporoch, *Ber.*, **64B**, 1357 (1931).

handled with care. Once during its preparation it was heated too hot and an explosion occurred. When it was treated with benzene the mixture ignited. It is possible that under controlled conditions a mixture of aluminum chloride and nitrobenzene might prove to be a valuable oxidizing agent to be used in the absence of water.

In the study of the mechanism of the condensation of acyl chlorides with aromatic hydrocarbons by the Friedel and Crafts reaction, it is usually considered that the halogen in the halogen hydride formed is the halogen present in the acyl halide. To test this view the condensation of acetyl chloride with benzene by means of aluminum bromide and the condensation of acetyl bromide with benzene by means of aluminum chloride were studied. In the two cases both hydrogen chloride and hydrogen bromide were formed. When acetyl chloride and aluminum bromide were used 70 mole per cent. of the mixture of gases evolved was hydrogen bromide. When acetyl bromide and aluminum chloride were used, 77 mole per cent. of hydrogen chloride was obtained. Much the larger part of the halogen liberated as the halide was the halogen which was originally in combination with the aluminum. These facts lead to conclusions which will be tested.

Details of Experiments

The Complex $Al_2Br_6 \cdot s\text{-}C_6H_3(C_2H_5)_3 \cdot HBr$.—Aluminum bromide was distilled under anhydrous conditions into a flask and *s*-triethylbenzene was added. The weights used were 17.811 g. of Al_2Br_6 and 5.564 g. of hydrocarbon (mole ratio 1:1). When the mixture was heated to 100° a solution was obtained from which about one-half of the bromide crystallized out on cooling. Hydrogen bromide was passed into the mixture at room temperature as long as it dissolved. The increase in weight was 2.997 g. equivalent to 1.10 moles of hydrogen bromide. When the product which was an oil was held at 15 to 25 microns pressure for 1.4 hours, the loss in weight was 0.373 g. The hydrogen bromide left in the complex was equivalent to 0.970 mole. The complex was held at the same pressure for an additional eight and one-third hours; the loss in weight was 0.04 mole. A control experiment showed that under the same conditions a saturated solution of aluminum bromide in *s*-triethylbenzene lost 1.1 g. in seven hours. A repetition of the preparation in which 32.3 g. of Al_2Br_6 was used gave closely checking results.

Samples of the complex after evacuation were analyzed in the way described by Norris and Ingraham with the following results: % hydrocarbon, 20.21, 19.45; bromine, 70.4, 70.6; aluminum 7.56, 7.52. Calcd.: 20.85, 72.07, 6.97, respectively.

The Complex $Al_2Br_6 \cdot s\text{-}C_6H_3(CH_3)_3 \cdot HBr$.—The compound was prepared in a way similar to that described above. The product after the removal of excess hydrogen bromide was found to contain 0.95 mole of hydrogen bromide.

The Complex $Al_2Br_6 \cdot s\text{-}C_6H_3(CH_3)_3 \cdot C_2H_5Br$.—A mixture was made at 0° of equal molecular quantities of the components, Al_2Br_6, 23.58 g., mesitylene, 4.98 g., and ethyl bromide, 4.59 g. The mixture was shaken for one hour; at the end of this time a homogeneous red liquid was formed. This oil was held at 12 mm. pressure for three and one-quarter hours; the loss in weight was 0.02 g. The pressure was then reduced to 15–30 microns. At the end of a total of four and one-half hours the loss in weight was 0.03 g. To gain further evidence as to whether the ethyl bromide was chemically combined, the product was shaken with about 10 cc. of petroleum ether and the latter after separation and washing with water was tested for bromine with a copper wire. No halogen was found. A control experiment with a mixture of petroleum ether and ethyl bromide gave a positive test.

The Complex $Al_2Br_6 \cdot s\text{-}C_6H_3(C_2H_5)_3 \cdot C_2H_5Br$.—A sample of this complex was made in the way described above and the same tests were applied. Petroleum ether did not remove any ethyl bromide. The complex was slowly decomposed under diminished pressure; 41.5 g. of the complex which contained 5.65 g. of ethyl bromide when held at 15–30 microns pressure lost 0.10 g. in one-quarter hour and 0.40 g. in 5.5 hours.

A sample of this complex which weighed 30.6 g. and contained 3.45 g. of ethyl bromide stood at room temperature in a closed tube for seventeen days with no apparent change. At the end of this time 5 cc. of ethyl bromide was added; the complex dissolved at once. In a few minutes hydrogen bromide was evolved freely.

The Reaction of the Complexes with Carbon Dioxide.—In all the experiments the substances in a glass vessel were placed in an autoclave. After the air was displaced by carbon dioxide, the autoclave was connected directly with a cylinder containing liquid carbon dioxide. When 31.9 g. of the complex $Al_2Br_6 \cdot 2s\text{-}C_6H_3(C_2H_5) \cdot HBr$ was kept for fifty hours at 50° in contact with carbon dioxide, carbonation took place to a very small extent. Enough *s*-triethylbenzoic acid was obtained to make its identification possible by the melting point of the acid and its amide. A very small amount of a substance which probably was the corresponding ketone also was isolated.

Experiments with the complex $Al_2Br_6 \cdot 3s\text{-}C_6H_3(CH_3)_3 \cdot HBr$ yielded unsatisfactory results. A small amount of the dimesityl ketone was isolated, but no acid was identified.

The complex $Al_2Br_6 \cdot s\text{-}C_6H_3(CH_3)_3 \cdot HBr$ when treated with carbon dioxide at room temperature for fifty hours gave no ketone and no acid; 96.5% of the mesitylene in the complex was recovered.

The Carbonation of Mesitylene in the Presence of Aluminum Bromide.—A mixture of 51.3 g. of aluminum bromide and 23.1 g. of mesitylene (mole ratio $1AlBr_3$ to 1 hydrocarbon) was treated with carbon dioxide for sixty hours at room temperature. The product was decomposed by water in the way described above, and steam distilled; 6 g. of mesitylene was recovered. The aqueous part of the distillate was returned to the flask from which it had been distilled and the mixture was cooled in an ice-bath. The solid was separated by filtration and digested

with 10 g. of sodium hydroxide dissolved in 200 cc. of water. The insoluble residue weighed 11.5 g. The alkaline solution after acidification and cooling gave 8.5 g. of an acid. The material insoluble in alkali was crystallized three times from petroleum ether; it melted at 138.5–139.1°. The recorded melting point of dimesityl ketone is 136–137°. The acid formed was crystallized once from a mixture of alcohol and water and twice from petroleum ether; it melted at 152.0–152.4° (short range standardized thermometer). The recorded melting points of *s*-trimethylbenzoic acid vary from 147 to 155°. A sample of the acid which melted at 152.3° was converted into the amide; this melted at 185–186° (recorded m. p. 187–188°). The neutralization equivalent of the acid was 162.7 (theoretical 164.1). The yield of dimesityl ketone was 44.9% of the theoretical and of *s*-trimethylbenzoic acid 26.9%; 26.3% of the mesitylene used was recovered. When 2 moles of $AlBr_3$ and 1 mole of mesitylene were used the yields were 47.2% ketone, 26.4% acid, and 19.6% hydrocarbon.

Electrolysis of the Complex $Al_2Br_6 \cdot s\text{-}C_6H_3(C_2H_5)_3 \cdot HBr$.—In a preliminary experiment two solutions of aluminum bromide in toluene (mole ratio 1:1) were prepared. One solution was converted into the complex by passing into it hydrogen bromide until no free toluene was present. The conductivities of the solution and of the complex were determined in a conductivity cell of the usual type. The conductance of the simple solution was 1.5×10^{-4} mhos; that of the complex was 0.18 mho.

In another experiment the complex $Al_2Br_6 \cdot s\text{-}C_6H_3(CH_3)_3 \cdot C_2H_5Br$ was placed in a conductivity cell and a potential of 6 volts was applied. The current produced measured 0.05 ampere. For comparison a 0.1 *N* solution of sodium chloride was placed in the cell and a potential of 6 volts was applied; the current measured 0.18 ampere.

The complex $Al_2Br_6 \cdot s\text{-}C_6H_3(C_2H_5)_3 \cdot HBr$ was prepared and placed in a cell consisting of a 100-cc. beaker and a thin-walled alundum cup. Platinum electrodes were used. During the electrolysis a stream of dry nitrogen was passed over the cell. A potential of 18 volts across the electrodes was applied; the current was 0.1 ampere. Bubbling and darkening of the material was observed at both electrodes; no aluminum was deposited. At the end of nineteen hours the material at the cathode was a dark viscous substance and a light colorless oil which was shown to be *s*-triethylbenzene by the melting point of its trinitro derivative. There was no separation of hydrocarbon in the anode compartment of the cell.

The dark viscous material from the anode compartment and that from the cathode compartment were analyzed separately for aluminum, bromine and hydrocarbon. The results were as follows: anode, % Al, 8.29, 8.34; % Br, 74.3, 74.9; % hydrocarbon 14.0, 14.6; mole ratio Al:Br, 1 to 3.0. Cathode, % Al, 6.69, 6.54; % Br, 65.8, 63.5; % hydrocarbon 25.4, 27.6; mole ratio Al:Br, 1:3.3. Seven cc. of the insoluble oil obtained as the result of decomposition of the anolyte with water was distilled through a 2-inch (5 cm.) Podbielniak column; there were obtained 5.5 cc. of a liquid which boiled at 215° (*s*-triethylbenzene) and 1 cc. of a higher boiling fluorescent fraction which was shown to contain bromine.

Halogen Interchange in Complexes.—When hydrogen chloride is passed into a mixture of benzene and aluminum chloride a complex is formed very slowly; when, however, hydrogen bromide is used an oily complex soon begins to separate at room temperature. Hydrogen bromide was passed at room temperature into a mixture of 45 g. of aluminum chloride and 132 g. of benzene which was stirred (mole ratio Al_2Cl_6 to C_6H_6, 1:3). At the end of sixteen hours the heavy oily layer was separated from the benzene and aluminum chloride that had not reacted. The product contained chlorine and bromine in the atomic ratio of approximately 1:1. The treatment with hydrogen bromide was continued until all the aluminum chloride had passed into the lower layer; eleven hours were required. The atomic ratio in the complex was approximately bromine 4 to chlorine 1. Continued treatment with hydrogen bromide did not appreciably alter the ratio.

A similar replacement of chlorine by bromine took place when toluene and aluminum chloride were used. In this case the reaction was more rapid; with benzene twenty-seven hours were required to effect solution of the aluminum chloride, whereas with toluene two hours were sufficient.

The complex having the formula $AlCl_3 \cdot 2C_6H_5NO_2$ was kept at 90–100° and treated with hydrogen bromide for eleven hours. It was then held at diminished pressure for several hours to remove any dissolved hydrogen halides. The product was decomposed by water; it contained about 43% bromine and 2% chlorine; 92% of the chlorine had been replaced by bromine.

The complex $AlCl_3 \cdot C_6H_5NO_2$ was treated with hydrogen bromide for eight hours; at the end of this time 85% of the chlorine had been replaced by bromine. Hydrogen chloride was then passed into the product for eight hours at room temperature. The treatment increased the percentage of chlorine from 6.4 to 24.4%.

In an experiment in which $AlCl_3 \cdot C_6H_5NO_2$ was treated with hydrogen bromide for thirty hours at 90–100°, a small amount of a precipitate appeared in the solution. This was separated and treated with water. The product was shown by its melting point and that of its acetyl derivative to be 2,4-dibromoaniline.

About 39 g. of the complex $AlCl_3 \cdot C_6H_5NO_2$ was made in a tube and treated with hydrogen iodide at dry-ice temperature until 20 g. of the gas condensed. The tube was sealed and stood at room temperature for ten days. It was then heated at 65° for twenty hours. From the product was isolated a small amount of 2,4,6-triiodoaniline.

The Condensation with Benzene of Acetyl Chloride in the Presence of Aluminum Bromide and of Acetyl Bromide in the Presence of Aluminum Chloride.—The two reactions were carried out under the same conditions and equal molecular quantities were used. The molecular ratio was 1 aluminum halide, 1 acyl halide, 5 benzene. The weight of acetyl bromide was 45 g. During the reaction the flask containing the reactant was surrounded by ice and the contents were stirred. The aluminum halide was added slowly to the acyl halide and the benzene was allowed to drop, during one hour, onto the mixture. The evolved gases were collected in water. When the reaction was complete the flask was heated on a steam-bath until the evolution of gas ceased. The mixture of hydrogen halides in the water was analyzed. When acetyl bromide and aluminum chloride were used the mole per-

centage of hydrogen bromide was 23 and of hydrogen chloride 77; for each mole of hydrogen bromide there was formed 3.3 moles of hydrogen chloride. When acetyl chloride and aluminum bromide were used the mole percentage of hydrogen chloride was 30 and of hydrogen bromide 70; for each mole of hydrogen chloride there was 2.3 moles of hydrogen bromide. The yields of acetophenone in the two cases were nearly the same, 72 and 76%, respectively.

Summary

1. The preparation and some of the properties of the complexes having the following formulas are described: $Al_2Br_6 \cdot s\text{-}C_6H_3(CH_3)_3 \cdot HBr$, $Al_2Br_6 \cdot s\text{-}C_6H_3(C_2H_5)_3 \cdot C_2H_5Br$, $Al_2Br_6 \cdot s\text{-}C_6H_3(CH_3)_3 \cdot C_2H_5Br$.

2. The complex $Al_2Br_6 \cdot s\text{-}C_6H_3(C_2H_5)_3 \cdot HBr$ did not react with CO_2 at 60 atmospheres, but a mixture of Al_2Br_6 and $s\text{-}C_6H_3(CH_3)_3$ under the same conditions gave high yields of the dimesityl ketone and *s*-trimethylbenzoic acid.

3. When a complex which contains aluminum chloride and benzene, toluene, triethylbenzene or nitrobenzene was treated with hydrogen bromide at room temperature an exchange of halogen atoms took place. When the complex which contained aluminum bromide was treated with hydrogen chloride, exchange also took place.

4. When acetyl chloride was condensed with benzene by means of aluminum bromide 77 mole per cent. of the hydrogen halides formed was hydrogen bromide. When acetyl bromide and aluminum chloride were used the mole per cent. of hydrogen chloride was 70.

CAMBRIDGE, MASS. RECEIVED FEBRUARY 27, 1940

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, No. 223]

The Preparation of Nitriles and Amides. Reactions of Esters with Acids and with Aluminum Chloride. The Use of the Salt $NaCl \cdot AlCl_3$ in the Friedel and Crafts Reaction

BY JAMES F. NORRIS AND ALBERT JOHN KLEMKA[1]

In a former paper[2] the preparation was described of benzonitrile from benzamide or ammonium benzoate by means of aluminum chloride. Since the results were satisfactory, the method has been studied further and applied to the preparation of a number of typical compounds. As a guide in the use of the method the steps involved in the reaction were investigated. The results are indicated as follows

$$C_6H_5CONH_2 + AlCl_3 \xrightarrow{\text{heated}}$$

$$HCl + C_6H_5CONHAlCl_2 \xrightarrow{\text{higher temperature}} C_6H_5CN + HCl + AlOCl$$

In one experiment a part of the product formed after the first evolution of hydrogen chloride had ceased was decomposed by water; benzamide was recovered. The second part was heated to a higher temperature; more hydrogen chloride was formed and the nitrile distilled.

Eleven nitriles were prepared by this method; the yields were from 63 to 97%. In most cases, the double salt of aluminum chloride and sodium chloride ($NaCl \cdot AlCl_3$) was used. This compound can be prepared easily, is convenient to handle and has the added advantage that it gives higher yields and does not melt during the reaction and cause frothing. The method cannot be applied to amides containing functional groups which react with aluminum chloride; unsatisfactory yields were obtained from amides of dibasic acids.

A simple procedure was devised for a semi-micro method to be used in the identification of certain amides by converting them into nitriles and determining the melting point of the latter; about 10 milligrams of the amide is sufficient for the identification.

When ammonium salts of the acids were used the yields were low. It was shown that the first step in the reaction with aluminum chloride was not the formation of an amide.

Since this method of preparing nitriles involved the use of amides, the preparation of the latter directly from acids was studied. Biehringer and Borsum[3] have reported the interaction of an acid and an amide, as the result of which there is an interchange of the hydroxyl and amino groups. The reactions were carried out in sealed tubes at a high temperature and the yields were low.

(1) From a part of the thesis of Albert John Klemka presented in partial fulfillment of the requirements for the degree of Doctor of Philosophy, 1939.

(2) Norris and Sturgis, THIS JOURNAL, **61**, 1413 (1939).

(3) Biehringer and Borsum, *Ber.*, **39**, 3348 (1906).

In our experiments a mixture of the acid and acetamide was heated in a flask and the volatile material was condensed and collected; the latter consisted chiefly of acetic acid.

When the method was applied to 2,6-dichlorobenzoic acid a quantitative yield of *m*-dichlorobenzene was obtained in two hours. The acid was heated with acetamide at the temperature (225–235°) at which decomposition takes place to a slight extent in six hours. The effect of acetamide on other acids that lose carbon dioxide when heated will be investigated.

The interchange reaction between an acid and amide was shown to be a reversible one; an interchange took place between benzoic acid and acetanilide as the result of which benzanilide was formed. Certain esters were shown to interchange groups with acids; for example, benzoic acid and phenyl acetate were converted by heating into phenyl benzoate and acetic acid.

The use of the compound of aluminum chloride and sodium chloride in Friedel and Crafts condensations was studied in a few cases. Since the reagent was found to be much less reactive than aluminum chloride, it could be used with advantage in the case of halogen compounds that are decomposed by aluminum chloride. A good yield of diphenylmethane was obtained from benzyl chloride. With chloroform and carbon tetrachloride the condensation took place to a slight degree only.

A number of miscellaneous reactions related to the work being done in this Laboratory are described in the Experimental Part of this paper. These include the reaction between ethyl 2,6-dichlorobenzoate and aluminum chloride as the result of which the ester was quantitatively converted into a salt of the acid and ethyl chloride; the reaction between benzoyl chloride and ammonium chloride; and the condensation of benzoic acid with toluene.

Details of Experiments

Preparation of Nitriles.—The double salt $NaCl \cdot AlCl_3$ was prepared as follows. Thirty grams of dry sodium chloride was intimately mixed with 68 g. of pulverized aluminum chloride (equal molecular quantities) and heated in a flask for one hour at 230–250°. The liquid was poured into a beaker and stirred as it solidified to a meal. The product was kept in a tightly stoppered bottle and ground before use.

The process used in making nitriles was as follows. A mixture of the amide and the salt $NaCl \cdot AlCl_3$ was heated in a flask connected with a condenser and a receiver. The mixture was heated cautiously with a free flame until the evolution of hydrogen chloride had nearly ceased; it was then heated at a higher temperature until no more distillate was obtained and a charred solid remained in the flask. The volatile product was the nitrile in pure condition. The liquids were redistilled to free them from a small amount of dissolved hydrogen chloride. The boiling and melting points agreed closely with those given in the literature.

The yields of pure nitriles were as follows. CH_3CN (b. p. 81–82°) 91% (moles amide to moles $NaCl \cdot AlCl_3$, 0.2 to 0.26; decrease in $NaCl \cdot AlCl_3$ gave lower yields; aluminum chloride alone, 0.2 to 0.2 mole gave 43%). $(C_6H_5)_2CHCN$ (m. p. 72–73°) 52% (0.031 to 0.044 mole). *n*-$C_5H_{11}CN$ (b. p. 158–159°) 63% (0.052 to 0.068 mole). C_6H_5CN (b. p. 190.7° (cor.) (97% (0.2 to 0.2 mole). *o*-ClC_6H_4CN (m. p. 43–44°) 93% (0.03 to 0.036 mole). *p*-$CH_3C_6H_4CN$ (b. p. 217–220° (cor.)) 89% (0.062 to 0.077 mole). *p*-$NO_2C_6H_4CN$ (m. p. 149–150°) 29%. 2,6-$Cl_2C_6H_3CN$ (m. p. 142.5–143.5°) 67% (0.026 to 0.029 mole). 2,4,6-$Cl_3C_6H_2CN$ (m. p. 75–76°) (50 mg. of acid used). α-$C_{10}H_7CN$ (m. p. 31–32°) 79% (1 g. of amide used). β-$C_{10}H_7CN$ (m. p. 65–66°) 80% (2 g. amide and 2.3 g. $NaClAlCl_3$).

In the study of the mechanism of the reaction, equal molecular quantities of benzamide and $NaCl \cdot AlCl_3$ were heated; when the temperature reached 140–150° hydrogen chloride began to be evolved. When the reaction ceased the temperature was raised to 290–295° before any more gas was formed. At this temperature hydrogen chloride was evolved freely and benzonitrile distilled from the flask; two moles of hydrogen chloride was formed.

Equal molecular quantities of benzamide and aluminum chloride were heated. At the melting point of the amide hydrogen chloride was evolved and the aluminum chloride dissolved in the liquid. The product, after solidification, was hydrolyzed by water; 86% of the amide was recovered.

p-Nitrobenzamide was heated with $NaCl \cdot AlCl_3$ (equal moles) at 180° until one mole of hydrogen chloride was formed. More of the salt was added but no additional hydrogen chloride was formed. The product was steam distilled; no nitrile was obtained. The amount of amide recovered was 94% of the amount used.

The Semi-micro Procedure.—The following procedure is recommended. A powdered mixture of 10 mg. of the amide and the equivalent weight of $NaCl \cdot AlCl_3$ or aluminum chloride is introduced into a 6-mm. tube closed at one end. In order to prevent the mixture from coming into contact with the sides of the tube, it is introduced through a second tube drawn out so that it can be placed in the reaction tube. The latter is then heated about 4 cm. from the closed end and drawn down to the diameter of a melting point tube. The mixture is heated cautiously above a flame until the hydrogen chloride has been given off. It is then heated slowly at a higher temperature until the nitrile formed has sublimed into the narrow part of the tube. When cold, the narrow tube is cut off and the melting point of the nitrile determined in a melting point block. The observed and the recorded melting points (in parentheses) are given of the nitriles made in this way; *o*-ClC_6H_4 45–46° (42–43°); 2,6-$Cl_2C_6H_3CN$ 144.5–146.5° (143°); 2,4,6-$Cl_3C_6H_2CN$ 75–76° (77.5°); 4-$NO_2C_6H_4CN$

144.5–146.5° (149°); α-$C_{10}H_7CN$ 31–32° (33.5°); β-$C_{10}H_7CN$ 63–64° (66°).

Nitriles from Ammonium Salts.—Attempts were made, without success, to isolate an amide as an intermediate product in the formation of nitriles from ammonium salts. In all cases the acid was recovered, although much hydrogen chloride was formed. The yields of acetonitrile (50%) and benzonitrile (48%) were about one-half of those obtained from the amides, when the ammonium salts and $NaCl \cdot AlCl_3$ were heated together in the molecular ratio of 1 to 2.

The Reaction between Acids and Amides.—The reactions were carried out in a 125-cc. distilling flask in the neck of which was placed a 3 cm. layer of glass beads. The latter served to prevent the acetamide used from distilling from the flask which was connected with a condenser and heated in a metal-bath.

One-tenth mole of benzoic acid was heated for two and one-half hours at 220–230° with 0.125 mole of acetamide. The distillate contained a little water, acetic acid and a small amount of benzonitrile. The benzamide formed in three experiments was 46, 51, and 53% of the theoretical yield. When equal molecular quantities of the acid and amide were refluxed for seven hours, the yield of benzamide was 30%.

The reaction was shown to be a reversible one. When equal molecular quantities of acetic acid and benzamide were refluxed for twenty-four hours, 42% of the benzamide and 31% of the acetic acid were recovered. The amount of benzoic acid formed showed that the interchange had taken place to the extent of 35%.

o-Chlorobenzoic acid gave 39% of its amide when heated with acetamide. The acid which did not react was recovered. When 16.1 g. of 2,6-dichlorobenzoic acid was heated at 225–235° for six hours with acetamide, the distillate was 93% of the theoretical yield of *m*-dichlorobenzene. When aliphatic dibasic acids were heated with acetamide the yield of amides was small. When formamide or urea was substituted for acetamide the yields were unsatisfactory.

An interchange of groups took place when benzoic acid was heated with acetanilide for three hours at 230–240°. The acetic acid formed was 65% of the theoretical and the benzanilide 50% after recrystallization.

Interchange between an Acid and an Ester.—An interchange of groups took place when 0.1 mole each of benzoic acid and phenyl acetate and 4 drops of sulfuric acid were heated at 175–177° for two and one-half hours; 49% of the benzoic acid was converted into phenyl benzoate.

The interchange reaction between benzoic acid and ethyl acetate gave 15% ethyl benzoate. No reaction took place between benzoic acid and phenetole.

The Use of the Compound $NaCl \cdot AlCl_3$ in Friedel and Crafts Condensations. Preparation of Diphenylmethane.—Into a mixture of 32 g. of $NaCl \cdot AlCl_3$ and 100 cc. of benzene was allowed to drop, during one hour, a solution of 63 g. of $C_6H_5CH_2Cl$ in 75 cc. of benzene, the temperature being held at 15–20°. Dry air was drawn over the mixture for one hour. It was then hydrolyzed. The product was distilled at 33 mm. pressure. The yield of diphenylmethane (b. p. 154–155°) obtained was 44 g. Diphenylmethane, which is converted into a tar by aluminum chloride, was not appreciably affected when a solution of 5 g. of the hydrocarbon in 15 cc. of benzene was allowed to stand with 3.5 g. of $NaCl \cdot AlCl_3$ for one hundred hours at room temperature. Stilbene and phenanthrene are rapidly changed by aluminum chloride; they were unaffected by $NaCl \cdot AlCl_3$ at room temperature.

Benzene condensed with chloroform or carbon tetrachloride in the presence of $NaCl \cdot AlCl_3$ at room temperature to only a very slight extent. The salt was active enough to bring about the usual reaction between benzene and alkyl halides.

Benzoyl Chloride and Ammonium Chloride.—The acyl chloride (0.20 mole) was refluxed with 0.34 mole of ammonium chloride for two hours; at the end of this time the odor of benzoyl chloride was no longer apparent. The product was treated with a solution of sodium hydroxide; the oil formed (9.8 g.) was shown to be benzonitrile; 10.2 g. of benzoic acid was recovered from the alkaline solution. An explanation of the reaction was evident from the results of Titherly and Holden,[4] who showed that benzoyl chloride and benzamide react and form benzonitrile and benzoic acid. In our experiment the benzamide probably formed from the chloride and ammonium chloride reacted with benzoyl chloride. The yield of nitrile obtained was close to that theoretically possible.

Reaction between Esters and Aluminum Chloride.—The study of this reaction[5] has been extended. Ethyl benzoate (0.1 mole) and aluminum chloride (0.1 mole) were mixed and heated cautiously in a flask, placed in a metal-bath, until the heat generated by the formation of the molecular compound had been given off. The flask was connected with a receiver cooled by dry-ice. The temperature was raised at the rate of about 1° per minute. At about 150–155° the solid melted. At 165° ethyl chloride began to condense. At the end of five hours the reaction ceased. The ethyl chloride obtained was 95% of the theoretical yield. The residue in the flask melted at 245°. When twice the amount of aluminum chloride was used only a few drops of ethyl chloride were obtained; a viscous mass was left in the flask.

Ethyl 2,6-Dichlorobenzoate and Aluminum Chloride.—The ester was prepared by treating the acid with thionyl chloride, removing the excess of the latter by heating and final heating with alcohol. The yield of the pure ester was 82%. To 7.1 g. of the ester 4.5 g. of aluminum chloride was added slowly while the mixture was cooled. The molecular compound melted at 90–95°; at 110° the rate of formation of ethyl chloride was appreciable. The temperature was raised to 120–130°. At the end of two and one-half hours reaction ceased. The weight of ethyl chloride formed was 91% of the theoretical. The residue was treated with water and acidified. The weight of 2,6-dichlorobenzoic acid (m. p. 141.5–142.5°, recorded 139–140°) was 92% of the theoretical yield. It should be noted that this ester of a diortho acid reacted with aluminum chloride at a much lower temperature than did ethyl benzoate or ethyl acetate. This fact is added evidence of the lability of the alkyl–oxygen bond produced by two groups in the ortho position to the carboxyl group. Treatment of these esters with hydrobromic acid or aluminum chloride

(4) Titherly and Holden, *J. Chem. Soc.*, **101**, 1876 (1912).

(5) Norris and Arthur, THIS JOURNAL, **62**, 874 (1940).

appears the best method of converting them into acids, since hydrolysis is effected with difficulty.

The ester and acetamide were distilled slowly at 200–210° for three hours to discover whether an interchange of groups would take place. Twenty-eight per cent. of the ester was converted into *m*-dichlorobenzene and the rest was recovered. The temperature used (200–210°) was below that at which the acid first loses carbon dioxide (235°).

Phenyl Tolyl Ketones from Toluene and Benzoic Acid.—Groggins[6] has shown that chlorobenzophenone can be prepared by condensing chlorobenzene with benzoic acid by means of aluminum chloride. We have applied the reaction to toluene. A mixture of 0.20 mole of benzoic acid, 0.40 mole of aluminum chloride and 0.44 mole of toluene was refluxed for six hours. About two-thirds of the 60% yield of ketones was a mixture which contained *p*-tolyl phenyl ketone and a smaller amount of the ortho isomer. When benzene was used with benzoic acid about 90% of the acid was recovered.

Summary

1. Eleven examples are given of the preparation with excellent yields of nitriles by the reaction between amides and aluminum chloride or the compound $NaCl \cdot AlCl_3$. The process can be used on a semi-micro scale as an aid in the identification of amides.

2. It has been shown that a reversible reaction takes place between an acid and an amide as the result of which the NH_2 and OH groups exchange places.

3. 2,6-Dichlorobenzoic acid loses its carboxyl group quantitatively when heated with acetamide at a temperature at which it is relatively stable when heated alone. The ester of the acid is quantitatively converted into the acid and ethyl chloride when it is heated at 110° with aluminum chloride.

4. The following are described: the reaction between benzoyl chloride and ammonium chloride, the use of the compound $NaCl \cdot AlCl_3$ in the Friedel and Crafts reaction and the condensation of benzoic acid with toluene by means of aluminum chloride.

(6) Groggins, Nagel and Stearton, *Ind. Eng. Chem.*, **26**, 1317 (1934).

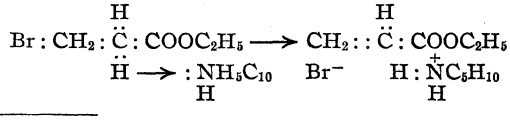
CAMBRIDGE, MASS. RECEIVED FEBRUARY 27, 1940

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

The Reaction of Organic Halides with Piperidine. V. Negatively Substituted Ethyl Bromides

BY E. LEON FOREMAN AND S. M. MCELVAIN

In the preceding paper[1] of this series it was shown that esters with a β-bromo substituent are very much more reactive toward piperidine than are other types of bromo-esters. Also it was shown that the reaction involves, first, the elimination of hydrogen bromide from the β-bromo-ester, and then the addition of piperidine to the resulting acrylic ester. The mechanism by which the acrylic ester is formed was thought to be the removal of a proton from the α-carbon atom of the bromo-ester by the nucleophilic reagent, piperidine, followed by the release of the bromide ion from the molecule,[2] thus



On the basis of such a mechanism it is obvious that the reactivity of β-substituted ethyl bromides, YCH_2CH_2Br, should parallel the electronegativity of the group Y.

The present paper reports the preparation and reactivity of a number of such negatively substituted ethyl bromides with piperidine. In the cases that Y is carbethoxy, cyano or benzoyl the rate of reaction of the bromide with piperidine is so rapid (*e. g.*, ethyl β-bromopropionate reacts to the extent of 94% in fifteen minutes at room temperature) that it cannot be measured readily. For this reason negatively substituted phenylethyl bromides, $YC_6H_4CH_2CH_2Br$, were used. These vinylogs of the more simply substituted ethyl bromides are, in most cases, more easily prepared and generally show a lower and more readily determined reaction rate.

Experimental

Preparation of β-Substituted Ethyl Bromides.—Ethyl β-Bromopropionate was prepared from ethylene cyano-

(1) Drake and McElvain, THIS JOURNAL, **56**, 697 (1934).

(2) A similar idea as to the mechanism of this type of elimination reaction has been expressed in a footnote of a paper by Noller and Dinsmore, *ibid.*, **54**, 1025 (1932), and also by Hauser and coworkers, *ibid.*, **57**, 1056 (1935); **59**, 1823 (1937).

hydrin.[3] **β-Bromopropionitrile**[4] was prepared by the reaction of ethylene cyanohydrin with phosphorus tribromide in benzene solution. The yield of product, boiling at 68–69° (7 mm.), d^{25}_4 1.6234, $n^{25}D$ 1.4789, was 43% of the theoretical. **β-Bromopropiophenone.** This compound had been prepared several years ago in this Laboratory by Frederick Beyerstedt and William Rinelli according to the following procedure. In a 2-liter round-bottom, 3-neck flask, fitted with a reflux condenser, an efficient stirrer and a dropping funnel were placed 500 ml. of carbon bisulfide, 100 g. of thiophene-free benzene and 260 g. of anhydrous aluminum chloride. The flask was set in an ice–salt mixture, stirring started, and 171 g. of β-bromopropionyl chloride[5] added through the dropping funnel at such a rate that the carbon bisulfide refluxed gently. After the addition of the halide, the ice-bath was removed and stirring continued until no more halogen acid was evolved. The reaction mixture then was poured carefully onto a mixture of ice and hydrochloric acid and, after thorough stirring, the carbon bisulfide layer separated. This layer was washed well with water and the solvent removed by distillation from a steam-bath. The remaining residue on cooling solidified. The yield of crude product amounted to 200 g. (93%). After recrystallization from petroleum ether the product melted at 58–59°.

Anal. Calcd. for C_9H_9OBr: Br, 37.5. Found: Br, 37.7.

Preparation of Substituted β-Phenylethyl Bromides. β-Phenylethyl Bromide.—This compound was prepared from Eastman Kodak Co. β-phenylethyl alcohol by the procedure of Norris.[6] The product boiled at 86° (8 mm.); $n^{25}D$ 1.5545.

***o*- and *p*-Nitrophenylethyl Bromide.**—A mixture of 204 g. of acetic anhydride and 120 g. of acetic acid was chilled to 0° in a 1-liter 3-necked flask equipped with a stirrer, thermometer and dropping funnel. There was added slowly 126 g. of fuming nitric acid, after which the mixture was chilled to −5°. One hundred and eighty-five grams of phenylethyl bromide was added slowly (three hours) through the dropping funnel, while the temperature was maintained below 0°. Stirring was continued for two and one-half hours after the addition was complete. The reaction mixture was then poured into a suspension of 265 g. of sodium carbonate in 2 liters of ice water. The yellow product was taken up in benzene and thoroughly washed with water and then with a saturated sodium bicarbonate solution. The benzene was removed as completely as possible on the steam-bath, the final portion under reduced pressure. The remaining product was recrystallized from 3 liters of petroleum ether (b. p. 60–68°). A yield of 124 g. (54% of the theoretical) of the *p*-nitro compound, m. p. 69–70°,[7] was obtained.

The solvent was removed from the mother liquors and the residue fractionally distilled under reduced pressure. Seventy grams (30.4% of the theoretical) of the *o*-nitro compound boiling at 115–120° (0.5 mm.) with some decomposition was obtained. After recrystallizing from petroleum ether, the product melted at 36–38°. This product on oxidation with potassium permanganate yielded *o*-nitrobenzoic acid. An additional 18 g. of the *p*-nitro compound may be recovered from the still residues, if desired. These two compounds were previously prepared by Sobotka,[7] who, however, did not obtain the ortho isomer in pure form.

Anal. Calcd. for $C_8H_8NO_2Br$: Br, 34.7. Found: Br, (ortho) 34.3, (para) 34.5.

***p*-Acetylphenylethyl Bromide.**—In a 1-liter 3-necked flask equipped with an efficient stirrer, dropping funnel, and reflux condenser were placed 83 g. of anhydrous aluminum chloride, 300 ml. of carbon disulfide, and 47 ml. of acetyl chloride. The flask was set in an ice-bath and a solution of 124 g. of phenylethyl bromide in 95 ml. of acetyl chloride added as rapidly as possible. Stirring was continued until no more hydrogen chloride was evolved (two to two and one-half hours), after which the reaction product was decomposed with a mixture of concentrated hydrochloric acid and crushed ice. The carbon disulfide layer was removed and the aqueous layer extracted twice with benzene. The combined benzene and carbon disulfide layers were washed with dilute hydrochloric acid, water, 10% sodium hydroxide solution, and again with water. The solvent was removed and the product fractionally distilled under reduced pressure. A recovery of 22.5 g. of phenylethyl bromide was effected, so that the 101.5 g. of product boiling at 117–118° (0.1 mm.) amounted to 83% of the theoretical based on the phenylethyl bromide actually used; $n^{25}D$ 1.5724; d^{25}_4 1.3784; MD calcd. 53.26, found 52.91. Permanganate oxidation converts this product to terephthalic acid.

Anal. Calcd. for $C_{10}H_{11}OBr$: Br, 35.2. Found: Br, 35.2.

***p*-Carboxyphenylethyl Bromide and *p*-Carbethoxyphenylethyl Bromide.**—An alkaline hypobromite solution prepared in a 1-liter 3-necked flask from 48 g. of the bromine and 33 g. of sodium hydroxide dissolved in 280 ml. of water and 200 ml. of dioxane, was chilled to 0° and 23 g. of *p*-acetylphenylethyl bromide added with stirring. Stirring was continued until the hypobromite was exhausted (2 hours), the temperature being maintained below 0°. The solution was acidified with an excess of hydrochloric acid and the precipitated acid filtered from the aqueous solution and bromoform, washed with water and dried. The yield of *p*-carboxyphenylethyl bromide was 20 g. (87%). After crystallization from a mixture of petroleum ether and benzene, the acid melted at 205–207°.

Anal. Calcd. for $C_9H_9O_2Br$: Br, 34.9. Found: Br, 35.0.

The acid was converted to the ester in 79% yield by first converting it to the acid chloride with a slight excess of thionyl chloride, then refluxing the crude chloride with ethanol. The ester boils at 111–114° (0.1 mm.); d^{25}_4 1.2918; $n^{25}D$ 1.5404; MD calcd., 59.19; obsd. 62.84.

Anal. Calcd. for $C_{11}H_{13}O_2Br$: Br, 31.1. Found: Br, 30.5.

***p*-Cyanophenylethyl Bromide.**—*p*-Carboxyphenylethyl bromide (64 g.) was converted to the corresponding acyl chloride by refluxing with a slight excess of thionyl chloride. This crude chloride was poured into cold concentrated ammonia water. The precipitated amide was

(3) "Organic Syntheses," Coll. Vol. I, 1932, p. 241.
(4) Moureu and Brown, *Bull. soc. chim.*, [4] **27**, 901 (1920).
(5) Hamilton and Simpson, THIS JOURNAL, **51**, 3158 (1929).
(6) Norris, Walt and Thomas, *ibid.*, **38**, 1071 (1916).
(7) Sobotka, *Ber.*, **62**, 2191 (1929).

TABLE I

RATE AND COURSE OF THE REACTION OF PIPERIDINE WITH NEGATIVELY SUBSTITUTED β-PHENYLETHYL BROMIDES, $YC_6H_4CH_2CH_2Br$, AT 60°

	Y is	Reaction time, hr.	A % Reaction	B Moles × 10^2 piperidine HBr	C Moles × 10^2 unreacted piperidine	D % Tertiary amine calcd.	E % Olefin calcd.
1	*o*-NO_2	0.25	78	0.78	1.01	21	57
		2.0	98	.98	0.62	40	58
2	*p*-NO_2	0.25	83	.83	.90	27	56
		2.0	98	.98	.55	47	51
3	*p*-CN	0.25	58	.58	1.11	31	27
		2.0	91	.91	0.62	47	44
4	*p*-CH_3CO	0.25	40	.40	1.26	34	6
		2.0	80	.80	0.58	62	18
5	*p*-$CO_2C_2H_5$	0.25	26	.26	1.52	22	4
		2.0	67	.67	0.81	52	15
6	H	0.25	16	.16	1.62	24	..
		2.0	55	.55	0.86	59	..
		48[a]	95	.95	.05	100	..

[a] The values for this time are taken from a table in ref. 9 and were determined at 90°.

filtered off, dried, and converted to the nitrile by refluxing with a mixture of 100 ml. of benzene and 100 ml. of thionyl chloride according to the procedure of Michaelis and Siebert.[8] When the reaction was complete, the excess thionyl chloride and solvent was removed on the steam-bath, the remaining product taken up in benzene and the insoluble residue discarded. The benzene solution was washed with water and saturated sodium bicarbonate solution, after which the solvent was removed by distillation. The yield of *p*-cyanophenylethyl bromide amounted to 35.5 g. (60% of theoretical) after recrystallization from petroleum ether and melted at 49–50°.

Anal. Calcd. for C_9H_8NBr: Br, 38.1. Found: Br, 38.5.

Reaction of Negatively Substituted Ethyl Bromides with Piperidine.—Ethyl β-bromopropionate, β-bromopropionitrile and β-bromopropiophenone each react too rapidly with piperidine to allow for rate determinations. The least reactive of these compounds, ethyl β-bromopropionate, was found to react practically completely with piperidine in fifteen minutes at room temperature. Determinations of the course of these reactions by the procedure described below in each case showed that the rate at which piperidine added to the resulting unsaturated compound to form the tertiary amine was practically as rapid as that at which the unsaturated compound was formed from the bromide. As may be seen from the table such is not the case with the negatively substituted phenylethyl bromides.

Reaction of Substituted Phenylethyl Bromides with Piperidine.—Due to the insolubility of these compounds in petroleum ether, the procedure used to follow the course and extent of the reaction was modified slightly from that previously reported.[1]

To 10 ml. of *M* solution of the bromide in benzene, contained in a test-tube prepared for sealing, was added two equivalents of piperidine by means of a calibrated pipet. The tubes were then sealed and immersed in the thermostat for the desired length of time, after which they were cooled and opened. The precipitated piperidine hydrobromide was washed onto a filter with petroleum ether and the washings made up to 50 ml. with petroleum ether. Unreacted piperidine was determined by treating an aliquot of this solution with phenyl isocyanate and collecting the piperidinoformanilide as described previously,[9] except that no corrections were applied.

After drying, the piperidine hydrobromide was dissolved in water and made up to 100 ml. An aliquot of this solution was titrated for bromide ion with standard silver nitrate solution.

It is believed that the results in column B of Table I are accurate to about 1%, while those in column C are probably less than 5% in error.

Discussion of Results

It may be seen from columns A and B of Table I that the reactivity of the substituted phenylethyl bromides increases with the negativity of the substituent in the benzene nucleus. Such a result would be expected from a reaction mechanism of the type postulated in the introductory portion of the paper. Inspection of columns D and E in the above table shows that the percentage of tertiary amine in the amine–olefin mixture of reaction products increases with a decrease in the negativity of the substituent groups. This fact indicates that the mechanism involving the elimination of hydrogen bromide is replaced, to an increasing extent, by one that operates directly at the carbon atom holding the bromine.[10] This

(8) Michaelis and Siebert, *Ann.*, **274**, 312 (1893).

(9) Semb and McElvain, THIS JOURNAL, **53**, 690 (1931).

(10) Another alternative, which would require the rate of addition of piperidine to the olefin to increase with a lowering of the negativity of the substituent, was readily eliminated by the failure of piperidine to add to styrene under the conditions of the reaction. Also the high yields of tertiary amine (the formation of which certainly involves the addition of piperidine to the olefin (*cf.* ref. 1)) in the cases of negatively substituted ethyl bromides, which were discussed in the experimental part of the paper, show that the strongly negative group promotes rather than hinders the addition of piperidine to an adjacent carbon to carbon double bond.

other mechanism may involve the approach of the reagent to the carbon holding the bromine, the ionization of the bromine, or some other mode of reaction. Similar transitions from one mechanism to another have been noted in other series of variously substituted bromides.[11]

A strong indication that the elimination reaction under discussion first involves a removal of a proton from the carbon in the β-position to the bromine is the striking difference in the reactivities of the negatively substituted phenylethyl bromides of the present paper and similarly substituted benzyl bromides. With the latter type of bromide it has been found that an increase in the negativity of the substituent group causes a *decrease* in the reactivity of the benzyl bromide with such bases as pyridine and aniline[11a] as well as with aqueous alcohol.[12] This behavior has been taken to indicate that the bromine is removed from the molecule of the benzyl bromide as a negative ion because such an ionization would be hindered by the presence of a substituent in the benzene ring which, by both an inductive and an electromeric effect, is strongly electron attracting.

(11) (a) Baker, *J. Chem. Soc.*, 1128 (1933); (b) Gleave, Hughes and Ingold, *ibid.*, 238 (1935).

(12) Shoesmith and Slater, *ibid.*, 214 (1926); Olivier, *Rec. trav. chim.*, **42**, 775 (1923).

The fact that such a negative group has just the opposite effect on the reactivity of a phenylethyl bromide with piperidine suggests that the opposite type of ion, *viz.*, a positive proton, is removed from the carbon adjacent to the benzene nucleus by the reagent. There seems to be no reason to believe that the electrophilic character of such a substituent group would not exert some of the same hindering effect on the reactivity of a bromine in the β-position to the ring as it does on the bromine of a benzyl bromide. If this be true, then a carbon–hydrogen bond adjacent to the aromatic nucleus is the only apparent point at which a negative substituent in the nucleus can activate a phenylethyl bromide for reaction with a base such as piperidine.

Summary

The rate and course of the reaction of some negatively substituted ethyl bromides with piperidine have been determined. Evidence is presented to show that the removal of a proton from the carbon atom in the α-position to the negative substituent (and in the β-position to the bromine) is the initial step in the elimination of hydrogen bromide from such a negatively substituted bromide.

MADISON, WISCONSIN RECEIVED JANUARY 26, 1940

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

The Reaction of Organic Halides with Piperidine. VI. Some Branched Chain β-Bromo-esters

BY E. LEON FOREMAN AND S. M. MCELVAIN

If the high reactivity of the β-bromo-esters with piperidine, reported in the fourth paper[1] of this series, is due, as suggested, to the presence of a hydrogen on the α-carbon atom of the ester, a study of the behavior of branched chain β-bromo-esters, particularly those having no α-hydrogen, should be of some interest. The present paper reports the behavior of two such esters, ethyl bromopivalate and ethyl α,α-dimethyl β-bromobutyrate (1 and 2 in the table below) in this reaction. Since such esters are halides of the neopentyl type, which are known to be very unreactive,[2] it seemed necessary to study also ethyl β-bromo-isocaproate and ethyl γ,γ-dimethyl-β-bromovalerate (3 and 4). These esters contain the unreactive isobutyl bromide[3] and neopentyl bromide structure, respectively, and also have hydrogens on the α-carbon atom and a bromine on the β-carbon atom to the carbethoxy group.

In the first paper[3] of this series cyclohexyl bromide, of all that were studied, was found to be the most inert toward piperidine. In order to ascertain the effect of a carbethoxy group in the β-position to the bromine atom on the reactivity of this bromide, ethyl 2-bromocyclohexanoate (no. 6) was included in the present study.

(1) (a) Drake and McElvain, THIS JOURNAL, **56**, 697 (1934); (b) Paper V is Foreman and McElvain, *ibid.*, **62**, 1435 (1940).

(2) Whitmore, Wittle and Popkin, *ibid.*, **61**, 1586 (1939).

(3) *Cf.* Semb and McElvain, *ibid.*, **53**, 690 (1931).

(4) Blaise and Marcilly, *Bull. soc. chim.*, [3] **31**, 158 (1904).

Experimental

Preparation of the Bromo-esters

Ethyl bromopivalate is best prepared by esterification of bromopivalic acid.[4] The treatment of ethyl hydroxypiva-

late[5] with phosphorus tribromide according to the procedure of Lease and McElvain[6] gives only a poor yield of the desired ester. The ethyl bromopivalate used boiled at 62–63°[4] (7 mm.); d^{25}_4 1.2713; $n^{25}D$ 1.4469; MD calcd., 43.91; found, 44.21.

Ethyl α,α-Dimethyl-β-bromobutyrate.—After chilling each in an ice-bath, a solution of 54 g. of phosphorus tribromide in 100 ml. of benzene was added to a solution of 80 g. of ethyl α,α-dimethyl-β-hydroxybutyrate[7] in 100 ml. of benzene. The mixture was allowed to stand in an ice-bath and gradually to come to room temperature as the ice melted. After standing for six days at room temperature, the benzene solution was poured into 500 ml. of ice water and the benzene layer separated, washed with water, then with a saturated solution of sodium bicarbonate and finally with water. On fractionation 28 g. (25% of the theoretical) of the bromo-ester, boiling at 90–92° (20 mm.) was obtained. In addition to this product 36 g. of the phosphite ester of the starting hydroxy ester remained as an undistilled residue. From this residue additional α,α-dimethyl-β-bromobutyric acid could be recovered by slow distillation with 48% hydrobromic acid.

The bromo-ester as prepared above was found to contain some of an isomeric ester, presumably ethyl α,β-dimethyl-α-bromobutyrate, a rearrangement product analogous to that obtained by Whitmore and Johnston[8] by the replacement of the hydroxyl group of methylisopropylcarbinol by halogen. This isomeric bromo-ester was removed readily from the desired product by reaction with piperidine. A solution of 20 g. of the crude bromo-ester and 25 ml. of piperidine in 50 ml. of benzene was refluxed for two hours. After this time the benzene solution was fractionated, whereupon 4 g. of a product boiling at 145–150° and 12 g. of a product boiling at 70–74° (8 mm.) were obtained. The lower boiling fraction was unsaturated and corresponded in properties to trimethylacrylic ester.[9] On refractionation the desired ethyl α,α-dimethyl-β-bromobutyrate boiled at 72–74° (8 mm.); d^{25}_4 1.2430; $n^{25}D$ 1.4531; MD calcd., 48.51; found, 48.58.

Anal. Calcd. for $C_8H_{15}O_2Br$: Br, 35.8. Found: Br, 35.4.

Ethyl β-Bromoisocaproate.—In a 3-liter round-bottomed flask were placed 960 g. (6 moles) of diethyl malonate, 50 g. of piperidine acetate and 432 g. (6 moles) of isobutyraldehyde. After stirring until homogeneous, the mixture was allowed to stand for forty-two hours at room temperature. Then 600 ml. of benzene was added and the aqueous layer separated. The benzene layer was washed with four 200-ml. portions of water and then fractionally distilled.

The yield of isobutylidene malonic ester[10] boiling at 117–119° (13 mm.) amounted to 629 g. (48% of the theoretical). To a hot solution of 450 g. of potassium hydroxide in 450 ml. of water was added slowly with stirring 428 g. (2 moles) of isobutylidenemalonic ester. After standing for two hours on the steam-bath without a reflux condenser, the hydrolysis mixture was chilled in an ice-bath and a cold solution of 450 g. of concentrated sulfuric acid in 450 ml. of water added. The precipitated potassium sulfate was filtered off and washed thoroughly with isopropyl ether. The aqueous solution was extracted with four 250-ml. portions of isopropyl ether and the combined ethereal extracts washed once with a little saturated sodium sulfate solution and then dried over anhydrous sodium sulfate. After removal of the ether, the malonic acid was decarboxylated by heating at 150° in an oil-bath and under a pressure of 20 mm. The monocarboxylic acid which distilled over was then fractionally distilled under reduced pressure. A yield of 46 g. (20.2%) of isocaprolactone[11] boiling at 96–98° (18 mm.), $n^{25}D$ 1.4312, and 48 g. (21%) of isobutylideneacetic acid[11] boiling at 114–115° (18 mm.), $n^{25}D$ 1.4466, neutral equivalent 114, was obtained. A portion of the acid on oxidation with cold 2% potassium permanganate yielded isobutyric acid, which was identified through its *p*-bromophenacyl ester. The isobutylideneacetic acid (42 g.) was esterified by refluxing it for two hours with 100 ml. of absolute ethanol using 2 ml. of concentrated sulfuric acid as a catalyst. The yield of ethyl isobutylideneacetate,[12] boiling at 171–173°, $n^{25}D$ 1.4301, amounted to 44 g. (84% of the theoretical).

Dry hydrogen bromide was passed into a cold solution of 14.2 g. (0.1 mole) of ethyl isobutylideneacetate in 100 ml. of chloroform until twice the amount theoretically required for addition to the unsaturated ester had been absorbed. The flask was then tightly stoppered, allowed to stand in the ice-bath and gradually to come to room temperature after the ice had melted. After six hours, the reaction mixture was poured into cold water and the chloroform layer separated, washed with water, then sodium bicarbonate solution, and finally with water. After drying over calcium chloride, the chloroform was removed at room temperature under reduced pressure and the product distilled at 0.1 mm. pressure so as to minimize the possibility of thermal rearrangement. The yield of ethyl β-bromoisocaproate amounted to 19.3 g. (86.5%); b. p. 63–64° (0.1 mm.); d^{25}_4 1.2464; $n^{25}D$ 1.4557; MD calcd., 48.51; found, 48.89.

Anal. Calcd. for $C_8H_{15}O_2Br$: Br, 35.8. Found: Br, 35.3.

An attempted preparation of this ester from the corresponding hydroxy ester and phosphorus tribromide yielded a product which appeared to be a mixture of the β- and γ-bromo-isocaproic esters, judging from the incompleteness of the reaction of this product with piperidine. In order to make the comparison, ethyl γ-bromo-isocaproate was prepared from isocaprolactone by the procedure of Bredt.[13] This bromo-ester distilled with some decomposition at 57–58° (0.1 mm.) and was found to contain 34.6% instead of the required 35.8% bromine. Previous workers[13,14] have reported it as undistillable. When this γ-bromo-ester was allowed to react with piperidine under the conditions used for the other bromo-esters listed in Table I it showed only 31% reaction in four hours.

Ethyl γ,γ-Dimethyl-β-bromovalerate.—Trimethylacetaldehyde[15] was condensed with diethyl malonate in 50%

(5) Blaise and Marcilly, *Bull. soc. chim.*, [3] **31**, 110 (1904).
(6) Lease and McElvain, THIS JOURNAL, **55**, 806 (1933).
(7) Adkins, Connor and Cramer, *ibid.*, **52**, 5192 (1930).
(8) Whitmore and Johnston, *ibid.*, **60**, 2265 (1938).
(9) Von Auwers and Eisenlohr, *J. prakt. Chem.*, [2] **82**, 167 (1910).
(10) Shryver, *J. Chem. Soc.*, **63**, 1344 (1893).
(11) Braun, *Monatsh.*, **17**, 207 (1896).
(12) Howles, Thorpe and Udall, *J. Chem. Soc.*, **77**, 942 (1900).
(13) Bredt, *Ber.*, **19**, 513 (1886).
(14) Jones and Tattersall, *J. Chem. Soc.*, **85**, 1691 (1904).
(15) The authors are indebted to Mr. E. W. Reeve of this Laboratory for the trimethylacetaldehyde used in this preparation. The catalytic dehydrogenation process used in its preparation will be described in a forthcoming publication.

TABLE I

RATE AND COURSE OF THE REACTION OF PIPERIDINE WITH CERTAIN β-BROMO-ESTERS AT 90°

	Bromo-ester (Y = $COOC_2H_5$)	Reaction time, hr.	A % Reaction	B Moles × 10^2 piperidine HBr	C Moles × 10^2 unreacted piperidine	D % t-amine calcd.	E % Olefin calcd.
1.	$BrCH_2C(CH_3)_2Y$	48	4	0.04	1.84	12[a]	..
		96	7	.07	1.71	20[a]	..
2.	$CH_3CHBrC(CH_3)_2Y$	96	9	.09	1.79	11	..
3.	$(CH_3)_2CHCHBrCH_2Y$	0.25	93[b]	.93	0.99	8	85
		4	94	.94	.97	9	85
4.	$(CH_3)_3CCHBrCH_2Y$	0.25	97[b]	.97	.94	9	88
		4.0	96	.96	.91	13	83
5.	$BrCH_2CH_2Y$	0.25	97[b]	.97	.18	84	13
6.	1,2-$C_6H_{10}BrY$	.25	74	.74	1.21	4	70
		4	90	.90	1.09	2	88

[a] For some reason, as yet undetermined, the values of unreacted piperidine in column C, from which the yields of tertiary amine in column D were calculated, were consistently low. The most obvious explanation of such a result, *viz.*, amide formation, could not be substantiated.

[b] These values carry no rate significance. As pointed out in the fifth paper of this series (ref. 1b) an ethyl bromide with a carbethoxy, cyano or benzoyl group as a β-substituent is much too reactive toward piperidine to allow for rate determinations at or above room temperature. The values are included in the above table to show that the reaction is complete insofar as the elimination of bromine from the ester molecule is concerned.

yield, using the process of Cope and Hancock,[16] except that the refluxing time was reduced from sixty to thirty-six hours. Trimethylethylidenemalonic ester boils at 138–140° (23 mm.); $n^{25}D$ 1.4449; d^{25}_4 0.9347; M_D calcd., 60.46; found, 65.24; exaltation, 4.78.

Anal. Calcd. for $C_{12}H_{20}O_4$: C, 63.12; H, 8.83. Found: C, 63.13; H, 8.86.

The malonic ester was saponified and the acid decarboxylated in 89% yield, using the procedure described above for the preparation of isobutylideneacetic acid. The 4,4-dimethyl-2-pentenoic acid boils at 126–131° (23 mm.), and melts at 62–63° after recrystallization from petroleum ether. The yield of recrystallized acid, neutral equivalent 127, amounted to 73% of the theoretical. A portion of the acid on oxidation with cold 2% potassium permanganate yielded trimethylacetic acid, which was identified by its *p*-bromophenacyl ester.

A solution of 25.6 g. (0.2 mole) of the dimethylpentenoic acid in 100 ml. of absolute ethanol was chilled in an ice-salt-bath and saturated with dry hydrogen bromide. After standing at room temperature for twelve hours, the reaction mixture was poured onto crushed ice, extracted with benzene, and worked up as described above for ethyl β-bromo-isocaproate. The yield amounted to 35.5 g. (75% of theoretical) of product boiling at 65–66° (0.1 mm.); d^{25}_4 1.2149; $n^{25}D$ 1.4588; M_D calcd., 53.29; found, 53.17.

Anal. Calcd. for $C_9H_{17}O_2Br$: Br, 33.8. Found: Br, 32.9.

Ethyl 2-bromocyclohexanoate was prepared in 50% yield from ethyl hexahydrosalicylate[17] by the procedure used above for ethyl α,α-dimethyl-β-bromobutyrate. It boils at 75–76° (0.1 mm.); d^{25}_4 1.3272; $n^{25}D$ 1.4909; M_D calcd., 51.17; found, 53.66.

Anal. Calcd. for $C_9H_{15}O_2Br$: Br, 34.0. Found: Br, 33.8.

(16) Cope and Hancock, THIS JOURNAL, **60**, 2901 (1938).

(17) Connor and Adkins, *ibid.*, **54**, 4678 (1932).

Reaction of Bromo-esters with Piperidine.—A ratio of two moles of piperidine to one of the bromo-esters was used. The general procedure for the determination of the extent and course of this reaction was the same as that described in the fifth paper of this series.[1b] The results of these determinations are summarized in Table I. It is believed that the values in column A can be duplicated within 1%, and that the maximum error for the values in column C is 5%.

Discussion of Results

It is apparent that those β-bromo-esters (1 and 2) that have no hydrogen on the α-carbon atom are very unreactive toward piperidine. It also should be noted that these particular bromo-esters show practically the same amount of reaction after ninety-six hours, even though one is a primary and the other a secondary bromide. With the simple alkyl halides there is a considerable difference in the reactivity of these two types.[3] In this connection mention should be made of Bouveault's observation[18] that ethyl α,α-dimethyl-β-chlorobutyrate is not attacked by alcoholic potassium hydroxide.

The high reactivities of the bromo-esters 3 and 4 show that the neopentyl bromide type of structure is not responsible for the low reactivity of esters 1 and 2. There is practically no difference in the rate at which esters 3 and 4 and ethyl β-bromopropionate[5] lose their bromine when allowed to react with piperidine. This fact definitely shows the powerful effect of the presence of an α-hydrogen, as well as the negligible effect of substitution

(18) Bouveault, *Bull. soc. chim.*, [3] **21**, 1064 (1899).

of such generally deactivating groups as isopropyl or *t*-butyl for a β-hydrogen atom of ethyl β-bromopropionate, on the reactivity of the halogen of β-bromoesters. It should be noted, however, that while the presence of these alkyl groups does not materially affect the rate at which these esters give up their bromine, such substitution does greatly affect the rate of addition of piperidine to the olefinic ester to form a tertiary amine.

The substitution of a carbethoxy group in the β-position to the halogen of cyclohexyl bromide changes it from an extremely inert halide to one with a quite high reactivity toward piperidine However, the ethyl 2-bromocyclohexanoate is not as reactive as the other β-bromo-esters with an α-hydrogen that have been studied and the resulting olefin, ethyl cyclohexenoate, shows a surprising inability to add piperidine across its double bond.

Summary

The rate and course of the reaction between piperidine and a number of β-bromo-esters with branched chains are reported. It is shown that those β-bromo-esters that have no α-hydrogen atom are extremely inert, while those that have such a hydrogen atom are very reactive regardless of the nature of the branching of the carbon chain. Such branching, however, greatly reduces the ability of the unsaturated ester that is formed from the bromo-ester to add piperidine to form a tertiary amine.

MADISON, WISCONSIN RECEIVED JANUARY 26, 1940

[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, UNIVERSITY OF NORTH CAROLINA]

Vicinal Substituted Resorcinols. I. Alkyl Resorcinols. The Synthesis of γ-Ethyl, γ-*n*-Propyl and γ-*n*-Butyl Resorcinols

BY ALFRED RUSSELL, JOHN R. FRYE AND WM. L. MAULDIN

The occurrence of γ-isoamylresorcinol as a fission product of natural rotenone, the possible value as antiseptics of γ-alkyl resorcinols and the potential usefulness as initial materials in various types of syntheses of γ-substituted resorcinols make it of considerable interest to exploit possible routes to such compounds.

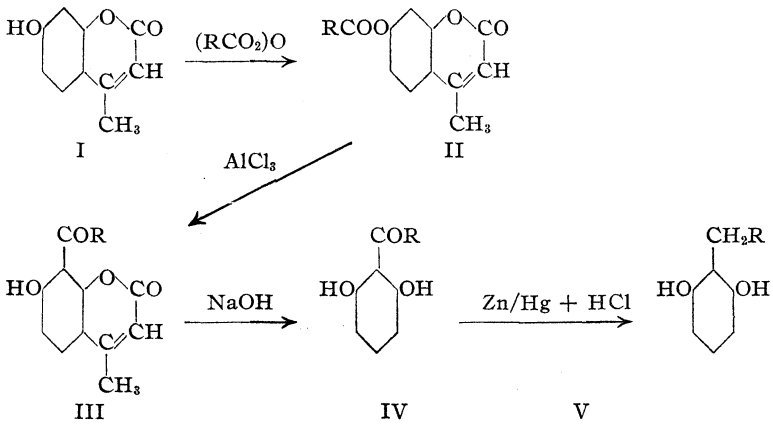
It is comparatively easy to obtain good yields of β-substituted derivatives of resorcinol; thus by treatment of resorcinol by a modification of the Gattermann process[1] it is possible to obtain upward of 90% of the theoretical amount of β-resorcylaldehyde; by carboxylation of resorcinol[2] some 60% of the theoretical amount of β-resorcylic acid may be obtained; again treatment of resorcinol with aliphatic acids and anhydrous zinc chloride gives good yields of alkyl β-resorcyl ketones, a process that involves ester formation followed by a Fries rearrangement; moreover, the ketones so obtained reduce readily by the Clemmensen method to the corresponding β-alkylresorcinols and this process is actually used in the manufacturing of hexylresorcinol.[3] There has also recently been described[4] the synthesis of some *n*-5-(or α)-alkyl resorcinols through the intermediate ketones obtained by the action of appropriate Grignard reagents on 3,5-dimethoxybenzamide.

However, the preparation of vicinal (or γ) substituted resorcinols has been attended with such difficulty that very few such compounds have been made and the yields have been poor. The tedious synthesis of 2,6-dihydroxyacetophenone[5] or vicinal resacetophenone starting with *m*-dinitrobenzene gives a yield amounting at the best to only a few per cent. of the theoretical. The synthesis of γ-resorcylaldehyde which has been described recently gives only a small yield of aldehyde.[6]

The synthesis of 4-methyl-7-hydroxy-8-acetylcoumarin (III, R = CH_3) is on record[7] and from this compound by fission with alkali 2,6-dihydroxyacetophenone[8] is obtained in better than 90% yield. It is obvious that a Clemmensen reduction of 2,6-dihydroxyacetophenone would give γ-ethylresorcinol and such a reduction of 2,6-dihydroxyisovalerophenone recently has been described[9] yielding γ-isoamylresorcinol.

(1) Adams and Levine, THIS JOURNAL, **45**, 2373 (1923).
(2) "Organic Syntheses," Volume X, John Wiley and Sons, Inc., New York, N. Y., 1930, p. 94.
(3) U. S. Patents 1,649,667 and 1,197,168.
(4) Suter and Weston, THIS JOURNAL, **61**, 234 (1939).
(5) Mauthner, *J. prakt. Chem.*, **139**, 290 (1934).
(6) Shah and Laiwalla, *J. Chem. Soc.*, 1828 (1938).
(7) Limaye, *Ber.*, **65**, 375 (1932).
(8) Baker, *J. Chem. Soc.*, 1954 (1934).
(9) Robertson and Subramanian, *ibid.*, 278 (1937).

This general route to γ-alkyl resorcinols appears to be very satisfactory and has now been applied to the preparation of γ-ethyl-, γ-*n*-propyl- and γ-*n*-butylresorcinols. Attempts to prepare the corresponding γ-*n*-hexylresorcinol have not been successful up to the present as the intermediate 4-methyl-7-caproyloxycoumarin did not undergo the Fries rearrangement.



Preliminary tests[10] indicate that saturated aqueous solutions of each of the three alkyl resorcinols described are ineffective against *B. typhosus* and *Staph. aureus*. Further tests are in progress and will be described in a later report.

Experimental Part

4-Methyl-7-hydroxycoumarin.—A mixture of acetoacetic ester (260 g.) and resorcinol (220 g.) was added in portions to 2000 cc. of concentrated sulfuric acid in a round-bottom flask which had been immersed in an ice-bath and mechanically stirred until the temperature of the sulfuric acid was below 5°. Mechanical stirring was continued during the addition of the acetoacetic ester–resorcinol mixture. The temperature was kept below 10° until the end of the addition and it was allowed to stand overnight at room temperature.

The mixture was poured, with stirring, onto ice (6 kg.) in a beaker. The product was filtered, washed twice with water, dissolved in 5% sodium hydroxide (1500 cc.) filtered and reprecipitated by the slow addition of dilute hydrochloric acid with mechanical stirring.

The precipitate was washed thoroughly with water and air-dried overnight. It recrystallizes from 95% ethanol in white needles, m. p. 187°, yield 290 g.

4 - Methyl - 7 - acetoxycoumarin.—4 - Methyl - 7 - hydroxycoumarin (286 g.) was refluxed with twice its weight of acetic anhydride for one and one-half hours. The reaction mixture was poured into cold water with stirring. The 4-methyl-7-acetoxycoumarin was collected, washed thoroughly with cold water to remove all acetic acid and the product air-dried for four days, when it was sufficiently pure for the next step, yield 333 g. Recrystallized from alcohol it formed slender white needles, m. p. 151°.

4-Methyl-7-hydroxy-8-acetylcoumarin.—Dry 4-methyl-7-acetoxycoumarin (200 g.) was thoroughly mixed with powdered anhydrous aluminum chloride (450 g.) in a 5-liter round-bottom flask, this immersed in an oil-bath at 125° and the temperature raised slowly over two and one-half hours to 170°. The reaction mixture was cooled, and 2400 cc. of dilute hydrochloric acid (1 hydrochloric acid to 7 water) added dropwise over a period of about five hours. It was then heated on a steam-bath for one-half hour while being stirred mechanically. The product was filtered, washed, recrystallized from 95% ethanol and dried; yield 197 g. It forms golden yellow leaflets, m. p. 163°.

2,6 - Dihydroxyacetophenone.—4 - Methyl - 7 - hydroxy - 8 - acetylcoumarin (197 g.) was placed in a 5-liter three-neck flask fitted with a dropping funnel, reflux condenser, and tube leading to the bottom of the flask. The solid was covered with water and nitrogen was passed in until the air was displaced. One and one-half times the theoretical quantity of sodium hydroxide solution of such concentration (165 g. of sodium hydroxide in 1350 cc. of water) that the final solution was about 12% sodium hydroxide, was added. The reaction mixture was heated on a steam-bath for five hours and then cooled. The alkaline mixture was neutralized with dilute sulfuric acid, and the precipitated 2,6-dihydroxyacetophenone collected, washed, and dried, yield 127 g. On recrystallization from water it forms stout yellow needles, m. p. 154–56°.

Vicinal Ethylresorcinol.—2,6 - Dihydroxyacetophenone (18 g.) was mixed with amalgamated zinc (45 g.) and hydrochloric acid (90 cc., 12% HCl) added. The whole was refluxed vigorously for five hours, with the addition of concentrated hydrochloric acid (15 cc.) at the end of each hour, cooled and extracted with ether. The ethereal extract was dried, the ether removed and the residue vacuum distilled. The solid distillate recrystallized from gasoline in long, slender, glittering needles, m. p. 94.5°; yield 8.5 g. *Anal.* Calcd. for $C_8H_{10}O_2$: C, 69.5; H, 7.25. Found: C, 69.4; H, 7.22.

4-Methyl-7-propionoxycoumarin and 4-Methyl-7-butyroxycoumarin.—From 220 g. of 4-methyl-7-hydroxycoumarin and 450 cc. of propionic anhydride, by refluxing for two hours, 262 g. of the propionoxy derivative was obtained as white needles from ethanol, m. p. 148.5°. Using the same amount of butyric anhydride and heating at 180° for three hours, 240 g. of the butyroxy derivative resulted as white needles from methanol, m. p. 91°. *Anal.* (propionoxy) Calcd. for $C_{13}H_{12}O_4$: C, 67.2; H, 5.18. Found: C, 66.9; H, 5.22. (butyroxy) Calcd. for $C_{14}H_{14}O_4$: C, 68.3; H, 5.7. Found: C, 68.3; H, 5.63.

4 - Methyl - 7 - hydroxy - 8 - propionylcoumarin and 4 - Methyl - 7 - hydroxy - 8 - butyrylcoumarin.—From 120 g. of the propionoxy compound and 300 g. of aluminum chloride heated to 120° and then over three hours to 170°

(10) Arranged through the courtesy of the Röhm and Haas Company, Inc.

there was obtained 90 g. of the rearrangement product as yellowish leaflets from ethanol, m. p. 187°. In a like manner 13 g. of the butyroxy compound gave 9.6 g. of rearrangement product as yellowish leaflets from ethanol, m. p. 141°. *Anal.* (propionyl) Calcd. for $C_{13}H_{12}O_4$: C, 67.2; H, 5.18. Found: C, 67.2; H, 5.34. (butyryl) Calcd. for $C_{14}H_{14}O_4$: C, 68.3; H, 5.7. Found: C, 68.1; H, 5.8.

2,6-Dihydroxypropiophenone and 2,6-Dihydroxybutyrophenone.—155 grams of the propionyl derivative treated with one liter of 12% aqueous sodium hydroxide for six hours on the steam-bath and in a nitrogen atmosphere gave, after cooling and acidification, 66 g. of 2,6-dihydroxypropiophenone, yellow needles from 25% aqueous methanol, m. p. 133.5°. By analogous treatment 16 g. of the butyryl derivative gave 9.4 g. of 2,6-dihydroxybutyrophenone as yellow needles from 25% aqueous methanol, m. p. 106°. *Anal.* (propiophenone) Calcd. for $C_9H_{10}O_3$: C, 65.1; H, 6.0. Found: C, 64.8; H, 6.0. (butyrophenone) Calcd. for $C_{10}H_{12}O_3$: C, 66.7; H, 6.7. Found: C, 66.9; H, 6.8.

Vicinal Propylresorcinol and Vicinal Butylresorcinol.—Clemmensen reduction of 36 g. of 2,6-dihydroxypropiophenone for six hours using 90 g. of amalgamated zinc, hydrochloric acid (180 cc. 12%) and with the addition of 15 cc. of concd. hydrochloric acid each hour gave, after separation, vacuum distillation and recrystallization from gasoline, 23 g. of vicinal propylresorcinol as white lustrous needles, m. p. 92.5°.

Using proportionate quantities, and continuing the reduction for seven hours, 60 g. of 2,6-dihydroxybutyrophenone yielded 44 g. of vicinal butylresorcinol as slender white needles from gasoline, m. p. 83°. *Anal.* (propyl) Calcd. for $C_9H_{12}O_2$: C, 71.1; H, 7.9. Found: C, 70.8; H, 8.0. (butyl) Calcd. for $C_{10}H_{14}O_2$: C, 72.3; H, 8.44. Found: C, 72.1; H, 8.5.

4-Methyl-7-caproyloxycoumarin.—4-Methyl-7-hydroxycoumarin (17 g.) was dissolved in dry pyridine (25 cc.) and the solution treated with caproyl chloride (35 g.). The whole was heated at the temperature of the steam-bath for ten minutes, cooled and poured into cold water (500 cc.) with good stirring. The solid was collected, washed, dried and recrystallized from methanol. It forms white prisms, m. p. 72°, yield 15.3 g. *Anal.* Calcd. for $C_{16}H_{18}O_4$: C, 70.0; H, 6.6. Found: C, 70.0; H, 6.9.

Summary

6- or β-substituted resorcinols are obtained easily in good yield whatever the nature of the substituting group. Moreover, methods are available for obtaining good yields of resorcinols substituted in the 5- or α-position. However, although some vicinal substituted resorcinols are known, up until the present no easy method has been exploited whereby substituents could be introduced into the resorcinol nucleus in the inaccessible 2-, γ- or vicinal position. Such a process is now described for obtaining vicinal alkyl resorcyl ketones and the corresponding vicinal alkyl resorcinols.

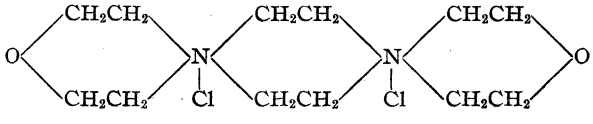
CHAPEL HILL, NORTH CAROLINA
RECEIVED FEBRUARY 14, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BOSTON UNIVERSITY]

Preparation and Polymerization of β-4-Morpholinoethyl Chloride

BY J. PHILIP MASON AND HARRY W. BLOCK[1]

The only morpholinoethyl halide derivative which we have found described in the literature is β-4-morpholinoethyl bromide hydrobromide obtained by Prelog and Blozek[2] by heating triethanolamine hydrobromide with 64% hydrobromic acid in a sealed tube at 160°. Their yield was 25%. We have prepared β-4-morpholinoethyl chloride hydrochloride by treating β-4-morpholineëthanol hydrochloride with thionyl chloride, obtaining a yield of 63.5%, and also by treating β-4-morpholineëthanol with thionyl chloride, obtaining yields varying from 73 to 88%. Treatment of this hydrochloride with alkali yielded a colorless liquid, β-4-morpholinoethyl chloride. After standing for a few days, a solid appeared in the liquid, and the amount of solid increased slowly on standing. It was found that the formation of the solid could be accelerated by refluxing an alcohol solution of β-4-morpholinoethyl chloride. This solid was found to be a dimeric quaternary ammonium salt having the formula



and which can be named N,N′-dispiromorpholinopiperazonium dichloride or N,N′-di-[1,5-(3-oxapentylene)]-piperazonium dichloride. Knorr[3] previously had prepared β-chloroethyldimethylamine and had found that it polymerized on standing or on refluxing in alcohol solution to N,N′-tetra-

(1) Taken from the thesis to be submitted by Harry W. Block to the faculty of the Graduate School of Boston University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) Prelog and Blozek, *C. A.*, **29**, 4011 (1935).

(3) Knorr, *Ber.*, **38**, 3136 (1905); **39**, 1420 (1906).

methylpiperazonium dichloride. Knorr's proof of structure consisted in determining the decomposition products obtained when the compound was heated with concentrated potassium hydroxide solution. He obtained acetylene, symmetrical tetramethyldiaminoethane and dimethylaminoethanol. Knorr's quaternary piperazonium salt can decompose in two ways, (a) to yield acetylene and tetramethyldiamineëthane, and (b) to yield dimethylvinylamine which was apparently hydrated to form dimethylaminoethanol. If our compound is analogous to Knorr's compound, it should decompose on treatment with potassium hydroxide to yield (a) acetylene and 1,2-dimorpholinoethane and (b) β-4-morpholineëthanol. We have obtained both acetylene and 1,2-dimorpholineëthane, but did not obtain any morpholineëthanol. In this connection, we have tried, unsuccessfully, to make vinylmorpholine by the catalytic dehydration of β-4-morpholineethanol. It is, of course, possible that our quaternary piperazonium salt decomposes in only one way, to yield acetylene and 1,2-dimorpholinoethane.

When β-4-morpholinoethyl chloride was digested with absolute alcohol, the yield of N,N'-di-[1,5-(3-oxapentylene)]-piperazonium dichloride obtained after refluxing for forty-eight hours was about 34%, and the formation of the solid had practically ceased. Evaporation of the alcohol yielded a solid which was identified as the hydrochloride of β-4-morpholinoethyl ether. Since we obtained more of this solid than of the dimer, the reaction between β-4-morpholinoethyl chloride and the solvent alcohol proceeds more rapidly than the polymerization reaction.

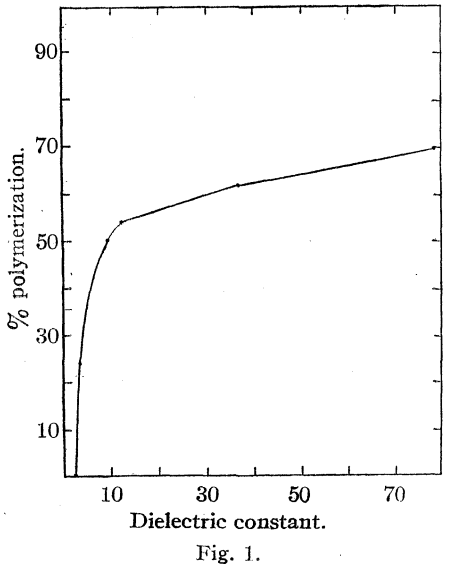


Fig. 1.

β-4-Morpholinoethyl chloride was then refluxed with separate portions of propyl alcohol, acetone and benzene. With propyl alcohol, a yield of 26.6% of the dimer was obtained after 218 hours of refluxing. β-4-Morpholinoethyl propyl ether hydrochloride was obtained after evaporation of the alcohol. Polymerization in acetone occurred very slowly, only 5% of the dimer being obtained after refluxing for a period of four months. There was no evidence of any reaction between β-4-morpholinoethyl chloride and acetone. A benzene solution of β-4-morpholinoethyl chloride was refluxed for one hundred eight hours without forming any trace of solid. At the end of this period, the benzene was distilled and 97% of the original β-4-morpholinoethyl chloride was recovered. In this connection, it is interesting to note that when benzene is used in place of ether for the extraction of β-4-morpholinoethyl chloride from the alkaline solution in which it is prepared, the β-4-morpholinoethyl chloride obtained does not form a solid as quickly as when ether is used for the extraction.

The above observations concerning the polymerization of β-4-morpholinoethyl chloride suggested the possibility that the extent of polymerization was dependent upon the dielectric constant of the solvent. Consequently, a number of polymerizations were carried out in water, dioxane and mixtures of these solvents. The results are given in Table I and represented graphically in Fig. 1.

TABLE I

% Dioxane	Dielectric constant[a]	β-4-Morpholinoethyl chloride used, g.	Dimer,[b] g.	Dimer, %
100	2.2	5	0	0
93.6	4.4	5	1.2	24
85.0	9.0	5	2.5	50
80.0	12.0	5	2.7	54
47.0	37.0	5	3.1	62
0	78.6	7.6	5.3	69.7

[a] Kraus and Fuoss, THIS JOURNAL, 55, 21 (1933).
[b] All mixtures refluxed for twenty-four hours.

It is to be noted that whenever water is present in the solvent, hydrolysis occurs, causing the formation of β-4-morpholineëthanol hydrochloride. In spite of this competing reaction, the evidence does indicate that, for this particular pair of liquids, the extent of dimerization of β-4-morpholinoethyl chloride is a function of the di-

electric constant of the solvent. That no general conclusion can be drawn concerning the extent of dimerization and the dielectric constant is shown by the following facts: (a) absolute ether and benzene, with dielectric constants of 4.35 and 2.28, respectively, did not cause any dimerization in twenty to twenty-four hours; (b) acetone, with a dielectric constant of 21.3, caused only slight polymerization (5%) in four months; (c) ethyl alcohol and propyl alcohol, with dielectric constants of 25.8 and 22, respectively, yielded 34% (forty-eight hours of refluxing) and 22.6% (two hundred and twenty-eight hours refluxing), respectively, of polymer. However, when comparing the dimerization of β-4-morpholinoethyl chloride in alcohols and in dioxane–water mixtures, it should be remembered that our evidence indicates that dimerization proceeds faster than hydrolysis but slower than alcoholysis. The possibility that some relationship exists between the rate of dimerization and the dielectric constant of the solvent is being studied further, using solvents which do not react with β-4-morpholinoethyl chloride.

When it was first planned to make β-4-morpholinoethyl chloride, we intended to make the Grignard reagent, β-4-morpholinoethylmagnesium chloride, and to cause that to react with various carbonyl compounds. All of our attempts to make this Grignard reagent have proved unsuccessful. It is interesting to note that while β-4-morpholinoethyl chloride does not polymerize in absolute ether when the solution is refluxed for twenty-four hours, it does polymerize appreciably (10%) in a few hours in absolute ether solution when magnesium is present. The rate of polymerization is much slower than the rate of formation of most Grignard reagents. Inasmuch as other work in this Laboratory indicates that the chlorine in β-4-morpholinoethyl chloride is a fairly reactive chlorine, we are puzzled over the inability of this compound to form a Grignard reagent.

Experimental Part

β-4-Morpholinoethyl Chloride Hydrochloride. (A) **From β-4-Morpholineëthanol and Thionyl Chloride.**—Two moles (262 g.) of redistilled β-4-morpholineëthanol was dissolved in 200 cc. of chloroform[4] in a three-necked flask equipped with a mercury sealed mechanical stirrer, a reflux condenser and a dropping funnel. A gas absorption bottle was connected to the top of the condenser. By means of a water-bath the solution was warmed to 40°, while stirring, and a few drops of a solution of 2.75 moles (200 cc.) of thionyl chloride in 200 cc. of chloroform[4] was added. After the initial reaction had abated, the thionyl chloride solution was added dropwise at such a rate that the temperature of the reaction mixture did not rise above 55°. After the first thirty minutes, the thionyl chloride solution could be added at the rate of two drops a second. After the first hour, the thionyl chloride was added more rapidly and external heating was necessary to keep the reaction mixture at 50–55°. About two hours was required for the addition. After all of the thionyl chloride solution was added, the reaction flask was heated very slowly and intermittently, until the mixture refluxed smoothly and the refluxing was continued for an hour. After cooling, the white crystals were removed by filtration and recrystallized from one liter of absolute alcohol, using 20 g. of Norit to decolorize the solution; yield, 263.6 g. (70.9%). The alcohol filtrate was concentrated to a volume of about 100 cc. An additional 26 g. was obtained, making a total yield of 289.6 g. (78%), m. p. 182–182.5°.

Anal. Calcd. for $C_6H_{13}Cl_2NO$: total Cl, 38.10; ionic Cl, 19.05; N, 7.53. Found: total Cl, 38.28, 38.40; ionic Cl, 18.59, 18.74; N, 7.15, 7.26.

(B) **From β-4-Morpholineëthanol Hydrochloride.**—β-4-Morpholineëthanol hydrochloride was made by adding slowly 56.4 cc. (10% excess) of concentrated hydrochloric acid to 70 g. of β-4-morpholineëthanol with good cooling and stirring. After evaporating to dryness on a steam-bath under reduced pressure, the solid was dissolved in 200 cc. of water and the solution decolorized by two treatments with Norit. Evaporation of the colorless solution under reduced pressure gave a solid which was recrystallized twice from *n*-amyl alcohol (absolute ethyl alcohol can also be used); yield 62.9 g. (70.2%), m. p. 109–110° (softens at 100°). A second crop of 3.4 g. was obtained by concentrating the combined filtrates.

Anal. Calcd. for $C_6H_{14}ClNO_2$: Cl, 21.15. Found: Cl, 20.91, 20.90.

Since β-4-morpholineëthanol picrate has not been reported in the literature, it was analyzed for nitrogen. It melted at 126°.

Anal. Calcd. for $C_{12}H_{16}N_4O_9$: N, 15.60. Found: N, 15.65, 15.66.

Six-tenths of a mole (100.5 g.) of β-4-morpholineëthanol hydrochloride was suspended in 150 cc. of chloroform. A solution of 108 g. of thionyl chloride in 150 cc. of chloroform was added and the mixture digested on the steam-bath for one hour. Complete solution occurred, followed by the separation of some solid. The mixture was then cooled and filtered and the crystals washed with a little chloroform. Two recrystallizations from *n*-amyl alcohol (absolute alcohol can also be used) yielded 67.2 g. of β-4-morpholinoethyl chloride hydrochloride, m. p. 182°. An additional 2.3 g. was obtained by concentrating the amyl alcohol filtrates and recrystallizing from amyl alcohol. Only 1.4 g. of purified product was obtained from the chloroform filtrate. The total yield was 70.9 g. (63.5%).

β-4-Morpholinoethyl Chloride.—Three-fourths of a mole (139.5 g.) of β-4-morpholinoethyl chloride hydrochloride

(4) When the amount of β-4-morpholineëthanol is considerably smaller, *e. g.*, 0.5 mole, the ratio of chloroform to reactants should be doubled in order to prevent the final reaction mixture from solidifying when cooled.

was dissolved in 150 cc. of water and 75 cc. of ether was added. To this mixture, 15% sodium hydroxide solution was added slowly until the aqueous solution was distinctly alkaline. The ether layer was removed and the aqueous solution was extracted with ten 50-cc. portions of ether. The combined ether extracts were dried over potassium hydroxide pellets. After distillation of the ether, the β-4-morpholinoethyl chloride distilled at 93–4° (12 mm.); yield, 95 g. (84.7%). In some later experiments, benzene was used instead of ether to extract the β-4-morpholinoethyl chloride. Five extractions with benzene were sufficient and the product could be kept for a longer period of time before polymerization was observed.

Anal. Calcd. for $C_6H_{12}ONCl$: Cl, 23.70; N, 9.36. Found: Cl, 23.48, 24.09; N, 9.39, 9.36.

β-4-Morpholinoethyl Chloride Picrate.—Since β-4-morpholinoethyl chloride reacts with both water and alcohol, the picrate was made by adding an excess of a saturated solution of picric acid in dry benzene to a solution of 1 cc. of β-4-morpholinoethyl chloride in 2 cc. of dry benzene. The precipitate, which formed immediately, was recrystallized from hot benzene in which it was soluble only to the extent of about 1.5%. However, it appears to be completely insoluble in cold benzene. It melted at 130°. Since the m. p. of β-4-morpholineëthanol picrate is 126°, a mixed melting point determination was made, m. p. 116°.

Anal. Calcd. for $C_{12}H_{15}ClN_4O_8$: N, 14.80. Found: N, 14.85, 14.96.

Reactions of β-4-Morpholinoethyl Chloride in Ethyl Alcohol. (A) N,N'-Di-[1,5-(3-oxapentylene)]-piperazonium Dichloride.—Fifty grams of freshly distilled β-4-morpholinoethyl chloride was refluxed with 250 cc. of absolute alcohol. The precipitated solid was removed by filtration at one, two, four, four, twelve, twelve, twenty-four, and forty-eight hour intervals. The amount of solid formed during the last period of digestion was very small. The total weight of solid was 16.8 g. (34%). This solid was soluble in water, insoluble in organic solvents and did not melt. It was identified by the following data as N,N'-di-[1,5-(3-oxapentylene)]-piperazonium dichloride.

Anal. Calcd. for $C_{12}H_{24}Cl_2N_2O_2$: Cl, 23.70; N, 9.36. Found: Cl, 23.97, 23.76; N, 9.23, 9.16.

Sixteen grams of this dimer was dissolved in a solution of 32 g. of potassium hydroxide dissolved in 32 cc. of water in an Erlenmeyer flask fitted with a tube leading to an ammoniacal silver nitrate solution. The flask was heated on a steam-bath until all of the acetylene had been driven off. The precipitate of silver acetylide was filtered, and a small portion of it exploded when heated on the end of a spatula. A positive test for acetylene also was obtained when the gas was passed into a 1% solution of phenylmercuric bromide in 10% potassium hydroxide solution, using the procedure developed by Spahr, Vogt and Nieuwland.[5]

After all of the acetylene had been liberated, the solution was cooled and extracted first with 100 cc. of ether, followed by eight more extractions, using 50 cc. of ether for each extraction. These extracts were combined and dried over solid potassium hydroxide. The ether solution was concentrated to a volume of about 25 cc. Five grams of Norit was added to decolorize the solution and the colorless filtrate was evaporated to a volume of 15 cc. The ether solution was cooled to about −75° by placing it in a bath of dry-ice in methanol. The solid was filtered and washed with dry ether previously cooled to this temperature. In this way, 4.4 g. of solid was obtained. By concentrating the filtrate and washings to 5 cc. and then cooling to −75° (dry-ice in methanol) an additional 1.0 g. was obtained. The total yield was 5.4 g. (51%) and the solid melted at 71–72°. Recrystallization from ether solution by cooling in a bath of dry-ice and methanol yielded pure 1,2-dimorpholinoethane melting at 73.5°. Knorr[6] reported a melting point of 74° for 1,2-dimorpholinoethane and 230–236° for the picrate. Our picrate melted with decomposition at 234–236°.

Anal. Calcd. for $C_{10}H_{20}N_2O_2$: N, 13.99. Found: N, 14.23, 13.89.

β-4-Morpholinoethyl Ethyl Ether Hydrochloride.—Since only one-third of the β-4-morpholinoethyl chloride was accounted for as the dimer after refluxing with alcohol, the alcohol filtrate was distilled and the residue transferred to an evaporating dish, using a little alcohol to rinse out the flask. This residue was heated on the steam-bath for four hours. On cooling, the mass solidified and weighed 30.7 g. The solid was pulverized, divided into 6 g. portions and each portion extracted repeatedly with hot toluene. In this way, 12.8 g. of solid was extracted, leaving a resinous residue of 4.2 g. which was insoluble in toluene. Five grams of the solid extracted by toluene was recrystallized twice from 250 cc. of toluene. The weight of pure product was 3 g. and it melted at 138°. This solid was very soluble in water, ethyl alcohol and *n*-amyl alcohol, soluble in the hot solvents, acetone, dioxane, cellosolve, diethylene glycol, β,β'-dichlorodiethyl ether, benzene and toluene, but could be recrystallized satisfactorily only from the last two solvents. It was insoluble in ligroin, cyclohexane and ether. That this compound was β-4-morpholinoethyl ethyl ether hydrochloride was shown by analysis and mixed melting point determination with some β-4-morpholinoethyl ethyl ether hydrochloride prepared from β-4-morpholinoethyl ethyl ether. The picrate of our ether melted at 102–3°, the picrate from the commercial ether melted at 103° and a mixture of the two melted at 102°.

Anal. Calcd. for $C_8H_{18}ClNO_2$: Cl, 18.12; N, 7.16; mol. wt., 195.6. Found: Cl, 18.01, 18.06; N, 6.80, 7.02; mol. wt. (acetic acid), 195.5, 198.5.

Picrate.—Calcd. for $C_{14}H_{20}N_4O_9$: N, 14.43. Found: N, 14.46, 14.65.

Reactions of β-4-Morpholinoethyl Chloride in Propyl Alcohol.—Twenty-one grams of freshly distilled β-4-morpholinoethyl chloride was refluxed with 100 cc. of *n*-propyl alcohol. Filtrations were made at two, twelve, thirty-six, sixty, and one hundred and eight hour intervals. At the end of 218 hours, a total of 5.6 g. (27%) of N,N'-di-[1,5-(3-oxapentylene)]-piperazonium dichloride was obtained. This was identified by decomposition with 50% sodium hydroxide solution as described above.

The propyl alcohol was distilled from the filtrate and

(5) Spahr, Vogt and Nieuwland, THIS JOURNAL, **55**, 2465 (1933).

(6) Knorr, *Ber.*, **35**, 4472 (1902).

the residue transferred to an evaporating dish, which was heated to remove the last trace of solvent. When cooled, the entire mass solidified; weight, 21.5 g. The pulverized solid was extracted repeatedly with hot toluene, and the toluene solution was decolorized with Norit. In this way, 10.5 g. of β-4-morpholinoethyl propyl ether hydrochloride was obtained. When recrystallized from toluene and dried, it melted at 130–131°.

Anal. Calcd. for $C_9H_{20}ClNO_2$: C, 51.54; H, 9.61; Cl, 16.91; N, 6.68. Found: C, 51.14, 51.65; H, 10.13, 10.20; Cl, 17.02, 17.12; N, 6.80, 6.82.

Reactions of β-4-Morpholinoethyl Chloride in Acetone.—Twenty grams of freshly distilled β-4-morpholinoethyl chloride was dissolved in 100 cc. of acetone and the solution refluxed. A solid formed very slowly, only 1 g. being obtained after refluxing for four months. During this period acetone was added frequently because of evaporation losses. The solid was identified as N,N′-di-[1,5-(3-oxapentylene)]-piperazonium dichloride by decomposition with 50% sodium hydroxide as described above.

The acetone was removed from the filtrate by distillation and the remaining liquid (3.7 g.) distilled at 91–2° (12 mm.). This corresponds to the b. p. of β-4-morpholinoethyl chloride. The liquid gave a precipitate with alcoholic silver nitrate solution only when heated, which is characteristic of β-4-morpholinoethyl chloride. The loss of β-4-morpholinoethyl chloride during the digestion can be accounted for by assuming that it was carried off by evaporation along with the acetone during the long period of refluxing.

Digestion of β-4-Morpholinoethyl Chloride in Benzene.—Twenty grams of freshly distilled β-4-morpholinoethyl chloride was refluxed for one hundred and eight hours with 100 cc. of benzene. No solid formed. The benzene was removed by distillation and the residue distilled at 91° (12 mm.). The distillate weighed 19.4 g. It was proved to be β-4-morpholinoethyl chloride by analysis for chlorine and nitrogen.

Digestion of β-4-Morpholinoethyl Chloride in Ether.—Three and eight-tenths grams of freshly distilled β-4-morpholinoethyl chloride was refluxed for twenty hours with 50 cc. of absolute ether. No solid appeared. After removal of the ether by distillation, 3.0 g. of β-4-morpholinoethyl chloride, b. p. 87° (7 mm.), was obtained.

Digestion of β-4-Morpholinoethyl Chloride in Dioxane.—Six grams of freshly distilled β-4-morpholinoethyl chloride was refluxed for twenty-four hours with 50 cc. of pure dioxane. Only the slightest trace of solid formed. After removal of the dioxane by distillation, 5.8 g. of β-4-morpholinoethyl chloride was recovered, b. p. 93° (12 mm.).

Reactions of β-4-Morpholinoethyl Chloride in Water.—Seven and six-tenths grams of freshly distilled β-4-morpholinoethyl chloride was refluxed with 50 cc. of water for twenty-four hours. The solution was then evaporated to dryness. The dry solid was pulverized and extracted three times with 10-cc. portions of hot *n*-amyl alcohol. The insoluble residue was washed three times with ether to remove adhering amyl alcohol. It weighed 5.3 g. (70%) and was identified as N,N′-di-[1,5-(3-oxapentylene)]-piperazonium dichloride by decomposing it with 50% sodium hydroxide solution and testing for acetylene with ammoniacal silver nitrate solution.

The *n*-amyl alcohol extracts were combined and concentrated to a volume of 10 cc. When cooled, a solid precipitated. When recrystallized from *n*-amyl alcohol, washed with ether and dried, 2.6 g. of solid was obtained which melted at 110°. This was identified as β-4-morpholineëthanol hydrochloride by means of a mixed melting point determination (109°) with some known β-4-morpholineëthanol hydrochloride. The weight of β-4-morpholineëthanol hydrochloride obtained is equivalent to 2.2 g. of β-4-morpholinoethyl chloride and accounts for 29% of the original chloride.

Reactions of β-4-Morpholinoethyl Chloride in Dioxane–Water Mixtures.—Five grams of freshly distilled β-4-morpholinoethyl chloride was refluxed for twenty-four hours in 50 cc. of the dioxane–water mixtures listed in Table I. A solid separated in each case except when the 47% dioxane–water solution was used. However, all mixtures were treated in the same way. After evaporation to dryness, the solids were extracted three times with 10-cc. portions of hot, 95% ethyl alcohol to remove β-4-morpholineëthanol hydrochloride. The insoluble N,N′-di-[1,5-(3-oxapentylene)]-piperazonium dichloride was washed with ether, dried and weighed. The results are given in Table I and Fig. 1.

Behavior of β-4-Morpholinoethyl Chloride on Standing and when Heated.—Fifty grams of freshly distilled β-4-morpholinoethyl chloride was placed in a tightly stoppered Erlenmeyer flask and stored in a dark closet. At the end of three months, 1.3 g. of solid was removed by filtration. At the end of an additional three months, 0.75 g. of solid was obtained. The remaining liquid was identified as β-4-morpholinoethyl chloride since it distilled at 92° (13 mm.) and left no residue. The solid was identified as N,N′-di-[1,5-(3-oxapentylene)]-piperazonium dichloride by the procedure described above.

Twenty-one grams of freshly distilled β-4-morpholinoethyl chloride was placed in a large test-tube in a flask of water which was heated on a steam-bath. The temperature of the water in the flask was 86° and the heating was continued for one week. When cold, the mixture was filtered and 1.2 g. of solid was obtained. This was identified as N,N′-di-[1,5-(3-oxapentylene)]-piperazonium dichloride and the remaining liquid distilled at the boiling temperature of β-4-morpholinoethyl chloride.

β-4-Morpholinoethyl Chloride and Magnesium.—Freshly distilled samples of β-4-morpholinoethyl chloride were added to magnesium in absolute ether, benzene and anisole. Even after adding iodine and refluxing for some time, no color test[7] indicating the presence of a Grignard reagent could be obtained. The use of activated catalysts[8,9] failed to cause the formation of any Grignard reagent. In some of these experiments, a white solid appeared. To determine the nature of the white solid, 9.5 g. of magnesium and 5 cc. of absolute ether were placed in a three-necked flask equipped with a mercury-sealed mechanical stirrer, a dropping funnel and a reflux condenser. At the top of the reflux condenser was placed a drying tube containing anhydrone. The flask was warmed on a steam-bath until the ether was refluxing and then a

(7) Gilman and Schulze, THIS JOURNAL, **47**, 2002 (1925).

(8) Gilman, Peterson and Schulze, *Rec. trav. chim.*, **47**, 19 (1928) [*C. A.*, **22**, 1134 (1928)].

(9) Underwood and Gale, THIS JOURNAL, **56**, 2118 (1934).

solution of 26.4 g. of freshly distilled β-4-morpholinoethyl chloride in 30 cc. of absolute ether was added slowly. The mixture was refluxed for one hour, allowed to stand overnight and refluxed for three hours the next day. After filtration, the white solid was dissolved in 10 cc. of water. Evaporation to dryness yielded 2.8 g. which was purified by dissolving in water, decolorizing with Norit, evaporating to 5 cc. and adding alcohol and ether to precipitate the solid. It was identified as N,N′-di-[1,5-(3-oxapentylene)]-piperazonium dichloride by decomposition with 50% sodium hydroxide solution as described above.

Summary

β-4-Morpholinoethyl chloride hydrochloride has been prepared from β-4-morpholineëthanol and also from β-4-morpholineëthanol hydrochloride.

The free base has been obtained and has been found to polymerize on standing. When refluxed with benzene, ether, dioxane, or acetone, it either does not polymerize or polymerizes extremely slowly. When refluxed with alcohols or water, it not only polymerizes but also reacts with the solvent. In dioxane–water solutions, the rate of polymerization appears to be related to the dielectric constant of the solvent.

BOSTON, MASS. RECEIVED MARCH 14, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF BOSTON UNIVERSITY]

Ethers and Amines from β-4-Morpholinoethyl Chloride

BY J. PHILIP MASON AND SAUL MALKIEL[1]

The preparation of β-4-morpholinoethyl chloride has been described by Mason and Block.[2] They found the chlorine in β-4-morpholinoethyl chloride to be fairly reactive because hydrogen chloride is removed when the chloride is refluxed with alcohol or water. Since the chlorine in β-chloro ethers is known to be quite unreactive toward some reagents,[3] we considered it worth while to investigate the reactivity of the chlorine in β-4-morpholinoethyl chloride toward a number of reagents which react with alkyl halides.

This communication describes the preparation of a number of ethers and amines. Two ethers of this series have been reported previously, namely, the ethyl ether[2,4] and the propyl ether.[2] Sand[5] reported a melting point of what he thought might be the picrate of β,β′-dimorpholinoethyl ether. He was doubtful about it, however, and we have shown that his picrate was actually the picrate of β-4-morpholinoethanol. Two of the amines have been reported in the literature, namely, dimorpholinoethane[6] and β-4-morpholinoethyl amine.[7]

The method used for the preparation of the ethers was essentially a Williamson synthesis. Since β-4-morpholinoethyl chloride polymerizes on standing, we used the more stable, solid β-4-morpholinoethyl chloride hydrochloride. The results are given in Table I.

The β-4-morpholinoethyl amines were made simply by heating the amine with freshly distilled β-4-morpholinoethyl chloride. The results are given in Table II. Swallen and Boord[3] obtained β-ethoxyethylaniline (no yield given) from β-chloroethyl ether and aniline after heating for ten hours.

Experimental

β-4-Morpholinoethyl Methyl Ether.—To 100 cc. of methanol in a 500-cc. wide-mouth Erlenmeyer flask was added 0.1 mole (2.3 g.) of metallic sodium. After all the sodium had dissolved, sufficient glass wool was added to cover the bottom of the flask. In an underwriter's extraction thimble was placed 0.05 mole (9.3 g.) of β-4-morpholinoethyl chloride hydrochloride. An underwriter's coil condenser was used in the top of the flask. The β-4-morpholinoethyl chloride hydrochloride dissolved in the condensed methanol and as soon as it reached the sodium methoxide solution a precipitate of sodium chloride appeared. About fifteen minutes was required for complete extraction of the β-4-morpholinoethyl chloride hydrochloride. The reaction mixture was refluxed for an additional five minutes and the excess methanol was removed as completely as possible by distillation. When the residue was cool, 100 cc. of 30% sodium hydroxide solution was added. After separation of the two layers, the aqueous solution was extracted with three 25-cc. portions of ether. The ether extracts and the original upper layer were combined and dried over Drierite. The ether and alcohol were removed by distillation and the residue was

(1) Abstracted from a thesis to be submitted by Saul Malkiel to the faculty of the Graduate School of Boston University in partial fulfillment of the requirements for the degree of Doctor of Philosophy. Present address: Massachusetts College of Osteopathy, Boston, Mass.

(2) Mason and Block, THIS JOURNAL, **62**, 1443 (1940).

(3) Swallen and Boord, *ibid.*, **52**, 651 (1930).

(4) (a) Cox and Carruthers, U. S. Patent 2,023,872; (b) Wilson, U. S. Patent 2,128,887.

(5) Sand, *Ber.*, **34**, 2906 (1901).

(6) Knorr and Brownsdon, *ibid.*, **35**, 4470 (1902).

(7) Hultquist and Northey, THIS JOURNAL, **62**, 447 (1940).

TABLE I

Alcohol	Yield, %	B. p., °C.	Mm.	Neut. equiv. Calcd.	Neut. equiv. Found	Nitrogen, % Calcd.	Nitrogen, % Found
Methyl (NaOR method)	75.9	104.0–105.8	(44)	145	145.7	9.66	9.65
Methyl (KOH method)[a]	64.8	105.3–107.3	(46)	145	145.2		
Ethyl	79.9	96.0–99.0	(17–19)[b]	159	159.9		
n-Propyl	82.2	120.0–123.0	(33)	173	172.5	8.09	8.07
i-Propyl	64.7	115.0–120.0	(34–35)	173	172.5	8.09	8.07
n-Butyl	81.3	134.5–137.5	(31)	187	186.2	7.49	7.48
s-Butyl	62.0	105.5–108.5	(7–8)	187	187.4	7.49	7.51
t-Butyl (20 min.)	58.8	114.0–119.0	(21–22)	187	187.0	7.49	7.48
t-Butyl (3 hr.)	53.5	113.0–116.0	(19)	187	186.3		
Morpholinoethyl[c]	66.2	178.0–180.5	(7)	122	122.1	11.48	11.47
Benzyl	67.8	196.0–202.0	(30–32)	221	220.4	6.33	6.30
Phenyl[d]	64.7	181.0–183.0	(21–22)	207	207.1	6.76	6.74

[a] 0.1 mole (5.6 g.) KOH dissolved in CH_3OH. [b] Cox and Carruthers (4a) report a b. p. 199.0–200.0° at 750 mm. and 80.0–81.0° at 10 mm. [c] M. p. of picrate, 175° (uncor.). Sand reported m. p. 123°. [d] 10 g. of C_6H_5OH dissolved in 50 cc. of 10% NaOH solution, and heated with 9.3 g. of β-4-morpholinoethyl chloride hydrochloride for 20 min.

TABLE II

β-4-Morpholinoethyl	Yield, %	B. p., °C.	Mm.	Nitrogen, % Calcd.	Nitrogen, % Found	Picrate M. p. (cor.), °C.	Picrate Nitrogen, % Calcd.	Picrate Nitrogen, % Found
Amine[a]	48.5	82	(6)[c]	21.54	21.59	188.0	19.05	19.27
Butylamine[b]	43.1	136–140	(20–21)	15.05	15.09	180.5	17.39	17.30
Aniline	57.3	186–188.5	(9)	13.59	13.68	179.4	16.87	16.79
Methylaniline	38.2	184–189	(9)	12.73	12.79	138–140.6	16.54	16.62
Morpholine	55.0	73[d]				234–237 (uncor.)[e]		

[a] Neut. equiv. calcd., 65. Found, 65.2. [b] Neut. equiv. calcd., 93. Found, 93.4. [c] Hultquist and Northey[7] report a b. p. of 204.5° at 768 mm. and 121–123° at 68 mm. [d] M. p. (uncor.); Knorr and Brownsdon,[6] m. p. 74°. [e] Knorr and Brownsdon,[6] m. p. 230–236°.

transferred to a 50-cc. Claisen flask whose side arm was well "vigreuxed" and was also packed with asbestos. After fractionation under reduced pressure, the high boiling fraction was dried over sodium and redistilled. The yield was 5.5 g. (76%) and the ether distilled at 105.3–107.3° (46 mm.).

The above procedure was used for the preparation of the ethyl, propyl, isopropyl, butyl, *s*-butyl, *t*-butyl, phenyl and benzyl ethers. All of the ethers were colorless mobile liquids possessing a strong ammoniacal odor. The methyl, ethyl, isopropyl, *s*-butyl and *t*-butyl ethers were soluble in water and typical organic solvents such as alcohol, ether and benzene. The butyl, benzyl and phenyl ethers were insoluble in water and soluble in the organic solvents just mentioned.

β,β'-Dimorpholinoethyl Ether.—Because of the high boiling point of β-4-morpholineëthanol (227°), 0.05 mole (7.5 g.) of β-4-morpholinoethyl chloride was added to 100 cc. of β-4-morpholineëthanol in which 0.05 mole (1.15 g.) of sodium had been dissolved. The mixture was heated to 200° in an oil-bath and kept at that temperature for twenty minutes. The separation and purification was carried out as described above. Dimorpholinoethyl ether is soluble in water and the above mentioned organic solvents.

β-4-Morpholinoethylamine.—To an excess of concentrated ammonium hydroxide (40 cc.) in a round-bottom flask was added 0.05 mole (7.5 g.) of freshly distilled β-4-morpholinoethyl chloride and sufficient water (45 cc.) to effect complete solution. A cork stopper was wired to the flask, which was then placed in an oven at 93–98° for five hours. After cooling, 80 cc. of 40% sodium hydroxide solution was added to the reaction mixture. The small upper layer was removed and the aqueous layer was extracted with three 25-cc. portions of ether. The ether solution was dried over Drierite, the ether removed by distillation and the residue distilled fractionally under reduced pressure. β-4-Morpholinoethylbutylamine was made by the same procedure, using 0.055 mole (4.0 g.) of *n*-butylamine. The results are given in Table II.

β-4-Morpholinoethylaniline.—A solution of 0.055 mole (5.2 g.) of aniline and 0.05 mole (7.5 g.) of freshly distilled β-4-morpholinoethyl chloride was heated under a reflux air condenser for two hours in an oil-bath at 200°. After cooling, the solution was treated with an excess of 40% sodium hydroxide solution and extracted three times with 25-cc. portions of benzene. The benzene solution was dried over Drierite, the benzene removed by distillation and the residue distilled using a fractionating column under reduced pressure. β-4-Morpholinoethylmethylaniline was made by the same procedure using 0.055 mole (5.5 g.) of methylaniline. When dimorpholinoethane was made by this procedure, a residue was left after distillation of the benzene. This was dissolved in hot ligroin, decolorized with Norit and recrystallized from ligroin. The results are given in Table II.

With the exception of dimorpholinoethane the amines are colorless liquids possessing an ammoniacal odor. The β-4-morpholinoethylamine and the β-4-morpholinoethylbutylamine are soluble in water and in the previously mentioned organic solvents. The β-4-morpholinoethylaniline and the β-4-morpholinoethylmethylaniline are

viscous liquids, insoluble in water but soluble in the organic solvents. Dimorpholinoethane is a white, water soluble solid.

Summary

The β-4-morpholinoethyl ethers of methyl, ethyl, propyl, isopropyl, butyl, *s*-butyl, *t*-butyl, benzyl and β-4-morpholinoethyl alcohols and phenol have been prepared from β-4-morpholinoethyl chloride and the corresponding sodium alkoxide or phenoxide. β-4-Morpholinoethyl amines have been made by the interaction of β-4-morpholinoethyl chloride with ammonia, *n*-butylamine, aniline, methylaniline and morpholine.

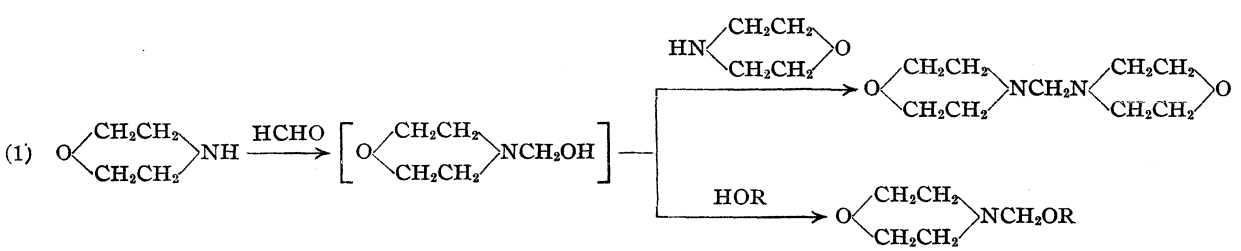
BOSTON, MASS. RECEIVED MARCH 14, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF BOSTON UNIVERSITY]

4-Morpholinomethyl Alkyl Ethers and N-Substituted Morpholines

BY J. PHILIP MASON AND MORRIS ZIEF[1]

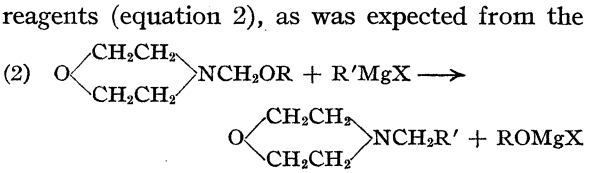
Dialkylaminomethyl alkyl ethers have been prepared by McLeod and Robinson[2] by the condensation of secondary amines with 40% aqueous formaldehyde solution and various alcohols. Stewart and Bradley[3] used paraformaldehyde instead of 40% aqueous formaldehyde solution. We have made a number of 4-morpholinomethyl alkyl ethers using the method described by Stewart and Bradley[3] with certain modifications.



It will be seen from equation (1) that there are two reactions possible when the three reactants are mixed. In order to increase the yield of the ether, we used two equivalents of alcohol to one each of morpholine and formaldehyde.

Table I shows the percentage of morpholine converted into the 4-morpholinomethyl alkyl ether and dimorpholinomethane, together with the boiling points, nitrogen analyses and neutral equivalents. Increasing yields of ether were obtained with increasing molecular weight of the primary alcohols from methyl to *n*-propyl and *n*-butyl. This may be due to the fact that the ethers obtained from higher alcohols are hydrolyzed less readily than those from lower alcohols.[2] Evidence that the hydrogen of the water split off during the formation of the ether comes from the alcohol and the hydroxyl from the hypothetical 4-morpholinemethanol is found in the lower yields of ethers obtained when secondary and tertiary alcohols were used. Picrates of these ethers could not be obtained by the usual method because all of the ethers hydrolyzed to form morpholine, and morpholine picrate was the only compound obtained.

These ethers reacted readily with Grignard reagents (equation 2), as was expected from the



work of McLeod and Robinson.[2] The results are reported in Table II.

Experimental

4-Morpholinomethyl Ethyl Ether.—Fifteen grams of paraformaldehyde (equivalent to 0.5 mole of formaldehyde), 23 g. (0.5 mole) of absolute ethyl alcohol and 100 cc. of dry benzene were placed in a 500-cc. three-necked flask which was equipped with a mercury-sealed mechanical stirrer, a separatory funnel and a fractionating column attached to a condenser for distilling the ternary mixture. The flask was heated in a water-bath kept at 85°. A mixture of 43.5 g. (0.5 mole) of morpholine and 23 g. (0.5 mole) of absolute ethyl alcohol was dropped slowly into the reaction mixture, which was stirred continuously. During this addition, which was completed in one hour,

(1) This material is taken from a thesis to be submitted by Morris Zief to the faculty of the Graduate School of Boston University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) McLeod and Robinson, *J. Chem. Soc.*, **119**, 1470 (1921).

(3) Stewart and Bradley, THIS JOURNAL, **54**, 4176 (1932).

TABLE I

Alcohol	% Morpholine converted to ether	% Morpholine converted to dimorpholinomethane	B. p. of ether °C.	Mm.	Neut. equiv. Calcd.	Found	Nitrogen, % Calcd.	Found
Methyl	46.2	35.5	55.6–57	8	131	131.9	10.68	10.58
Ethyl	59.3	26.2	58–63	6	145	144.8	9.66	9.64
n-Propyl	74.0	12.0	100–102	22	159	158	8.81	8.80
Isopropyl[a]	29.7	53.6	64–66	6	159	158	8.81	8.89
n-Butyl[a]	73.8	16.3	99.5–100.5	11	171	171	8.09	8.22
Isobutyl	68.0	17.2	90.5–92.5	10	171	172	8.09	8.12
s-Butyl	58.9	34.0	92–94	10	171	170.5	8.09	8.23
t-Butyl	9.4	75.4						
Allyl	52.4	36.3	82–83	7	157	156.6	8.92	8.93
Benzyl	76.8	4.4	152–154	7	207	206	6.76	6.83

[a] Harradence and Lions, *J. Proc. Roy. Soc. N. S. Wales*, **73**, 22 (1939).

TABLE II

N-Morpholine	B. p. °C.	Mm.	Yield, %	Neut. equiv. Calcd.	Found	Nitrogen, % Calcd.	Found	Picrate M. p. °C. (cor.)	Nitrogen, % Calcd.	Found
β-Phenethyl	147–151	13	66	191	190	7.33	7.31	166–167	13.33	13.27
α-Naphthylmethyl	185–190	9	57.7	227	225	6.17	6.00	209–211	12.28	12.40
n-Propyl	43–46	7	43.4	129	130.3	10.85	10.76	118–120	15.64	15.67
n-Hexyl	86–87	6	59.7	171	172	8.18	8.04	110–111	13.99	13.97
Benzyl	135–136.5	14	64.4	177	176.8	7.91	7.35	193.5–195	13.79	13.65

the ternary mixture of water, alcohol and benzene distilled at 65°.[4] After all of the morpholine was added, the temperature of the water-bath was raised to 100° and the remaining benzene and alcohol were distilled. The residue was transferred to a 500-cc. round-bottom flask to which was attached an efficient fractionating column. The distillate which came over up to 58° at 6 mm. pressure was discarded. The following fractions were collected.

Fraction	B. p., °C. (6 mm.)	Wt., g.	Neut. equiv.
I	58–63	26.7	144.8
II	63–110	24.3	120.5
III	110–113	4.1	97.3

Fraction I is pure 4-morpholinomethyl ethyl ether (neutral equivalent 145) while fraction III consists chiefly of dimorpholinomethane (neutral equivalent 93). If we make the reasonable assumption that fractions II and III are mixtures of the ether and dimorpholinomethane, it is possible to determine the amount of each component from the titration data and simultaneous equations. For example, 0.2546 g. of fraction II required 20.71 cc. of 0.1024

TABLE III

Alcohol used and temp. of external bath, °C.	Fraction	B. p., °C.	(Mm.)	Weight, g.	Neut. equiv.
Methyl[a]	I	55.6–57	(8)	20.0	131.9
75–80	II	57–113	(8)	8.8	127.7
	III	113–120	(8)	18.1	96.1
Propyl	I	100–102	(22)	40.9	158
87–92	II	102–128	(22)	12.7	152
	III	128–131	(22)	10.7	120
Isopropyl	I	89–93	(21)	3.9	155
80–85	II	93–98	(21)	5.8	155
	III	98–129	(21)	5.7	144
	IV	129–135	(21)	33.1	105
n-Butyl[a]	I	99.5–100.5	(11)	30.8	171
100	II	100.5–104	(11)	14.5	166
	III	104–110	(11)	8.8	158
	IV	110–122	(11)	17.3	134
Isobutyl[a]	I	90.5–92.5	(10)	29.9	172
100	II	92.5–97.5	(10)	15.1	170
	III	97.5–116	(10)	8.2	145
	IV	116–121	(10)	13.7	126
s-Butyl[a]	I	92– 94	(10)	10.3	170.5
100	II	94–100	(10)	17.0	165
	III	100–117	(10)	12.7	151
	IV	117–122	(10)	26.8	123
t-Butyl[a]	I	112–120	(11)	7.8	111
100	II	120–123	(11)	16.0	102
	III	123–125	(11)	19.5	98
Allyl[a,b]	I	82–83	(7)	10.8	156.6
100	II	83–88	(7)	12.3	153.4
	III	88–111	(7)	11.9	134.9
	IV	111–116	(7)	23.0	111.3
Benzyl[a,b]	I	140–146	(7)	6.5	173
100	II	146–152	(7)	10.8	187.4
	III	152–154	(7)	64.0	206

[a] No benzene used. Mixture was fractionally distilled after addition of morpholine was complete. First fraction was a binary mixture of the alcohol and water. [b] 0.75 mole of alcohol used.

N hydrochloric acid for neutralization. One gram of 4-morpholinomethyl ethyl ether requires 68.36 cc. of this acid and 1 g. of dimorpholinomethane requires 104.98 cc. of this acid for neutralization. Solving the simultaneous equations

$$x + y = 0.2546$$
$$68.36x + 104.98y = 20.71$$

x equals 0.1641. Therefore 64.5% of fraction II is 4-morpholinomethyl ethyl ether. This type of analysis was used in all subsequent experiments to determine the per-

(4) Jordan, "Technology of Solvents," Chemical Publishing Company, New York, N. Y., pp. 324–325.

centages of morpholine converted to the ether and dimorpholinomethane reported in Table I.

The other 4-morpholinomethyl alkyl ethers were made by the method described above, with the modifications given in the footnotes of Table III which summarizes all of the experimental data.

N-Substituted Morpholines.—The Grignard reagents were prepared in the usual way using 0.12 mole of magnesium and 0.12 mole of halide in 100 cc. of absolute ether. One-tenth mole of 4-morpholinomethyl ethyl ether dissolved in 50 cc. of absolute ether was then added slowly to the solution of Grignard reagent, the mixture refluxed for thirty minutes and allowed to stand overnight. The mixture was hydrolyzed with 10 cc. of concentrated sulfuric acid dissolved in 100 cc. of water. The ether layer was extracted with three 20-cc. portions of 20% sulfuric acid. Ten grams of ammonium chloride was added to the combined acid extracts to which concentrated ammonium hydroxide (about 65 cc.) was added until the solutions were alkaline. The alkaline solution was extracted with four 40-cc. portions of ether. The combined ether extracts were dried over calcium sulfate, the ether distilled and the remaining oil was distilled under reduced pressure. The results are given in Table II.

Summary

The preparation of eight new 4-morpholinomethyl alkyl (or aralkyl) ethers has been described and the amount of dimorpholinomethane formed by a competing reaction has been indicated in each preparation.

Five alkyl (or aralkyl) morpholines have been prepared from 4-morpholinomethyl ethyl ether and Grignard reagents.

BOSTON, MASS. RECEIVED MARCH 14, 1940

[CONTRIBUTION FROM THE RESEARCH LABORATORIES DIVISION, GENERAL MOTORS CORPORATION]

The Thermal Decomposition of the Acetate of 2,2-Dimethyl-3-pentanol

BY PAUL L. CRAMER AND VERLE A. MILLER

The dehydration of primary and secondary alcohols containing a neopentyl group to form the corresponding olefin is accompanied by a skeletal rearrangement.[1] Thus, the alcohol–olefin–paraffin method in many instances is not applicable in the synthesis of the tetra-alkylmethanes. The thermal decomposition of the methyl xanthate of the alcohol has provided a successful modification of the above method for the preparation of this type of hydrocarbon.[2]

The thermal decomposition of the acetate rather than the methyl xanthate of the alcohol has been employed in the synthesis of 3,3-dimethyl-1-butene.[1,3] The acetate gives much higher yields of the olefin than those obtained by the methyl xanthate procedure. Also the acetate method offers a more simple procedure in which no solvent is required. The main disadvantage of this method is the high temperature required to decompose the acetate, which would be expected to enhance the possible formation of isomeric olefins or other undesirable side reaction products. Thus, it seemed desirable to further test the acetate method as a possible general procedure for the synthesis of the above type of olefins and the corresponding paraffins.

In the present investigation a study has been made of the thermal decomposition of the acetate of 2,2-dimethyl-3-pentanol. As in the case of the acetate of 3,3-dimethyl-2-butanol,[3] a temperature of 400° is required to bring about an 80% conversion at contact times of reasonable length. Only about 12% conversion is obtained at 350°. The reaction is remarkably free of side reaction products, and the unchanged acetate may be recovered almost quantitatively.

4,4-Dimethyl-2-pentene is the principal olefin (93%) formed in the decomposition of the acetate of 2,2-dimethyl-3-pentanol. In contrast with the results obtained with the acetate of 3,3-dimethyl-2-butanol,[1,3] rearrangement occurs in this reaction to the extent of about 7%.[4] The rearranged products consist of a mixture containing about equal amounts of two olefins boiling in the 2,3-dimethylpentene and the 2,4-dimethylpentene range. Due to the very small amounts of these rearranged olefins, their separation and further identification by fractionation was unsuccessful.

(1) For references see Whitmore and Meunier, THIS JOURNAL, **55**, 3721 (1933).

(2) (a) Fomin and Sochanski, *Ber.*, **46**, 246 (1913); (b) Schurman and Boord, THIS JOURNAL, **55**, 4930 (1933).

(3) Cramer and Mulligan, *ibid.*, **58**, 373 (1936).

(4) To demonstrate that the rearranged olefins were not the result of the decomposition of the 2,2-dimethyl-3-pentanol contained as an impurity in the acetate, the pure alcohol, obtained by the saponification of a portion of the acetate, was found to be stable under the conditions employed in the decomposition of the acetate.

However, from the corresponding heptanes, obtained by the hydrogenation of the rearranged olefin mixture, pure 2,3-dimethylpentane was separated by fractionation. Thus, one of the rearranged olefins is identified as 2,3-dimethylpentene. The boiling point range, and in particular the refractive index curve for the second hydrogenated rearranged product, offer strong evidence in favor of the 2,4-dimethyl isomer. The above distillation analysis is shown in Fig. 1.

It is of interest to note that in the case of the principal olefin, 4,4-dimethyl-2-pentene, only a very small amount of evidence was obtained to indicate the presence of both *cis* and *trans* isomers. The entire distillation range, carried out in a column having an effectiveness equivalent to 100 plates, was only 0.1°. The refractive index of the first 20% of the distillate was slightly higher than that of the main portion. Hydrogenation of the first portion gave pure 2,2-dimethylpentane, Fig. 1. Thus, it seems reasonable to assume that the 4,4-dimethyl-2-pentene obtained by the above method is comprised largely of one form, presumably the higher boiling isomer.

A comparison of the results obtained by the acetate and the methyl xanthate methods in the synthesis of 4,4-dimethyl-2-pentene is shown by the following data: acetate, yield based on the carbinol 70.5%, b. p. 76.6–76.7°, d^{20}_4 0.6884, $n^{20}D$ 1.3983; methyl xanthate,[2b] 44%, 76–76.1°, 0.6881, 1.3986. No rearranged olefins have been reported for the methyl xanthate procedure.

Experimental

Materials.—2,2-Dimethyl-3-pentanol was prepared in the usual manner, namely, the reaction of *t*-butyl-magnesium chloride with propionaldehyde. The yield of the alcohol, b. p. 132–135°, was 35%.

The acetate of 2,2-dimethyl-3-pentanol, previously prepared by the acetylation of the alcohol with acetic anhydride,[5] was prepared here by the acetylation of the alcohol by a 10% excess of acetyl chloride. The acetyl chloride was added slowly to the alcohol with stirring. The reaction mixture finally was heated at 100° for two hours. The acetate was distilled from the reaction mixture. It was washed with water and with sodium bicarbonate solution, and dried over calcium chloride. The yield of acetate, b. p. 153–158°, containing a small amount of unchanged carbinol, was 80%.

The Thermal Decomposition of the Acetate of 2,2-Dimethyl-3-pentanol.—These reactions were carried out in a pyrex tube packed with glass wool, and heated in the conventional type of electric furnace. The reaction products were collected at 0°. The olefin containing unchanged acetate was separated from the acetic acid by washing with water and with sodium bicarbonate solution. After drying over calcium chloride, the olefin was separated by distillation.

(5) Favorsky, *J. prakt. Chem.*, (2) **88**, 672 (1912).

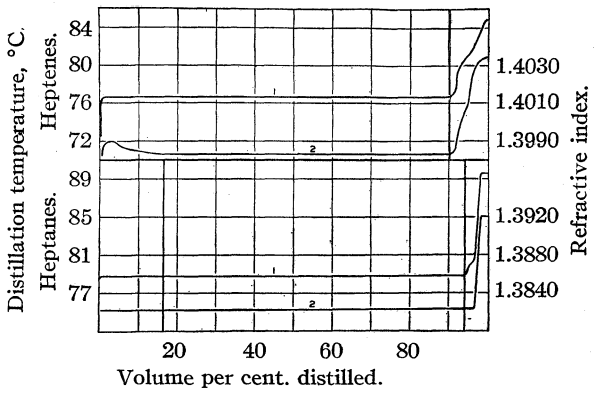


Fig. 1.—Distillation analyses of the heptenes and the corresponding heptanes obtained by the thermal decomposition of the acetate of 2,2-dimethyl-3-pentanol: curves 1, distillation temperature; curves 2, refractive index.

The decomposition of the acetate (238 g.) at 349° with a contact time of one hundred and nine seconds yielded 11.5% olefin. At 401° and a contact time of ninety-nine seconds the yield from 214 g. of the acetate was 77%.

The main portion of the acetate (538 g.), in which the olefins were analyzed by fractionation, was decomposed at 400° and a contact time of one hundred seconds. The yield of olefin, including that obtained from the second passage of the recovered acetate from the main run, was 88%. The main portion of the olefin (90.5%), pure 4,4-dimethyl-2-pentene, was separated by fractionation in a 100-plate column. The hold-up from this column, amounting to about 50 cc., was transferred to a small column having an effectiveness equivalent to 28 plates. In the latter column only a partial separation of a mixture (38 cc.) of 4,4-dimethyl-2-pentene, and two rearranged products, boiling in the 2,3- and 2,4-dimethylpentene range, was effected. The distillation analysis of the heptenes is shown in Fig. 1. The physical constants for 4,4-dimethyl-2-pentene are presented elsewhere in this paper.

The Hydrogenation of the Heptenes.—The hydrogenation of the heptenes was carried out in three separate batches: namely, the first 20%, the middle 70.5% and the last 8% of the total heptene distillate. The hydrogenation was effected by the use of Raney nickel catalyst in the absence of a solvent. The hydrogenated products in each case were purified by washing with water, concd. sulfuric acid, and finally by refluxing and fractionation over sodium. The fractionation was carried out in the 28-plate column. The distillation analysis of the heptanes is shown in Fig. 1. The physical constants for the pure heptanes thus obtained are as follows: 2,2-dimethylpentane, b. p. 78.8°, $n^{20}D$ 1.3823; 2,3-dimethylpentane, b. p. 89.6°, $n^{20}D$ 1.3920.

Summary

A study has been made of the thermal decomposition of the acetate of 2,2-dimethyl-3-pentanol

to yield 4,4-dimethyl-2-pentene and acetic acid.

About 7% rearrangement occurred in this reaction. One of the two rearranged olefins obtained in this reaction was identified as a 2,3-dimethylpentene.

In the case of the principal olefin, 4,4-dimethyl-2-pentene, little evidence was obtained of the presence of both *cis* and *trans* isomers.

2,2-Dimethylpentane, 2,3-dimethylpentane and an unidentified isomer were obtained by the hydrogenation of the heptenes.

DETROIT, MICH. RECEIVED MARCH 11, 1940

[CONTRIBUTION FROM THE AVERY LABORATORY OF CHEMISTRY OF THE UNIVERSITY OF NEBRASKA]

The Ternary Systems Involving Cyclohexene, Water, and Methyl, Ethyl, and Isopropyl Alcohols

BY E. ROGER WASHBURN, C. LOREN GRAHAM,[1] GEORGE B. ARNOLD AND LAURENCE F. TRANSUE

In continuation of a series of investigations of similar binary and ternary systems the solubility relationships for the systems formed from cyclohexene, water and methyl, ethyl and isopropyl alcohols have been studied at 25.0°. In order to provide an indication of the changes to be expected with changes in temperature the system involving isopropyl alcohol was also studied at 15.0 and 35.0°. The proportions in which the alcohols are distributed between the water-rich and cyclohexene-rich layers have been measured.

Materials.—Good commercial grades of methyl and ethyl alcohol, and isopropyl alcohol from Eastman Kodak Company were dried by refluxing over active lime for many hours. The alcohols were then distilled from the lime into a carefully dried all-glass still. They were then slowly distilled from this still through an efficient fractionating column and preserved in carefully dried glass-stoppered bottles. The specific gravities and refractive indices of the purified materials are listed in Table I.

Several studies carried out in this Laboratory indicate that both the density and the refractive index of cyclohexene change with the passage of time if the material is in contact with oxygen. That this is probably due to the formation of a peroxide is indicated by the fact that while the freshly distilled material fails to liberate iodine from an iodide, the material which has been in contact with oxygen for some time gives positive results when added to an acidified potassium iodide–starch solution. Accordingly our cyclohexene, the better of the two grades sold by Eastman Kodak Company, was repeatedly fractionated through a carefully controlled Snyder column[2] in an atmosphere of purified nitrogen. It was collected in carefully dried, nitrogen-filled bottles and kept under nitrogen until used. It was our experience that the specific gravity and refractive index were constant at the values indicated in Table I as long as tests with potassium iodide and starch indicated no peroxide.

There is little consistency in the recorded values for the specific gravity, or for the refractive index, of cyclohexene. Therefore, since considerable effort was made in this work to obtain material of a high degree of purity, more than the usual amount of interest may attach to the value which we record. In one distillation these observations were made. Three hundred twenty-five cc. of stock material of d^{25}_4 0.80919 was distilled. The first 50 cc. collected had a value of d^{25}_4 of 0.80558, the second fraction (210 cc.) had a specific gravity of 0.80566, while the 50 cc. of residue showed the high value of 0.82152. The second fraction was then fractionated yielding 35 cc. with d^{25}_4 of 0.80564, 55 cc. of 0.80562 and leaving 50 cc. of residue of 0.80576.

A large number of similar distillations carried out by different investigators in this Laboratory lead us to believe that the specific gravity of cyclohexene d^{25}_4 is 0.8056 ± 0.0001.

TABLE I

Material	Specific gravity, d^{25}_4	Refractive index $n^{25}D$
Methyl alcohol	0.7866	1.32659
Ethyl alcohol	.7851	1.35942
Isopropyl alcohol	.7809	1.37487
Cyclohexene	.8056 d^{15}_4 0.8151	1.4434

Procedure and Results.—The ternary solubility curves were determined by a titration method similar to that described elsewhere.[3] The titrations were carried out at the temperatures

(1) Present address: Eastman Kodak Company, Rochester, New York.

(2) Hill and Ferris, *Ind. Eng. Chem.*, **19**, 379 (1927).

(3) THIS JOURNAL, **62**, 579 (1940).

indicated within ±0.05°. Weighed quantities of the components were used, the titrant being added from a weight pipet. Care was taken to avoid overstepping the end-point and also to avoid confusing the opalescence obtained with certain proportions of the components with the true end-point as indicated by the appearance of a second phase. The angle and intensity of the illumination was varied so as to provide conditions most favorable for the particular titration. To make certain that the end-point had been reached the titration mixture was shaken automatically in the constant-temperature bath for at least fifteen minutes and then reëxamined.

The determinations of the refractive indices of the saturated solutions containing methyl alcohol were particularly difficult with the solutions where the end-point was preceded by an opalescence. In order to overcome this difficulty these solutions were warmed to 30.0° in order to clear up the solutions and the refractive indices were determined at that temperature. These values are indicated in Table I. When solutions in this range of concentrations were encountered in the distribution studies they were, of course, also heated to 30.0° for the refractive index determination.

The results of these determinations of solubilities and refractive indices are recorded in Tables II to VI. The concentrations of the conjugate solutions are recorded in Tables VII to XI.

TABLE II

METHYL ALCOHOL, CYCLOHEXENE AND WATER AT 25.0°[a]

Cyclohexene, wt. %	Methyl alcohol, wt. %	Refractive index	Cyclohexene, wt. %	Methyl alcohol, wt. %	Refractive index
89.03	10.86	1.4259[a]	6.57	74.36	1.3416
79.09	20.65	1.4135[a]	3.52	70.79	1.3403
68.09	31.43	1.4000[a]	2.05	64.56	1.3409
56.88	42.35	1.3868[a]	0.87	55.87	1.3410
44.13	54.30	1.3745	.48	47.96	1.3410
30.20	66.31	1.3603	.20	37.12	1.3400
17.87	74.04	1.3490	.10	24.92	1.3380
10.67	76.11	1.3435	.05	15.31	1.3356
	Cyclohexene saturated with water				1.4405[a]
	Water saturated with cyclohexene				1.3320

[a] These refractive indices were measured at 30.0°.

TABLE III

ETHYL ALCOHOL, CYCLOHEXENE AND WATER AT 25.0°

Cyclohexene, wt. %	Ethyl alcohol, wt. %	Refractive index	Cyclohexene, wt. %	Ethyl alcohol, wt. %	Refractive index
95.48	4.25	1.4387	16.13	64.31	1.3730
85.65	13.86	1.4302	7.39	61.32	1.3659
68.96	28.31	1.4151	3.08	54.54	1.3612
53.61	40.90	1.4018	0.59	41.56	1.3547
39.57	51.92	1.3903	.17	23.94	1.3475
29.46	58.86	1.3832	.12	19.85	1.3453
	Cyclohexene saturated with water				1.4428
	Water saturated with cyclohexene				1.3320

TABLE IV

ISOPROPYL ALCOHOL, CYCLOHEXENE AND WATER AT 25.0°

Cyclohexene, wt. %	Alcohol, wt. %	Refractive index	Cyclohexene, wt. %	Alcohol, wt. %	Refractive index
94.29	5.25	1.4389	5.94	44.85	1.3679
81.12	17.37	1.4284	5.21	43.87	1.3669
67.49	28.86	1.4182	1.29	33.34	1.3594
54.31	38.58	1.4087	0.48	20.34	1.3501
44.89	44.27	1.4024	.35	14.33	1.3450
30.39	50.39	1.3914	.09	7.10	1.3382
18.76	51.37	1.3816	.06	3.21	1.3348
11.73	49.27	1.3750			

TABLE V

ISOPROPYL ALCOHOL, CYCLOHEXENE AND WATER AT 15.0°

Cyclohexene, wt. %	Alcohol, wt. %	Refractive index	Cyclohexene, wt. %	Alcohol, wt. %	Refractive index
97.82	2.02	1.4470	11.38	49.30	1.3779
91.11	8.41	1.4414	7.22	47.52	1.3743
83.16	15.70	1.4348	2.09	39.56	1.3662
77.87	20.34	1.4312	1.28	35.76	1.3634
70.74	26.44	1.4258	0.34	27.44	1.3580
58.60	35.62	1.4171	.11	22.94	1.3541
43.91	44.95	1.4060	.11	17.95	1.3499
31.16	50.67	1.3958	.20	9.72	1.3415
21.63	51.42	1.3884	.08	3.89	1.3361

TABLE VI

ISOPROPYL ALCOHOL, CYCLOHEXENE AND WATER AT 35.0°

Cyclohexene, wt. %	Alcohol, wt. %	Refractive index	Cyclohexene, wt. %	Alcohol, wt. %	Refractive index
94.30	5.13	1.4336	13.76	49.53	1.3726
84.54	14.31	1.4254	7.31	45.01	1.3653
66.88	29.40	1.4119	1.23	31.80	1.3557
51.88	40.47	1.4017	0.46	24.08	1.3507
40.62	46.52	1.3940	.18	14.39	1.3433
31.81	50.10	1.3878	.06	4.79	1.3348
23.62	51.31	1.3814			

TABLE VII

CONJUGATE SOLUTIONS CONTAINING METHYL ALCOHOL AT 25.0°[a]

Water layer			Cyclohexene layer		
Refractive index	Alcohol, wt. %	Water, wt. %	Refractive index	Alcohol, wt. %	Cyclohexene, wt. %
1.3341	9.6	90.4	1.4404[a]	0.1	99.9
1.3362	17.8	82.1	1.4403[a]	.2	99.8
1.3384	27.0	72.9	1.4403[a]	.2	99.8
1.3392	31.0	68.9	1.4402[a]	.3	99.7
1.3404	40.0	59.7	1.4401[a]	.4	99.6
1.3406	72.8	22.2	1.4390[a]	1.2	98.8
1.3435	76.0	14.0	1.4378[a]	2.1	97.9

[a] These refractive indices were measured at 30.0° for purposes of analysis.

A comparison of the solubility curves for these systems indicates that isopropyl alcohol is the

TABLE VIII

CONJUGATE SOLUTIONS CONTAINING ETHYL ALCOHOL AT 25.0°

Water layer			Cyclohexene layer		
Refractive index	Alcohol, wt. %	Water, wt. %	Refractive index	Alcohol, wt. %	Cyclohexene, wt. %
1.3405	12.3	87.4	1.4425	0.3	99.7
1.3491	27.8	72.3	1.4422	.6	99.3
1.3539	39.7	60.0	1.4418	1.0	98.8
1.3580	48.7	49.5	1.4410	1.8	98.0
1.3635	58.4	37.0	1.4399	3.1	96.9
1.3690	63.3	25.6	1.4372	5.9	93.7
1.3730	64.3	19.6	1.4360	7.3	92.4

TABLE IX

CONJUGATE SOLUTIONS CONTAINING ISOPROPYL ALCOHOL AT 25.0°

Water layer			Cyclohexene layer		
Refractive index	Alcohol, wt. %	Water, wt. %	Refractive index	Alcohol, wt. %	Cyclohexene, wt. %
1.3398	8.8	91.1	1.4428	0.6	99.3
1.3496	19.8	79.9	1.4385	5.7	93.8
1.3569	29.6	69.7	1.4283	17.6	80.9
1.3605	34.9	63.6	1.4181	28.8	68.0
1.3623	37.5	60.2	1.4132	34.2	60.6
1.3643	40.4	55.5	1.4060	41.3	50.0
1.3695	46.0	47.1	1.3920	50.2	31.4
1.3734	48.3	41.5	1.3839	51.6	21.3

most effective in bringing about complete miscibility of the system cyclohexene, water and alcohol, and methyl alcohol is the least effective. In the study of the conjugate solutions very little

TABLE X

CONJUGATE SOLUTIONS CONTAINING ISOPROPYL ALCOHOL AT 15.0°

Water layer		Cyclohexene layer	
Refractive index	Alcohol, wt. %	Refractive index	Alcohol, wt. %
1.3439	12.0	1.4480	0.7
1.3521	20.5	1.4457	3.5
1.3600	30.6	1.4366	14.1
1.3636	36.1	1.4284	23.2
1.3685	42.4	1.4159	36.7
1.3740	47.3	1.4021	47.3
1.3770	48.8	1.3970	50.2

TABLE XI

CONJUGATE SOLUTIONS CONTAINING ISOPROPYL ALCOHOL AT 35.0°

Water layer		Cyclohexene layer	
Refractive index	Alcohol, wt. %	Refractive index	Alcohol, wt. %
1.3390	9.6	1.4368	1.8
1.3455	17.2	1.4338	4.9
1.3507	23.9	1.4259	14.0
1.3545	29.9	1.4162	24.7
1.3563	32.8	1.4100	31.6
1.3573	34.5	1.4054	36.5

methyl alcohol is found in the cyclohexene layer, even when a considerable portion of the system is alcohol. A slightly larger proportion of ethyl alcohol is found in the hydrocarbon layer especially when the alcohol content is high. As has been found with other systems containing isopropyl alcohol, the proportion of it found in the

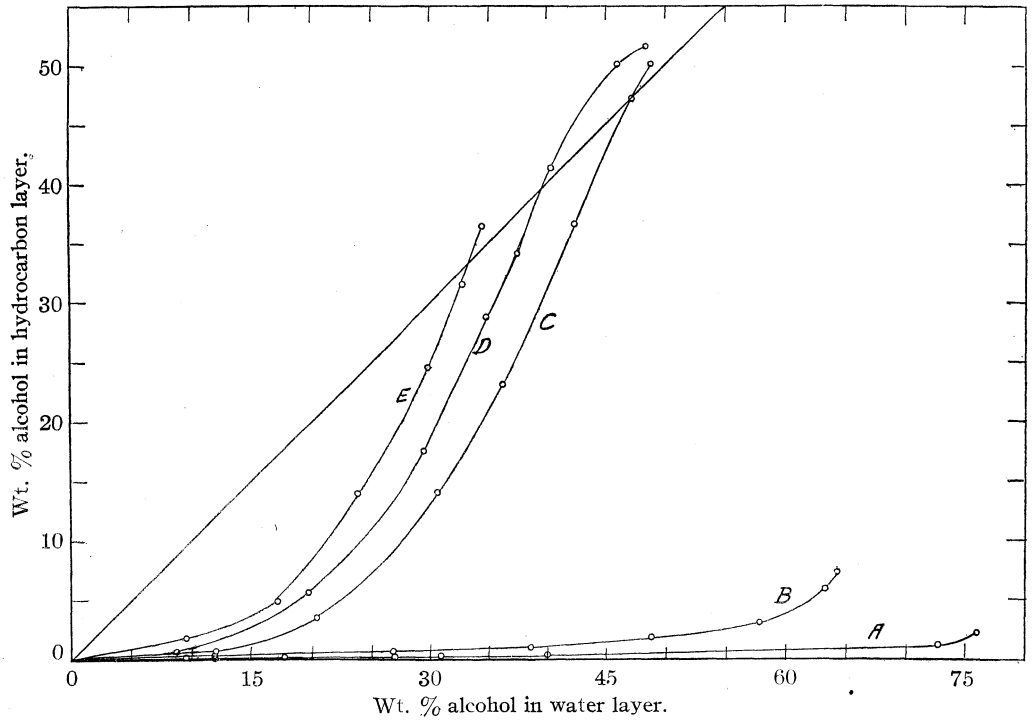


Fig. 1.—A, methyl alcohol; B, ethyl alcohol; C, D, E, isopropyl alcohol at 15, 25, 35°, respectively.

hydrocarbon layer increases rapidly with increasing total amount of alcohol until the tie lines change the sign of their slope. These facts are clearly indicated in Fig. 1 in which the % of alcohol in the cyclohexene layer is plotted against the % of alcohol in the water layer.

Increasing the temperature from 15 to 35° causes very little change in the area in which conjugate solutions are found; the area is slightly larger at the lower temperature. The slopes of the tie lines change by a large amount. The plait point at 15° is not far from the highest point of the solubility curve, while at 25° it is farther down on the water-rich side of the curve. It was experimentally difficult to approach very closely to the plait point at 35° but the indications are that at this temperature it is still farther down on the water side of the curve.

Summary

The solubility relationships for the ternary systems containing water and cyclohexene and methyl, ethyl or isopropyl alcohol have been determined at 25°. The system containing isopropyl alcohol has been investigated at 15 and 35°.

LINCOLN, NEBRASKA RECEIVED APRIL 20, 1940

[CONTRIBUTION FROM THE U. S. DEPARTMENT OF AGRICULTURE]

Hydration Mechanism of the Clay Mineral Montmorillonite Saturated with Various Cations[1]

BY S. B. HENDRICKS,[2a] R. A. NELSON[2b] AND L. T. ALEXANDER[2b]

Introduction

The hydrous magnesium aluminum silicate mineral montmorillonite, because of its unusual properties and widespread occurrence in clays and soils, has attracted the attention of workers in many fields. It is extremely plastic when moist and can be dispersed in water, readily forming thixotropic gels at moderate concentrations. The dispersed material upon drying reorganizes, forming a crystalline material one lattice constant of which depends upon the humidity. Montmorillonite is a salt of a moderately strong acid, from which other salts and the free acid can be prepared by cation replacement, that is, base exchange. It strongly absorbs organic bases with formation of the corresponding salts and also shows marked adsorption for neutral organic compounds, which is the basis for its use as a clarifying agent. Many reactions are catalyzed by montmorillonite.

Study of montmorillonite as a base exchange complex has come about largely because it is a component of many soils showing high base exchange capacity. Replacement of one cation by another has been investigated to a considerable extent and several series have been set up showing ease of replacement. The one generally accepted shows[3,4]: $H^+ > Ba^{++} > Sr^{++} > Ca^{++} > Mg^{++} > Cs^+ > Rb^+ > K^+ > Na^+ > Li^+$; thus, for example, a greater fraction of the K^+ ions is displaced at equivalent concentrations by Ca^{++} than by Li^+. These differences usually have been attributed to "ionic hydration."[5] A successful correlation has been found with zeta potentials[6] derived from migration velocities of clay micelles in suspensions. No attempt has been made, however, to determine the environment of the ion in the clay, which is fundamental to understanding the nature of the replacements.

For a number of years the authors have been interested in the identification and structures of minerals present in clays. During the course of this work it became evident that a study of water sorption by the various salts of montmorillonite probably would go far toward determining the environment of the replaceable cation. The material is one of the few in which sorption can be followed by means of lattice changes.

Methods and Materials

Since montmorillonite might be expected to differ in behavior depending upon its origin, samples were obtained from several localities. All of these were bentonites, that is, they were formed by devitrification of volcanic ash. One was a commercial material from Wyoming, sold under the trade name "Volclay," which is known to contain finely divided quartz and appreciable silica that can be dissolved in weak bases. This particular sample has not been ana-

(1) Not copyrighted.

(2a) Bureau of Agricultural Chemistry and Engineering.

(2b) Bureau of Plant Industry.

(3) G. W. Robinson, "Soils, Their Origin, Constitution, and Classification," D. Van Nostrand Co., New York, N. Y., 1936, Chapter V.

(4) H. Jenny, *J. Phys. Chem.*, **36**, 2217 (1932).

(5) G. Wiegner, *J. Soc. Chem. Ind.*, **50**, 65T, 103T (1931).

(6) H. Jenny and R. F. Reitemeier, *J. Phys. Chem.*, **39**, 593 (1935).

lyzed. Two other samples were furnished by Dr. C. S. Ross and Dr. P. G. Nutting of the U. S. Geological Survey. One was a fine white specimen from Otay, California (Sample G in 7) and the other was a slick yellowish material from the vicinity of Laurel, Mississippi (Sample B in 7). Both are considered to be very pure montmorillonite and analyses for them have been published.[7]

The clays were electrodialyzed to obtain the free acids and these were titrated to *p*H 8.0 with dilute calcium hydroxide or sodium hydroxide solutions to form the corresponding salts. Cesium, potassium, and barium salts of the Mississippi sample were made by titration of the free acid obtained by treatment of the clay for short times with successive lots of dilute (1:10) hydrochloric acid in large excess which was removed by washing with water. Lithium, magnesium, strontium (Miss.), and cerium (Calif.) salts were prepared from the original clays (predominantly the calcium salt) by base exchange from neutral chloride solutions. Base exchange capacities, expressed in milliequivalents per gram, of the three clays as obtained by titration of the hydrogen clays to *p*H 8.0 with sodium hydroxide solution are as follows: Mississippi 0.95, California 0.80, Wyoming 0.85.

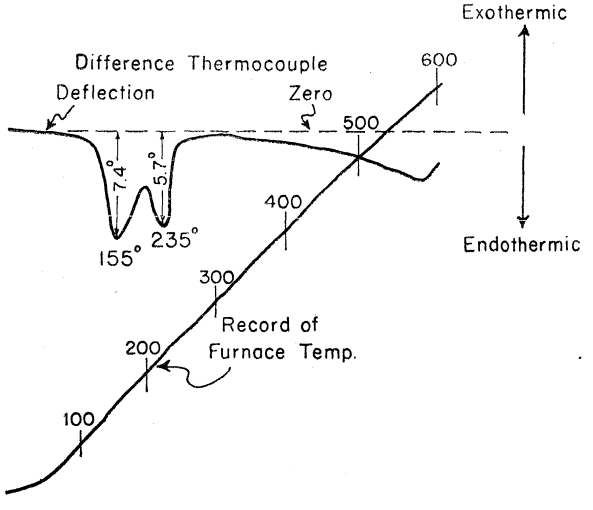


Fig. 1.—Photographic record from differential thermal analysis apparatus.

The clay salts were dried over phosphorus pentoxide in vacuum to constant weight and were then exposed at 30° to water vapor, at various relative humidities, for a week or longer. Amounts of water adsorbed were recorded and samples were removed for differential thermal analysis and for X-ray examination. The samples for X-ray examination were protected from change in water content by sealing them with plastocene in small tubes, 0.5 mm. in diameter, made from Lindemann glass. Unoriented samples were used since the procedure was simple and gave satisfactory results, even though it was realized that oriented samples would have been preferable. Nickel Kα radiation was used throughout.

Differential thermal analyses were made, according to the Le Chatelier[8] method, in an apparatus similar to that described by Norton.[9,10] In this method the temperature of a sample relative to that of an inert material is followed as the two are heated at an equal and approximately constant rate. An endothermic change, such as accompanies loss of water from a clay, results in a temperature lag relative to the inert material. The heating rate used was approximately 12° per minute which is rapid; a photographic record from the apparatus is reproduced as Fig. 1.

Some Structural Features of Montmorillonite.—The approximate crystal structure of montmorillonite, the essential mineral component of bentonites, was suggested by Hofmann, Endell and Wilm.[11] They showed that the lattice consisted of superimposed silicate sheets, similar to those found in the mineral pyrophyllite, having the ideal composition $(OH)_2Al_2Si_4O_{10}$, with replacement of Al^{+++} by Mg^{++}, Fe^{+++} and Fe^{++}, and silicon by aluminum. There is perfect cleavage between the sheets. Water sorption was shown to result in increase of the lattice spacing normal to the cleavage, (001). The water molecules were thus presumably located on the surfaces of the sheets.

Montmorillonite differs from pyrophyllite in having a smaller particle size, a more variable composition, a larger amount of water lost above 300°, and in showing base exchange. The replaceable ions are apparently external to the silicate sheets and usually amount to slightly less than 1 m. e. per gram, which is equivalent to about one-third the amount of potassium in muscovite. Their presence indicates that the sheets have some deficiency of positive ions resulting in an over-all negative charge. Attempts to locate the replaceable ions relative to the lattice have largely been speculative. Hofmann and Bilke[12] assumed that these ions were chiefly around the edges of the layers and to a lesser extent between the layers. Marshall[13] considered them to be between the layers and to be associated with water molecules. The behavior of organic salts of montmorillonite[14] when analyzed in detail shows that the exchangeable ions are predominantly between the silicate sheets. Gieseking, who has carried out the most extensive study of these salts, actually reproduces a drawing due to Hofmann and Bilke, without particular comment, but it is not to be thought that his results support their hypothesis. Results obtained in the present work also show that the most of the ions, probably more than 80%, are between the silicate sheets.

There has been some discussion of the manner in which water molecules are arranged between the silicate layers. A considerable body of opinion contends that they are in some type of close packed arrangement.[15] However, there are several arguments against this hypothesis, the simplest of which is that water usually has tetrahedral coordination. A suggested arrangement of water molecules which is supported by the known structure of vermiculite and which explains the observations that have been made on montmorillonite is shown in Fig. 6. A water layer of this type is of such a structure that if preserved would

(7) "U. S. Geological Survey Bulletin," No. 878, p. 107, 1937.
(8) H. Le Chatelier, *Z. physik. Chem.*, **1**, 396 (1887).
(9) F. H. Norton, *J. Am. Ceram. Soc.*, **22**, 54 (1939).
(10) S. B. Hendricks and L. T. Alexander, *Soil Sci.*, **48**, 257 (1939).
(11) U. Hofmann, K. Endell and D. Wilm, *Z. Krist.*, **86**, 340 (1933).
(12) U. Hofmann and W. Bilke, *Kolloid. Z.*, **77**, 238 (1936).
(13) C. E. Marshall, *Z. Krist.*, **91**, 446 (1935).
(14) J. E. Gieseking, *Soil Sci.*, **47**, 1 (1939).
(15) See S. B. Hendricks and M. E. Jefferson, *Amer. Mineral.*, **23**, 863 (1938), for a discussion.

propagate the lattice as a whole which is a very strong argument in its favor. If it is assumed that the upper surfaces of all silicate layers in montmorillonite are covered by a single water sheet of this type then 0.10 g. of water will be required for 1.0 g. of mineral.

Addition of a layer of water molecules results in a change of about 3.0 Å. in the separation of the silicate layers. The first layer hydrate would thus have a spacing of about 12.0–13.0 Å., and a hydrate with two water layers about 15.0–16.0 Å.[16] Bradley, Grim and Clark have shown that definite hydrates can at least be formed for a sample of hydrogen Wyoming montmorillonite that they studied. Others have failed to repeat this observation, which, however, does not detract from its possible validity. The more usual situation, and one in accord with all except a single observation made in this work, is that the characteristic cleavage spacing varies continuously but not uniformly with water content.[12] This apparently is a result of an averaging effect from a lattice that contains various numbers of water layers in different parts.[15]

Results and Discussion

Previous studies of water sorption by clays have largely been restricted to measurement of lattice constants and weight increases as functions of humidity or loss on drying to constant weight at fixed temperatures. With one exception, which will be discussed later (note reference 16), the results indicated that water was gained or lost in a monotonous way. Differential thermal analyses, however, carried out in this Laboratory for identification of clay minerals indicated that probably more than one process was involved in water sorption since the low temperature endothermic region had considerable structure (note Fig. 1).

Results obtained by differential thermal analysis for the various clays are reproduced in Figs. 2–5. Curves in these figures show the galvanometer response, in series with the differential couple, as the sample is heated. Ordinates thus are proportional to lag in temperature of the sample, behind the reference body, which depends upon the rate of energy uptake accompanying evolution of water.

(16) W. F. Bradley, R. E. Grim and G. L. Clark, *Z. Krist.*, **97**, 216 (1937).

Energy of desorption is constant to within 10% irrespective of the temperature of water evolution. Thus the area under a curve is a measure of the amount of water associated with each component curve provided it is referred to a uniform dry weight of sample. Values listed in the second line beneath the curves were obtained in this manner and can probably be trusted to within 20%. Amounts of water adsorbed per gram of dry material at room temperature, which of course are accurate, are shown in the first line beneath the curves. Results of X-ray diffraction measurements are given in the third line.

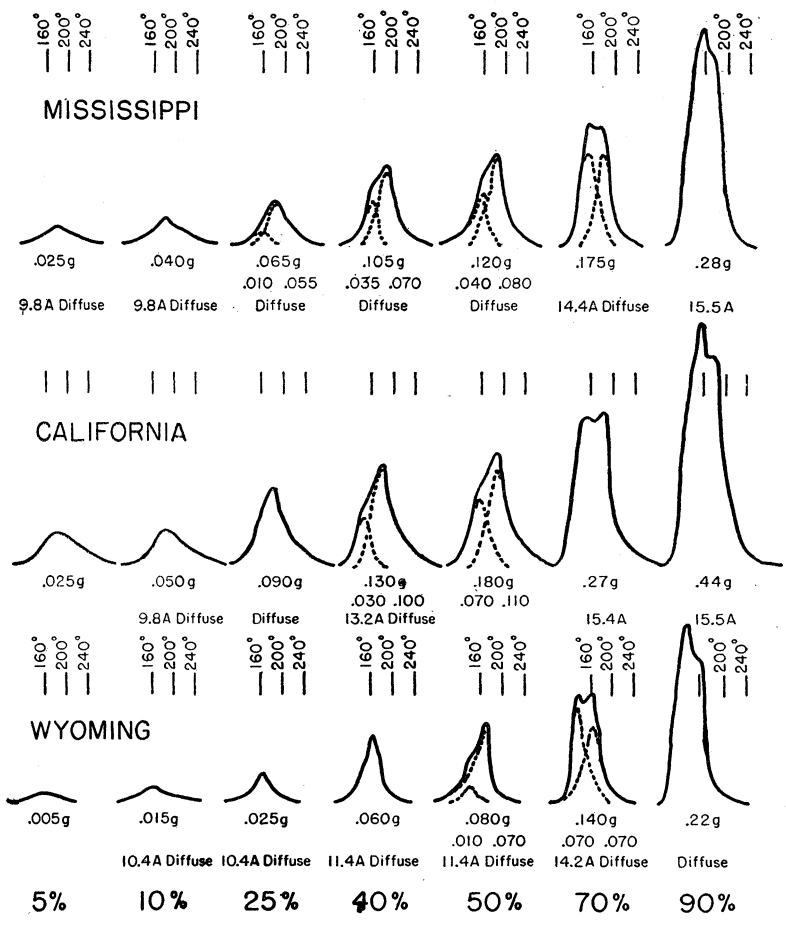


Fig. 2.—Thermal analysis curves of the sodium salts of various montmorillonites. Amounts of adsorbed water and values of the apparent cleavage spacing are given below the curves.

Although differential thermal analysis is a crude method measuring no real physical constant of a system, it enables one to distinguish variations in the binding of water even though such variations might be very small. Temperature of maximum rate of energy absorption is perhaps the best meas-

ure of order of binding energy. Maxima produced by loss of water adsorbed at low humidities occur at the higher temperatures, which is evidence that such water has the higher heat of binding.

Differential thermal analysis curves of the sodium and calcium clays from different localities are reproduced in Figs. 2 and 3. It can perhaps be seen that origin of material is relatively unimportant. For this reason only salts of the Mississippi material were prepared for further examination. Results obtained from them are reproduced in Figs. 4 and 5.

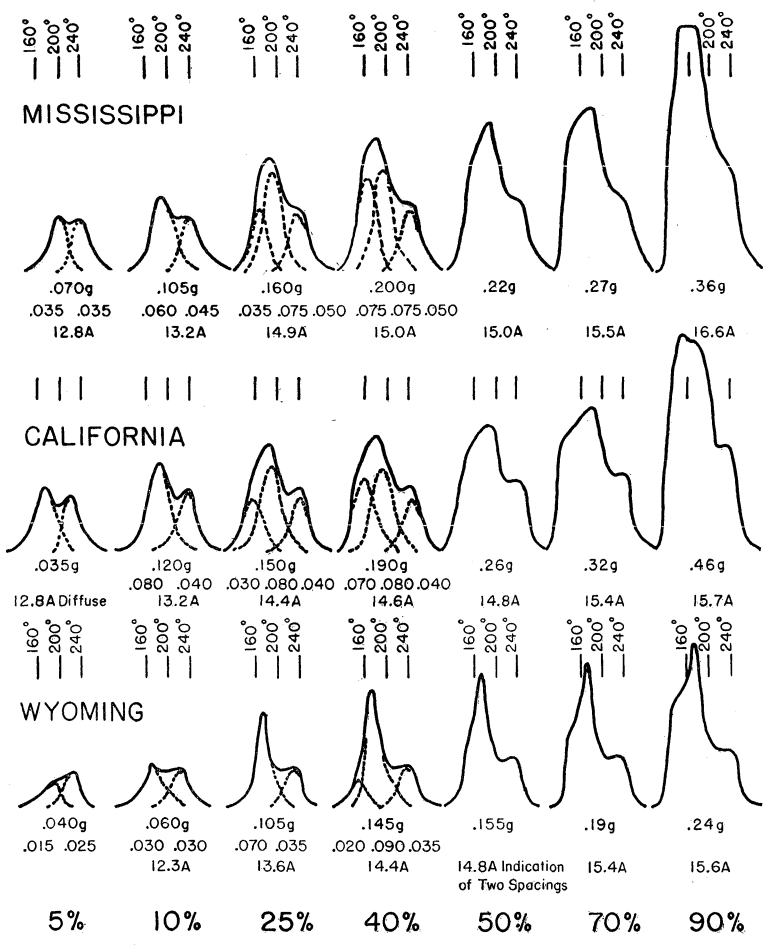


Fig. 3.—Thermal analysis curves, amounts of adsorbed water and values of the apparent cleavage spacing of the calcium salts of various montmorillonites.

An attempt was made, as shown in the figures, to resolve some of the curves into ones with single maxima. This presented some difficulties, but was aided by the fact that the contribution to one maximum was rather well completed before that to another had started. An example will be discussed to illustrate the general procedure. At a 5% R. H. (relative humidity as given at the bottom of the charts) the magnesium salt of Mississippi montmorillonite has a curve that comparison with the alkaline earth salts at the same R. H. indicates is formed from two incompletely resolved components. Moreover, the shape of the curve on the high temperature side shows that the high temperature component is somewhat smaller than the other. At 10% R. H. the second component has increased with little accompanying change of the high temperature component since that part of the curve above 240° has changed but slightly. The slightly convex shape of the low temperature part of the curve, below 180°, suggests that a third component is appearing. This is questionable at 10% R. H. but at 25% R. H. the third component is prominent and apparently accounts for the added water sorption as it also does at 40% R. H. Although the curves of samples with high water content obviously have several components, it was not considered justifiable to attempt the resolution. Attention is called to the cesium salt of Mississippi montmorillonite where the presence of two component curves between 40% and 70% R. H. is indicated by the shifting of the apparent single maximum and the shape of the curve above 180°.

The total area under the two peaks with highest maximum lags in temperature (max. T°C.) of the magnesium and calcium salts of Mississippi montmorillonite represents about 0.12 g. of adsorbed water which is approximately the amount, 0.10 g., required for formation of a single layer of water molecules arranged in the manner shown in Fig. 6. Moreover, the cleavage spacings of the hydrates are between 13.0 and 13.5 Å. which is but slightly more than the expected value, 12.0 to 13.0 Å., for a silicate sheet covered by a single layer of water molecules. Thus it would seem that at least two distinct processes are involved in the formation of the first layer hydrate.

It appears that the peaks having the highest max. T°C. for the magnesium and calcium Mississippi montmorillonites are to be correlated with hydration of the exchangeable cations. The base exchange capacity of this clay is about 0.95 milliequivalent per gram, the actual value varying slightly with the method used for determining it. This is equivalent to 0.00047 mole of Ca^{++} which would require 0.050 g. of water to form a hexahydrate. From the curves it appears that about 0.045 g. of water is associated with the peak having the highest max. T°C. The remaining water contributing to the formation of the first layer hydrate must be that required to hydrate the surface not contiguous to the exchangeable cations. It apparently is held somewhat less strongly since the max. T°C. of the peak associated with it is about 40° lower than the first peak.

Strontium and barium salts of Mississippi montmorillonite show characteristics similar to those discussed above. It is necessary, however, to go to higher humidities in order to have water sorption equivalent to that of the magnesium and calcium salts. As would be expected, accordingly, corresponding max. T°C. peaks are shifted to somewhat lower temperatures, about 20°, for the strontium and barium compounds. This shift makes it difficult to effect the resolution of the experimental curve into three maxima at the higher humidities and thus to determine the point at which the second peak is completed.

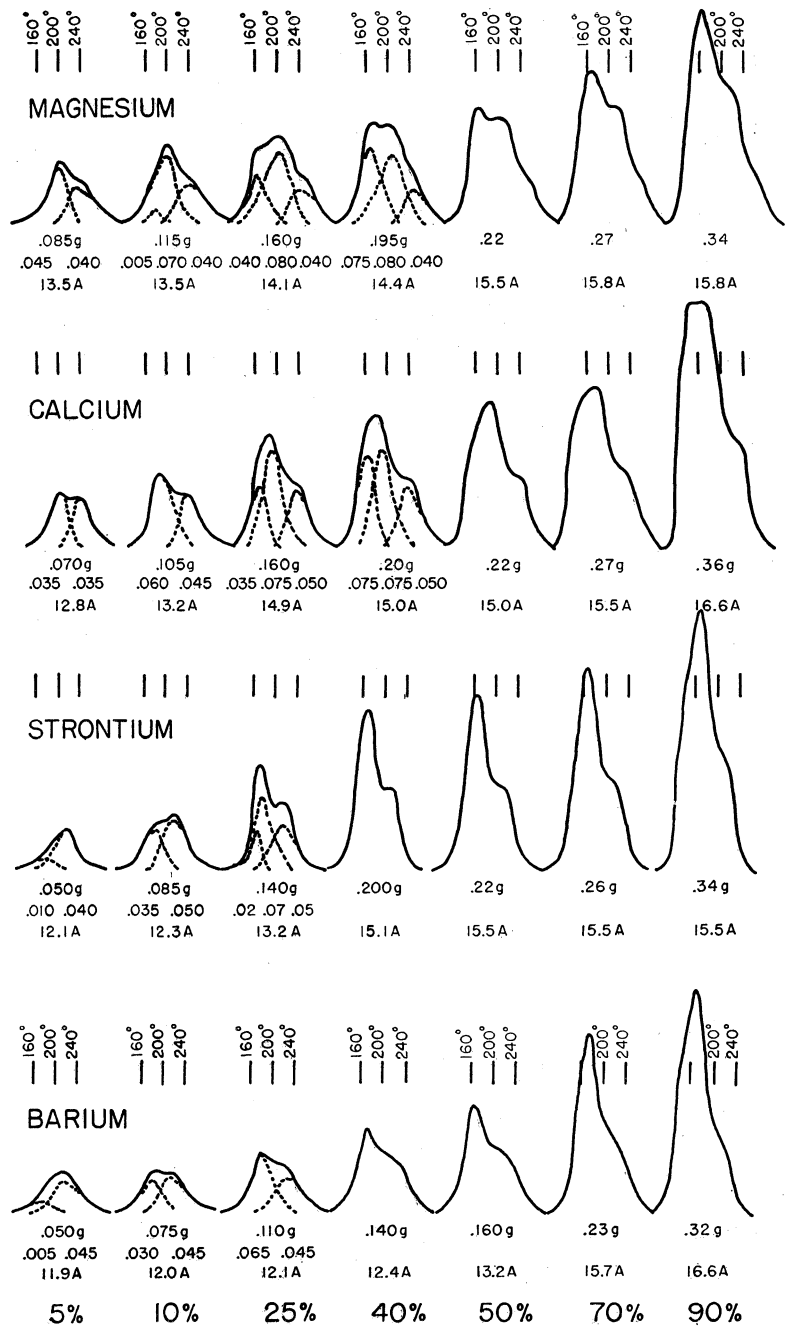


Fig. 4.—Thermal analysis curves, amounts of adsorbed water and values of the apparent cleavage spacing of magnesium, calcium, strontium and barium salts of Mississippi montmorillonite.

Lithium Mississippi montmorillonite is somewhat like the alkaline earth salts in behavior. At low humidities two well-resolved peaks are present. The peak with the highest max. T°C. (235°), which is almost complete at 5% relative humidity, corresponds to about 0.055 g. of water. This is about three (actually 3.3) water molecules for each Li^+ ion, which is the amount expected for plane coördination about a small ion. The second peak has a considerably lower max. T°C. (170°) than does the second peak of the alkaline earth salts. This, as was the case for the strontium and barium salts, makes it difficult to determine when the third peak begins to appear. The

cleavage spacing, however, is constant, as far as can be told, between 5 and 25% relative humidities but increases at 40%.[17] It would appear that the third peak must contribute to the curve at 40% relative humidity and that the second peak is essentially complete at 25%. The total water sorption at 25% relative humidity is about 0.12 g. which again is approximately the same as that required for a single layer of water molecules. While the six-fold coordination of magnesium and the alkaline earth ions would be expected to enhance the stability of a layer of the type shown in Fig. 6, there would possibly be some disrupting effect of lithium. This effect, however, need not completely destroy the structure in the water layer.

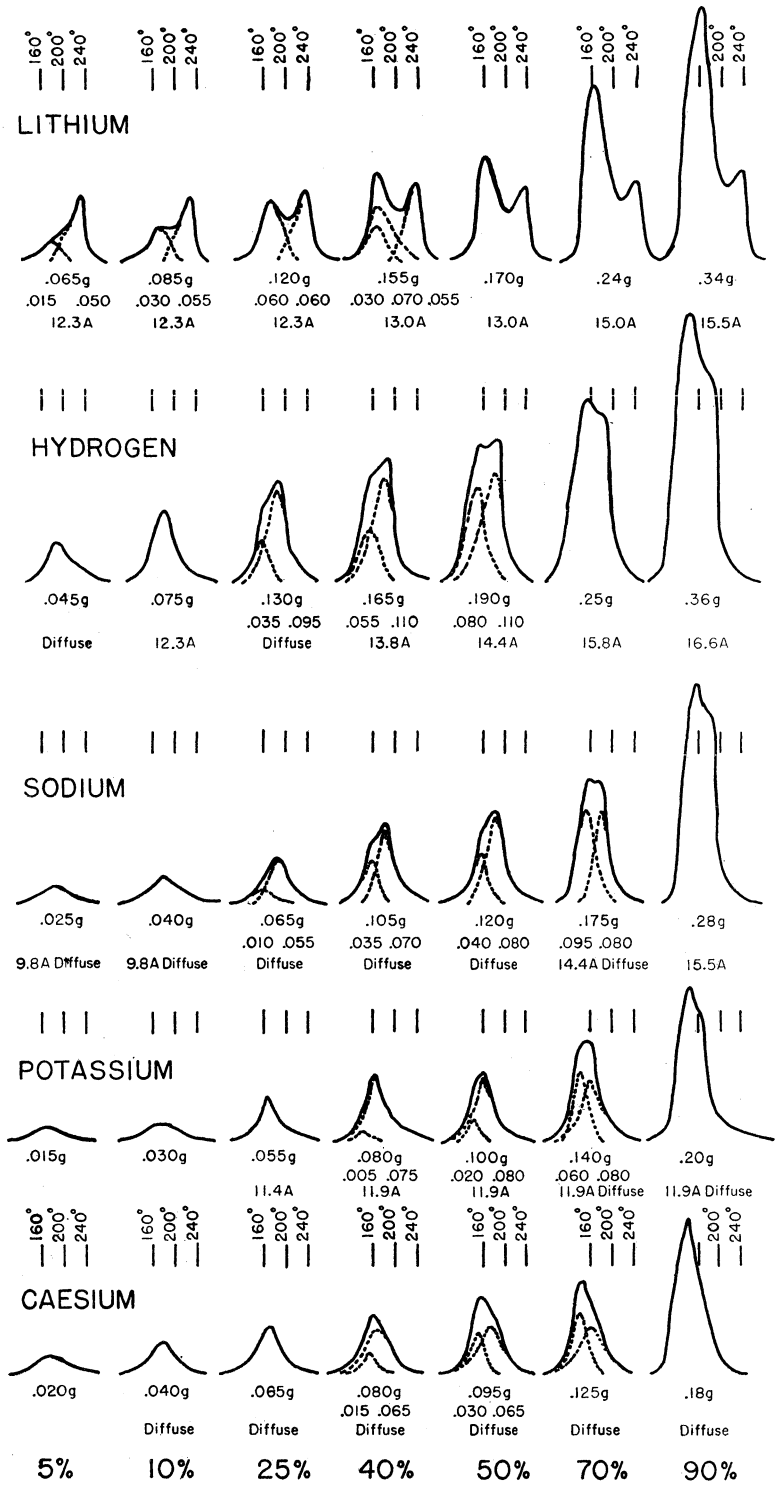


Fig. 5.—Thermal analysis curves, amounts of adsorbed water and values of the apparent cleavage spacing of lithium, hydrogen, sodium, potassium and cesium salts of Mississippi montmorillonite.

The third peak that appears for the lithium, magnesium and alkaline earth salts is probably to be associated with introduction of another layer of water molecules since the cleavage spacing increases, finally reaching a value of 15.0 to 16.0 Å., as the relative humidity is increased. Introduction of a second layer of water molecules is not a particularly simple process since it must influence the energy of binding of water that is already present. As a second layer is started molecules of the first layer are probably redistributed, some of the hydrated ions being in one layer and some in the other. Since the analysis is really made by successive removal of water it does not show what the binding conditions are before any water is removed. Finally at high relative humidities increased water sorption does not further change

(17) It is outside the scope of this work to discuss the crystal structures of montmorillonite and its hydrates in detail, but attention should be called to several facts. The measured interplanar spacings recorded on the figures are definitely not those of the first observed order (n) for some of the lithium, calcium, and hydrogen samples, but rather appear to be the second order ($2n$) since an apparent third order ($3n$) is present. We suspect, without analysis, that this is a result of the averaging effect previously mentioned.

the apparent cleavage spacing. Either the additional water is not between silicate layers or the diffraction pattern is due to only a minor part of the total sample. Both actually seem to play a part.

The most striking difference in the behavior of the sodium, potassium and cesium salts of Mississippi montmorillonite from that of the salts already considered is that only a single peak is present at low humidities. Furthermore, the value of max. T °C. is about the same for this peak, about 180°, as for the second peak of the strontium and barium salts. The two are completed at about the same value of the relative humidity and correspond to approximately the same amount of water, 0.06 to 0.08 g. These features indicate that the exchangeable cation is probably not hydrated in the sodium, potassium and cesium salts, although this interpretation is open to some question. Such a result might be expected for the cesium ion[18] from its behavior in solutions and to a lesser extent for the potassium ion.

Sodium, potassium and cesium salts are further characterized by a very poor degree of organization, as evidenced by the diffuseness of the X-ray diffraction patterns. Even at 90% relative humidity the potassium salt although containing enough water for two layers still shows the spacing of a single layer hydrate. The general character of these photographs, however, indicates that probably only a small portion of the material is sufficiently organized to give a diffraction pattern. This organized portion then is the single layer hydrate, which is indicative of an even more difficult formation of the multiple layer hydrate. The sodium salt is well enough organized to show the expected increase in X-ray spacing when a considerable amount of the double layer hydrate is present.

The free acid of the Mississippi clay has perhaps the simplest behavior of any of the materials examined. A single peak with a max. T °C. of 180° corresponding to the second peak of the alkaline earth salts is completed at about 25% relative humidity. The cleavage spacing is that of a single layer hydrate and the degree of organization as judged by diffuseness is high. Water sorption associated with this peak is about 0.10 g., which is the amount required for hydration of a layer according to the structure shown in Fig. 6. It would appear therefore that the hydrogen ion has little influence on the hydration. This is

(18) J. D. Bernal and R. H. Fowler, *J. Chem. Phys.*, **1**, 515 (1933).

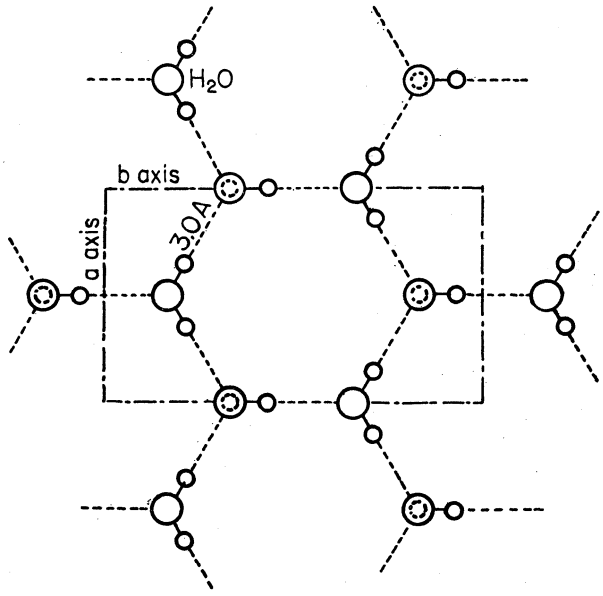


Fig. 6.—Possible arrangement of water molecules in a hydrated layer of vermiculite or montmorillonite.

reasonable when it is remembered that the hydrogen ion, being very small, is probably embedded in the silicate sheet near the site of the effective negative charge. There is no indication of hydration of the proton with formation of a hydronium $(H_3O)^+$ ion which in turn would hydrate.

Consideration of the preceding discussion shows that the evidence for the base exchange ions being between the silicate layers in montmorillonite is rather conclusive.

The total surface of water sorption by montmorillonite is about 8×10^6 sq. cm. per g., which is of the order of fifty times the observed surface for sorption of gases such as nitrogen and oxygen.[19] In other words, the internal surface reached by water in montmorillonite, as might be expected, is not available for van der Waals adsorption of most gases. Adsorption of nitrogen and oxygen rather measure the external surface area of the organized montmorillonite crystal which would not be greatly changed in formation of the internally hydrated material. Comparison of these areas shows that the individual montmorillonite crystals contain fifty to a hundred silicate layers, which is within the range indicated by electron diffraction and interference of visible light.

Summary

The water sorptions at relative humidities between 5 and 90% were measured for the Li^+, Na^+,

(19) B. Makower, T. M. Shaw and L. T. Alexander, *Proc. Soil Sci. Soc. Am.*, **2**, 101 (1937).

K^+, Cs^+, Mg^{++}, Ca^{++}, Sr^{++}, and Ba^{++} salts as well as the free acid of the clay mineral montmorillonite. Variations in X-ray diffraction patterns and behaviors upon differential thermal analyses were determined for the materials at the various relative humidities.

Results obtained indicate that the exchangeable cations are located between the silicate layers of which the mineral is formed. In the magnesium and alkaline earth salts, the first step of water sorption is the hydration of the cation with six molecules of water which is followed by completion of a water layer having a hexagonal type structure. A second water layer of similar structure is taken up at high relative humidities. Similar results were obtained for the lithium salt except that only three molecules of water were required for the hydration of the lithium ion. In sodium, potassium, and cesium salts the cation apparently was not hydrated. This was also true for the hydrogen ion in the clay acid.

The methods used in the work although inexact give a clear picture of the sorption process for water, which is entirely different from van der Waals adsorption of gases such as nitrogen.

WASHINGTON, D. C. RECEIVED FEBRUARY 10, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

The Heats of Dilution, Heat Capacities, and Activities of Urea in Aqueous Solutions from the Freezing Points to 40°[1,2]

BY FRANK T. GUCKER, JR., AND HUGH B. PICKARD

Introduction

In the study of solutions of non-electrolytes, a number of thermodynamic properties of aqueous solutions of urea have been determined in this Laboratory. We have found that, up to a concentration of 3 *M*, the apparent molal volume[3] of urea at 25 and 30° and the apparent molal expansibility[4] at 27.5° are linear functions of the first power of the concentration. Such a relationship is to be expected for many properties of non-electrolytes. Redlich and Klinger[5] found that it was the limiting law for the apparent molal volume of sucrose, and work in this Laboratory showed that it also was the limiting law for the apparent molal heat capacity[6] and heat content[7] of sucrose. An exhaustive study of the specific heats of aqueous solutions of urea[8] failed to determine unequivocally what limiting law was obeyed by the apparent molal heat capacity of urea. Heats of dilution can be measured in very dilute solutions, the specific heats of which differ from unity by an amount too small to measure directly. Hence the limiting value of the apparent molal heat content can be determined more accurately than that of the heat capacity. We therefore undertook a study of the heats of dilution of solutions of urea in order to find the limiting law for this property.

Our results also provide the final thermal data necessary for an accurate calculation of the change of the osmotic and activity coefficients of urea over a temperature range from 2 to 40°. Thus we can compare the results of vapor pressure measurements at different temperatures, and of freezing point depressions, with recent precise measurements of the vapor pressures of aqueous solutions of urea at 25°.

Heats of Dilution at 25°

Materials and Solutions.—The urea used in experiments 1–6 had been purified and used in the density determinations carried out in this Laboratory. It had been reclaimed several times by precipitation from 50% alcohol, as described in this work.[3] The urea used in experiments 7–23 was prepared from Mallinckrodt analytical reagent. It was recrystallized once from water, washed once with 95% alcohol, filtered on a sintered glass filter and dried overnight in a vacuum desiccator connected to a water aspirator. After being ground in an agate mortar, it was dried for seven or eight hours *in vacuo* at 50–60°. This purified material showed a conductance corresponding to only 0.004% electrolyte calculated as sodium chloride.

The distilled water used in making up the solutions had a specific conductance of 3×10^{-6} reciprocal ohm or less.

(1) Most of the material in this paper was presented before the Division of Physical and Inorganic Chemistry at the Boston Meeting of the American Chemical Society, September 14, 1939.

(2) This work was supported by grants from the Penrose Fund of the American Philosophical Society and from the Committee on Research of the Graduate School of Northwestern University.

(3) Gucker, Gage and Moser, THIS JOURNAL, **60**, 2582 (1938).

(4) Gucker and Moser, *ibid.*, **61**, 1558 (1939).

(5) Redlich and Klinger, *Sitzber. Akad. Wiss. Wien.*, Abt. IIb, **143**, 489 (1934); *Monatsh.*, **65**, 137 (1934).

(6) Gucker and Ayres, THIS JOURNAL, **59**, 447 (1937).

(7) Gucker, Pickard and Planck, *ibid.*, **61**, 459 (1939).

(8) Gucker and Ayres, *ibid.*, **59**, 2152 (1937).

The solutions used in experiments 1, 5, 7–10, 13, 14, 16 and 19–23 were made up determinate. Those used in the other experiments were the products of previous dilutions.

Experimental Methods.—The twin-calorimeter apparatus, sensitive to 1 microdegree, which was used to measure the heats of dilution of urea, has been described in a previous paper.[7] The experimental procedure was the same except for a few slight modifications. In order to increase the rate of heating, the 50-ohm calorimeter heaters were replaced by 25-ohm heaters in experiments 19–23.

In our apparatus, electrical heating cannot always be supplied rapidly enough to balance the heat of dilution at each instant. Since the thermal conductance constant is very low, no appreciable error is caused by heat leakage unless a heat change of more than a quarter of a calorie is involved. In these experiments, the pipet is opened not at the *beginning* but in the *middle* of the heating period.

Two types of experiment were carried out. In the first, a small amount of water (2.8–58 ml.) in the pipet was added to a large volume of solution (900 ml. to 1 liter) in the calorimeter. This caused a small change in molality, Δm, and gave a short chord on the heat content–molality curve. In the second type of experiment, a small quantity of solution was diluted with a large amount of water, giving a long chord on the heat content–molality curve.

In most of the experiments, the pipets were only partially filled with liquid. For example, in experiments 13 and 14 at 3 m, the pipets contained only about 3 ml. of water and 57 ml. of air. This introduced unexpected complications. The air is saturated with water vapor, at the vapor pressure of pure water, p_0. After the pipet is opened, this same air is in contact with the *solution*, having a vapor pressure $(p_0 - \Delta p)$. A small quantity of water therefore will condense and the heat of condensation will be added to the observed heat of dilution. This is practically the same as the heat of condensation of the same amount of water vapor on pure water, since the values of $\bar{L}_1$ which we calculate later are quite small. Taking the recent value of Osborne, Stimson and Ginnings[9] for the latent heat of vaporization of water at 25°, the heat evolved for V ml. of air in the pipet is

$$-\delta q = \frac{273}{298} \times \frac{\Delta p}{760} \times \frac{V}{22{,}400} \times 10{,}510$$
$$= 0.000566\, V \Delta p \text{ cal.}_{15}$$

Values of the vapor pressure of urea solutions, which are very nearly those calculated from Raoult's law, were taken from the paper of Scatchard, Hamer and Wood.[10] This correction then was applied to the experimentally measured values of q to give the actual heat effect caused by the dilution.

In experiments 13, 14, and 19–23, a small amount of solution was added to a large amount of water. In this case δq was positive (heat was absorbed) since the vapor pressure of the final 0.01 m solution was greater than that of the 3 m solution over which the air originally stood. In experiments 3–7 the volume of air in the pipet was 10 ml. or less and Δp was small so that δq was negligible and no correction was applied.

(9) Osborne, Stimson and Ginnings, *Bur. Standards J. Research*, **23**, 197 (1939), Table 13.

(10) Scatchard, Hamer and Wood, THIS JOURNAL, **60**, 3061 (1938).

Experimental Results.—The experimental results are summarized in Table I, which includes all but eight dilutions. Seven of these could not be completed, because of mechanical failures. One dilution of experiment 13 was rejected. This result was very low, probably because the valves of the pipet leaked.

The temperature at which the dilution took place was read from a standardized Beckmann thermometer. This temperature seldom varied from 25° by more than 0.03° and never by more than 0.05°. No correction was necessary for this difference, since the slope of the apparent molal heat capacity curve for urea at 25° is small.

We analyzed the results by the same methods we had used for sucrose.[7] The values of $\Delta H/\Delta m$ obtained from the short chord experiments, when plotted against m, were found to lie along a smooth curve, which could be represented by the equation

$$\Delta H/\Delta m = -85.87 + 12.88\, m - 0.795\, m^2 \qquad (1)$$

The coefficients of this equation were determined by the method of least squares, weighting each experiment in proportion to the heat change which was measured. The experimental results, together with the graph of this equation, are plotted in Fig. 1. The chords are short, corresponding to a change of only 0.01 in m, so that they are plotted simply as points. The satisfactory agreement is apparent from the graph.

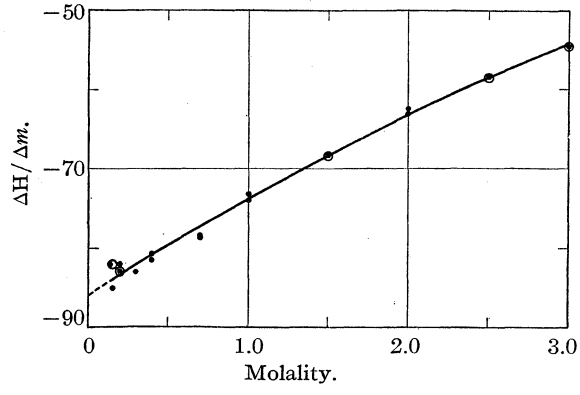


Fig. 1.—Slopes of dilution curve for urea at 25°.

Integration of equation (1) gave for the apparent relative heat content the equation

$$\Phi L_2 = \Phi H_2 - \Phi H_2^0 = -85.87\, m + 6.44\, m^2 - 0.265\, m^3 \qquad (2)$$

From this equation we calculated the values of q which are given in column 5 of Table I. The values for the two dilutions of an experiment usu-

TABLE I

HEATS OF DILUTION OF UREA SOLUTIONS AT 25°

Expt.	Initial concn., m_1	Final concn., m_2	q (cal.$_{15}$) (obsd.)	Equation 2: q (cal.$_{15}$) (calcd.)	Equation 2: $10^3\Delta q$ (obsd. − calcd.)	Equation 3: q (cal.$_{15}$) (calcd.)	Equation 3: $10^3\Delta q$ (obsd. − calcd.)	ΔH, cal.$_{15}$/mole	$-\Delta H/\Delta m$
6	0.1420	0.1340	0.091	0.093	− 2	0.093	− 2	0.66	82
5	.1500	.1420	.096	.098	− 2	.098	− 2	.66	82
	.1500	.1420	.100	.099	+ 1	.099	+ 1	.68	85
4	.2000	.1900	.163	.163	0	.163	0	.83	83
3	.2100	.2000	.174	.175	− 1	.174	0	.83	83
	.2100	.2000	.171	.175	− 4	.174	− 3	.82	82
2	.3100	.3000	.247	.245	+ 2	.244	+ 3	.829	82.9
	.3100	.3000	.247	.244	+ 3	.243	+ 4	.830	83.0
1	.4100	.4000	.330	.331	− 1	.330	0	.807	80.7
	.4100	.4000	.332	.330	+ 2	.329	+ 3	.814	81.4
15	.7000	.6900	.506	.497	+ 9	.496	+10	.786	78.6
	.7001	.6901	.505	.499	+ 6	.497	+ 8	.783	78.3
11	1.0100	1.0000	.680	.685	− 5	.682	− 2	.732	73.2
	1.0154	1.0053	.703	.702	+ 1	.699	+ 4	.746	73.9
10	1.4997	1.4900	.867	.867	0	.867	0	.663	68.4
	1.4997	1.4900	.854	.855	− 1	.855	− 1	.662	68.2
18	2.0100	2.0000	1.111	1.126	− 15	1.131	−20	.625	62.5
	2.0100	2.0000	1.118	1.122	− 4	1.127	− 9	.631	63.1
17	2.5100	2.5000	1.291	1.295	− 4	1.314	−25	.584	58.4
	2.5100	2.5000	1.278	1.278	0	1.296	−18	.586	58.6
16	3.0100	3.0000	1.314	1.312	+ 2	1.343	−29	.545	54.5
	3.0100	3.0000	1.385	1.382	+ 3	1.415	−30	.545	54.5
9	0.2000	0.0050	0.078	0.080	− 2	0.081	− 3	15.8	
	.2000	.0050	.083	.080	+ 3	.081	+ 2	16.8	
8	.2000	.0050	.078	.080	− 2	.081	− 3	15.8	
	.2000	.0050	.085	.080	+ 5	.081	+ 4	17.2	
7	.2000	.0100	.157	.160	− 3	.159	− 2	15.8	
	.2000	.0100	.157	.160	− 3	.159	− 2	15.8	
14	3.007	.0100	1.970	1.963	+ 7	1.968	+ 2	207.1	
13	3.007	.0100	2.108	2.105	+ 5	2.110	− 2	206.7	
19	6.002	.0100	3.435	3.338	+ 97	3.425	+10	349.7	
	6.002	.0100	3.442	3.371	+ 71	3.459	−17	347.0	
20	8.010	.0100	4.174	4.033	+141	4.171	+ 3	424.3	
	8.010	.0100	4.184	4.038	+146	4.176	− 8	424.8	
21	10.003	.0100	4.619	4.585	+ 34	4.636	−15	484.4	
	10.003	.0100	4.825	4.808	+ 17	4.861	−36	482.5	
23	11.992	.0100	5.168	5.436	−258	5.171	− 3	532.2	
	11.992	.0100	5.204	5.469	−265	5.202	+ 2	532.7	

ally were slightly different, because different quantities were used in the two calorimeters, although the change in concentration was the same. As the figures in column 6 show, equation (2) reproduces the experimental results up to 3 m very satisfactorily, with an average deviation of ±3.3 microdegrees. The equation shows increasing deviations, however, when applied to our later results at higher concentrations. When all of our results were employed to calculate the coefficients by the method of least squares, the resulting cubic equation gave better agreement at high concentrations but yielded a limiting slope inconsistent with our experiments at low concentration.

Finally we obtained a fourth degree equation, retaining the limiting slope of equation (2) and calculating the other coefficients from the results of experiments 13 and 14, 20 and 23 at 3, 8 and 12 m. This equation was

$$\Phi L_2 = -85.87\, m + 6.815\, m^2 - 0.4569\, m^3 + 0.01471\, m^4 \quad (3)$$

Values of q for each dilution, calculated from this equation, are included in column 7 of Table I. As the figures in column 8 show, this gives reasonably satisfactory agreement with all our experimental results. Up to 1.5 m concentration, the difference averages ±2.7 microdegrees, and over the whole range it averages ±7.6 microdegrees.

From equation (3), the partial relative molal

heat contents of urea and water were calculated by the methods used in our previous work.[7] The results are plotted in Fig. 2.

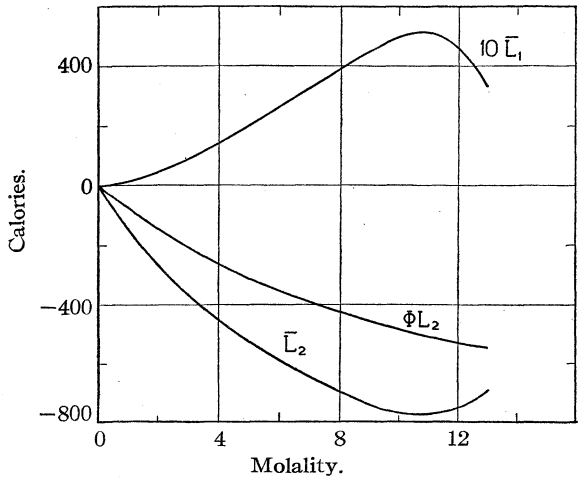


Fig. 2.—Apparent and partial relative molal heat contents for urea and water at 25°.

Discussion of the Heats of Dilution.—In magnitude, the heat of dilution of urea is even smaller than that of sucrose, showing that urea is more nearly an ideal solute. Our results are in general agreement with those of Naudé[11] at 18°, as we shall show in more detail after a discussion of the heat capacities.

In dilute solutions, the apparent molal heat content of urea is a linear function of the first power of the molality. It therefore parallels the volume properties. This is to be expected on the basis of what little theory has been developed for such solutes. For instance, Fuoss[12] has calculated the free energy of a dipolar solute of small dipole moment. From his theory, we can show that the apparent molal heat content of such a solute should be a linear function of the first power of the concentration. The surprising thing about the results is the *sign* of the heat of dilution. The separation of electrical dipoles, like that of ions, should cause a *liberation* of heat in a solvent having a dielectric constant with a temperature coefficient like that of water. It is hard to see how any purely electrostatic forces could account for a negative limiting slope. However, we have found the same negative slope in the case of glycine, which we expect to publish shortly.

(11) S. M. Naudé, *Z. physik. Chem.*, **135A**, 209 (1928).
(12) Fuoss, THIS JOURNAL, **58**, 982 (1936).

Apparent Molal Heat Capacities

Since the apparent molal heat content is a linear function of the molality at low concentrations, its temperature coefficient, the apparent molal heat capacity, doubtless obeys the same limiting law and should be expressed by a power series in m

$$\Phi C_{p_2} = \Phi C^0_{p_2} + am + bm^2 + cm^3 + \ldots \quad (4)$$

Accordingly we took the data of Ayres[6] and plotted the apparent molal heat capacity against the molality at each of the six temperatures he investigated. The results, as shown in Fig. 3, lie along smooth curves. The best coefficients for cubic equations in m were determined by the method of least squares. Each value of the apparent molal heat capacity was weighted in proportion to its accuracy, assuming the same precision for the specific heat s at all concentrations.

The resulting equations reproduced all 74 of the experimental points satisfactorily. Only one deviation was greater than 0.03% in s, seven were between 0.02 and 0.03%: and eighteen between 0.01 and 0.02%. The average deviation, $\pm 0.007\%$ in s, is slightly smaller than the average of $\pm 0.0085\%$ from the third degree equations in $m^{1/2}$ which were used in the original publication[6]

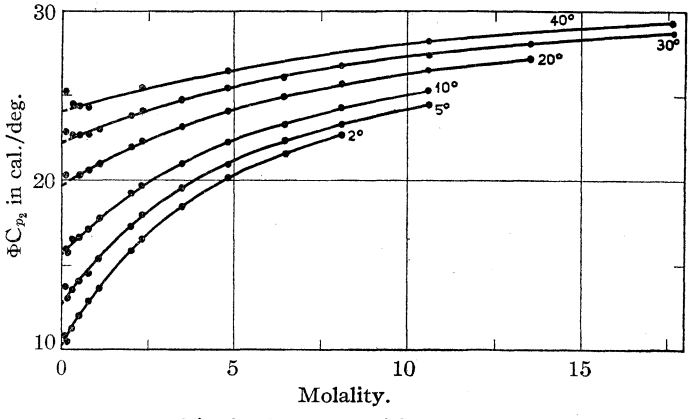


Fig. 3.—Heat capacities of urea.

of these data. This comparison emphasizes the difficulty in determining the limiting law from specific heat measurements. However, it shows that the limiting slope linear in m, indicated by the more sensitive measurements of heats of dilution, is consistent with the specific heats.

The coefficients of equation (4) are measured in calories at the experimental temperature. In order to be combined with our heats of dilution they are first changed to 15°-calories, using the values of the heat capacity of water at different

temperatures recently determined by Osborne, Stimson and Ginnings at the National Bureau of Standards.[13] The coefficients then were plotted against the centigrade temperature, t. As shown in Fig. 4, all four change in about the same way with temperature. The values of $\Phi C^0_{p_2}$ and b increase more rapidly at low temperatures, while those of a and c decrease correspondingly. Assuming the change of each coefficient is a quadratic function of $(t - 25)$, *e. g.*

$$\Phi C^0_{p_2} = \Phi^0_{25} + k_1(t - 25) + k_2(t - 25)^2 \qquad (5)$$

we evaluated the constants k_1 and k_2 by the method of least squares, weighting each according to the accuracy with which it was calculated from the original data. Thus the value of c, the coefficient of m^3 in equation (4), is fixed 20 times as accurately at 30°, by the series of fourteen experiments extending up to 17.6 m, as at 2°, where the twelve experiments extended only to 8.1 m. The differences in the accuracy of the coefficients of the lower powers of m were progressively less.

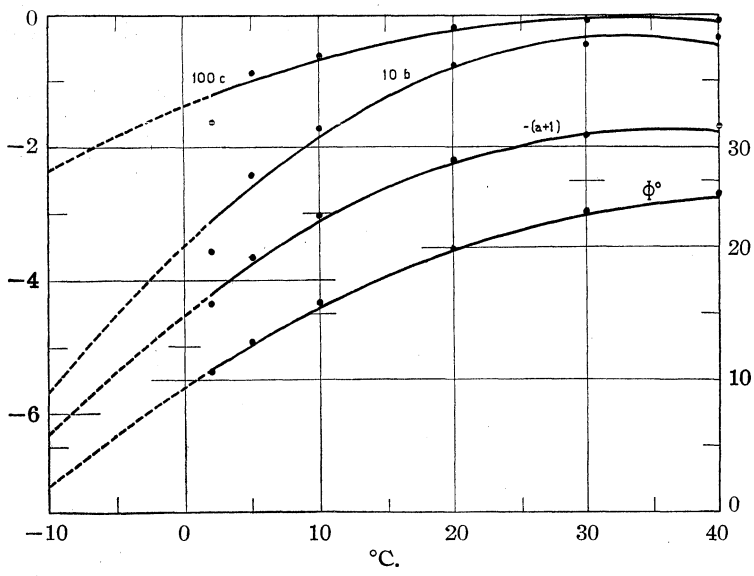


Fig. 4.—Constants for heat capacities of urea.

The curves of Fig. 4 represent these equations. The deviations, which appear to be random, average ±0.236 in $\Phi C^0_{p_2}$, ± 0.0898 in a, ±0.0175 in b and ±0.00120 in c. Because of the decreased accuracy of the coefficients of higher powers of m at low temperatures, the scattering in Fig. 4 is more pronounced at low temperatures. Fortunately the importance of these coefficients also decreases at low temperature, because of the decreased solubility of urea. Using the equations thus derived, coefficients of equation (4) were calculated at all six temperatures. Values of specific heats, calculated from these smoothed equations, were compared with the original experiments. The average deviation was ±0.033%. The two largest deviations, −0.236 and −0.500%, were for the 17.6 m solution at 30 and 40°. The average deviation of all the other results, up to and including 13.5 m, was ±0.024%. Of the individual deviations, 22 are less than 0.01%, 26 lie between 0.01 and 0.02%, 4 between 0.02 and 0.03%, 7 between 0.03 and 0.04%, 5 between 0.04 and 0.05%, 4 between 0.05 and 0.06%, 2 between 0.06 and 0.07% and 1 (13.5 m at 20°) is 0.22%. At any one temperature, the deviations are of the same sign, but the average net deviation is only −0.01%.

These figures indicate that, up to 12 m, which is the limit of the heats of dilution, the results can be expressed fairly satisfactorily by means of quadratic equations in the temperature, over the range from 2 to 40°. The values plotted in Fig. 4 indicate, however, that the coefficients of equation (4) approach zero at higher temperatures, instead of going through a maximum value and then decreasing as demanded by a quadratic equation in the temperature. A different type of equation might be required to fit the results of a series of heat capacity measurements extended to higher temperatures. At the lower temperatures, our equations are consistent with the experimental results and seem reasonable bases for extrapolation. Also, the decreased solubility at low temperatures limits the range to which the equations can be applied, and this helps to compensate some of the uncertainty of extrapolation.

Apparent and Partial Relative Heat Contents at Different Temperatures.—From equation (4) we can obtain the apparent relative heat capacity of the solute, $\Phi C_{p_2} - \Phi C^0_{p_2}$. Since this is the temperature coefficient of the apparent relative heat content, and a, b and c are known functions of temperature, we can integrate to obtain the apparent relative heat content at any temperature between 2 and 40°. The equation is

(13) Reference 9, Table 6.

$$\Phi L_2 = \Phi L_2'' + \Delta\Phi C_{p_2}(t - 25) + \Phi P_2(t - 25)^2 + \Phi Q_2(t - 25)^3 \quad (6)$$

where $\Phi L_2''$ at 25° is given by equation (3), and the other terms are

$$10^3\Delta\Phi C_{p_2} = 940.0\ m - 49.4\ m^2 + 1.11\ m^3 \quad (7)$$

$$10^5\Phi P_2 = -2306\ m + 236.9\ m^2 - 1.88\ m^3 \quad (8)$$

$$10^7\Phi Q_2 = 7423\ m - 955\ m^2 + 1.71\ m^3 \quad (9)$$

In 1928, Naudé[11] studied the heats of dilution of urea from 1 to 0.001 M, at temperatures near 18°, using one of the first microcalorimeters. Previous work in this Laboratory[3] has shown that the apparent molal volume of urea changes very little with temperature, hence the difference between molarity (moles per liter) and molality, m, is practically the same at 18 as at 25°. On this basis we have converted Naudé's results to 25°. For dilutions from 0.333 M (0.340 m) to 0.0067 M (or m) at 18.51°, he found $\Delta H = 28.5$ cal./mole. From equation (6) the value should be 2.4 cal./mole less, or 26.1 cal./mole at 25°. Our equation (3) gives 27.8 cal./mole for this dilution. His value of 14.0 for the dilution from 0.1 to 0.003 M is decreased by 0.8 to 13.2 cal./mole, compared to 8.3 calculated from equation (3). These differences of −1.7 and +4.9 cal./mole correspond to −11 and +15 microdegrees. This agreement was typical of the five results up to 0.5 M. His 2 results at 1 M gave larger deviations of about 60 microdegrees.

From equation (3) for the apparent relative heat content of urea, the equations for $\bar{L}_2$ and $\bar{L}_1$, the partial relative heat contents of urea and water are calculated by the general thermodynamic relations. If G represents any extensive property of a solution of n_1 moles of water and n_2 of solute, and G_1 is the corresponding molal property of the water, the apparent molal property, ΦG_2 is defined by the equation

$$G = n_1G_1 + n_2\Phi G_2 \quad (10)$$

If ΦG_2 is represented by the equation

$$\Phi G_2 = \Phi G_2^0 + am + bm^2 + cm^3 + \ldots \quad (11)$$

the corresponding equations for $\bar{G}_2$ and $\bar{G}_1$, the partial molal properties of solute and water, respectively, are

$$\bar{G}_2 = \Phi G_2^0 + 2\ am + 3\ bm^2 + 4\ cm^4 + \ldots \quad (12)$$

$$\bar{G}_1 = G_1 - 0.018016[am^2 + 2\ bm^3 + 3\ cm^4 + \ldots] \quad (13)$$

These relationships hold for the arguments of equations (3), (7), (8) and (9).

The Change of Activity with Temperature

The difference between the activity a' of any component of a solution at a temperature T' and its activity a'' at a temperature T'' is given by the well-known thermodynamic equation[14]

$$\log a'' - \log a' = \frac{-0.43429}{R}\int_{T'}^{T''}\frac{\bar{L}}{T^2}\,dT \quad (14)$$

where R is the gas constant and $\bar{L}$ the partial relative heat content. If $\bar{L}$ is a cubic function of T, the integrated form of equation (14) is

$$\log a'' - \log a' = K_1\bar{L}'' + K_2\Delta\bar{C}_p'' + K_3\bar{P} + K_4\bar{Q} \quad (15)$$

where

$$K_1 = \frac{-0.43429}{R}\frac{\Delta T}{T'T''}, \text{ where } \Delta T = T'' - T' \quad (16)$$

$$K_2 = \frac{0.43429}{R}\left[\frac{\Delta T}{T'} - \ln\left(\frac{T''}{T'}\right)\right] \quad (17)$$

$$K_3 = \frac{-0.43429}{R}\left[\Delta T + T''\left\{\frac{\Delta T}{T'} - 2\ln\left(\frac{T''}{T'}\right)\right\}\right] \quad (18)$$

$$K_4 = \frac{0.43429}{R}\left[3T'\Delta T + 4.5(\Delta T)^2 + \frac{(\Delta T)^3}{T'} - 3T''^2\ln\left(\frac{T''}{T'}\right)\right] \quad (19)$$

The coefficients K_1, etc., are functions only of the temperatures involved. The first can be evaluated easily by direct substitution but the rest cannot, since the logarithmic term differs from the sum of the others by only 4, 0.1 and 0.005%, respectively. However, on expanding the logarithm in series, many of the largest terms cancel and we obtain the following expressions for the coefficients, chiefly in terms of the variable $v = \Delta T/T'$.

$$K_2 = \frac{0.43429}{R}v^2[1/2 - v/3 + v^2/4 + \ldots] \quad (20)$$

$$K_3 = -\frac{0.43429}{R}v^3[T' - 2T''/3 + 2\Delta T(1 + v)\,(1/4 - v/5 + v^2/6 + \ldots)] \quad (21)$$

$$K_4 = \frac{0.43429}{R}v^4\left[\frac{T'^2}{4} - \frac{T'\Delta T}{10} - \frac{9(\Delta T)^2}{20} - \frac{3(\Delta T)^2v}{5} + 3(\Delta T)^2(1 + v)^2\,(1/6 - v/7 + v^2/8 + \ldots)\right] \quad (22)$$

In evaluating the coefficients, only four or five terms of each power series in v are necessary to give results to 0.01%. In Table II we have recorded values of these coefficients for changes from the given initial temperatures T' to the standard temperature $T'' = 298.16°$.

The values of K_1 are 0.03% higher than those tabulated by Lewis and Randall (p. 615), because of our use of $R = 1.9869$ cal.$_{15}$ deg.$^{-1}$ mol.$^{-1}$ for the gas constant and 273.16° A. as the freezing point of water.[15] Our values of K_2 agree with

(14) Lewis and Randall, "Thermodynamics," McGraw-Hill Book Co., Inc., New York, N. Y., 1923, p. 289.

(15) These values were obtained from a critical compilation by Dr. F. D. Rossini, privately communicated to us through Professor Scatchard.

TABLE II[a]

COEFFICIENTS OF EQUATION (15) FOR THE CHANGE IN THE LOGARITHM OF THE ACTIVITY BETWEEN t AND 25°

t, °C.	K_1	K_2	K_3	K_4
−15	−0.00011359	0.0023807	−0.06500	1.9779
−14	− .00011032	.0022519	− .05991	1.7780
−13	− .00010708	.0021269	− .05510	1.5916
−12	− .00010387	.0020064	− .05058	1.4223
−11	− .00010067	.0018898	− .04632	1.2668
−10	− .00009750	.0017773	− .04233	1.1250
− 9	− .00009436	.0016688	− .03858	0.9958
− 8	− .00009123	.0015642	− .03508	.8784
− 7	− .00008814	.0014636	− .03181	.7721
− 6	− .00008507	.0013669	− .02876	.6761
− 5	− .00008201	.0012736	− .02592	.5894
− 4	− .00007898	.0011843	− .02328	.5116
− 3	− .00007598	.0010986	− .02084	.4420
− 2	− .00007300	.0010166	− .01859	.3800
− 1	− .00007003	.0009381	− .01651	.3248
0	− .00006709	.0008631	− .01460	.2761
10	− .00003884	.0002963	− .00299	.0338
20	− .00001250	.0000314	− .00011	.0004
30	.00001209	.0000301	.00010	.0004
40	.00003511	.0002590	.00257	.0288
50	.00005671	.0006899	.01134	.2127

[a] The energy unit of this table is the 15°-calorie, which is used throughout this paper: 1 $cal._{15}$ = 4.1858 abs. j. (ref. 9, p. 238).

those of Lewis and Randall, but are carried two places farther. T. F. Young,[16] in his excellent treatment of the calculation of activities from freezing points, has taken account of the quadratic change of $\bar{L}$ with temperature. He has tabulated values of Ω, the coefficient defined in equation (10) of his paper, which is equal to $-1/2\ K_3$. This unpublished tabulation, extending from −25 to 0°, he kindly sent to us in a private communication.

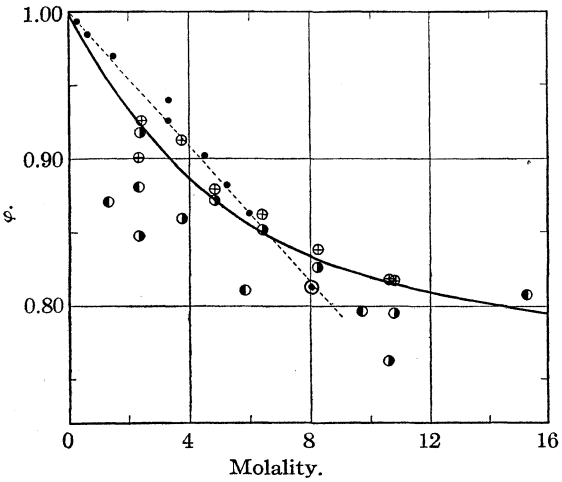


Fig. 5.—Osmotic coefficients of urea at 25° (curve from Scatchard, Hamer and Wood); ◑, Fricke at 0°; ⊕, Fricke at 10°; ◐, Perman and Lovett at 50°; ● and ○, Chadwell and Politi at f. p. (The first point represents 2 results.)

In describing the behavior of the solvent in an aqueous solution, Bjerrum's osmotic coefficient

$$\varphi = -\frac{55.506}{m} \ln a_1 \qquad (23)$$

is a convenient function since it can be calculated directly from measurements of the vapor pressure or freezing point of the solution.

The activity coefficient is related to the osmotic coefficient by the isothermal equation

$$\ln \gamma = (\phi - 1) + \int_0^m (\phi - 1)\, d \ln m \qquad (24)$$

If values of ϕ or γ at any temperature are known at definite concentrations, and the thermal terms are also known, the values of ϕ or γ at any other temperature can be calculated. If either ϕ or γ at any temperature is known as a function of m, and the thermal terms are also known as functions of m, ϕ or γ at any other temperature in the experimental range can be determined as a function of m by algebraic addition of the necessary equations. These methods are applicable to the results of isothermal vapor pressure measurements.

When solvent activities are determined from freezing points, they corrrespond to the temperature of the freezing point, which decreases with concentration. Knowing ϕ' at a definite freezing point, we can interpolate values of the coefficients from Table II and calculate ϕ at 25° from our thermal data.

The Osmotic Coefficient of Urea at 25°

Scatchard, Hamer and Wood[10] have made a very careful study of isotonic solutions at 25°. By intercomparison with the best results for several standard substances, they have determined the vapor pressure and tabulated the osmotic coefficient of urea at this temperature. The smooth curve of Fig. 5 represents their results. Our thermal data allow a comparison between their results and other studies at different temperatures, excluding the early work, in which the experimental uncertainty is large.

Fricke[17] has measured the vapor pressure of urea solutions at 0 and 10°. From these data we have calculated ϕ, first at the experimental temperature and then, by means of equations (15) and (23), at 25°. The resulting values are plotted in Fig. 5. The deviations from the curve corresponded to

(16) T. F. Young, *Chem. Rev.*, **13**, 103 (1933).

(17) Fricke, *Z. Elektrochem.*, **33**, 441 (1927); **35**, 631 (1929).

average differences of +0.010 mm. in the vapor pressure at 0° and −0.004 mm. at 10°, which appear to be within the experimental error. Perman and Lovett[18] measured vapor pressures at 50° and higher. We calculated values of ϕ from their results at 50°, which did not involve too great extrapolation of our thermal data. The points, plotted in Fig. 5, show an average deviation from the curve of +0.18 mm. in the vapor pressure, which also appears to be within the experimental error. The results of these three series of vapor pressure measurements therefore corroborate the curve of Scatchard, Hamer and Wood.

Recently, Chadwell and Politi[19] have determined the freezing points of aqueous solutions of urea from 0.3 to 8.08 *m*, the eutectic, and calculated ϕ', the osmotic coefficient at the freezing point. After interpolating the coefficients from Table II, we used equations (15) and (23) to calculate the corresponding values of ϕ, at 25°, which we plotted in Fig. 5. The deviations in ϕ are smaller than those among the vapor pressure measurements, but they are systematic. The points all lie along the dotted straight line which crosses the curve of Scatchard, Hamer and Wood at about 7 *m*. Below this concentration, the freezing point depressions observed by Chadwell and Politi are *higher* than those which would be expected from the vapor pressure and thermal data, while their two concordant results at 8.08 *m* are *lower*. The deviation is only +0.004° in the 0.3 *m* solution, but it increases to +0.25° at 3.4 *m* and −0.32° at 8.1 *m*.

We have estimated the part of this discrepancy which might be due to our thermal measurements, as follows. From the differences between the heats of dilution observed and those calculated from equation (3), the corresponding differences in $\bar{L}_1$ were determined at a series of even concentrations. The uncertainty in $\Delta\bar{C}_{p_1}''$ at the same concentrations was then estimated as the average difference between $\Delta\bar{C}_{p_1}$ at each temperature, calculated from the original equation (which best fitted the measured specific heats) and the final equation (which smoothed the results at all temperatures). The corresponding uncertainty in $\bar{P}_1$ and $\bar{Q}_1$ was estimated by assuming an error in $\Delta\bar{C}_{p_1}$ at 2 and 40° equal to that in $\Delta\bar{C}_{p_1}''$ at 25°, but opposite in sign. The resulting differences in these three terms, multiplied by the appropriate factors, gave the corresponding differences in ϕ. The sum of these differences, taken as a generous estimate of the error in the thermal terms, was 2, 3, 4, 5, 20 and 44 × 10^{-4} at 0.5, 1, 2, 4, 6 and 8 *m*. Up to 4 *m*, the three heat capacity terms made up 80–90% of the whole uncertainty, but at 6 and 8 *m* their contribution had fallen to about 50%. Up to 4 *m*, these figures would account for only 2% of the observed differences between ϕ calculated from freezing points and from vapor pressure measurements at 25°. At 6 and 8 *m* they would account for 38 and 20% of the difference. The remaining difference, at all but the lowest concentrations, is far larger than would be expected from the sensitivity of the measurements involved, and from the agreement between the results of freezing point and e. m. f. measurements in the case of hydrochloric acid, reported by Chadwell a few years ago.[20] We considered the possibility of solid solution of the urea in the ice, but this would lead to a negative error in ϕ at all concentrations.

Acknowledgments.—In addition to the grants-in-aid from the Penrose Fund of the American Philosophical Society and from the Graduate School of Northwestern University, it is a pleasure to acknowledge the courtesy of Professors George Scatchard and T. F. Young in reading the manuscript and making helpful suggestions in connection with it.

Summary

We have used a calorimeter sensitive to one millionth of a degree in measuring the heats of dilution of aqueous solutions of urea at 25°, from 12 *m* to 0.005 *m*. At low concentrations the heat of dilution is a linear function of *m*.

Combining these results with the heat capacities of urea from 2 to 40°, previously determined in this Laboratory, yields equations for the heat of dilution and the partial relative molal heat contents of urea and water as cubic functions of temperature.

These data are used to calculate ϕ, the osmotic coefficient at 25°, from measurements of freezing points and of vapor pressures at 0, 10 and 50°. The necessary equations are given and the numerical coefficients for the integration are tabulated.

The results of vapor pressure measurements

(18) Perman and Lovett, *Trans. Faraday Soc.*, **22**, 1 (1926).
(19) Chadwell and Politi, THIS JOURNAL, **60**, 1291 (1938).
(20) Chadwell, *ibid.*, **49**, 2795 (1927).

agree within their own rather large experimental uncertainty with the recent precise isotonic measurements of Scatchard, Hamer and Wood. The results calculated from freezing points show smaller but systematic deviations, which apparently are considerably beyond the experimental error of the thermal measurements.

EVANSTON, ILLINOIS RECEIVED JANUARY 29, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF DUKE UNIVERSITY]

The System Magnesium Sulfate, Cadmium Sulfate and Water at 25 and 40°

BY W. C. VOSBURGH, VERNON H. DIBELER, HELEN C. PARKS AND WILLIAM J. MILLER

In the study of modified Weston cells[1] some difficulty was experienced in the preparation of a double salt of magnesium and cadmium sulfates. Schiff[2] prepared a double salt with the composition $MgSO_4 \cdot CdSO_4 \cdot 14H_2O$ in 1857, but no mention of later work on this compound has been found. Attempts to make the double salt by slow evaporation at room temperature of a solution containing the two component salts failed, and it was apparent that further study of the system magnesium sulfate, cadmium sulfate and water was desirable.

Mixtures were prepared of carefully weighed quantities of recrystallized magnesium and cadmium sulfates and water and brought to equilibrium in closed tubes which were rotated in an air-bath at 25 ± 0.1°. The time allowed for equilibrium varied considerably, but in only a few cases was it less than forty-eight hours. Often it was much longer than this, and the consistency of the data is an indication that equilibrium was attained in the time allowed.

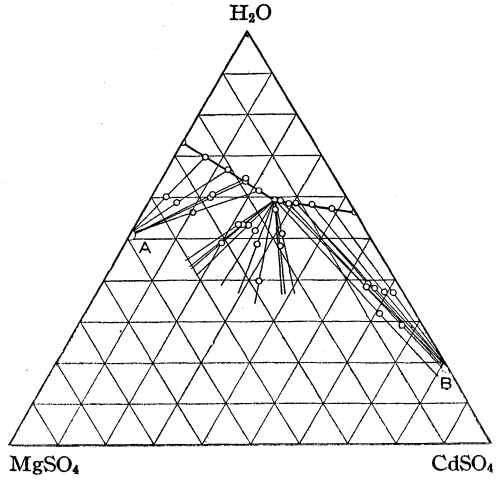


Fig. 1.—The system magnesium sulfate, cadmium sulfate and water at 25°. Points A and B represent the calculated compositions, in weight percentage, of hydrated magnesium and cadmium sulfates, respectively.

After sufficient rotation, the saturated solution was drawn off through a glass-wool filter, this operation being carried out within the air-bath. The solution was weighed, diluted to a known volume and aliquot portions taken for analysis. Total solids were determined by evaporation to dryness and ignition in a muffle at 500°. Other samples were acidified with sulfuric acid, the cadmium was precipitated as sulfide, and the magnesium sulfate determined in the filtrate by evaporation, ignition at 500° and weighing. The cadmium sulfide was dissolved by hydrochloric acid, and the solution evaporated to dryness after addition of an excess of sulfuric acid. The cadmium sulfate was ignited at 500° and weighed.

TABLE I

COMPOSITIONS OF SATURATED SOLUTIONS AND ORIGINAL MIXTURES AT 25°

Saturated solutions		Original mixtures	
$CdSO_4$, wt. %	$MgSO_4$, wt. %	$CdSO_4$, wt. %	$MgSO_4$, wt. %
6.5	23.8	3.1	36.8
12.5	20.9	5.9	35.4
17.2	18.3	12.2	26.9
17.4	18.9	12.3	27.8
21.7	17.0	10.3	33.2
25.5	15.2	27.1	16.3
25.7	14.9	20.0	31.1
25.8	15.4	32.4	19.4
26.0	15.0	21.2	25.5
26.1	15.0	31.3	17.6
26.2	15.3	22.2	24.4
26.2	15.1	25.5	22.6
26.4	15.0	32.3	28.1
26.4	15.2	23.4	23.4
26.4	15.2	27.6	21.9
26.9	14.9	60.9	7.2
27.0	13.9	55.0	6.6
29.1	12.5	54.9	5.9
30.5	11.2	56.8	5.1
30.5	11.0	67.0	3.9
34.0	8.0	59.3	3.6
38.6	4.3	61.3	1.9

(1) Vosburgh, Derr, Cooper and Pettengill, THIS JOURNAL, **61**, 2687 (1939).

(2) Schiff, *Ann.*, **104**, 327 (1857); **107**, 73 (1858).

The compositions of the original mixtures and saturated solutions are given in Table I and plotted in Fig. 1.

It is apparent from Fig. 1 that no double salt was formed at 25°. Consequently, some experiments were carried out to see whether a transition temperature could be detected, since the temperature range within which the double salt of Schiff[2] is capable of existence might not include 25°. Two modified Weston cells[1] were constructed with an electrolyte saturated with magnesium and cadmium sulfates and with an excess of both hydrated solids present. On measurement of the electromotive force at several temperatures between 20 and 40° it was found that the temperature coefficient ($\Delta E/\Delta T$) changed abruptly and considerably at about 30°. The reproducibility and constancy of the cells were not good, and the error might amount to a few tenths of a degree. Following this, equimolecular quantities of magnesium and cadmium sulfates and a little water were rotated together for several days at 40° and a cooling curve for the mixture determined. It gave clear evidence of an evolution of heat at about 30.2°.

TABLE II

COMPOSITIONS OF SATURATED SOLUTIONS AND ORIGINAL MIXTURES AT 40°

Saturated solutions		Original mixtures	
$CdSO_4$, wt. %	$MgSO_4$, wt. %	$CdSO_4$, wt. %	$MgSO_4$, wt. %
2.6	29.6	2.0	36.0
5.0	28.8	3.2	36.5
7.6	27.8	5.1	35.1
9.2	28.0	8.5	34.9
9.6	27.8	12.3	31.1
10.2	27.5	14.5	28.9
9.6	28.3	13.2	31.0
12.1	24.4	24.0	23.2
17.2	20.0	25.6	20.4
14.5	22.4	27.3	22.0
20.0	17.6	31.4	20.4
20.9	17.1	31.7	19.3
24.2	14.3	32.4	18.8
28.2	12.2	32.4	16.4
33.5	10.4	34.4	14.5
38.8	9.2	37.7	13.2
39.6	9.2	40.3	14.8
40.1	8.8	44.7	13.8
40.9	7.7	57.1	4.7
42.7	4.5	59.4	2.5

The solubilities were determined again at a temperature of 40 ± 0.2°, and the data in Table II (shown graphically in Fig. 2) obtained. It is clear that a double salt can exist at 40° in equilibrium with solutions of a wide range of compositions. Point C in Fig. 2 represents the calculated composition of the compound $MgSO_4 \cdot CdSO_4 \cdot 14H_2O$ while D represents that of a double salt with twelve molecules of water. Points A and B represent $MgSO_4 \cdot 7H_2O$ and $3CdSO_4 \cdot 8H_2O$, respectively, in both Figs. 1 and 2. The solubilities of these salts in water were taken from "International Critical Tables."

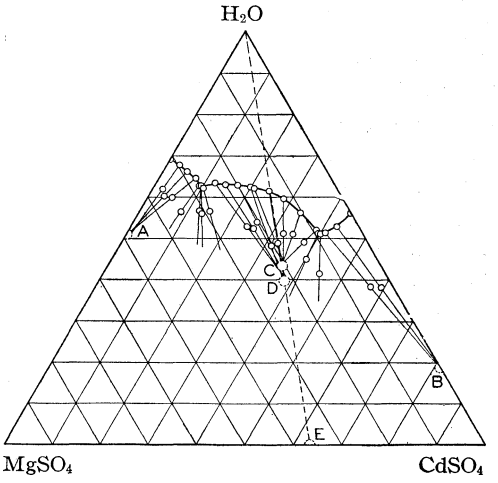


Fig. 2.—The system magnesium sulfate, cadmium sulfate and water at 40°. Points A and B are the same as in Fig. 1. Point C represents the calculated composition of the compound $MgSO_4 \cdot CdSO_4 \cdot 14H_2O$, point D a double salt with twelve molecules of water and point E the anhydrous double salt.

As a further check on Schiff's formula for the double salt, samples of the salt were prepared by rotation of equimolecular mixtures of hydrated magnesium and cadmium sulfates with some excess water at 40° and filtering and drying in the air-bath at the same temperature. Determination of water lost at 500° and of magnesium and cadmium sulfates gave the following results for three different preparations of the double salt.

	Calcd. for $CdSO_4 \cdot MgSO_4 \cdot 14H_2O$	Observed 1	2	3
$MgSO_4$, %	20.72	20.74	20.76	20.83
$CdSO_4$, %	35.88	35.85	35.83	35.87
H_2O, %	43.41	43.41	43.39	43.40

Summary

A double salt of magnesium and cadmium sulfates, $MgSO_4 \cdot CdSO_4 \cdot 14H_2O$, can exist in equilibrium with saturated solutions at 40°, but not at 25°. A transition point for the system was found at about 30.2°.

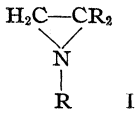
DURHAM, NORTH CAROLINA RECEIVED MARCH 29, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF ROCHESTER]

The Stability toward Racemization of Optically Active Compounds—with Especial Reference to Trivalent Nitrogen Compounds

BY JOHN F. KINCAID AND F. C. HENRIQUES JR.

Although a tremendous amount of work has been done in attempts to resolve trivalent nitrogen compounds into optically active forms, the attempts have been uniformly unsuccessful.[1] On the other hand, other compounds in which the central atom is surrounded by only three groups have been resolved. Thus active forms of the sulfoxides, sulfinic esters, and sulfonium salts have been obtained. The present investigation was undertaken in order to explain this apparent anomaly as well as to gain information which would lead to a prediction of the stability toward racemization of a substituted ethyleneimine of the type (I), which is being investigated at the present time by Dr. T. L. Cairns of this Laboratory.[2]



I

Since all previous attempts to prepare optically active nitrogen compounds have proved fruitless, the energy required to bring about a planar configuration, through vibrations, must be low. The computations which are to follow are based on the fact that one of the normal modes of vibration, ν_3 of Fig. 1, leads to such a configuration. A

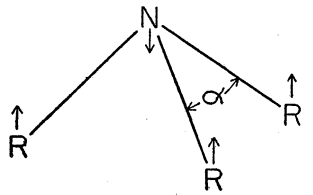


Fig. 1.—A diagrammatic representation of the normal vibration ν_3.

similar type of calculation by Rice and Teller[3] of the amount of energy required to bring three of the hydrogen atoms of the methane molecule into a plane containing the carbon has led to an approximately correct value of the activation energy of the reaction $D + CH_4 \rightarrow CH_3D + H$.[4]

(1) Gilman, "Organic Chemistry, an Advanced Treatise," John Wiley and Sons, 1938, Chapter 3 by Shriner, Adams, and Marvel.
(2) *Cf.* Adams and Cairns, THIS JOURNAL, **61**, 2464 (1939).
(3) Rice and Teller, *J. Chem. Phys.*, **6**, 489 (1938).
(4) Gorin, Kauzman, Walter and Eyring, *ibid.*, **7**, 633 (1939).

Let us consider a compound of the type R_3N. If the nitrogen is not in the plane of the R groups, then the potential energy of the molecule as a function of the distance of the nitrogen atom from the plane of the other groups will have the form illustrated by the dotted curve in Fig. 2.

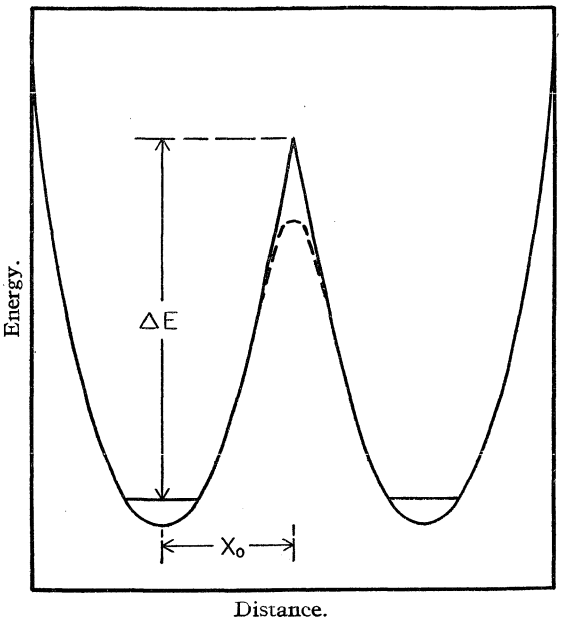


Fig. 2.—The energy, V, as a function of the displacement, x, for the normal vibration ν_3.

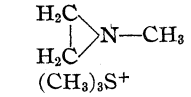
Therefore, racemization may take place either by passing over or through the potential hill. The rate of racemization by either of these mechanisms is determined by the dimensions of the barrier, the frequency ν_3, and the temperature. For ammonia several methods have been employed to obtain these dimensions.[5,6,7] By far the simplest of these leading to agreement between theory and experiment is that employed by Wall and Glockler[7]; and it is this function which has been used in these computations. Their expression for the potential energy, V, is

$$V = {}^1/_2k(|x| - |x_0|)^2 \qquad (1)$$

where x is the distance of the nitrogen from the

(5) (a) Morse and Stueckelberg, *Helv. Phys. Acta*, **4**, 373 (1931); (b) Dennison and Uhlenbeck, *Phys. Rev.*, **41**, 313 (1932); (c) Rosen and Morse, *ibid.*, **42**, 210 (1932).
(6) Manning, *J. Chem. Phys.*, **3**, 136 (1935).
(7) Wall and Glockler, *ibid.*, **5** 314 (1937).

TABLE I

Compd.	Bond distance in Å.	Bond angle see Figs. 1 and 3	Equil. height in Å. x_0	Frequency[d] in cm.$^{-1}$, ν_3	Reduced mass in g., μ	Activ. energy in kcal.
NH_3	N–H = 1.01[9]	α = 109.5°[9]	0.34	945	2.5	11
$N(CH_3)_3$	C–N = 1.47[10]	α = 109.5°[10]	.49	374	11	15
	C–N = 1.47[a] C–C = 1.54	α = 109.5°[a] β = 63°	.77	~374[e]	11	38
$(CH_3)_3S^+$	C–S = 1.82[10]	$\alpha \approx$ 109.5°[c]	.61	~600[f]	19	100
PH_3	P–H = 1.40[b]	$\alpha \approx$ 100°[c]	.65	990	2.7	47
$P(CH_3)_3$	C–P = 1.87[11]	α = 100°[11]	.87	~340[g]	18	67
PCl_3	P–Cl = 2.00[12]	α = 101°[12]	.91	260	24	57
PBr_3	P–Br = 2.24[12]	α = 100°[12]	1.04	162	28	34
$C(CH_3)_4$[h]	C–C = 1.54[13]	α = 111.5°[13]	0.87	377	9.6	88

[a] The angle β, see Fig. 3, is uniquely determined by the bond distances. Since the C–C bond distance in cyclopropane has been found to be 1.53 Å.,[13] it is quite reasonable to assume that the above bond distances for ethyleneimine are correct. Angle α, see Fig. 3, has been assumed to have the normal tetrahedral value. This assumption is substantiated by the value of 110° found for the C—N=N angle of azomethane by Boersch.[15] [b] This distance has been calculated from the covalent radii of the atoms.[14] [c] From a comparison of homologous compounds, values of 100° for the HPH angle and 109.5° for the C–S–C angle are upper limits. A smaller angle would only make the calculated activation energies higher. [d] All of the experimental frequencies are those summarized by Hibben.[16] [e] Since the vibrational levels for ethyleneimines are unknown, the value for $N(CH_3)_3$ has been used. Due to the formation of a three-membered ring the actual frequency for this vibration must be somewhat greater; however, this would only lead to a higher activation energy than that calculated. [f] The vibrational spectrum of this ion has not been determined. Since the C–C bending frequencies,[16] 377 cm.$^{-1}$ for $(CH_3)_2CH_2$ and 413 cm.$^{-1}$ for $(CH_3)_2NH$ are very close to the respective values of the normal mode corresponding to ν_3, 372 cm.$^{-1}$ for $(CH_3)_3CH$ and 374 cm.$^{-1}$ for $(CH_3)_3N$; a good approximation for ν_3 of $(CH_3)_3S^+$ can be obtained from the 648 cm.$^{-1}$ bending frequency of dimethyl sulfide. 600 cm.$^{-1}$ is probably a lower limit, and a higher value would only tend to increase the activation energy. [g] The vibrational frequencies for this compound are also unknown. A comparison of ν_3 for PH_3 and NH_3 together with the known value for $N(CH_3)_3$ (see table) yield 390 cm.$^{-1}$ for $P(CH_3)_3$. A similar comparison using the corresponding frequencies[16] of 1304 cm.$^{-1}$ and 372 cm.$^{-1}$ for methane and isobutane, respectively, yields a value of 300 cm.$^{-1}$. An average value, 340 cm.$^{-1}$, has been used; even if ν_3 were as low as 300 cm.$^{-1}$, the calculated ΔE would still be 55 kcal. [h] The method of calculating the activation energy for this compound is given later. α is the C–C–C angle in propane, and ν_3 its bending frequency; x_0 is the height of one carbon from a line joining the other two; $1/\mu \approx (1/14) + 1/(2 \times 15)$.

plane of the R groups, x_0 is this distance at equilibrium, and k, the force constant, is given by the expression

$$k = 4\pi^2\nu_3^2\mu \qquad (2)$$

where ν_3 (Fig. 1) is the frequency leading to inversion of the molecule and μ is the reduced mass defined by

$$\mu \approx 3ab/(3a + b) \qquad (3)$$

where a is the mass of the R group and b that of nitrogen.[8]

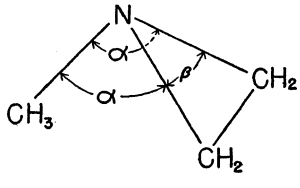


Fig. 3.—A diagrammatic representation of N-methyl ethyleneimine.

The results of the computations are given in Table I. A necessary condition for resolution is that the intramolecular first order rate constant for racemization be less than 10^{-5} sec.$^{-1}$. Thus

(8) It is a well-known fact that a potential curve of the form illustrated in Fig. 2 leads to a quantum mechanical interaction, *tunneling*, and gives rise to a separation of the ν_3 vibrational levels into doublets. Previous investigations have been made with the view in mind of obtaining these observed doublet separations. In order to obtain the observed separation of the first vibrational level of ν_3, Wall and Glockler[7] used an arbitrary equilibrium distance, x_0, for ammonia. It is of interest to compare their activation energy of 9.5 kcal./mole with our value for ammonia of 11 kcal. Both these values are possibly high since the form of the curve given by equation (1) is that of the solid curve rather than the dotted curve of Fig. 2. The more elaborate function, $V = A(\csc^2\Theta - \csc^2\Theta_0)^2$, was employed by Manning and gives rise to a smooth curve. The arbitrary parameters in this function were chosen so as to give the observed doublet separations of the zero-th and first vibration levels. Manning[6] obtained 6 kcal./mole for the height of the potential hill, 0.38 Å. for x_0, and 1050 cm.$^{-1}$ for ν_3 (see also Howard, *J. Chem. Phys.*, **3**, 208 (1935)). Although this value of 6 kcal./mole is considerably lower than our value, it should be noted that Manning's values for x_0 and ν_3 are both too high. Since the doublet separation for a fixed reduced mass is a function of the area under the barrier, it is clear that a more reasonable value for x_0 and the correct value for ν_3 would lead to a considerably higher activation energy. These considerations lead to the conclusion that about 8 kcal./mole is the most probable barrier height for ammonia.

(9) Wright and Randall, *Phys. Rev.*, **44**, 391 (1933).
(10) Brockway and Jenkins, THIS JOURNAL, **58**, 2036 (1936).
(11) Springall and Brockway, *ibid.*, **60**, 996 (1938).
(12) Creeg, Hampson, Jenkins, Jones and Sutton, *Trans. Faraday Soc.*, **33**, 852 (1937).
(13) Pauling and Brockway, THIS JOURNAL, **59**, 1223 (1937).
(14) Pauling, "Nature of Chemical Bond," Cornell University Press, Ithaca, N. Y., 1939.
(15) Brockway, *Rev. Mod. Phys.*, **8**, 261 (1936).
(16) Hibben, "The Raman Effect and its Chemical Applications," Reinhold Publishing Corp., New York, N. Y., 1939.

one readily obtains from the Arrhenius equation

$$k \approx 10^{13} \exp.(-\Delta E/RT) \qquad (4)$$

that ΔE must be greater than 25 kcal./mole if resolution at room temperature is to be possible. For the moment tunneling through the barrier has been neglected. It will be shown later that for room temperature and above the effective activation energy for tunneling is only a few % lower than the height of the barrier.

Before discussing specific cases it should be emphasized that our method of obtaining ΔE leads to rather approximate results and values which are too high. However, the relative values are undoubtedly quite significant. An estimate of the probable error may be obtained by comparing our value of 11 kcal. for ΔE for NH_3 with the more reasonable value of 8 kcal.[8] Due to mutual repulsions, neopentane is an exception, the calculated ΔE being too low.

Compounds Similar to Trimethylamine.—The activation energy obtained for trimethylamine is 15 kcal./mole. One would expect other compounds of the type $NR_1R_2R_3$ to have a somewhat lower value for the following reasons. (1) The activation energy calculated for ammonia is less than that of trimethylamine. Thus if R_1, R_2, or R_3 is a hydrogen atom, ΔE should be slightly less than 15 kcal. (2) If R_1, R_2, and R_3 are aliphatic groups, the force constant, k, which appears in equation (1) will be approximately independent of the weight, *i. e.*, an increase in the reduced mass will be compensated by a corresponding decrease in the numerical value of ν_3. However, due to mutual repulsions, x_0, the height of the pyramid, will actually tend to decrease with increasing size of the R groups, thus lowering ΔE. Hence, three large normal saturated aliphatic groups attached to nitrogen would not lower the activation energy as much as would branched groups, such as *t*-butyl radicals. (3) Aromatic groups attached directly to nitrogen tend to lower ΔE through making the molecule more planar both because of the size of the groups, and the contribution to the stability of the compound through the resonance structure involving a double bonded nitrogen. This effect has been pointed out by Pauling.[17] (4) A comparison of ΔE for PH_3, PCl_3, and PBr_3 indicates that the attachment of an electronegative group to the central atom will not result in an appreciable increase in stability.

(17) Gilman, *loc. cit.*, p. 334.

The resolution of a compound of the type $NR_1R_2R_3$ is impossible at room temperature.

From the reasons given above, the activation energy for inversion of these compounds is certainly no more than 15 kcal./mole. This value almost suffices for resolvability at −80° (dry-ice temperature). Since, however, 15 kcal./mole is an upper limit for the activation energy, it appears very improbable that these compounds can be resolved even at dry-ice temperatures.[1]

Cyclic Compounds.—The activation energy obtained for N-methyl ethyleneimine was 38 kcal./mole. Even if rounding off the barrier should decrease it as much as 10 kcal., this compound would be stable with respect to racemization at room temperature. It can be shown that the increase in the rate of racemization through tunneling is negligible.[18] Thus a substituted ethyleneimine containing an asymmetric nitrogen atom appears to offer an excellent possibility for the resolution of a trivalent nitrogen compound.

Many attempts have been made to resolve cyclic compounds in which the nitrogen is enclosed in a five- or six-membered ring.[1] From simple considerations of strain it is evident that such systems will be only slightly more stable than the analogous open chain compounds.

Trivalent Phosphorus Compounds.—Although no examples of activity due to trivalent phosphorus have been reported, the values of ΔE recorded in Table I for these compounds are so high that it appears certain that they can be

(18) The B. K. W. approximation for tunneling rate is given by Rojansky ("Introductory Quantum Mechanics," Prentice-Hall, New York, N. Y., 1938, p. 221).

$$T_{\epsilon_i} = f(\epsilon_i) \exp.\left(-(4\pi/h)\int_{x_1}^{x_2}\sqrt{2\mu(V-\epsilon_i)}\,dx\right)$$

where T_{ϵ_i} is the probability of penetration through the barrier for a harmonic oscillator with energy ϵ_i, and V is defined by equation (1). It is easy to show that in our case $f(\epsilon_i)$ is about two. Assuming a Boltzmann distribution, the rate constant for tunneling is

$$k_t = c\nu_3 \sum_i T_{\epsilon_i} \exp.(-\epsilon_i/kT) \Big/ \sum_i \exp\,(-\epsilon_i/kT)$$

where ν_3 has been previously defined and c is the velocity of light. From the above equations it is found that for trimethylamine the ratios of the rate of tunneling to that of going over the barrier, k_t/k, at 300, 200, and 150°K. are 60, 3×10^3, and 10^3, respectively. The numerical values of k_t at these temperatures were, respectively, 10^3, 10^{-1} and 6×10^{-5} sec.$^{-1}$ and resolution should be possible only at or below 150°K. For the ethyleneimine considered, k_t/k at 300, 400, and 500°K. is 300, 30, and 10, respectively. Since the rate in the reverse direction has been neglected, these computations are an upper limit for the rate of tunneling. It should be pointed out that if the calculations had been based on the type of potential function illustrated by the dotted line in Fig. 2, the tunneling rate would be much smaller, but the thermal rate would be correspondingly greater. Thus for the type of barrier employed, the effect of tunneling is essentially to round off the barrier.

resolved if the chemical difficulties can be overcome. Comparison of the values recorded for $P(CH_3)_3$, phosphorus trichloride, and phosphorus tribromide lead to the conclusion that the most favorable case is one in which three alkyl groups are attached directly to phosphorus.[19]

Active Sulfonium Salts.—The calculated activation energy is so high that racemization through an intramolecular conversion is out of the question. In fact, not only have these compounds been resolved,[20] but it has also been demonstrated that the mechanism by which they racemize is dissociation of the molecule, $R_3S^+X^-$, into the compounds R_2S and RX.

Asymmetric Carbon Atoms.—A mechanism which has been suggested[21] for the racemization of a compound of the type $CR_1R_2R_3R_4$ is one in which the four R groups and the asymmetric carbon atom are postulated to assume momentarily a planar configuration during inversion. Computations of the energy required show that this mechanism is entirely unreasonable.

From inspection of models it is clear that ΔE for this mechanism should be approximately twice the energy required to bend the propane molecule so that the three carbons lie on a line. Using the carbon bending frequency for propane[16] and the appropriate reduced mass, ΔE is found to be 88 kcal./mole. A value computed directly from data for neopentane is even higher. Since the attachment of groups other than methyls would not be expected to reduce greatly this value it may be stated *that the racemization of an asymmetric carbon cannot occur except through some process which results in the breaking of a bond attached to the central carbon.* A search through the literature has revealed no clear-cut experimental evidence for inversion through an intramolecular process.

(19) Sutherland, Lee and Wu (*Trans. Faraday Soc.*, **XXXV**, 1373 (1939)) have recently computed about 4 kcal./mole for the height of the barrier in PH_3 from a doublet observed by Fung and Barker (*Phys. Rev.*, **45**, 238 (1934)) at 990 cm.$^{-1}$. The separation of 2.4 cm.$^{-1}$ was interpreted as arising from a splitting of the ν_2 vibrational levels. We do not agree with this interpretation since it leads to a ten-fold reduction in the barrier height, thus necessitating an unreasonable anharmonicity. It should be noted that if the same anharmonicity were employed in the calculation of ΔE for R_3S^+, a value of 10 kcal./mole would be obtained compared to a minimum value of 25 kcal./mole required for stability at room temperature. There is no reason to expect much difference in the behavior of S^+ and P since the orbitals available for bond formation are the same in each case.

(20) (a) Gilman, *loc. cit.*, p. 344; (b) Balfe, Kenyon and Phillips, *J. Chem. Soc.*, 2554 (1930).

(21) Gilman, *loc. cit.*, p. 177.

Summary

1. Approximate calculations of activation energy from spectroscopic data have shown that no compound of the type $NR_1R_2R_3$ can be resolved into active forms at room temperature.

2. Substituted ethyleneimines appear to offer the best possibility for the resolution of trivalent nitrogen compounds since the calculated activation energy is considerably above the minimum value required for stability.

3. Trivalent compounds of phosphorus can be resolved if the chemical difficulties can be overcome.

4. The calculations provide an explanation of the observation that the mechanism of racemization of active sulfonium salts is through dissociation of the molecule, $R_3S^+X^-$, into RX and R_2S, rather than through an intramolecular mechanism.

5. It is concluded that the activated complex for racemization of a compound of the type $CR_1R_2R_3R_4$ cannot be a planar structure, and thus that the racemization of a compound of this type cannot occur except through some process which results in the breaking of a bond attached to the central atom.

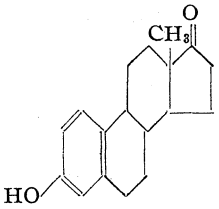
ROCHESTER, NEW YORK RECEIVED MARCH 20, 1940

[CONTRIBUTION FROM THE RESEARCH LABORATORY OF ORGANIC CHEMISTRY, MASSACHUSETTS INSTITUTE OF TECHNOLOGY, No. 224]

Experiments on the Synthesis of Oestrone. I. The 2-(β-Phenylethyl)-furans as Components in the Diene Synthesis

BY ROBERT BURNS WOODWARD[1,2]

The synthetic approach to substances of the hormone or sterol group, culminating in the brilliant synthesis of equilenin by Bachmann, Cole and Wilds,[3a] and of a stereoisomer of oestrone by Dane,[3b] has attracted much attention in recent years. The investigation undertaken in this Laboratory had as its ultimate object the synthesis of oestrone (I) or a stereoisomer. In view of its wide applicability in the synthesis of cyclic systems, the diene synthesis of Diels and Alder was investigated as a favorable vehicle for such a



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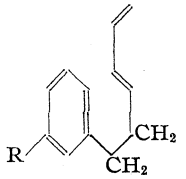

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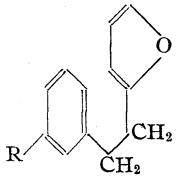


III

project. Other investigators[4] have explored the possibilities of this method. Cohen[4a] was able to add maleic anhydride to 1-(β-phenylethyl)-$\Delta^{1,3}$-butadiene (II, R = H). The yield, however, was small and the extension of the reaction to the pertinent case of 1-[β-(*m*-methoxyphenyl)-ethyl]-$\Delta^{1,3}$-butadiene (II, R = OCH_3) was unsuccessful. The use of 1-vinylnaphthalenes[4b] and 1-vinyl-$\Delta^{1,2}$-dihydronaphthalenes[4c] has been attended with more success.

Cohen attributed his difficulties to isomerism to derivatives of 1-vinyl-tetralin, and their subsequent polymerization. Our success in view of his failure is easily explained on this basis. The choice of 2-(β-phenylethyl)-furans (III) as diene components affords compounds whose individual double bonds are not active enough to be subject to prototropic isomerization, but whose diene character is still so marked as to permit their participation in the Diels and Alder reaction.

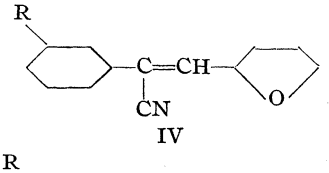
(1) Submitted in partial fulfillment of the requirements for the degree of Doctor of Philosophy at the Massachusetts Institute of Technology, June, 1937.

(2) At present member of the Society of Fellows, Harvard University.

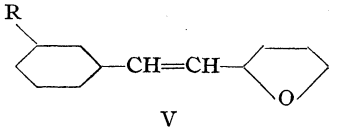
(3) (a) Bachmann, Cole and Wilds, THIS JOURNAL, **62**, 824 (1940); (b) Dane and Schmitt, *Ann.*, **537**, 246 (1939).

(4) (a) Cohen, *J. Chem. Soc.*, 429 (1935); (b) Cohen and Warren, *ibid.*, 1318 (1937); Bachmann and Kloetzel, THIS JOURNAL, **60**, 2204 (1938); (c) Dane and co-workers, *loc. cit.*

The parent compound, 2-(β-phenylethyl)-furan (III, R = H) had been prepared by Freund and Immerwahr.[5] Phenylacetonitrile was condensed with furfural to give α-phenyl-β-(2-furyl)-acrylic nitrile (IV, R = H). The reduction of the latter substance by molten sodium and absolute alcohol gave the desired compound in addition to β-phenyl-γ-(2-furyl)-propylamine.



IV



V

Since this method involved two concurrent reactions, one of which gave a product unsuitable for further synthetic work, it was hoped that a more direct method could be used. Two alternatives were investigated. The reaction of benzylmagnesium chloride with furfuraldehyde proceeded smoothly but it was impossible to obtain a homogeneous sample of benzyl-(2-furyl)-carbinol, water being split to some extent even on distillation in a high vacuum. Dehydration of the crude carbinol gave the new stilbene isolog α-phenyl-β-(2-furyl)-ethylene (V, R = H), characterized by the ease with which it forms a beautifully crystalline dibromide, and by its catalytic hydrogenation to the desired 2-(β-phenylethyl)-furan. The over-all yield of the latter substance obtained by this method, however, was slightly less than that obtained by the older process.

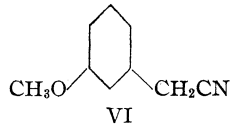
Again, the reaction of benzylmagnesium halide with 2-furfuryl bromide was the subject of considerable investigation. Certain 2-substituted furans had been prepared in this manner by Paul.[6] This investigator found that unless a large excess of the Grignard reagent was used, a small quantity of unchanged 2-furfuryl bromide invariably induced conjunct polymerization during the working up of the reaction mixture, with the result

(5) Freund and Immerwahr, *Ber.*, **23**, 2847 (1890).

(6) Paul, *Compt. rend.*, **200**, 1481 (1935).

that no product was obtained. Such a procedure was not feasible when a relatively rare substance such as *m*-methoxybenzyl bromide was being used. Accordingly the device was adopted of using equimolecular proportions of the (un)substituted benzyl halide and of 2-furfuryl bromide, and adding a large excess of butylmagnesium bromide after the reaction was complete to destroy the sensitive 2-furfuryl bromide. It was found also that greater success was obtained with this type of reaction if certain variations were made in the original preparation[7] of 2-furfuryl bromide. While Zanetti and Paul freed the crude bromide of water, unchanged 2-furfuryl alcohol, and other impurities, a better product is obtained by treating the crude ethereal solution with a small molar proportion of freshly prepared methylmagnesium iodide or butylmagnesium bromide. The separation of small amounts of 2-ethyl- or 2-(*n*-amyl)-furans formed by this process from the desired 2-(β-phenylethyl)-furans is easily effected by distillation. If these conditions are carefully observed, it is possible by this method to obtain better yields of the 2-(β-phenylethyl)-furans than by the older process. On the other hand, since the reactions of the latter method may be carried out more easily and quickly, it is the better method for preparative purposes.

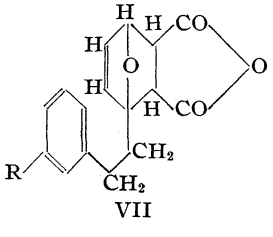
m-Methoxyphenylacetonitrile (VI) was obtained in 70% over-all yield by the following four-step process. *m*-Hydroxybenzaldehyde[8] was methylated according to Reimer[9] with methyl sulfate in dilute alkaline solution. The methylation of the aldehyde by means of diazomethane was unsatisfactory.[10] The methoxybenzaldehyde was reduced quantitatively by hydrogen using the Adams catalyst with ferrous ions to *m*-methoxybenzyl alcohol. The conversion of the alcohol into *m*-methoxybenzyl bromide by the action of hydrogen bromide in benzene proceeded essentially as described by Lapworth.[11] The bromide gave an excellent yield of *m*-methoxyphenylacetonitrile (88%) (VI) on treatment in the usual manner with aqueous alcoholic potassium cyanide.



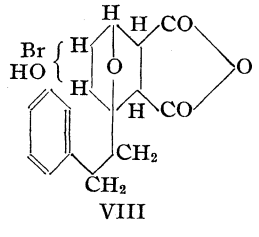
VI

The condensation of *m*-methoxyphenylacetonitrile with furfural to α-(*m*-methoxyphenyl)-β-(2-furyl)-acrylic nitrile (IV, R = OCH_3) proceeded smoothly; the product, an oil, may if desired be isolated by distillation *in vacuo*, but it was more convenient for synthetic work to reduce the crude condensation product directly by molten sodium and absolute alcohol to 2-[β-(*m*-methoxyphenyl)-ethyl]-furan (III, R = OCH_3).

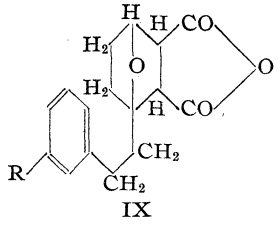
2-(β-Phenylethyl)-furan reacted on standing with pure maleic anhydride in anhydrous ether to give a beautifully crystalline addition product, 3-(β-phenylethyl)-3,6-endoxo-Δ^4-tetrahydro-*o*-phthalic anhydride (VII, R = H). This substance on heating above the melting point alone or in solvents dissociated into its components. On dissolving in ligroin, particularly, a clear solution was obtained which deposited crystals of maleic anhydride on standing in the ice-box for a short time. Again, the colorless solution in dimethylaniline on heating developed the characteristic orange color of maleic anhydride in this reagent. When the substance is warmed on the steam-bath in a current of nitrogen, maleic anhydride sublimes into the condenser. A bromo-hydroxy derivative (VIII) of the addition product was prepared by the action of bromine on a neutralized solution of the addition product in sodium carbonate. As would be expected, this latter substance exhibited no tendency to dissociate.



VII



VIII



IX

Similar phenomena are observed in the reaction of 2-[β-(*m*-methoxyphenyl)-ethyl]-furan with maleic anhydride. A beautifully crystalline addition product, 3-[β-(*m*-methoxyphenyl-)-ethyl]-3,6-endoxo-Δ^4-tetrahydro-*o*-phthalic anhydride

(7) Zanetti, THIS JOURNAL, **49**, 1066 (1927).

(8) The *m*-hydroxybenzaldehyde used in this research was obtained through the kindness of the General Aniline Company of New York.

(9) Reimer, THIS JOURNAL, **55**, 4644 (1933).

(10) *Cf.* Asahina and Yasue, *Ber.*, **68**, 2026 (1935).

(11) Lapworth, *J. Chem. Soc.*, **121**, 1396 (1922).

(VII, R = OCH_3) is obtained in excellent yield. This substance, like the unsubstituted adduct, dissociates readily into its components.

The original synthetic plan involved the catalytic hydrogenation of the addition products to dihydro derivatives (IX, R = H, OCH_3), theoretically susceptible of isomerization to substances possessing a substituted hydrophenanthrene template similar to oestrone or its degradation products. In practice the addition products were found to be remarkably resistant to hydrogenation. 3-(β-Phenylethyl)-3,6-endoxo-Δ^4-tetrahydro-*o*-phthalic anhydride was unaffected on shaking with hydrogen for long periods in ethyl acetate solution, in the presence of palladium or platinum black. Hydrogenation in glacial acetic acid with a platinum catalyst over a period of twelve hours gave succinic acid as sole crystalline product, dissociation evidently taking place. Similar difficulties were experienced in reducing the methoxylated addition product.[12]

Experimental

α-Phenyl-β-(2-furyl)-acrylic nitrile (IV, R = H) was obtained by Frost's method[13] from phenylacetonitrile and furfuraldehyde in the presence of alcoholic sodium ethylate. The substance crystallized from aqueous alcohol as slightly yellow needles, m. p. 42–43°.

2-(β-Phenylethyl)-furan (III, R = H).—(a) The material was first prepared according to Freund and Immerwahr.[5] The substance was purified more easily by steam distillation than by the procedure recommended by these authors. From 63 g. of the nitrile an average of 30 g. of the furan, b. p. (760 mm.) 241–243°, was obtained as a colorless oil of pleasant aromatic odor, reminiscent of stilbene.

(b) 9.6 grams of freshly turned magnesium was dissolved in 50 g. of benzyl chloride and 200 cc. of anhydrous ether in a three-necked flask equipped with dropping funnel, reflux condenser, and mercury seal with mechanical stirrer. To the large excess of benzylmagnesium chloride obtained in this manner, 2-furfuryl bromide, prepared as described below from 40 g. of 2-furfuryl alcohol, was added slowly with good stirring. A white or slightly yellow precipitate began to form immediately and precipitation continued throughout the course of the reaction. When the addition was complete, the reaction mixture was decomposed in the usual manner with ammonium chloride solution, the yellow ethereal extract was washed with water and dried over anhydrous sodium sulfate. After removal of the ether, the residual oil was fractionated. Twenty grams of 2-(β-phenylethyl)-furan was obtained, identical with that obtained by the method outlined in (a).

The preparation could also be carried out using equimolecular proportions of the reactants if the precautions mentioned in the theoretical part are observed (*cf.* 2-[β-(*m*-methoxyphenyl)-ethyl]-furan, (b), below).

α-Phenyl-β-(2-furyl)-ethylene (V).—To the Grignard solution from 12.2 g. of magnesium, 63 g. of benzyl chloride and 300 cc. of anhydrous ether, 48 g. of furfuraldehyde was added slowly, with mechanical stirring. When the addition had been completed, the reaction mixture was heated on the steam-bath for a short time. There was now suspended in the ether a yellow crystalline precipitate. The whole was poured into ice and stirred well to effect decomposition. The ethereal solution was separated, the residual sludge of magnesium oxychloride was dissolved by the addition of dilute acetic acid, and the resulting solution was extracted with ether. The ether extract was dried over anhydrous sodium sulfate, and the ether was removed. The deep yellow residual oil (35 g.) was distilled *in vacuo* over 20 g. of pure potassium hydrogen sulfate, or 7 g. of anhydrous aluminum sulfate. The fraction b. p. (3 mm.) 150–165° solidified on cooling and was purified further by crystallization from alcohol. Ten grams of α-phenyl-β-(2-furyl)-ethylene was obtained in long yellowish needles, of pleasant aromatic odor, reminiscent of stilbene (m. p. 49–50°).

Anal. Calcd. for $C_{12}H_{10}O$: C, 84.7; H, 5.88. Found: C, 84.6; H, 5.93.

2-(β-Phenylethyl)-furan (III, R = H) is obtained readily from the above substance by shaking with hydrogen in the presence of Adams catalyst. The reduction is complete in less than one-half hour, and the product is identical in every respect with that obtained above.

Dibromide.—One-half gram of the ethylenic compound was dissolved in 15 cc. of pure chloroform, 0.5 g. of bromine was added, and the reaction mixture allowed to stand for three days. At the end of this time magnificent crystals of the dibromide had separated as long transparent prisms, m. p. 232.0–232.3°, reminiscent in appearance of hydroxylamine hydrochloride.

Anal. Calcd. for $C_{12}H_{10}OBr$: Br, 48.48. Found: Br, 48.5.

***m*-Methoxybenzaldehyde** was obtained in 83% yield by the methylation of *m*-hydroxybenzaldehyde in weakly alkaline solution by means of dimethyl sulfate. The yield of pure product obtained when the crude aldehyde is distilled *in vacuo* in a current of nitrogen is appreciably higher than that obtained when no precaution is taken to protect the substance from oxidation (b. p. (30 mm.) 129–130°).

***m*-Methoxybenzyl alcohol** was prepared in quantitative yield by the catalytic hydrogenation of the aldehyde. In a typical experiment, 40 g. of *m*-methoxybenzaldehyde, 200 cc. of reagent ethyl alcohol, 0.2 g. of freshly prepared Adams platinum oxide, and 2.0 cc. of 0.1 *M* ferrous sulfate solution were placed in the pressure bottle of the Adams hydrogenation apparatus. Shaking was started at three atmospheres. Within ten minutes, the theoretical absorption (0.294 mole = 23 lb.) had taken place. It was possible to use the same catalyst for a second or third reduction, but the time required for complete hydrogenation in this case was considerably longer. The alcohol was removed by distillation under reduced pressure, and the residual oil distilled *in vacuo* in a current of nitrogen.

(12) More recent work which will be described in a subsequent communication has led to the quantitative hydrogenation of 3-[β-(*m*-methoxyphenyl)-ethyl]-Δ^4-tetrahydro-*o*-phthalic anhydride by shaking a suspension in methyl alcohol with hydrogen in the presence of platinum black.

(13) Frost, *Ann.*, **250**, 159 (1888).

m-Methoxybenzyl alcohol is a clear colorless liquid of peculiar odor, b. p. (25 mm.) 150°.

***m*-Methoxybenzyl Bromide.**—167 grams of *m*-methoxybenzyl alcohol was dissolved in 300 cc. of dry thiophene-free benzene, and saturated with dry hydrogen bromide in the cold. Water collected under the clear benzene solution of the bromide which was decanted and allowed to dry overnight over calcium chloride. The benzene was removed *in vacuo* in a current of dry nitrogen; 238 grams of *m*-methoxybenzyl bromide, b. p. (8 mm.) 116° was obtained. The substance is a clear, highly refractive liquid which rapidly turns green or greenish purple on standing. Care must be taken not to inhale the substance nor allow it to come in contact with the skin, since it is an extremely irritating lachrymator and vesicant.

***m*-Methoxyphenylacetonitrile** (VI).—100 grams of *m*-methoxybenzyl bromide was refluxed for two and a half hours with 32 g. of sodium cyanide, 30 cc. of water and 55 cc. of reagent ethyl alcohol. At the end of this time the alcohol was distilled *in vacuo* from the orange-brown mixture, the residual sludge was shaken with water, and the oil which separated dried over a small amount of anhydrous sodium sulfate. On distillation 64 g. (87.5%) of *m*-methoxyphenylacetonitrile, b. p. (20 mm.) 164–165°, was obtained as a highly refractive liquid, of faint characteristic nitrile odor.

Anal. Calcd. for C_9H_9ON: C, 73.5; H, 6.10; N, 9.50. Found: C, 73.6; H, 6.3; N, 9.6.

α-(*m*-Methoxyphenyl)-β-(2-furyl)-acrylic Nitrile (IV, R = OCH_3).—To a mixture of 64 g. of *m*-methoxyphenylacetonitrile and 42 g. of furfural, 20 cc. of 20% alcoholic sodium ethylate was added, in small portions, with shaking. A good deal of heat was liberated, and the color of the reaction mixture deepened considerably. From time to time the flask was cooled under the tap. Considerable water separated on the sides of the vessel. When the reaction was complete, the dark brown oil was washed several times with water, dried over a small amount of anhydrous sodium sulfate and distilled in a high vacuum (b. p. (1 mm.) 180°). Ninety grams of α-(*m*-methoxyphenyl)-β-(2-furyl)-acrylic nitrile was obtained as a clear yellow oil. For conversion into 2-(β-(*m*-methoxyphenyl)-ethyl)-furan, the purification was superfluous. The crude brown oil gave satisfactory results.

Anal. Calcd. for $C_{14}H_{11}O_2N$: C, 74.8; H, 4.98; N, 6.23. Found: C, 74.6; H, 5.2; N, 6.4.

2-[β-(*m*-Methoxyphenyl)-ethyl]-furan (III, R = OCH_3).—(a) (The preparative method.) Ninety grams of α-(*m*-methoxyphenyl)-β-(2-furyl)-acrylic nitrile was dissolved in 1200 cc. of absolute ethyl alcohol and poured onto 138 g. of metallic sodium cut into chips (this was an excess of two and a half times the theoretical amount for complete reduction to β-(*m*-methoxyphenyl)-γ-(2-furyl)-*n*-propylamine). A three-necked flask equipped with two reflux condensers and one stopper was used for the reduction. If the reaction became too violent, the clogging of the condensers was easily remedied by removing the stopper for a moment. The flask was set in a pail, or in the sink, so that cold water could be dashed on the sides of the flask in case the reaction got out of control. When the reduction was complete, the greenish reaction mixture was made acid with hydrochloric acid. Since a good deal of free sodium remained in the flask, it was advisable to conduct this operation with considerable care. It was advantageous to place a quantity of dry-ice on the surface of the reaction mixture before each addition of acid. The contents of the flask were then subjected to a vigorous steam distillation, when the desired product passed over as a yellowish oil. Since this process was very slow, it was found that it was quite as satisfactory to extract the contents of the flask with ether, wash with dilute hydrochloric acid, then with water, and evaporate the ether after drying over sodium sulfate. In either case, the oil was distilled *in vacuo*. Thirty-nine grams of 2-[β-(*m*-methoxyphenyl)-ethyl]-furan was obtained as a colorless oil, b. p. (10 mm.) 153°, of aromatic odor, which turned yellow on standing. The same change was noticed with 2-(β-phenylethyl)-furan and 2-(γ-phenyl-*n*-propyl)-furan.

(b) (By the Grignard reaction.) Three grams of magnesium was placed in a dry three-necked flask equipped with dropping funnel, reflux condenser, and mercury seal bearing a mechanical stirrer. A few drops of *m*-methoxybenzyl bromide were allowed to fall onto the magnesium. When the reaction had started, the remainder of the bromide, in all 25 g., dissolved in 60 cc. of anhydrous ether, was added slowly. The reaction was not vigorous. Stirring and refluxing were continued for three hours after the bromide had been added. To the solution of *m*-methoxybenzylmagnesium bromide obtained in this manner, an ethereal solution of 2-furfuryl bromide, prepared from 40 g. of 2-furfuryl alcohol as described below, was added slowly, with good stirring. A shiny purple precipitate of magnesium bromide covered the walls of the flask as the reaction proceeded. When the addition of 2-furfuryl bromide was complete, a large excess of freshly prepared butylmagnesium bromide was added rapidly and the reaction mixture was allowed to stand for one-half hour. Ammonium chloride solution was then added to decompose unreacted Grignard reagents, the yellow ethereal solution was separated, washed with water, and dried over anhydrous sodium sulfate. On fractionation *in vacuo*, 13 g. of 2-[β-(*m*-methoxyphenyl)-ethyl]-furan was obtained, identical in every respect with that prepared by method (a).

Anal. Calcd. for $C_{13}H_{14}O_2$: C, 77.3; H, 7.10. Found: C, 77.1; H, 7.1.

2-Furfuryl Bromide.—Forty grams of freshly distilled 2-furfuryl alcohol dissolved in 400 g. of absolute ether was treated in the course of a half hour with 40 g. of pure phosphorus tribromide dissolved in 60 cc. of anhydrous ether. The flask was cooled from time to time by running water. When the addition had been completed, the reaction mixture was allowed to stand for half an hour before decanting from the waxy precipitate of phosphorous acid which covered the walls of the flask. The decanted solution was treated with a solution of 0.1–0.2 mole of butylmagnesium bromide (from 18 g. of butyl bromide and 4.0 g. of magnesium) in 100 cc. anhydrous ether, and used directly in the reaction described above.

3-(β-Phenylethyl)-3,6-endoxo-Δ^4-tetrahydro-*o*-phthalic Anhydride (VII, R = H).—Three grams of pure maleic anhydride (twice recrystallized from chloroform) and 5.4 g. of 2-(β-phenylethyl)-furan dissolved in the smallest amount of anhydrous ether necessary for complete

solution were allowed to stand in a well-stoppered flask. In a few days the contents of the flask had become a solid mass of beautiful needles. On filtering and washing with anhydrous ether, the addition product was obtained in almost quantitative yield as white needles, m. p. 71–73°. Due to its tendency to dissociate, the substance was difficult to recrystallize. Satisfactory results were obtained, however, by dissolving in cold chloroform, adding petroleum ether, and allowing to stand in the ice-box, when long fine needles gradually separated, m. p. 73–74°.

Anal. Calcd. for $C_{16}H_{14}O_4$: C, 71.2; H, 5.18. Found: C, 71.2; H, 5.3.

If this substance was dissolved in warm ligroin (b. p. 70–90°) and the resulting solution allowed to stand in the icebox, needles separated, which proved to be maleic anhydride, m. p. 57–59°, mixed m. p. 57–59°; orange color on heating with dimethyl- or diethylaniline.

Bromohydroxy Derivative (VIII, R = H).—The addition product (1.0 g.) was dissolved in excess sodium carbonate and the basic solution was exactly neutralized. This solution was shaken vigorously with a slight excess of bromine. Recation took place immediately with the quantitative precipitation of the bromohydroxy acid. After recrystallization from boiling water (Norit) the acid melted at 142–143°, with decomposition.

Anal. Calcd. for $C_{16}H_{15}O_5Br$: C, 52.4; H, 4.18. Found: C, 52.1; H, 4.4.

3-[β-(*m*-Methoxyphenyl)-ethyl]-3,6-endoxo-Δ⁴-tetrahydro-*o*-phthalic Anhydride (VII, R = OCH_3) crystallized quantitatively in beautiful transparent rosets when 31.6 g. of 2-[β-(*m*-methoxyphenyl)-ethyl]-furan and 15.3 g. of pure maleic anhydride were dissolved in the least amount of anhydrous ether necessary for complete solution and allowed to stand for three days. After washing with anhydrous ether, drying and crystallizing by the chloroform–petroleum ether procedure, long, transparent needles were obtained, m. p. 78–80°.

Like the unsubstituted addition product, this methoxy derivative gave maleic anhydride on heating in ligroin, gave no color with dimethylaniline until heated, and was unstable to cold dilute alkaline permanganate.

Anal. Calcd. for $C_{17}H_{16}O_5$: C, 68.0; H, 5.33. Found: C, 68.0; H, 5.4.

Hydrogenation Experiments.—If 1 g. of 3-(β-phenylethyl)-3,6-endoxo-Δ⁴-tetrahydro-*o*-phthalic anhydride dissolved in 30 cc. of glacial acetic acid was shaken with 0.2 g. platinum (palladium) oxide under 3 atmospheres of hydrogen for fifteen hours, succinic acid was obtained after washing the residue from the acetic acid (removed *in vacuo*) with dry benzene; m. p. 186–187°, mixed m. p. 185–187°.

All attempts to isolate other crystalline products from the reaction, or from numerous runs made in ethyl acetate or inert solvents, failed.

Summary

The synthesis of 2-(β-phenylethyl)-furan and 2-[β-(*m*-methoxyphenyl)-ethyl]-furan has been accomplished.

The Diels–Alder reaction has been applied with success to these substances.

CAMBRIDGE, MASS. RECEIVED MARCH 11, 1940

[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Ketene Acetals. VI. The Preparation of Ketene Acetals from α-Bromo-orthoesters[1]

BY PHILIP M. WALTERS AND S. M. MCELVAIN

The procedure which has been used in this Laboratory for the preparation of ketene acetals involves the removal of the elements of halogen acid from a halogenated acetal by means of potassium *t*-butoxide

$$XCH_2CH(OEt)_2 + KOC_4H_9(t) \longrightarrow CH_2{=}C(OEt)_2 + KX + t\text{-}C_4H_9OH$$

By this reaction ketene diethylacetal and various halogenated derivatives of it have been prepared.[2] It is obvious that attempts to apply this procedure to the acetals of the higher α-halogenoaldehydes, $R_2CHCHXCH(OEt)_2$, might be unsuccessful due to the preferential loss of halogen acid from the α- and β-carbon atoms with the resultant formation of the acetals of the unsaturated aldehydes.[3]

Another route to the ketene acetal structure that was partially explored when the problem first was undertaken is the elimination of the elements of ethyl hypohalite, EtOX, from an α-halogenoorthoacetic ester in a manner similar to that used by Boord and co-workers[4] to prepare olefins. A

(1) Paper V of this series is Barnes, Kundiger and McElvain, THIS JOURNAL, **62**, 1281 (1940).

(2) Beyerstedt and McElvain, *ibid.*, **58**, 529 (1936); **59**, 2266 (1937); Magnani and McElvain, *ibid.*, **60**, 2210 (1938).

(3) In the cases of the acetals of the α-halogeno-propionaldehyde, -butyraldehyde and -isobutyraldehyde the larger numbers of hydrogens on the β-carbon atoms makes the α,β-loss of halogen acid much more probable than that between the α-carbon and the aldehyde carbon atom. However in the case of the acetal of α-halogeno-isovaleraldehyde, $(CH_3)_2CHCHXCH(OEt)_2$, in which there is only one hydrogen on the β-carbon atom it seems that there should be some chance of loss of halogen acid from the α-carbon and the aldehyde carbon atom. But Jones (B.S. Thesis, University of Wisconsin, 1939), working along this line found that each of the above acetals (X is Br) gave the corresponding unsaturated acetal, through an α,β-loss of hydrogen bromide, when treated with potassium *t*-butoxide in *t*-butyl alcohol.

(4) Boord, *et al.*, THIS JOURNAL, **52**, 3396 (1930); **53**, 1505 (1931) **54**, 751 (1932); **55**, 3293, 4930 (1933).

study of the reaction of the various ethyl orthohalogenoacetates with both zinc and magnesium showed that the loss of EtOX was not intramolecular to form ketene acetal, but instead was poly-intermolecular to form non-volatile condensation products of high molecular weight.[5]

Wislicenus[6] reported the removal of the elements of ethyl hypochlorite from chloro-acetal by means of sodium to form vinyl ethyl ether according to the following reaction:

$$ClCH_2CH(OEt)_2 + 2Na \longrightarrow CH_2{=}CHOEt + NaCl + NaOEt$$

The yield of the ether obtained was not reported by Wislicenus, but Lunsted[7] in this Laboratory has studied the reaction, using the bromo- instead of the chloro-acetal, and has found that vinyl ethyl ether is produced in yields of 75% of the theoretical.

Because of the success of this reaction with bromoacetal it seemed worth while to apply it to the preparation of ketene acetals from the α-bromo-orthoesters. It has proved to be most satisfactory for this purpose and the present paper reports the preparation of ketene diethylacetal and methylketene diethylacetal from ethyl orthobromoacetate and ethyl ortho-α-bromopropionate. Each of these bromo-orthoesters reacts smoothly with two equivalents of sodium to give the corresponding ketene acetal according to the following reaction:

$$RCHBrC(OEt)_3 + 2Na \longrightarrow RCH{=}C(OEt)_2 + NaBr + NaOEt$$

Ketene acetal (R is H) and methylketene acetal (R is CH_3) were obtained from the above reaction in yields of 66 and 80% of the theoretical, respectively. Methylketene diethyl acetal boils at 133–134°[8] and shows no tendency to rearrange into the isomeric acrolein diethyl acetal, $CH_2{=}CHCH(OEt)_2$ (b. p. 123–124°). It reacts vigorously, with the evolution of heat, with both water and alcohol at room temperature and yields the corresponding esters, ethyl propionate and ethyl orthopropionate.

It seems that this method should be of general applicability. The elements, EtOBr, which are eliminated from the orthoester can only come from the carbon atoms that are to carry the double bond of the ketene acetal, and since it appears from the behavior of methylketene acetal that there is no rearrangement of the ketene acetal into an unsaturated aldehyde acetal, the reaction should be applicable to the preparation of any of the higher homologs of ketene acetal.

(5) Beyerstedt and McElvain, THIS JOURNAL, **59**, 1273 (1937).

(6) Wislicenus, *Ann.*, **192**, 106 (1879).

(7) Lunsted, M.S. Thesis, University of Wisconsin, 1940.

(8) Scheibler, Marhenkel and Nikolic, *Ann.*, **458**, 21 (1927), reported the formation of this acetal in 7% yield from the reaction of sodium ethoxide on ethyl propionate. They list the following physical properties, b. p. 78–81°; d^{13}_4 0.8002; $n^{18}D$ 1.36732 (*cf.* other properties given in the experimental part of this paper).

Experimental

Ketene Diethylacetal from Ethyl Orthobromoacetate.—To a stirred mixture of 9.2 g. (0.4 atom) of powdered sodium and 200 ml. of anhydrous benzene heated under gentle reflux was added dropwise 48.2 g. (0.2 mole) of ethyl orthobromoacetate[5] over a period of forty minutes. After the first few ml. of the bromo-ester had been added, the reaction mixture turned a characteristic deep blue in color. The reaction mixture was stirred for an additional two hours with continued refluxing. The clear supernatant liquid was then decanted from the precipitated blue salts, and the salts thoroughly washed by several triturations with anhydrous benzene. These washings were combined with the filtrate, and the benzene removed under atmospheric pressure with the heating bath temperature not exceeding 120°. The remaining material was distilled under diminished pressure (100 mm.). The yield of ketene diethylacetal was 15.4 g. (66%), b. p. 68° (100 mm.); $n^{25}D$ 1.4110; d^{25}_{25} 0.877.

Ethyl Orthopropionate.—This ester was prepared in yields of 48% of the theoretical from propioniminoethyl ether hydrochloride, m. p. 92°, by the procedure of Sah.[9] It was found advantageous to carry out the distillation of the reaction mixture under diminished pressure sufficient to keep its temperature below 85°. The ethyl orthopropionate obtained boiled at 44° (9 mm.); $n^{25}D$ 1.4000.

Ethyl Orthobromopropionate.—This ester was prepared by the procedure used for the preparation of ethyl orthobromoacetate.[5] The yields amounted to 67% of the theoretical. The product boiled at 73° (8 mm.); $n^{25}D$ 1.4338; d^{25}_{25} 1.181.

Anal. Calcd. for $C_9H_{19}O_3Br$: C_2H_5O, 52.95. Found: C_2H_5O, 53.05.

Methylketene Diethylacetal.—This acetal was prepared from ethyl ortho-α-bromopropionate and sodium in yields of 80% of the theoretical by the same procedure as that given above for the preparation of the lower homolog, ketene diethylacetal. The product obtained boiled at 133–134° or 77–78° (100 mm.); $n^{25}D$ 1.4083; d^{25}_{25} 0.8654.

Anal. Calcd. for $C_7H_{14}O_2$: C, 64.61; H, 10.72; C_2H_5O, 69.23. Found: C, 64.48; H, 10.57; C_2H_5O, 68.50.

A 3-g. sample of methylketene diethylacetal was treated with the theoretical amount of water, and the reaction catalyzed with a trace of concentrated hydrochloric acid. The reaction mixture underwent almost spontaneous reaction and the temperature rose rapidly to 80–85°. The reaction mixture then was dried over anhydrous calcium chloride, and distilled under atmospheric pressure. The ethyl propionate so obtained boiled at 98–100°; $n^{25}D$

(9) Sah, THIS JOURNAL, **50**, 516 (1928).

1.3810; sap. equiv., 103 (calcd. 102); m. p. of the *p*-toluidide of the acid, 122–124°. When this experiment was repeated using absolute alcohol instead of water a decided evolution of heat was noticed and resulting ethyl orthopropionate boiled at 157–158° (752 mm.); $n^{25}D$ 1.4000. The yields of ester in each of these cases were practically quantitative.

Summary

Ketene diethylacetal and methylketene diethylacetal have been prepared in excellent yields by the action of sodium on the corresponding α-bromo-orthoesters. This method appears to be of general applicability for the higher homologs of ketene acetal. The properties of methylketene diethylacetal are described for the first time.

MADISON, WISCONSIN RECEIVED APRIL 4, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE OHIO STATE UNIVERSITY]

Osage Orange Pigments. IV. Degree of Unsaturation and Flavone Nature[1]

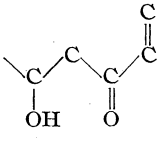
BY M. L. WOLFROM, P. W. MORGAN AND F. L. BENTON

The publication of the determination of the degree of unsaturation of osajin and pomiferin, the two pigments of the fruit of the osage orange (*Maclura pomifera* Raf.), has been withheld until enough data were obtained to warrant a satisfactory explanation. We believe that this can now be done.

Osajin could be hydrogenated catalytically at atmospheric pressure with platinum in a stepwise fashion. One double bond hydrogenated with great ease to yield dihydro-osajin. The second double bond also hydrogenated readily, although more slowly than the first, to yield tetrahydro-osajin. At this point further hydrogenation proceeded very slowly but a hexahydro-osajin was obtained. All of these hydrogenated derivatives showed the presence of the one easily acetylatable and of the one difficultly acetylatable hydroxyl group of the original osajin, a monoacetate and a diacetate of each hydrocompound being obtained. Hydrogenation thus produced no new hydroxyl groups and it was determined also that no carboxyl groups were formed. Similar results were obtained with pomiferin, except that the hexahydropomiferin has not yet been isolated. A diacetate and a triacetate of both dihydropomiferin and tetrahydropomiferin were obtained, this behavior on acetylation being identical with that of pomiferin. No carboxyl groups were produced.

Table I shows the results of the application of the perbenzoic acid titration procedure to the determination of the degree of unsaturation of the two pigments and of their reduction products. Osajin and pomiferin were found to undergo extensive general oxidation with perbenzoic acid, but when protected by acetylation, this effect was minimized, although not eliminated. If we consider the relatively low values given by the tetrahydro derivatives as a subtractable blank, it is seen that the data indicate the presence of two active double bonds in both osajin and pomiferin. The data indicate also that the third unsaturation, as represented by hexahydro-osajin, is of a different type and is not a simple aliphatic double bond. A negative Diels–Alder test with maleic anhydride denoted that the two active double bonds are not conjugated.

The nature of the unsaturation of this third double bond of osajin was therefore a presented problem. It was found that hexahydro-osajin gave a negative result with the boric acid test described by Wilson.[2] On the other hand, Table II shows that osajin and pomiferin and their dihydro and tetrahydro derivatives gave a positive color reaction. According to Wilson, flavanones give no color reaction with boric acid, and the grouping shown below is among those that do give a positive color reaction, the α,β-unsaturated carbonyl and a suitable *peri* auxochromic group, as the hydroxyl, being essential.



A phenolic group *peri* to a carbonyl group in osajin and pomiferin would be in harmony with the known fact of the presence of one hydroxyl group that is difficultly methylatable. This type of phenolic group is also frequently quite acidic and

(1) Previous publications in this series: (a) THIS JOURNAL, **60**, 574 (1938); (b) **61**, 2832 (1939); (c) **62**, 651 (1940).

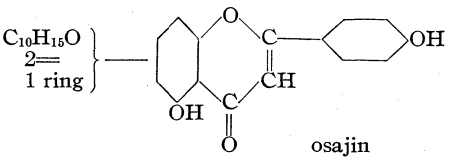
(2) C. W. Wilson, *ibid.*, **61**, 2303 (1939).

would explain the titratable phenolic acidity (one equivalent) of osajin, although pomiferin consumes less than one equivalent of alkali on direct titration.

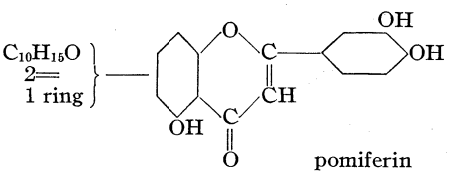
Asahina and co-workers[3] have shown that flavanones are reducible by both sodium amalgam and magnesium and hydrochloric acid; flavones are reducible by sodium amalgam and not by magnesium–hydrochloric acid; flavanols unsubstituted in position three are reducible by magnesium–hydrochloric acid and not by sodium amalgam; flavonols substituted in position three by a methoxyl group or a sugar residue are reducible by both methods. All reduction products exist in or separate from hydrochloric acid solutions as red substances of a flavylium salt nature. Application of these tests to our substances showed that hexahydro-osajin was reducible with magnesium–hydrochloric acid and that osajin, tetrahydro-osajin, pomiferin, and tetrahydro-pomiferin were not reducible by this reagent. Sodium amalgam, however, reduced all of the compounds, as shown in Table III.

The above results are indicative that osajin and pomiferin possess flavone structures and that the third double bond reduced in osajin was that between carbons two and three in a γ-pyrone nucleus, producing a flavanone structure. The absorption spectra obtained[1a,1b] for osajin and pomiferin (one band with maxima at 2730 and 2750 Å., respectively) are in harmony with the presence of a carbonyl group. These conclusions are based on color reactions and must be considered as tentative until supported by definite degradative results. Such confirmation has been obtained in part by the isolation of anisic acid from osajin dimethyl ether and of veratric acid from pomiferin trimethyl ether by oxidation with alkaline hydrogen peroxide.[1c]

If a flavone structure be subtracted from the molecular formulas of osajin ($C_{25}H_{24}O_5$) and of pomiferin ($C_{25}H_{24}O_6$), there is left a $C_{10}H_{15}O$ group. This is a monoterpene residue and would be attached very probably as shown in the formulas below. In this residue there must be two active double bonds which, when saturated, would produce the separate entity $C_{10}H_{20}O$. The one oxygen atom is unreactive, indicative of an oxide linkage. This entity has a deficiency of two atoms of hydrogen, indicative of one ring. On this basis, the formulas of osajin and pomiferin may be developed as shown below, although they are distinctly tentative and must be corroborated by further degradative work.



osajin



pomiferin

Further work on the structure of these two substances is in progress in this Laboratory.

Experimental[4]

Dihydro-osajin.—Platinum dioxide catalyst was freshly prepared and then dried for twenty-four to forty-eight hours in a vacuum desiccator over potassium hydroxide. The catalyst (0.10 g.) was suspended in 10 cc. of absolute ethanol and saturated with hydrogen. A solution of osajin (1 g. in 40 cc. of absolute ethanol) was then introduced and hydrogenation (atmospheric pressure) was stopped when 1 mol of hydrogen (55 cc., S. T. P.) had been absorbed. The time required varied with the activity of the particular catalyst preparation but with the amount of osajin cited it was generally about five minutes.

The catalyst was removed by filtration, the filtrate was concentrated to 30 cc. and the product was crystallized by the addition of water to the hot solution until turbidity appeared; yield 0.9 g. of m. p. 194.5° and 0.05 g. of m. p. 173–175°. The melting point was raised to 197°[5] by repeated crystallization from methanol and was unchanged on further crystallization from methanol, 95% ethanol or propylene chloride; yield 0.74 g.

The substance crystallized from methanol in fine, cottony needles of a light, dull yellow color. It was soluble in ethanol, less so in methanol and was moderately soluble in benzene. In alcoholic solution, it gave a dark green ferric chloride color, turning to a bright wine-red on the addition of ammonium hydroxide. In glacial acetic acid solution, it gave an immediate orange color on the addition of a few drops of concentrated sulfuric acid. In pyridine solution, it reduced Tollens reagent.

Anal. Calcd. for $C_{25}H_{26}O_5$: C, 73.87; H, 6.45; mol. wt., 406.5. Found: C, 73.88; H, 6.32; mol. wt. (Rast), 400, 380.

Dihydro-osajin Monoacetate.—Dihydro-osajin (0.44 g.) was acetylated overnight at icebox temperature with pyridine (10 cc.) and acetic anhydride (15 cc.) and the product obtained crystalline by pouring the acetylation mixture into ice and water; yield 0.48 g., m. p. 155°. Recrystal-

(3) Y. Asahina and M. Inubuse, *Ber.*, **61**, 1646 (1928); **64**, 1256 (1931); Y. Asahina, G. Nakagome and M. Inubuse, *ibid.*, **62**, 3016 (1929).

(4) All experimental work by Mr. P. W. Morgan, except where otherwise noted.

(5) All melting points recorded are uncorrected and were taken on a 360° thermometer with immersion to the −20° mark.

lization from 95% ethanol raised the melting point to 156.5° (yield 0.36 g.), unchanged on further crystallization from 95% ethanol or benzene.

The substance crystallized from ethanol as long, silky needles of a very light yellow tinge. It was very soluble in chloroform and was only moderately soluble in 95% ethanol, acetone and benzene. It gave an apple-green ferric chloride–alcohol test and gave a yellow color with sulfuric acid–acetic acid.

Anal. Calcd. for $C_{25}H_{25}O_5(CH_3CO)$: C, 72.30; H, 6.29; CH_3CO, 2.23 cc. 0.1 *N* NaOH per 100 mg.; mol. wt., 448.5. Found: C, 72.25; H, 6.19; CH_3CO,[6] 2.16 cc.; mol. wt. (Rast), 400.

Dihydro-osajin Diacetate.—Dihydro-osajin (0.6 g.) was acetylated by refluxing for three hours with fused sodium acetate (5 g.) and acetic anhydride (30 cc.) and the product isolated by pouring the acetylation mixture into ice and water; yield 0.7 g., m. p. 150°. Recrystallization from 95% ethanol and from methanol raised the melting point to 154° (yield 0.45 g.) unchanged on further recrystallization from 95% ethanol or benzene–petroleum ether; mixed m. p. with dihydro-osajin monoacetate (m. p. 156.5°), 142°.

The substance crystallized in radiating clusters of colorless, elongated plates, was very soluble in acetone and benzene and was only moderately soluble in cold alcohol. It gave no coloration with ferric chloride–alcohol and gave a yellow color slowly with sulfuric acid–acetic acid.

Anal. Calcd. for $C_{25}H_{24}O_5(CH_3CO)_2$: C, 71.03; H, 6.17; CH_3CO, 4.08 cc. 0.1 *N* NaOH per 100 mg.; mol. wt., 490.5. Found: C, 71.03; H, 6.01; CH_3CO, 4.16 cc.; mol. wt. (Rast), 460.

Dihydro-osajin diacetate also was obtained by similar treatment of dihydro-osajin monoacetate and was identified by melting point and mixed melting point.

Tetrahydro-osajin.—Osajin (1.0 g.) was reduced with hydrogen (platinum catalyst) at atmospheric pressure as described for the preparation of dihydro-osajin except that the hydrogenation was stopped when 2 mols of hydrogen (111 cc., S. T. P.) had been absorbed. With most catalyst preparations, this point was attained readily (about fifteen minutes) and further reduction proceeded very slowly. The substance was isolated as described for dihydro-osajin; yield 0.78 g., m. p. 198–200°. Pure material was obtained on recrystallization from benzene; yield 0.60 g., m. p. 206°, mixed m. p. with dihydro-osajin (m. p. 197°) 188–190°. This melting point was unchanged on further crystallization from propylene chloride. The substance crystallized from benzene or propylene chloride in the form of long, silky needles of a pale yellow color. If allowed to stand overnight in a benzene–petroleum ether mixture these needles slowly changed to short prisms of a lemon-yellow color, having the same melting point. This change in habit occurred more readily if the material was impure.

The solubilities and properties of the substance were similar to those of dihydro-osajin. In alcoholic solution, it gave an apple-green ferric chloride color, turning wine-red on the addition of ammonium hydroxide.

Anal. Calcd. for $C_{25}H_{28}O_5$: C, 73.50; H, 6.91; mol. wt., 408.5. Found: C, 73.70; H, 6.84; mol. wt. (Rast), 390, 360.

(6) All acetyl analyses recorded were made according to the procedure of K. Freudenberg and M. Harder, *Ann.*, **433**, 230 (1923).

Tetrahydro-osajin also was obtained on further hydrogenation of dihydro-osajin and was identified by melting point and mixed melting point.

Tetrahydro-osajin Monoacetate.—Tetrahydro-osajin (0.25 g.) was acetylated with pyridine and acetic anhydride as described for the preparation of dihydro-osajin monoacetate. Pure material was obtained on recrystallization from benzene–petroleum ether; yield 0.19 g., m. p. 179.5°, unchanged on further crystallization from benzene or ethanol.

The substance crystallized as silky needles of a very light yellow tinge. It was soluble in benzene and propylene chloride and was moderately soluble in ethanol. It gave an apple-green color with ferric chloride–alcohol.

Anal. Calcd. for $C_{25}H_{27}O_5(CH_3CO)$: C, 71.98; H, 6.71; CH_3CO, 2.22 cc. 0.1 *N* NaOH per 100 mg.; mol. wt., 450.5. Found: C, 71.96; H, 6.68; CH_3CO, 2.21 cc.; mol. wt. (Rast), 395, 370.

Tetrahydro-osajin was recovered from the acetyl[6] analysis by pouring the alcoholic solution into a large excess of water, removing the separated solid by filtration, and recrystallizing from benzene–petroleum ether (identification by m. p. and mixed m. p.).

Tetrahydro-osajin Diacetate.—Tetrahydro-osajin (0.30 g.) was acetylated with acetic anhydride and sodium acetate as described for the preparation of dihydro-osajin diacetate. The substance crystallized from 95% ethanol as colorless needles; yield 0.21 g. of m. p. 186°, unchanged on further crystallization from methanol. It gave no color with ferric chloride–alcohol.

Anal. Calcd. for $C_{25}H_{26}O_5(CH_3CO)_2$: C, 70.71; H, 6.55; CH_3CO, 4.06 cc. 0.1 *N* NaOH per 100 mg.; mol. wt., 492.6. Found: C, 70.89; H, 6.47; CH_3CO, 4.00 cc.; mol. wt. (Rast), 450.

This substance also was obtained by similar treatment of tetrahydro-osajin monoacetate (identification by m. p. and mixed m. p.). Tetrahydro-osajin was recovered from the acetyl analysis (identification by m. p. and mixed m. p.).

Hexahydro-osajin.[7]—This substance was prepared by the reduction of osajin (1.5 g.) with an active catalyst as described for the preparation of dihydro-osajin but allowing the hydrogenation to proceed until 3 mols of hydrogen (250 cc., S. T. P.) were absorbed. This required about three hours. It was isolated in the same manner and was purified by crystallization from methanol–water and benzene–petroleum ether; yield 1.0 g. of m. p. 162°.

The substance crystallized in the form of pale yellow needles. When impure, it crystallized with difficulty. It was water-insoluble but was soluble in the common organic solvents except low-boiling petroleum ether. It gave a dark dull-green color with ferric chloride–alcohol, turning to a dull wine-red color with ammonium hydroxide. In acetic acid solution, it gave an immediate yellow color on the addition of a few drops of concentrated sulfuric acid. In pyridine solution it reduced Tollens reagent. The compound was recovered unchanged on refluxing with either a pyridine or an alcoholic solution of hydroxylamine for two hours.

Anal. Calcd. for $C_{25}H_{30}O_5$: C, 73.15; H, 7.37; mol. wt., 410.5. Found: C, 73.16; H, 7.30; mol. wt. (Rast), 380.

(7) Preliminary experimental work by Mr. W. W. Hess.

The substance absorbed one equivalent of alkali when titrated directly in acetone solution according to the procedure described for osajin.[1a] This behavior is identical with that observed for osajin and accordingly no acid groups were formed in the reduction.

Hexahydro-osajin was obtained on further hydrogenation of tetrahydro-osajin (identification by m. p. and mixed m. p.).

Hexahydro-osajin Monoacetate.—This substance was prepared from hexahydro-osajin (0.50 g.) as described for the preparation of dihydro-osajin monoacetate and was purified by crystallization from 95% ethanol; yield 0.45 g., m. p. 138°, unchanged on recrystallization from benzene–petroleum ether.

The substance crystallized in radiating clusters of needles possessing a slight yellow tinge and was soluble in the common solvents except water and petroleum ether. It gave an apple-green color with ferric chloride–alcohol.

Anal. Calcd. for $C_{25}H_{29}O_5(CH_3CO)$: C, 71.66; H, 7.13; CH_3CO, 2.21 cc. 0.1 *N* NaOH per 100 mg.; mol. wt., 452.5. Found: C, 71.57; H, 7.03; CH_3CO, 2.28 cc.; mol. wt. (Rast), 390.

Hexahydro-osajin was recovered from the acetyl analysis (identification by m. p. and mixed m. p.).

Hexahydro-osajin Diacetate.—This substance was prepared from hexahydro-osajin (0.20 g.) as described for the synthesis of dihydro-osajin diacetate and was purified by crystallization from 95% ethanol; yield 0.17 g., m. p. 190°, unchanged on crystallization from benzene–petroleum ether, mixed m. p. with tetrahydro-osajin diacetate (m. p. 186°) 170–174°.

The substance crystallized in radiating clusters of fine, colorless needles. Its solubilities were similar to those of hexahydro-osajin monoacetate. It gave no color with ferric chloride–alcohol.

Anal. Calcd. for $C_{25}H_{28}O_5(CH_3CO)_2$: C, 70.44; H, 6.93; CH_3CO, 4.04 cc. 0.1 *N* NaOH per 100 mg.; mol. wt., 494.6. Found: C, 70.39; H, 6.82; CH_3CO, 4.01 cc.; mol. wt. (Rast), 450.

This substance also was obtained by similar treatment of hexahydro-osajin monoacetate (identification by m. p. and mixed m. p.). Hexahydro-osajin was recovered from the acetyl analysis (identification by m. p. and mixed m. p.).

Dihydropomiferin.[8]—This substance was prepared from pomiferin (2 g.) as described for the preparation of dihydro-osajin. It was purified by crystallization from propylene chloride, trichloroethylene and from ethanol–water; yield 1.3 g. of m. p. 212°.

The substance crystallized from ethanol–water as fine, lustrous, light yellow needles. It was very soluble in acetone, methanol and ethanol; moderately so in benzene and propylene chloride; and was insoluble in water. It gave an apple-green color with ferric chloride–alcohol, turning deep violet with ammonia. The compound gave an orange color with acetic acid–sulfuric acid.

Anal. Calcd. for $C_{25}H_{26}O_6$: C, 71.07; H, 6.20; mol. wt., 422.5. Found: C, 70.75; H, 6.10; mol. wt. (Rast), 390.

The substance consumed less than one equivalent of alkali when titrated directly in acetone solution according to the procedure described for osajin.[1a] This behavior is identical with that observed for pomiferin.

Dihydropomiferin Diacetate.—Dihydropomiferin (0.50 g.) was acetylated as described for the preparation of dihydro-osajin monoacetate and the product was purified from 95% ethanol; yield 0.50 g. of m. p. 166°, unchanged on crystallization from benzene–petroleum ether.

The compound formed long, silky needles of a slight yellow tint. It was readily soluble in acetone, benzene and chloroform; moderately so in 95% ethanol and carbon tetrachloride; practically insoluble in water and petroleum ether. The substance gave an apple-green color with ferric chloride–alcohol. It gave a deep yellow color with acetic acid–sulfuric acid.

Anal. Calcd. for $C_{25}H_{24}O_6(CH_3CO)_2$: C, 68.77; H, 5.97; CH_3CO, 3.95 cc. 0.1 *N* NaOH per 100 mg.; mol. wt., 506.5. Found: C, 68.80; H, 5.90; CH_3CO, 3.91 cc.; mol. wt. (Rast), 450.

Dihydropomiferin Triacetate.—Dihydropomiferin (0.60 g.) was acetylated as described for the preparation of dihydro-osajin diacetate and the product was purified from 95% ethanol and from methanol; yield 0.59 g. of m. p. 165.5°, unchanged on crystallization from benzene–petroleum ether, mixed m. p. with dihydropomiferin diacetate (m. p. 166°) 142–149°.

The substance crystallized from methanol as glistening plates and from benzene–petroleum ether as clusters of radiating needles. It was very soluble in benzene; moderately so in acetone, ethanol and methanol; practically insoluble in water and petroleum ether. It gave no color with ferric chloride–alcohol.

Anal. Calcd. for $C_{25}H_{23}O_6(CH_3CO)_3$: C, 67.84; H, 5.88; CH_3CO, 5.47 cc. 0.1 *N* NaOH per 100 mg.; mol. wt., 548.6. Found: C, 68.06; H, 5.85; CH_3CO, 5.41 cc.; mol. wt. (Rast), 520.

This substance also was produced by similar treatment of dihydropomiferin diacetate (identification by m. p. and mixed m. p.).

Tetrahydropomiferin.—This substance was prepared from pomiferin (1 g.) as described for the preparation of tetrahydro-osajin and the product was purified by crystallization from trichloroethylene–petroleum ether; yield 0.91 g. of m. p. 201.5°, unchanged on crystallization from 95% ethanol or benzene–petroleum ether.

The substance crystallized from trichloroethylene–petroleum ether as yellow plates. Its solubilities and properties were similar to those of dihydropomiferin. The substance was recovered unchanged on refluxing with a pyridine solution of hydroxylamine hydrochloride for four hours.

Anal. Calcd. for $C_{25}H_{28}O_6$: C, 70.71; H, 6.65; mol. wt., 424.5. Found: C, 70.71; H, 6.57; mol. wt. (Rast), 380.

The substance consumed less than one equivalent of alkali when titrated directly in acetone solution according to the procedure described for osajin.[1a] This behavior is identical with that observed for pomiferin. Tetrahydropomiferin also was obtained by further hydrogenation of dihydropomiferin (identification by m. p. and mixed m. p.).

Tetrahydropomiferin Diacetate.—Tetrahydropomiferin (0.35 g.) was acetylated as described for the preparation of

(8) Preliminary experimental work by Mr. F. L. Benton.

dihydro-osajin monoacetate and the product was purified from methanol; yield 0.35 g. of m. p. 154.5°, unchanged on crystallization from 95% ethanol or benzene–petroleum ether.

The compound crystallized from methanol as very long, radiating needles of a slight yellow tinge. Its solubilities and properties were similar to those of dihydropomiferin diacetate.

Anal. Calcd. for $C_{25}H_{26}O_6(CH_3CO)_2$: C, 68.49; H, 6.34; CH_3CO, 3.93 cc. 0.1 *N* NaOH per 100 mg.; mol. wt., 508.6. Found: C, 68.65; H, 6.41; CH_3CO, 3.96 cc.; mol. wt. (Rast), 500, 480.

Tetrahydropomiferin was recovered from the acetyl analysis (identification by m. p. and mixed m. p.).

Tetrahydropomiferin Triacetate.—Tetrahydropomiferin (0.50 g.) was acetylated as described for the preparation of dihydro-osajin diacetate and the product was purified from 95% ethanol; yield 0.62 g. of m. p. 181.5°, unchanged on crystallization from propylene chloride–petroleum ether or benzene–petroleum ether.

The compound crystallized from 95% ethanol as fine, colorless needles. Its solubilities and properties were similar to those of dihydropomiferin triacetate.

Anal. Calcd. for $C_{25}H_{25}O_6(CH_3CO)_3$: C, 67.62; H, 6.22; CH_3CO, 5.45 cc. 0.1 *N* NaOH per 100 mg.; mol. wt., 550.6. Found: C, 67.56; H, 6.15; CH_3CO, 5.38 cc.; mol. wt., 540, 490.

This substance was produced by similar treatment of tetrahydropomiferin diacetate and also was obtained by reduction of pomiferin triacetate[1b] (identifications by m. p. and mixed m. p.). Tetrahydropomiferin was recovered from the acetyl analysis (identification by m. p. and mixed m. p.).

Maleic Anhydride Treatment of Osajin and Pomiferin.—Osajin (0.30 g.) was recovered unchanged (0.20 g., identification by m. p. and mixed m. p.) on refluxing for two hours in xylene (20 cc.) containing 0.7 g. of maleic anhydride. Similar results were obtained with pomiferin.

Flavone and Flavanone Color Tests.—The substance to be tested[9] (10 mg.) was dissolved in 3 cc. of 95% ethanol, a small drop of mercury and 5 drops of concentrated hydrochloric acid were then introduced and the mixture heated to 40° and maintained at that temperature. Powdered magnesium was then added and from time to time more powdered magnesium and a few drops more of hydrochloric acid were added in order to maintain a constant evolution of hydrogen. A quercitin control gave a cherry-red coloration in ten minutes. No colorations were developed in five hours time by osajin, tetrahydro-osajin, pomiferin and tetrahydropomiferin. Hexahydro-osajin, however, developed on orange color in twenty minutes. This color deepened to a reddish-orange in one hour and when observed at five hours, the color was a dark cherry-red.

The sodium amalgam reductions were performed according to the general directions of Asahina and co-workers.[3] The substance (10 mg.) to be tested was dissolved in 3 cc. of 95% ethanol and the air displaced with nitrogen. Sodium amalgam (3%) was added and the tube stoppered. Standing at room temperature for ten hours or heating at 40° for two hours gave the same results. At the end of this treatment, the solution was decanted quickly from the excess amalgam and acidified with an excess of concentrated hydrochloric acid. The colored precipitates obtained were formed on dilution with water. Sodium chloride sometimes separated but redissolved on dilution. The results obtained are tabulated in Table III and indicate that osajin, pomiferin and their tetrahydro compounds possess the flavone structure and that hexahydro-osajin has the flavanone structure.

(9) *Cf.* R. Willstätter, *Ber.*, **47**, 2874 (1914).

TABLE I

DEGREE OF UNSATURATION OF OSAJIN AND POMIFERIN AS DETERMINED BY PERBENZOIC ACID TITRATION[a]

Substance	No. double bonds 2 hr.	24 hr.
Osajin diacetate	1.48	2.13
Dihydro-osajin diacetate	1.16	1.52
Tetrahydro-osajin diacetate	0.21	0.33
Hexahydro-osajin diacetate	.14	.60
Pomiferin triacetate	1.56	2.20
Dihydropomiferin triacetate	1.14	1.33
Tetrahydropomiferin triacetate	0.23	0.21

[a] Experimental work by Mr. F. L. Benton.

TABLE II

BORIC ACID COLOR REACTION (ACCORDING TO WILSON[2]) OF OSAJIN, POMIFERIN AND THEIR HYDRO COMPOUNDS[a]

Substance	Nature of test	Time for initiation of yellow color, min.
Quercitin	+	Immediate
Osajin	+	2
Dihydro-osajin	+	3
Tetrahydro-osajin	+	3
Hexahydro-osajin	−	
Pomiferin	+	2
Dihydropomiferin	+	3
Tetrahydropomiferin	+	3

[a] Experimental work by Mr. J. E. Mahan.

TABLE III

SODIUM AMALGAM REDUCTION OF OSAJIN, POMIFERIN AND THEIR HYDRO COMPOUNDS

Substance	Color of final HCl soln.	Color of ppt.
Osajin	Bright red	Dark red
Tetrahydro-osajin	Reddish-orange	Rust
Hexahydro-osajin	Reddish-orange	Brick-red
Pomiferin	Dark red	Purple
Tetrahydropomiferin	Cherry-red	Purple

We are indebted to Mr. John Walker (W. P. A. Project 18062) for assistance rendered in the analytical determinations and to Messrs. E. J. Penka and J. H. Tracht (N. Y. A. Project O. S. U. 181) for assistance in preparing the plant material.

Summary

1. Osajin has been hydrogenated stepwise to produce a dihydro, tetrahydro and hexahydro derivative, each of which has been characterized as a monoacetate and diacetate.

2. Pomiferin has been hydrogenated stepwise to produce a dihydro and a tetrahydro derivative,

each of which has been characterized as a diacetate and triacetate.

3. Perbenzoic acid titrations and non-reactivity with maleic anhydride indicate the presence of two non-conjugated, active double bonds in both osajin and pomiferin.

4. By a combination of the Wilson boric acid color reaction and the Asahina reduction tests, it is shown that a flavanone structure for hexahydro-osajin and a flavone structure for osajin and pomiferin are probable.

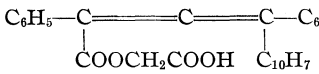
COLUMBUS, OHIO RECEIVED APRIL 8, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF HARVARD UNIVERSITY]

Optically Active α,γ-Diphenyl-α-carbomethoxy-γ-naphthylallene

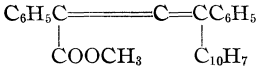
BY ELMER P. KOHLER AND WENDELL J. WHITCHER[1]

The glycolic acid ester of α,γ-diphenyl-γ-naphthylallene carboxylic acid (I) was recently



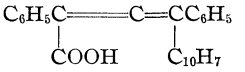
(I)

resolved in this Laboratory,[2] and we now describe the preparation and behavior of the optically active forms of the corresponding allenic methyl ester (II).



(II)

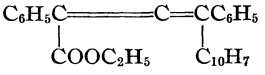
The solid inactive glycolic acid ester (I), with diazomethane, yielded its methyl derivative, but the active forms of (I), on similar treatment, or when subjected to hydrolysis in the attempt to prepare active forms of the simple allenic acid (III), gave only oily products.



(III)

The optically active methyl esters of the simple allenic acid (II), however, were synthesized by at least two of the following methods: (1) the active glycolic acid ester (I) was hydrolyzed by a large excess of alcoholic potassium hydroxide, the active form of the simple allenic acid (III) was converted into the silver salt, and the latter, with methyl iodide, to the active methyl ester (II); (2) the active allenic acid (III), prepared by the hydrolysis of active (I), was treated with diazomethane and yielded the active methyl ester (II); and (3) the active glycolic acid ester (I) was converted to the active methyl ester (II) by absolute methyl alcoholic potassium hydroxide.

A study of the formation of the active and inactive methyl esters (II) by the third method, as well as the rapid conversion of the inactive glycolic acid ester (I) to the inactive ethyl ester (IV)

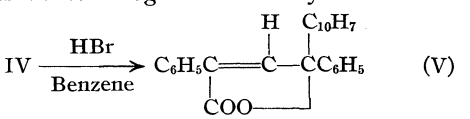


(IV)

by ethyl alcoholic potassium hydroxide, indicated that the reaction proceeded by ester interchange. The pure methyl esters (II) were obtained in yields increasing with the amount of potassium hydroxide used up to two equivalents. With 1.1 mole of potassium hydroxide (0.08 *M*), during one hour, 62% yield of methyl ester was obtained, but 80% was obtained with two moles (0.25 *M*) during a quarter hour. The sign of rotation of each optically active ester was the same as that of the parent glycolic ester no matter which method of transformation was employed.

That these enantiomeric methyl esters retained the allenic system was demonstrated by dissolving together equimolecular quantities of each in ether, and isolating from the solution only an inactive ester which proved to be identical with the inactive methyl ester (II) prepared by a method leaving no doubt as to its structure.[2]

Solutions of the active forms of the glycolic acid ester (I) and of the methyl ester (II) in benzene and in ethyl acetate remained optically active during long periods when kept in the dark, but on exposure to sunlight for a few days the solution developed a yellow color, became inactive, and the inactive form of (I) or (II) (50–60% yield) was isolated together with a yellow resin.



(V)

It has been shown that the inactive ethyl ester (IV) with hydrogen bromide in benzene solution yields the crotono lactone[3] (V).

(1) The experimental work described in this manuscript was completed before the death of Professor Kohler. The present manuscript has been prepared since that time by the junior author.

(2) Kohler, Walker and Tishler, THIS JOURNAL, **57**, 1743 (1935).

(3) Unpublished work of Dr. Max Tishler.

Whereas analogous treatment of the active methyl esters (II) seemingly offered an unprecedented opportunity for the conversion of a molecule with asymmetry due to its structure as a whole into one in which asymmetry is dependent upon a particular carbon atom, the dextro methyl ester, when subjected to this treatment, underwent ring closure as expected, but with complete loss of activity, and only the inactive form of the crotono lactone could be isolated.

Experimental Part

The Methyl Ester of the Glycolic Acid Ester, $C_6H_5C(COOCH_2COOCH_3)=C=C(C_{10}H_7)C_6H_5$.—An ether solution of 2.0 g. of inactive glycolic acid ester (I) was treated with enough diazomethane to esterify 1.2 g. Excess acid ester was removed by sodium bicarbonate extraction and 0.92 g. of crystalline methyl ester was recovered, m. p. 113°.

Anal. Calcd. for $C_{29}H_{22}O_4$: C, 80.16; H, 5.11. Found: C, 80.28; H, 5.32.

Active Methyl Esters of α,γ-Diphenyl-γ-naphthylallene Carboxylic Acid (II). (1) By Way of the Silver Salt.—Hydrolysis of 0.5 g. of levo glycolic acid ester (I) was carried out with excess alcoholic potassium hydroxide. The alcoholic solution was diluted with water, acidified with nitric acid and extracted with ether, from which extract any glycolic acid or unhydrolyzed acid ester was removed by aqueous sodium bicarbonate. The levo allenic acid (III) was taken up in aqueous sodium hydroxide and converted into the silver salt in the manner previously employed[2] in the case of the inactive acid. Boiling the salt with excess methyl iodide in ether led to isolation of 0.16 g. of levo methyl ester (II), m. p. 91°, $[\alpha]_D$ −49.8° in benzene at 25°.

Anal. Calcd. for $C_{27}H_{20}O_2$: C, 86.14; H, 5.36. Found: C, 86.14; H, 5.62.

(2) **By Means of Diazomethane.**—An ether solution of the active form of (III) prepared as above from 0.5 g. of the levo glycolic acid ester (I) when dried and treated with an equivalent quantity of diazomethane deposited 0.1 g. of levo methyl ester (II).

(3) **By Action of Potassium Hydroxide in Methyl Alcohol.**—A solution of 1.32 g. of dextro glycolic acid ester (I) in 25 cc. of a 0.25 *M* solution of potassium hydroxide in absolute methyl alcohol was boiled for fifteen minutes, poured into water and the aqueous solution extracted with ether. Ether and petroleum ether deposited 0.94 g. of the dextro methyl ester, m. p. 91°, $[\alpha]_D$ +49.3° in benzene at 25°.

Conversion of Active Ester to Crotono Lactone (V).—When 0.159 g. of the dextro methyl ester (II) was dissolved in 10 cc. of benzene containing 0.085 g. of hydrogen bromide, the rotation fell rapidly, practically disappearing in twenty minutes. From this solution was recovered 0.10 g. of the crotono lactone (V), m. p. 189°, readily identified by comparison with an authentic sample. A series of such conversions indicated that the rate and extent of lactone formation was dependent on the initial concentration of the hydrogen bromide.

Summary

Although the enantiomeric forms of α,γ-diphenyl-γ-naphthyl-allene carboxylic acid have not been obtained in the solid state, the crystalline methyl esters of this acid have been obtained from the active forms of its glycolic acid ester by three methods: (a) hydrolysis and subsequent treatment with diazomethane, (b) hydrolysis, formation of the silver salt of the acid, and subsequent reaction with methyl iodide, and (c) ester interchange in methyl alcoholic potassium hydroxide.

Whereas acids rapidly isomerize the above acid and its alkyl esters to a crotono lactone with one asymmetric carbon atom, the coversion of the active methyl esters to this lactone by hydrogen bromide in benzene was accompanied by loss of optical activity.

CAMBRIDGE, MASS. RECEIVED MARCH 18, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY AND CHEMICAL ENGINEERING OF THE STATE COLLEGE OF WASHINGTON]

Binary Liquid Systems. II. The Azeotropic Composition of Carbon Tetrachloride–Ethyl Acetate Mixtures as a Function of the Pressure

BY PHILIP W. SCHUTZ AND ROBERT E. MALLONEE

In the first article[1] of this series it was pointed out that, judging from the then existing values for the composition of the azeotrope formed by carbon tetrachloride–ethyl acetate mixtures at different pressures, it appeared that this system was unique since the rate of change of the azeotropic composition with pressure decreased as the pressure decreased.

The rapid change in composition with pressure at higher pressures evidenced by these data would indicate that in the vicinity of 900 mm. a complete separation of these compounds by ordinary fractional distillation would be possible (see curve 1, Fig. 1). As the data were so few in number and the phenomenon an entirely new one, the present work was undertaken in order to obtain a complete set of data over a wider pressure range.

Experimental

The materials and apparatus were identical with those previously described[1] except that a pressure regulator was incorporated, which, with careful operation, controlled the pressure within ±0.3 mm. All runs were made as described earlier. As we were interested only in the composition of the azeotrope and since the quantities of materials were limited, we did not cover the entire range of compositions at any pressure other than 685 mm. The azeotropic composition was determined at each pressure by means of the x–y diagram familiar in the analysis of distillation problems. The composition of the liquid (x) was plotted against that of the vapor (y), both in terms of the same constituent. A forty-five degree line on such a plot represents vapors and liquids of the same composition. The intersection of the curve through the points representing equilibrium compositions of the vapor and liquid on either side of the azeotrope with this forty-five degree line represents the azeotropic composition at the pressure under which the data were obtained. At each pressure, three or more vapor–liquid equilibrium compositions were determined on each side of the azeotropic composition. In every case the intersection was at such an angle as to lead to no uncertainty as to the azeotropic composition. All analyses were made by refractive index ($n^{20}D$) and all compositions are believed accurate to well within ±0.1 mole %.

Discussion of Results

The data obtained are given in Table I and plotted as composition *vs.* pressure in curve 2, Fig. 1. It is apparent from this curve that the rate of change of composition of the azeotrope formed by this system with pressure is increasing as the pressure is decreased. This result is in accord with all available data of a similar nature on other systems. It is also apparent that the present results are not in very good agreement with the three earlier values, indicated by curve 1 of Fig. 1, and we are unable to explain the large discrepancies at the present time. The value of 43 mole per cent. at 760 mm. given by Young[2] and by Lecat[3] has been widely quoted, but it is impossible

TABLE I

AZEOTROPIC DATA AT DIFFERENT PRESSURES

P, mm.	B. p., °C.	Mole % CCl_4
789.2	76.15	55.60
583.7	66.72	60.75
484.5	61.32	63.75
385.2	55.22	67.75
285.7	47.36	72.60

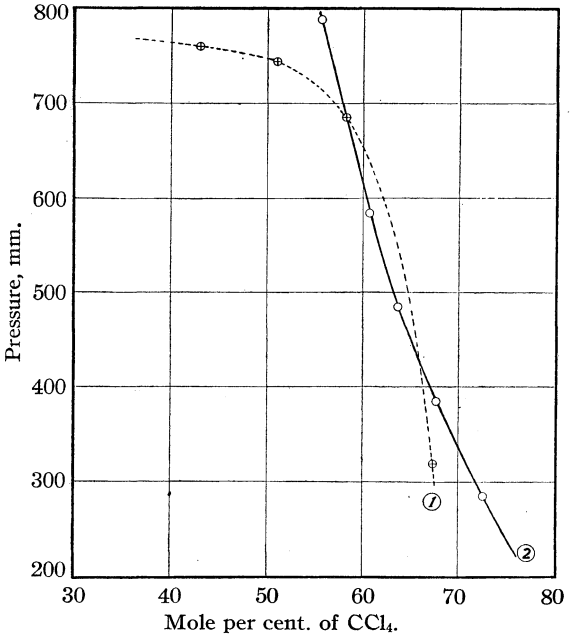


Fig. 1.—Change in composition of the azeotrope formed by the system carbon tetrachloride–ethyl acetate with pressure: 1, plot of data from Reference 1; 2, plot of data from Table I.

(1) THIS JOURNAL, **61**, 2691 (1939).

(2) Young, "Distillation Principles and Processes," Macmillan and Company, London, 1922, p. 52.

(3) Lecat, "l'Azeotropisme," Lamertin, Brussels, 1918, p. 136.

to find the original work in which this value was determined. Young records this value as 57 weight % of carbon tetrachloride. If by chance this should have been 57 mole per cent, the latter value agrees quite well with our results.

Conclusions

1. Data have been presented which show that the system carbon tetrachloride–ethyl acetate behaves in the same manner when subjected to pressure change as do all other systems for which similar data are available. The concentration of carbon tetrachloride in the azeotrope increases as the pressure decreases.

PULLMAN, WASH. RECEIVED MARCH 5, 1940

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY OF THE INSTITUTE OF TECHNOLOGY OF THE UNIVERSITY OF MINNESOTA]

Crystal-Chemical Studies of the Alums. I. Solid Solutions of Potassium Aluminum Alum and Ammonium Aluminum Alum

BY HAROLD P. KLUG AND LEROY ALEXANDER

Solid solution formation by potassium aluminum alum and ammonium aluminum alum was first observed by Krickmeyer,[1] who proved the existence of a continuous series of solid solutions by density measurements. More recently Hill and Kaplan[2] have studied this pair of alums and made analyses of the conjugate liquid and solid solutions. It was noted that the tie-lines pass through the water apex of the ternary diagram, indicating that the ratio of the two alums is the same in the aqueous phase as in the solid phase. The data when plotted with respect to these two ratios fall nearly upon the true diagonal, giving what Hill and Kaplan regarded as an ideal example of Roozeboom's class 1.[3] This appears to be the first example of this type to be noted. In such a case the deviation of the two phases from the properties of ideal solutions, whatever they are, are quantitatively similar.

It seemed of interest to investigate this series of solid solutions further by means of X-ray diffraction to determine whether they were ideal from the standpoint of Vegard's law,[4] which states that for two compounds of the same crystal structure, forming a continuous series of solid solutions, the lattice constants of the solid solutions are a linear function of the composition. The results of such a study are reported in this communication.

Experimental

The materials used were reagent grade alums each of which was recrystallized from conductivity water slightly acidified with sulfuric acid. To produce fine crystals the solutions were shaken vigorously during crystallization. The crystals were washed successively with water, alcohol, and ether, and then air dried overnight. Analyses of these alums for aluminum by precipitation with *o*-hydroxyquinoline, according to the method of Kolthoff and Sandell,[5] were in excellent agreement with the theoretical composition.

The preparation of the solid solutions followed that of Hill and Kaplan[2] each complex being made up in duplicate so that the final equilibrium solid solution was formed in one case (A) from the potassium alum and in the duplicate case (B) from the ammonium alum. The stoppered bottles containing the complexes were turned in a thermostat at 25 ± 0.1° until equilibrium was attained. Contrary to the observations of Hill and Kaplan, equilibrium was reached much more slowly under the conditions of this experiment. It was necessary to introduce four lengths of 8 mm. Pyrex glass rod into each bottle, thereby producing a miniature rod-mill effect, to prevent the crystals from becoming too coarse. Even under these conditions attainment of complete equilibrium required four months. The crystals of the equilibrium solid solution were filtered off with suction, washed successively with alcohol and ether, and air-dried.

The compositions of the solid solutions were determined by analyzing for ammonia by titrating with calcium hypochlorite solution according to the procedure of Kolthoff and Sandell.[5] This method proved to be much more accurate than the usual Kjeldahl method. From the ammonia content the amount of ammonium alum present was calculated, and the potassium alum determined by difference.

Using a Buerger powder camera[6] of 57.3 mm. radius, precision determinations of the lattice constants of the pure alums and their solid solutions were made at 25°. FeK radiation was used with the films in the asymmetric position,[7] and the camera was thermostated as described by Straumanis and co-workers.[8] For control of the air thermostat a hollow cylindrical mercury regulator[9] was

(1) Krickmeyer, *Z. physik. Chem.*, **21**, 53 (1896).
(2) Hill and Kaplan, THIS JOURNAL, **60**, 550 (1938).
(3) Roozeboom, *Z. physik. Chem.*, **8**, 504 (1891).
(4) Vegard, *Z. Physik*, **5**, 17 (1921).
(5) Kolthoff and Sandell, "Textbook of Quantitative Inorganic Analysis," The Macmillan Company, New York, N. Y., 1936.
(6) Buerger, *Am. Mineralogist*, **21**, 11 (1936).
(7) Ievins and Straumanis, *Z. Krist.*, **94**, 40 (1936).
(8) Straumanis, Ievins and Karlsons, *Z. anorg. allgem. Chem.*, **238**, 175 (1938).
(9) Heisig and Cameron, *Ind. Eng. Chem., Anal. Ed.*, **5**, 420 (1933).

used with a vacuum tube relay circuit. The temperature within the thermostat could be kept constant at 25 ± 0.2°, and the variation in sample temperature was probably considerably less than this.

The sample consisted of 200-mesh powder stuck on the outside of a fine Pyrex glass capillary tube with an adhesive such as glyptal varnish.

Diffraction lines on the films were measured to ±0.02 mm. Then, using only lines with angle θ greater than 60°, the lattice constants were calculated by Cohen's analytical method.[10]

Results

In Table I are the compositions of the pure alums and their solid solutions, and their lattice contants at 25°. The criterion for the attainment of equilibrium in the solid solutions was the close agreement in composition for the two members of a pair, each of which had approached equilibrium from opposite directions.

TABLE I

COMPOSITION AND LATTICE CONSTANTS FOR POTASSIUM ALUM AND AMMONIUM ALUM AND THEIR SOLID SOLUTIONS

Substance	Wt. % NH_3 (by analysis)	Mole % $NH_4Al(SO_4)_2 \cdot 12H_2O$	Lattice constant in Å. at 25 ± 0.1°
$KAl(SO_4)_2 \cdot 12H_2O$	0.00	0.00	12.1328
S. S. 1A	1.036	28.52	12.1537
S. S. 1B	1.039		12.1527
S. S. 2A	1.904	51.76	12.1717
S. S. 2B	1.900		12.1722
S. S. 3A	2.770	74.57	12.1926
S. S. 3B	2.767		12.1923
$NH_4Al(SO_4)_2 \cdot 12H_2O$	3.750	100.0	12.2136

The results are presented graphically in Fig. 1. A straight line has been drawn through the points representing the lattice constants of the pure alums. It is seen that the deviations from Vegard's additivity law are extremely small. The deviations are, however, believed to be real, and the pair can be said to be not quite ideal from the standpoint of their solid solutions and Vegard's law.

(10) Cohen, *Rev. Sci. Instruments*, **6**, 68 (1935); **7**, 155 (1936).

The values of the lattice constants reported above are believed to be accurate to ±0.001 Å. In the case of the pure alums the values may be compared with those of Lipson and Beevers,[11] who report for $KAl(SO_4)_2 \cdot 12H_2O$, 12.133 Å., and for $NH_4Al(SO_4)_2 \cdot 12H_2O$, 12.215 Å., each with an accuracy of ±0.002 Å., but with no indication of the temperature of their observations.

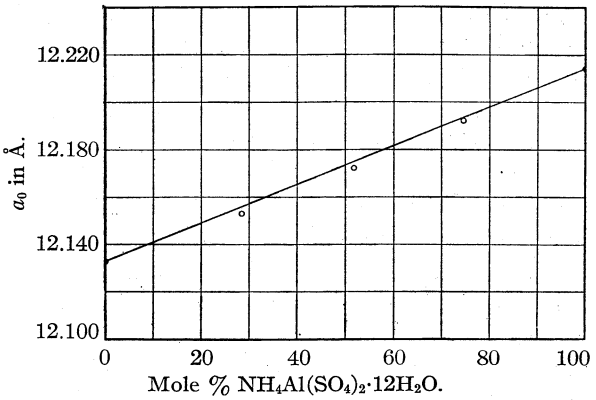


Fig. 1.—Lattice constants as a function of composition for solid solutions of potassium and ammonium alums.

The authors are indebted to G. B. Heisig for the loan of the vacuum tube relay. They also wish to acknowledge gratefully a grant from the Graduate School of the University of Minnesota which made this study possible.

Summary

1. The solid solutions of potassium aluminum alum and ammonium aluminum alum have been studied by means of X-rays and found to deviate slightly from Vegard's law of additivity.

2. The following values are reported for the lattice constants of the pure alums at 25 ± 0.1°:

$KAl(SO_4)_2 \cdot 12H_2O$ $a_0 = 12.133 \pm 0.001$ Å.

$NH_4Al(SO_4)_2 \cdot 12H_2O$ $a_0 = 12.214 \pm 0.001$ Å.

MINNEAPOLIS, MINNESOTA RECEIVED APRIL 12, 1940

(11) Lipson and Beevers, *Proc. Roy. Soc.* (London), **A148**, 664 (1935).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF SOUTH DAKOTA STATE COLLEGE AND THE SCHOOL OF CHEMISTRY OF THE INSTITUTE OF TECHNOLOGY OF THE UNIVERSITY OF MINNESOTA]

The Distribution of Protons between Water and Other Solvents

BY L. S. GUSS AND I. M. KOLTHOFF

In a study of acid–base indicator equilibria in methanol[1] buffer solutions, it was found that traces of water have a negligible effect upon the equilibrium of the system, unless the water reacts with the indicator itself.[2] In unbuffered solutions of strong acids in alcohols, traces of water have a pronounced effect upon the color equilibrium of an indicator since water is a much stronger base than the alcohols.

Qualitatively, the effect of the addition of water to alcoholic solutions of strong acids is comparable to the effect of ammonia added to aqueous solutions of strong acids. In the present paper, the effect of traces of water added to a dilute solution of a strong acid in an alcohol, ROH, has been studied quantitatively with the aid of a suitable acid–base indicator. In anhydrous alcoholic solution, the strong acid is assumed to be completely ionized into alcoxonium ions, ROH_2^+ and anions. Upon addition of traces of water, the protons distribute themselves between the alcohol and water molecules according to the equation

$$ROH + H_3O^+ \rightleftharpoons ROH_2^+ + H_2O$$

The equilibrium of this reaction is given by

$$K_p = \frac{a_{ROH_2^+} a_{H_2O}}{a_{H_3O^+}}$$

At very small ionic strengths, the activity coefficients of the ROH_2^+ and H_3O^+ ions may be taken equal. When the concentration of the water is very small, the activity of the water may be written equal to the concentration. Hence, under the specified conditions we may write

$$K_p = \frac{c_{ROH_2^+} c_{H_2O}}{c_{H_3O^+}} \qquad (1)$$

The equilibrium between the acid and alkaline forms, I_a and I_b, of an indicator in alcoholic medium is given by the expression

$$\frac{a_{I_b}}{a_{I_a}} = \frac{K_I}{a_{ROH_2^+}}$$

or

$$r = \frac{c_{I_b}}{c_{I_a}} = \frac{K_I}{c_{ROH_2^+}} \frac{f_{I_a}}{f_{I_b} f_{ROH_2^+}} \qquad (2)$$

If c is the concentration of the strong acid in the alcohol and c_{H_2O} the concentration of the water added, we have

$$c_{H_3O^+} + c_{ROH_2^+} = c \qquad (3)$$

From this and equation (1), it is derived that in the water-containing alcoholic solution

$$c_{ROH_2^+} = \frac{K_p c}{c_{H_2O} + K_p} \qquad (4)$$

Introducing this expression in equation (2), we find that

$$r = \frac{c_{I_b}}{c_{I_a}} = \frac{K_I}{c} \left[\frac{c_{H_2O}}{K_p} + 1 \right] \frac{f_{I_a}}{f_{I_b} f_{ROH_2^+}} \qquad (5)$$

If we use a simple indicator base, such as methyl yellow, I_a is a positively charged univalent ion. It has been shown[3] that in such a case f_{I_a} can be taken equal to $f_{ROH_2^+}$ at small ionic strengths. Since I_{I_b} is a neutral molecule we then have, instead of (5)

$$r = \frac{c_{I_b}}{c_{I_a}} = \frac{K_I}{c} \left[\frac{c_{H_2O}}{K_p} + 1 \right] \qquad (6)$$

By plotting values of the indicator color ratio, r, against water concentration, the intercept is K_I/c and the slope, K_I/cK_p, leads to the evaluation of K_p. Since $C_{H_3O^+}$ is negligible, compared with C_{H_2O}, the latter may be taken equal to the concentration of water added.

By studying the change in conductivity of hydrochloric acid solutions on the addition of traces of water, Goldschmidt and co-workers obtained the values of K_p of 0.0583 in ethanol[4] and of 0.235 in methanol.[5] These values are substantiated in this investigation and the method is extended to the solvent *n*-butanol.

Materials.—Methanol and ethanol were purified by methods already described,[1,6] the final product having less than 0.01% of water as estimated from density measurements. *n*-Butanol was dehydrated with aluminum amalgam[7] and distilled from anhydrous copper sulfate. Its density (d^{25}_4) measured with a 100 ml. pycnometer was found to be 0.80579. Methyl yellow was recrystallized from a water–methanol solution.

Dry hydrogen chloride was prepared by dropping concentrated sulfuric acid into concentrated hydrochloric acid, passing the gas through a wash bottle of concentrated sulfuric acid, then through a plug of glass wool. It was

(1) I. M. Kolthoff and L. S. Guss, THIS JOURNAL, **60**, 2516 (1938).
(2) I. M. Kolthoff and L. S. Guss, *ibid.*, **61**, 16 (1939).
(3) I. M. Kolthoff and L. S. Guss, *ibid.*, **61**, 330 (1939).
(4) H. Goldschmidt, *Z. physik. Chem.*, **89**, 129 (1914).
(5) H. Goldschmidt and P. Dahll, *ibid.*, **108**, 121 (1924).
(6) L. S. Guss and I. M. Kolthoff, THIS JOURNAL, **62**, 249 (1940).
(7) P. Walden, H. Ulich and F. Laun, *Z. physik. Chem.*, **114**, 275 (1925).

finally washed in the solvent to be used. Such solutions were prepared immediately before use to diminish errors due to esterification. Standard solutions of water were prepared as previously described.[2]

Method.—A measured volume of hydrogen chloride was introduced into a test-tube, 0.5 ml. of methyl yellow solution (0.0001 *M*) added and the volume made up to 5.0 ml. with the pure solvent. The ratio r was measured by the Gillespie method. The procedure was then repeated with the same solution containing known concentrations of water. These data are listed in Tables I, II and III.

TABLE I

EFFECT OF WATER ON METHYL YELLOW IN METHANOL

c_{H_2O}	r		
	$c_{HCl} = 0.00080$	$c_{HCl} = 0.00107$	$c_{HCl} = 0.00160$
0	0.67	0.47	0.33
0.12	.905	.67	.43
.24	1.22	.92	.67
.36	1.50	1.13	.82
.48	1.70	1.44	.89
.60	2.33	1.78	1.22
Intercept	0.63	0.42	0.32
Slope	2.44	2.16	1.36
K_p	0.258	0.194	0.235

TABLE II

EFFECT OF WATER ON METHYL YELLOW IN ETHANOL

c_{H_2O}	r		
	$c_{HCl} = 0.0016$	$c_{HCl} = 0.0024$	$c_{HCl} = 0.032$
0	0.54	0.33	0.25
0.02	.75	.43	.30
.04	.89	.54	.37
.06	1.13	.67	.47
.10	1.50	.89	.59
.16	2.03	1.22	.89
Intercept	0.58	0.326	.225
Slope	9.4	5.6	4.0
K_p	0.062	0.058	0.056

TABLE III

EFFECT OF WATER ON METHYL YELLOW IN BUTANOL

c_{H_2O}	r		
	$c_{HCl} = 0.00118$	$c_{HCl} = 0.00178$	$c_{HCl} = 0.00236$
0	0.67	0.47	0.37
0.02	1.13	0.72	.59
.04	1.63	1.00	.67
.06	2.33	1.38	.82
.08	2.57	1.50	1.04
.10	3.0	1.63	1.38
.12			1.50
.14		2.33	
.16			1.86
Intercept	0.70	0.48	0.32
Slope	23.8	12.8	9.8
K_p	0.029	0.038	0.033

Values of r were plotted against c_{H_2O} and from the curves K_p was evaluated. As an example, the data obtained in methanol are plotted in Fig. 1. For the sake of brevity, the figures referring to the data in ethanol and *n*-butanol are omitted. All determinations were carried out in the temperature range 25 ± 2°.

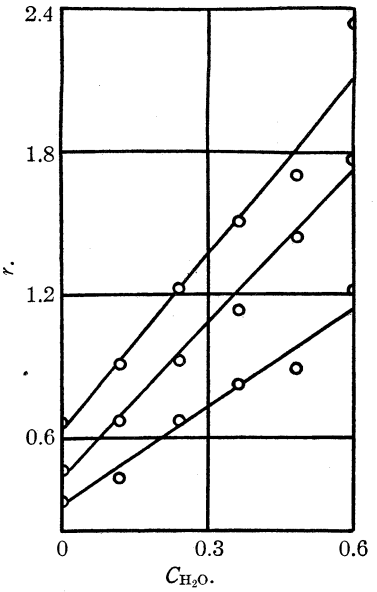


Fig. 1.—Effect of water on methyl yellow in methanol.

Discussion

The average values of K_p obtained by these measurements are 0.23, 0.059 and 0.033 for methanol, ethanol, and butanol, respectively. The first two are in agreement with the values obtained by Goldschmidt of 0.235 and 0.0583. While ethanol is a much weaker base than methanol, *n*-butanol is not much less basic than ethanol.

The fact that all points fall fairly well on straight lines substantiates the validity of the derivation in the introduction. There might, however, be a doubt in the assumption that hydrogen chloride is completely dissociated in such solvents of low dielectric constant. If we take this into consideration, equation 3 would become

$$c = c_{H_3O^+} + c_{ROH_2^+} + c_{HCl} = c_{ROH_2^+}\left[\frac{c_{H_2O}}{K_p} + 1 + \frac{c_{Cl^-}}{K_{HCl}}\right]$$

where K_{HCl} is the dissociation constant of hydrogen chloride. Equation 6 then becomes

$$r = \frac{K_I}{c}\left[\frac{c_{H_2O}}{K_p} + 1 + \frac{c_{Cl^-}}{K_{HCl}}\right]$$

Hence, if the acid were not completely dissociated, we would expect an increase in K_p with an increase in acid concentration. Since the values of K_p check within experimental error in all three cases, our assumption of complete dissociation is valid.

The results of the experiments give us a method of evaluating the dissociation constant of methyl yellow in these solvents. In Table IV are listed

these values, along with values obtained by other methods.

TABLE IV

DISSOCIATION CONSTANT OF METHYL YELLOW

Solvent	pK_I	pK_I (lit.)
Methanol	3.3	3.4[1]
Ethanol	3.1	3.1[a]
Butanol	3.1	2.8[b]

[a] The value reported by us in a previous paper (ref. 5) was erroneously given as 3.55 instead of 3.1. [b] R. B. Mason and M. Kilpatrick, THIS JOURNAL, **59**, 372 (1937).

There is a satisfactory check in the case of methanol and ethanol. The lack of agreement in butanol might be due to the presence of water in the butanol used by Mason and Kilpatrick. The amount of water can be estimated from these data. From equation (6) we find

$$K_I' = K_I \left[\frac{c_{H_2O}}{K_p} + 1\right]$$

where K_I' is the apparent dissociation constant. So

$$pK_I - pK_I' = \log\left(\frac{c_{H_2O}}{K_p} + 1\right)$$

Setting $pK_I - pK_I' = 0.3$, and $K_p = 0.033$, we get $c_{H_2O} = 0.033$ mole per liter, corresponding to 0.075% water in the butanol used by the above authors.

The colorimetric method could be used for the determination of traces of water in ethanol and butanol. From equation (6) it follows that

$$C_{H_2O} = K_p\left(\frac{rc}{K_I} - 1\right)$$

It is seen from Table II that the ratio r increases about 2.5 times when 0.18% water is added to pure ethanol.

Summary

1. The effect of traces of water on the color equilibrium of methyl yellow in dilute solutions of hydrogen chloride in methanol, ethanol and butanol, has been studied.

2. The relative basicities of these solvents have been determined and were found to decrease in the order: methanol, ethanol, butanol.

3. The dissociation constant of methyl yellow in these solvents has been calculated.

BROOKINGS, SOUTH DAKOTA
MINNEAPOLIS, MINNESOTA RECEIVED MARCH 8, 1940

[CONTRIBUTION FROM THE GEORGE HERBERT JONES CHEMICAL LABORATORY OF THE UNIVERSITY OF CHICAGO AND THE GEORGE FISHER BAKER LABORATORY OF CORNELL UNIVERSITY]

The Change with Time of the Surface Tension of Solutions of Sodium Cetyl Sulfate and Sodium Lauryl Sulfate

BY G. C. NUTTING, F. A. LONG AND WILLIAM D. HARKINS

Introduction

The static value of the surface tension of a pure liquid is attained within a very minute time after the surface is formed, for in order to reduce the surface free energy to its minimum value only a reorientation of molecules already present is necessary. With solutions, however, there is in general at equilibrium an excess or deficiency of solute in the surface layer and an appreciable time interval may be required for the transport of solute molecules from the bulk of the solution into the surface or *vice versa*.

Bond and Puls[1] have measured the surface tension of surfaces whose age is about 0.003 sec. and find that for a variety of aqueous solutions, including solutions of inorganic salts and the lower aliphatic alcohols, the surface tension even in so short a time changes to approximately the static value. They have been able to show that their experimental values of the surface tension change agree reasonably well with predicted values if diffusion alone is responsible for the time effect.

In the case of certain other solutions the final surface tension is not reached until days or weeks have passed. Examples are solutions of paraffin chain salts and of other molecules which are in part strongly hydrophobic, yet which dissociate into ions in water.[2] Doss[3] has presented evidence that unhindered diffusion would lead to establishment of equilibrium in the surface in a far shorter time than is observed, and that the rate of diffusion of the ions is slowed up enormously near the surface by the electrostatic repulsion of the ions already present in the surface layer.

In the present paper data are presented on the change with time of the surface tension of solutions of sodium cetyl sulfate and sodium lauryl

(1) W. N. Bond and H. O. Puls, *Phil. Mag.*, **24**, 864 (1937).

(2) N. K. Adam and H. L. Shute, *Trans. Faraday Soc.*, **34**, 758 (1938).

(3) K. S. G. Doss, *Kolloid-Z.*, **86**, 205 (1939).

sulfate. The time effect has been studied over the interval between two minutes and about six hours, over a wide range of concentrations, and at particular concentrations in the presence of various inorganic salts.

Experimental Methods

Sodium lauryl sulfate and sodium cetyl sulfate are salts of strong acids and are thus much better suited for a study of time effects than are the soaps since with the latter a small change in *p*H, induced perhaps by atmospheric carbon dioxide, has a large effect on the surface tension. Samples of these two salts were generously supplied by E. I. du Pont de Nemours and Co. and were supposedly of high purity. In addition a partial analysis was carried out and the amount of barium sulfate and alcohol formed indicated a purity of 99% or better.

Surface tensions were measured by the ring method, with the apparatus used by Harkins and Jordan.[4] The apparatus was immersed in a thermostat kept at 40.00 ± 0.05°. A slow current of water-pumped nitrogen, saturated with water vapor at the temperature of the thermostat, was passed through the apparatus. That this eliminated evaporation was shown by the fact that the volume of the liquid in the cup did not change measurably in two weeks. The ring used in the measurements was of platinum iridium and its mean radius was 0.6378 cm. After precautions had been taken to prevent condensation of water on the suspension wire, it was found that the weight of the wire and ring remained constant to within 0.1 mg. over a two-day period.

Since it was found that electrolytes in small amounts affected considerably the rate of change of surface tension, much care was taken in preparing the solutions. The water used was conductivity water, redistilled in a quartz still. Solutions were made up in very clean soft glass volumetric flasks by diluting stock solutions of 0.01 *M* alkyl sulfate. The solutions were used shortly after they were prepared since experiments showed that solutions kept for a long time in glass vessels gave results different from either fresh solutions or solutions kept in quartz vessels.

The solutions were brought to 40° and then introduced into the surface tension apparatus. The level of the liquid was adjusted to that of the rim of the cup and at the same time the surface was swept free from bubbles. Initial time was taken as the instant when the surface was swept level and free of bubbles. The first measurement was taken within two to three minutes and then measurements were taken at intervals thereafter. The maximum pull on the ring was determined to 0.1 mg., equivalent to 0.013 dyne per cm.

The suitability of the ring method for measuring surface tensions changing with time has been questioned[3] because of the inevitable disturbance of the surface by the (small) motion of the ring. Tests were made by agitating the surface with the ring as violently as possible and in no case was a change in the surface tension of over 1% observed. It appears from this evidence that solute particles once in the surface-film are averse to reëntering the solution. However, it is still true that a small error is involved in the expansion of the closed surface inside the ring as this is pulled from the surface.

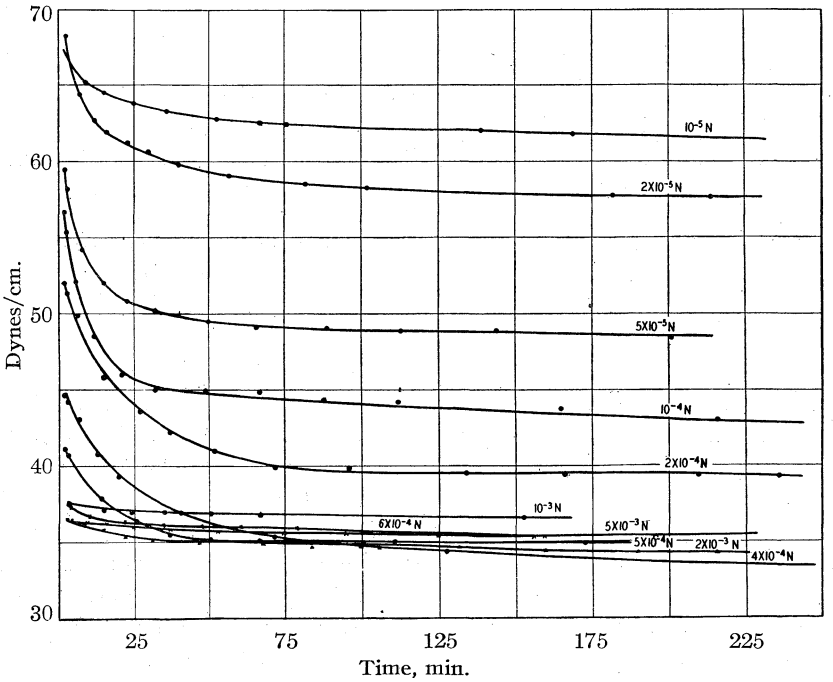


Fig. 1a.—Sodium cetyl sulfate solutions at 40°: surface tension *versus* time curves for various concentrations. At ten minutes time the concentrations of the sclutions are, in order of increasing surface tensions: 2×10^{-3}, 5×10^{-3}, 6×10^{-4}, 10^{-3}, 5×10^{-4}, 4×10^{-4}, 2×10^{-4}, 10^{-4}, 5×10^{-5}, 2×10^{-5}, 10^{-5} mole per liter.

Decrease of Surface Tension with Time

Sodium Cetyl Sulfate.—Surface tension *versus* time curves for sodium cetyl sulfate, $Na(Cet)SO_4$, have been obtained at 19 concentrations between 10^{-5} and 10^{-2} *N*. Most of the curves are shown in Figs. 1a and 1b. It is to be noted that at concentrations below 0.0006 *N* there is a considerable decrease in the surface tension in the first few minutes, while at higher concentrations the tension measured after two minutes is about the same as that measured after several hours. After the initial, more or less rapid, decrease in surface tension a much slower decline sets in which is linear

(4) W. D. Harkins and H. F. Jordan, THIS JOURNAL, **52**, 1751 (1930).

with time and nearly the same for all the solutions. The work of Adam and Shute[2] on cetylpyridinium bromide and cetyltrimethylammonium bromide suggests that the linear decrease may continue for weeks in the case of the more dilute solutions. Figure 1b shows clearly that the form of the surface tension curve at times below fifty minutes changes entirely from a very rapidly decreasing slope at 0.0002 M to an almost flat curve at 0.0007 M. Figure 1a shows that at 4 and 5 $\times$ 10^{-4} M the curve has the same general form as at 2 $\times$ 10^{-4} M. Thus the abrupt change in the time relation occurs very close to 6 $\times$ 10^{-4} M.

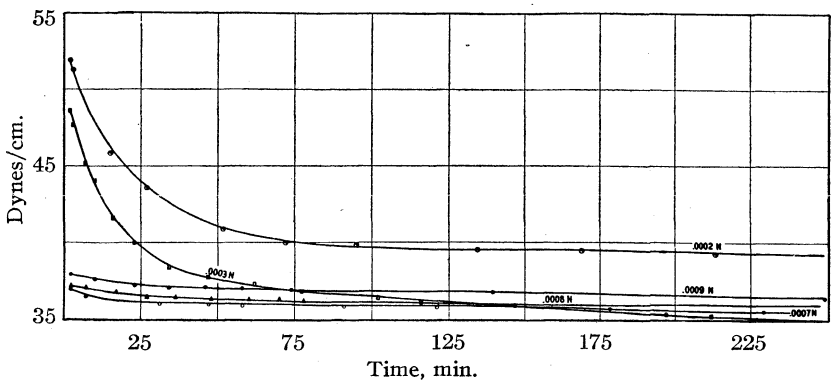


Fig. 1b.—Sodium cetyl sulfate solutions at 40°: surface tension *versus* time curves for various concentrations. At ten minutes the concentrations of the solutions are, in order of increasing surface tension: 7 $\times$ 10^{-4}, 8 $\times$ 10^{-4}, 9 $\times$ 10^{-4}, 3 $\times$ 10^{-4}, 2 $\times$ 10^{-4} mole per liter.

The abruptness with which the large initial drop in surface tension ceases at 0.0006 M is exhibited in Fig. 2 where the ratio of the surface tension after five minutes to that after two hundred minutes, σ $5/\sigma$ 200, is plotted against the logarithm of the concentration. The true value of the surface tension of all the solutions at zero time is doubtless the surface tension of water at 40° (69.6 dynes) and the final value of the surface tension for all concentrations is not far from 35 dynes. The course of the attainment of this final value is very different for different concentrations. Our experiments do not show the true final value of the surface tension but the ratio of σ at five minutes to σ at two hundred minutes serves to show clearly the sharp change in the time decrease of the surface tension which occurs at about 0.0006 M, since it is in the first fifty-minute period that the great differences are manifest.

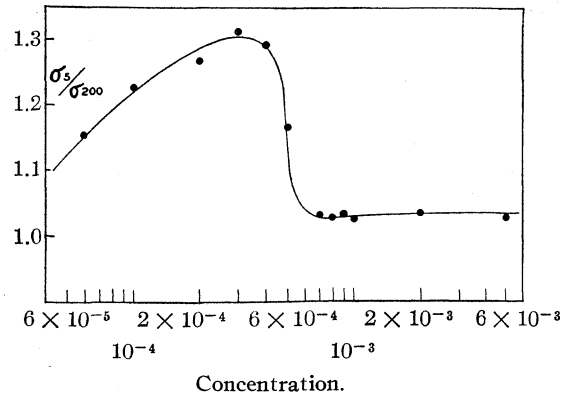


Fig. 2.—Sodium cetyl sulfate solutions at 40°: the ratio of the surface tension at a surface age of 5 min. to the surface tension at 200 min. for various concentrations.

Figures 3a and 3b exhibit the influence of added electrolytes on the rate of change of the surface tension of 0.0004 N Na(Cetyl)SO_4. It is seen from Fig. 2 that there is a large difference between the "initial" and "final" surface tensions of solutions of this concentration, and the primary effect of added electrolytes is to diminish this difference, producing S. T. *vs.* time curves similar to solutions 6 $\times$ 10^{-4} N and stronger. Thus 0.01 N sodium chloride, hydrochloric acid, sulfuric acid and sodium hydroxide give almost identical curves, while the curve of 0.01 N lithium nitrate is similar in shape, but lies above even the curve of the cetyl sulfate solution alone and thus resembles the 0.001 N solution without added electrolyte. Increasing the concentration of the electrolyte lowers and further flattens the curves.

Silver ions are much more effective in lowering the surface tension than the alkali metal ions and H^+, but the greatest effect is shown by Mg^{++} at 10^{-4} and 10^{-3} N. These solutions which contained Mg^{++} were extremely viscous, but clear throughout the experiments, and had surface tensions of about 30 dynes which scarcely changed with time. 10^{-8} N Ca^{++} lowered the surface tension slightly, but 10^{-6} N and higher concentrations raised it considerably. At the highest concentration, 10^{-4} N Ca^{++}, there was visible precipitation during the measurements, and the obvious removal of the alkyl sulfate ions from the solution accounts for the increased surface tension. In other solutions containing polyvalent positive ions, even though permanently free from turbidity, the tight binding

of the metal and cetyl sulfate ions is expressed in the heightened surface tension.

Sodium Lauryl Sulfate ($Na(Lauryl)SO_4$).—Figure 4 presents curves for this salt at ten concentrations from 5×10^{-4} to 5×10^{-2} N. At concentrations below 5×10^{-4} N the results were very erratic and are not reported. The surface tension of the solutions decreases in a rather regular fashion with concentration. The amount of the decrease is not nearly so great at the lower concentrations as with cetyl sulfate. The most remarkable result is that, except for 0.01 N and stronger solutions, whose curves are very flat anyway, the surface tension *vs.* time curves have broad minima which are followed by a rise of gentle, nearly constant upward slope. The surface tension variation of none of the solutions was followed for more than six hours, so that it is not possible to estimate either the value of the static surface tension or the time required to approach it.

Salt effects were observed with 0.004 N solutions. The results are in Figs. 5a and 5b. In none of the solutions, even those containing 0.6 N Na^+, 0.006 N Mg^{++} or 0.001 N Al^{+++}, was there ever any trace of turbidity. The unvarying effect of addition of electrolytes was to decrease the surface tension, sometimes to values nearly 4 dynes lower than observed in even the most concentrated lauryl sulfate solutions. The minimum was displaced both to shorter and longer times and was most often broadened or rendered nonexistent, but a conspicuous exception is provided by the solution which contains 1×10^{-5} N aluminum sulfate.

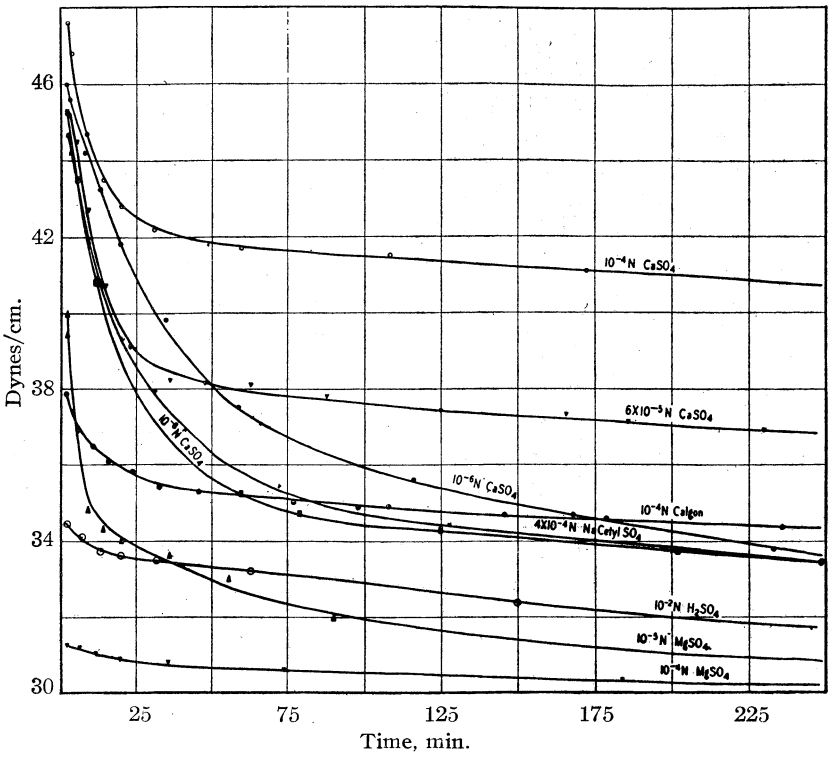


Fig. 3a.—0.0004 N sodium cetyl sulfate solutions at 40°: the effect of added salts on the lowering of the surface tension with time.

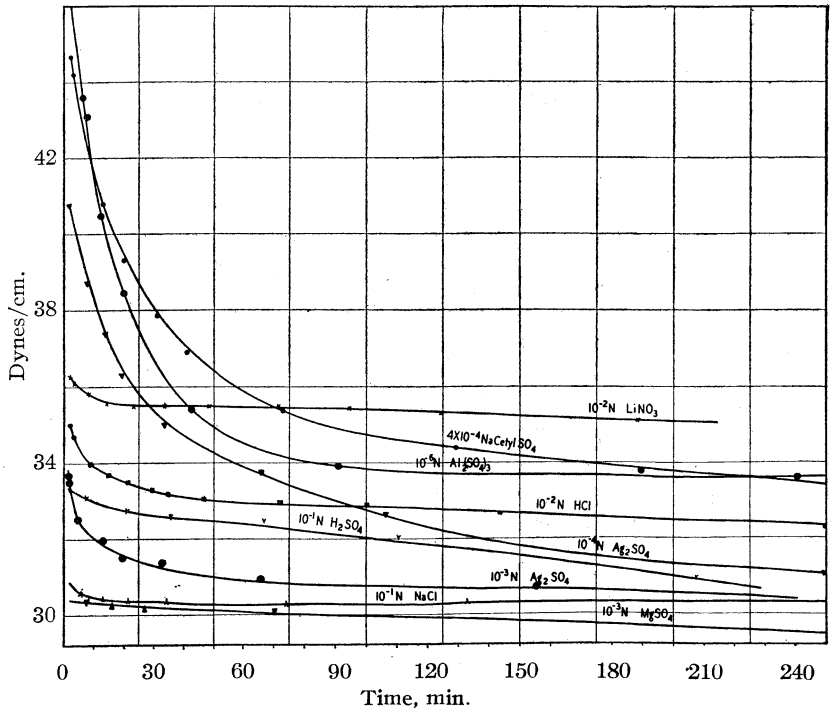


Fig. 3b.—0.0004 N sodium cetyl sulfate solutions at 40°: the effect of added salts on the lowering of the surface tension with time.

Discussion

At the instant of its formation the surface of the strongest alkyl sulfate solution employed contains about five thousand and the most dilute about five million water molecules to each molecule of solute, so that the initial surface tension approximates that of pure water. At all surface concentrations the solute particles adsorbed from the solution presumably behave like a two-dimensional gas in the sense that their cohesional forces are too feeble to produce permanent agglomeration and that they cover uniformly the entire surface area of the solution. Except in the very first stages of adsorption, however, the surface film cannot approach the behavior of an ideal gaseous film, and when the surface is nearly saturated and the film pressure is around 40 dynes per cm. the gas must be highly imperfect.

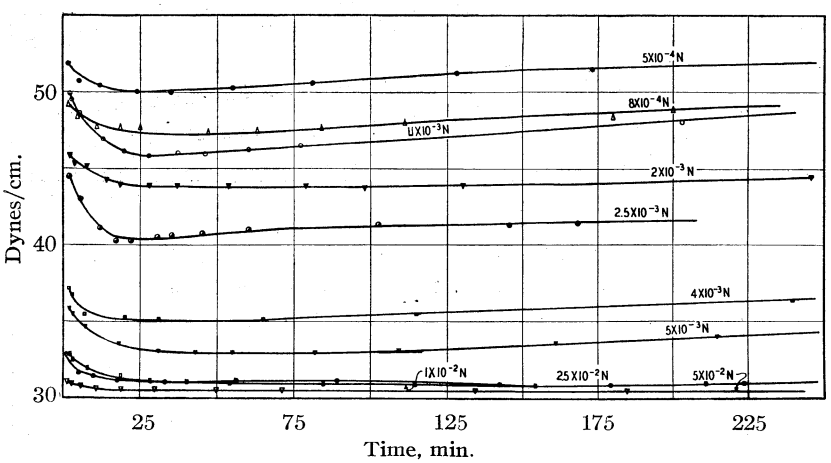


Fig. 4.—Sodium lauryl sulfate solutions at 40°: surface tension *versus* time curves for various concentrations.

The great amount of work which has been done on films of materials which contain long, unbranched paraffin chains, indicates that the area per molecule of films of sodium cetyl and lauryl sulfate under pressures of 40 dynes may fall as low as 20 sq. Å. The number of molecules per sq. cm. is then 5×10^{14}. The depth from which *all* solute would have to be removed in order to thus saturate the surface is inversely proportional to the bulk concentration of the solution and for a 10^{-6} N solution the depth is 0.8 cm.; for a 10^{-3} solution, 0.008 cm. Transfer of solute from such depths to the surface will be by no means instantaneous and attainment of the ultimate surface tension is correspondingly delayed.

Bond and Puls[1] and Doss[3] have given expressions for the order of magnitude of the time necessary for the attainment of the static value of the surface tension of solutions, assuming that the time is determined principally by the rate of diffusion of the surface-active material. The methods of Bond and Puls are not applicable to the present work since they involve a knowledge of the change of the static surface tension with concentration. An application of Doss' equation indicates that the time necessary to half saturate the surface with solute would be of the order of one second for the concentrations employed in this work. The actual times, both from the present investigation on sodium cetyl sulfate and from Adam and Shute's work on cetylpyridinium bromide and cetyltrimethylammonium bromide, are of the order of one thousand times the predicted values. While the assumptions made by Doss are probably not strictly valid no plausible variations could account for this *extreme* disagreement. It should be mentioned that the work of Harkins and King shows that a period of half an hour is required to give equilibrium with the surface in the case of a 0.000067 M solution of decylic acid. Consequently it is quite improbable that the rate of simple diffusion alone can account for the excessively slow accumulation of the solute in the surface layer which was found in our work.

The capillary active material in solutions of the alkyl sulfates is doubtless a collection of alkyl sulfate ions, each with a single negative charge. At a solution–air interface the adsorbed ions are firmly joined to water molecules through the sulfate groups, while the hydrocarbon "tails" above may assume practically any orientation with respect to the surface. At high surface concentrations the tails are closely packed and inclined steeply to the surface, and thus constitute an upper layer of liquid hydrocarbon, and a lower negative ionic layer. Sodium ions must then concentrate below this negative sheet in a diffuse positive layer. The electrical double layer thus set up provides a potential barrier to the entrance of additional alkyl sulfate ions into the surface. The height of the barrier increases with the density of ions in the surface and initially is zero.

An accurate calculation of the effect of this double layer on the speed with which ions diffuse into the surface would undoubtedly be difficult. In a rough calculation Doss, however, has shown that the hindering potential, even when the surface density of ions is small, is probably much larger than kT, the energy magnitude which determines the speed of diffusion of the ions. Thus the first ions could diffuse into the surface with rapidity but the electrical double layer caused by these ions would repel other negative ions and the rate of attainment of the equilibrium surface tension would be considerably delayed.

Evidence which qualitatively confirms this picture of the time effect can be obtained from the work of Schulman and Rideal[5] on mixed films. These investigators worked with partially compressed films of various insoluble substances, cetyl alcohol for example, on an approximately neutral substrate into which they injected very small amounts of sodium cetyl sulfate. The sodium cetyl sulfate was at a concentration (approximately 10^{-5} M) such as to cause the surface tension of water alone to be lowered only slowly, about 5 dynes in the first hour. But this same concentration of sodium cetyl sulfate causes a film of cetyl alcohol, initially present at a film pressure of 10–12 dynes and thus rather highly compressed, to show a surface tension lowering of nearly 50 dynes in a few minutes.

By the use of a different technique Harkins and Florence[6] have obtained an increase in the pressure of the cetyl alcohol film by a much greater factor. A 10^{-5} M sodium cetyl sulfate solution was found to increase its film pressure to about 6 dynes in four hours. The film of this material was then swept off quickly by the use of barriers. Then a few drops of a solution of cetyl alcohol in a low boiling ligroin were put on the surface. The solution spreads rapidly and pushes off any trace of the sodium cetyl sulfate. Even although the amount of cetyl alcohol used on the area gives by itself a pressure of only about 0.2 dyne/cm. the sodium cetyl sulfate diffused into the surface so rapidly that the pressure had risen to over 50 dynes per cm. in less than three minutes.

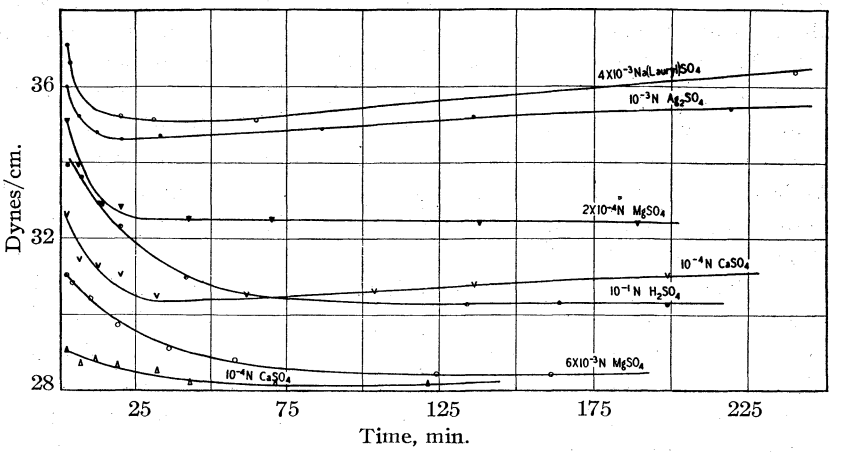


Fig. 5a.—0.004 N sodium lauryl sulfate solutions at 40°: salt effects.

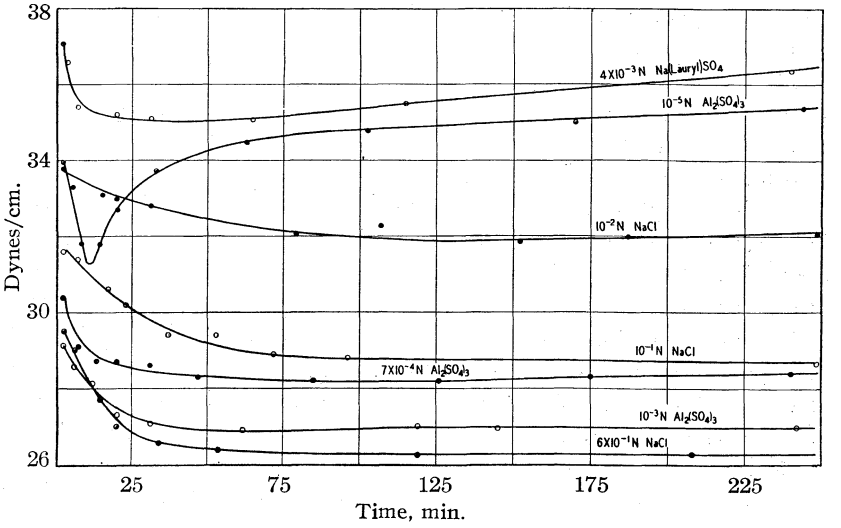


Fig. 5b.—0.004 N sodium lauryl sulfate solutions at 40°: salt effects.

Although in the last experiment described the pressure of the alcohol film alone is very low, nevertheless the surface was almost completely covered by the alcohol since its molecular area was only slightly above that found for a completely condensed liquid film (21.85 sq. Å. for cetyl alcohol at 20°).

Thus in either of the cases cited above the sur-

(5) J. H. Schulman and E. K. Rideal, *Proc. Roy. Soc.* (London), **B122**, 29 (1937).

(6) W. D. Harkins and R. T. Florence, unpublished work.

face was so completely covered by the alcohol that the sodium cetyl sulfate molecules in general moved into holes, in the film, completely surrounded by alcohol molecules. Thus no potential barrier was present to slow down their entrance and the diffusion into the surface was rapid. Also, since very few molecules of the solute were required to fill these holes, the adjacent solution was only very slightly depleted. In such a case both of these factors coöperate to make the rise of film pressure a very rapid one.

In the case of films of the sodium cetyl sulfate by itself a phenomenon appears which is even more spectacular than the time effect itself. This is its sudden cessation at a definite concentration. As is shown in Figs. 1 and 2, the time effect for sodium cetyl sulfate at 40° stops abruptly at about 6×10^{-4} M. For sodium lauryl sulfate the similar change comes at about 7×10^{-3} M. A very similar result has been reported by Adam and Shute for the salts investigated by them. Although the explanation of the time effect as being due to the electrostatic repulsion of the surface layer of ions seems fairly straightforward, the problem as to just why this effect should almost disappear at a definite concentration needs further consideration.

There is a close correlation for a given salt between the concentration at which the time effect stops and that at which the conductivity of the solution of the salt shows an abrupt break. Thus for sodium cetyl sulfate at 40° an abrupt decrease in the conductivity sets in at a concentration of about 5×10^{-4} M and for sodium lauryl sulfate at 6×10^{-3} M.[7]

The concentrations above which the time effect disappears are almost the same, that is, respectively, 6×10^{-4} and 7×10^{-3} M. Other properties of these solutions also show abrupt changes in the same concentration regions.[8]

These sharp changes have been explained by Hartley as due to a formation of ionic micelles, spherical aggregates of around 60 paraffin-chain ions with about half this number of "gegenions" attached more or less firmly to the aggregate. The concentration at which this abrupt change enters has been called the "critical concentration for micelles." And it is clear, not only from our results but from results of other workers on essentially "fresh" solutions,[9] that the surface properties of these solutions also show sharp changes at concentrations close to the critical concentration for micelles. The difference when surface tension is the phenomenon involved is, however, that it is not so much the final value which shows a change but the rate of attainment of the final, equilibrium value.

The results which are presented here on the effect of added salts on the surface tension are just what are to be expected from a consideration of the action of added salts on the critical concentration for micelles. It has been shown[8,10] that the effect of added salt is to lower the critical concentration and this effect is larger for divalent than for monovalent cations. Hence it is not surprising that solutions of 0.0004 M sodium cetyl sulfate which contain added electrolyte show surface tensions similar to solutions of the pure salt of somewhat larger concentrations (Figs. 1 and 3). The observation that small concentrations of magnesium salts have a pronounced action offers still further evidence that divalent cations adhere more strongly to the micelles than do monovalent ones, as they should on the basis of electrostatic theory.

It is not easy to see just why the presence of micelles allows the final surface tension to be attained so much more rapidly, but the change must be due to changes in the bulk of the solution, since it is quite unlikely that there is any essential change in the surface conditions in the small concentration ranges involved. It is plausible, however, that the ease with which an ion in a micelle can get up to the surface is greater than that for the simple ion. In the first place the mobility of a micelle is such that the rate of diffusion per ion is larger for the ions in a micelle than for simple ions. Probably still more important is the condition near the surface in the region of the double layer. The double layer offers a barrier to the simple ion of many times kT. But consider the behavior of a micelle in this region, assuming for convenience a micelle of 60 simple ions with approximately half this many gegenions. As the micelle approaches the surface it will encounter the diffuse region in which gegenions are concentrated. The greater potential gradient at the surface of the micelle (compared to a simple ion) will result in a still larger number of gegenions be-

(7) Howell and Robinson, *Proc. Roy. Soc.* (London), **A155**, 386 (1936); Lottermoser and Puschel, *Kolloid-Z.*, **63**, 175 (1933).

(8) G. S. Hartley, "Aqueous Solutions of Paraffin-chain Salts," Hermann et Cie., Paris, 1936.

(9) J. Powney and C. C. Addison, *Trans. Faraday Soc.*, **33**, 1243 (1937); A. Lottermoser and F. Stoll, *Kolloid-Z.*, **63**, 49 (1933).

(10) G. S. Hartley, *J. Chem. Soc.*, 1968 (1938).

coming attached to it. Consequently the net charge of the micelle will be reduced as it approaches the surface region. The surface will still offer an electrostatic barrier to the approach of the micelle, but the force per ion will be considerably less than for the simple ion case. As a result the rate at which ions present in micelles reach the surface may be many times that for simple ions.

In addition to these coulombic interactions which tend to hinder the formation of the surface layer, there are undoubtedly short-range noncoulombic forces between the surface layer and the ions or micelles in the solute. The noncoulombic forces will in general be attractive and thus tend to accelerate the formation of the surface layer. If these forces are greater for the micelle than for the simple ions, the result would be that, with micelles present, the height of the potential barrier for entrance into the surface would be decreased and the rate of formation of the surface accelerated. At present, however, it does not seem possible to ascertain whether these forces are of sufficient importance and sufficiently different for the micelles than for the ions to explain the observed results. It is, of course, unlikely that the micelle remains in or even enters the surface as such, since it is strongly hydrophilic and cannot decrease the surface free energy by orientation but only by dissociation. At an air–solution interface the condition essential for the existence of a small spherical micelle which is stable in the bulk of the solution is removed, the micelle dissociates and its fragments orient in the infinitely large two-dimensional micelle.

Lottermoser[7] and McBain[11] have not accepted the concept of Hartley and believe, rather, that the critical concentration for micelles represents a formation, not of ionic micelles, but of neutral colloid. This latter is considered to consist of aggregates of paraffin-chain salt molecules, each aggregate carrying only a very low net charge. This theory, although it does not seem to agree with certain other properties of solutions of paraffin chain salts,[7] allows an easy interpretation of the change in the time effects noted at the critical concentration. An electrical double layer would not be expected to offer any large hindering potential to a neutral or practically neutral aggregate and consequently if neutral colloid is present it could diffuse to the surface and permit the formation of a saturated surface layer in a comparatively short time.

If, as seems likely, the surface layer of these solutions is formed from ions, a comparison of the observed surface tensions with those for neutral molecules is rather difficult. Considerable numbers of gegenions will adhere to the ionic layer, but even so the electrostatic repulsion of like ions will cause the surface layer to be less concentrated. The ionic layer will act in the opposite way to produce a lower surface tension. These two opposing effects must be approximately equal since the final surface tension is about the same as that for neutral molecules of about the same chain length.

An interesting result is obtained from an application of Gibbs' theorem to the surface tension data for paraffin-chain salts or in other cases in which the surface tension though below that of water remains constant, or even increases with concentration. Here, *if the activity is proportional to concentration*, the theorem indicates a zero, or even a negative adsorption. The apparent explanation of this is that the equation gives correctly the adsorption in the whole surface region, but that the organic solute is more concentrated in the monolayer and less just below it, than in the three-dimensional phase.

Behavior like that of the alkyl sulfates might be expected from solutions of the soaps, which we have regarded as less suitable for the present work than the alkyl sulfates since the former hydrolyze. However, Bond and Puls have found that observed and predicted values of $t_{1/2}$ for 1% and 0.25% solutions of Lux are in good agreement. Assuming that the paraffin salt in Lux is sodium stearate and that the weight of water and other electrolyte is negligible, the respective molal concentrations are approximately 0.02 and 0.008.

At these concentrations the soap is largely in micellar form and the time of half-saturation of the surface would be small. That it should be as small as predicted from diffusion theory seems to indicate that the solute in the surface film is not in the form of ions but of fatty acid molecules. These have no potential barrier hindering their entrance into the surface and would pass in preferentially from a mixture of fatty acid ions and molecules. The static surface tension would be that of a liquid hydrocarbon, 25 to 30 dynes, as is observed. The *p*H of the soap solutions is doubtless not far above 7 so that the concentration of

(11) M. L. McBain, *Proc. Roy. Soc.* (London), **A170**, 415 (1939).

neutral particles in the solutions must be considerable. If the *p*H of the Lux solutions were raised, so that the surface active particles were fatty acid ions, it is predicted that the approach to equilibrium would be far slower and that the discrepancy between $t_{1/2}$ as calculated and observed would be as great as in the case of the alkyl sulfates and the pyridinium compounds.

Observations made by the writers on the change of surface tension of sodium nonylate and sodium laurate solutions with *p*H may be reinterpreted on the basis of the time effects which have been discussed.[12] It was found that the surface tension of dilute soap solutions increased markedly with *p*H. The film at *p*H 7 was supposed to consist principally of fatty acid molecules; at *p*H 12 principally of fatty acid ions. It was also supposed that the observed film pressure was characteristic of the film species in the equilibrium proportion at each *p*H. But the surface tension lowering by an ion layer should be comparable to the lowering by a layer of molecules of the same length of hydrocarbon chain. In reporting the increase in surface tension with *p*H it was tacitly assumed that the surfaces at the time of measurements were in all cases saturated. It seems at present likely that at low *p*H, adsorption of the fatty acid molecules was so rapid that the surface at the time of measurement was indeed saturated; while at higher *p*H adsorption of the fatty acid ion was so slow that the measured surface tension corresponded to only a partly filled surface. If the measurements had been postponed for several hours saturation would have been approached and the surface tension probably about the same as for the less alkaline solutions.

Adam and Shute's measurements on sodium lauryl sulfate are not in very good agreement with our own. Their surface tensions are invariably *higher* by 5 or 10 dynes per cm., even though the error to be expected in the ring method used by us is such as to give a value slightly too high. Also, their curves do not have the minima which we have observed. The minima suggest a change in the nature of the adsorbed particles but the character of the change cannot yet be specified.

Summary

The change with time of the surface tension of solutions of sodium cetyl sulfate has been measured in the concentration range 10^{-5} to 10^{-2} N at 40°; and of sodium lauryl sulfate in the range 5×10^{-4} N to 5×10^{-2} N. The changes were followed in the interval two minutes to from three to six hours.

The effects of various uni-, di- and trivalent ions at several concentrations have been measured on 0.0004 N sodium cetyl sulfate and 0.004 N sodium lauryl sulfate.

In the cetyl sulfate solutions without added electrolyte at concentrations below 6×10^{-4} N a rapid fall in tension is found followed by a slow fall, linear with time, at the same rate for all solutions. At concentrations higher than 6×10^{-4} N the initial fall is small and the surface tension soon reaches a value of about 35 dynes per cm. The effect of electrolytes is the same as an increase in cetyl sulfate concentration, namely, greatly to hasten attainment of static values of the surface tension near 30 dynes. The effectiveness of the positive ions increases rapidly with the valence.

In the lauryl sulfate solutions the initial fall is not so marked and is followed usually by a broad minimum surface tension. The nature of this phenomenon cannot now be specified. The effect of electrolytes is again to hasten attainment of a static tension of about 25–30 dynes, and the order of effectiveness is the same as for the cetyl sulfate.

The slow fall is considered due principally to the potential barrier set up against alkyl sulfate ions diffusing into the surface by the ions already in the surface film. No quantitative account of the effect of this electric double layer on the rate of fall of surface tension has yet been possible.

The sudden change in the time effect at a definite concentration has been correlated with the appearance of micelles in the bulk of the solution. The reasons for this change are obscure but a tentative explanation is considered. The effects of added electrolytes are shown to be related to the critical concentration for micelles.

The apparent increase of surface tension of solutions of soaps with increasing *p*H is accounted for on the basis of slow accumulation of fatty acid ions in the surface films at high *p*H, and rapid accumulation of fatty acid molecules by simple diffusion at low *p*H.

(12) F. A. Long, G. C. Nutting and W. D. Harkins, THIS JOURNAL, **59**, 2197 (1937).

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RECEIVED FEBRUARY 28, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF STANFORD UNIVERSITY]

Thermal Data on Organic Compounds. XX. Modern Combustion Data for Two Methylnonanes, Methyl Ethyl Ketone, Thiophene and Six Cycloparaffins

BY GEORGE E. MOORE,[1] MELVIN L. RENQUIST AND GEORGE S. PARKS

In a continuation of the thermochemical studies initiated by Richardson and Parks[2] in this Laboratory, we have recently measured very accurately the heats of combustion of 2-methylnonane, 5-methylnonane, methyl ethyl ketone, thiophene, and six cycloparaffins, *viz.*, methylcyclopentane, ethylcyclopentane, cyclohexane, methylcyclohexane, *n*-heptylcyclohexane and *n*-dodecylcyclohexane. These thermochemical results will be summarized in the present paper. In subsequent publications they will be combined with the proper entropy data to yield values for the free energies of the several compounds.

Apparatus and Method

The apparatus and general method were essentially the same as in the previous study of Richardson and Parks. Three cylinders of oxygen were used in this investigation and with each a new series of calibrations of the calorimeter, involving five to eight combustions, was carried out with standard benzoic acid (sample 39e) supplied by the United States Bureau of Standards. For the "standard" conditions of our calorimeter the three series of calibrations yielded the mean results 3211.4 (±0.2) cal., 3211.2 (±0.5) cal., and 3211.3 (±0.2) cal. for the energy equivalent per degree at 25.0°. These values are in excellent agreement with the result (3211.3 ± 0.4 cal.) reported previously.

The combustions were made with the bomb filled with oxygen to a pressure of 30 atm. at 23° and, except in the case of thiophene, with 1 ml. of water initially in the bomb. In general, most of the air originally in the bomb was washed out by two preliminary fillings with oxygen to a pressure of 5 atm. and thus the correction for nitric acid formation was kept down to about 1 calorie in a total of approximately 6000 calories.

In the case of thiophene, however, this washing out was omitted because we found that the air originally in the bomb was very essential as a catalyst for the complete oxidation of the sulfur to sulfuric acid. After each combustion of this substance we analyzed for both nitric acid and nitrous acid and corrected for the small heat effects of these according to the procedure of Huffman and Ellis.[3] In this work with thiophene appropriate corrections were also made on the standard energy equivalent of our calorimetric system (a) for the omission of the 1 ml. of water usually placed within the bomb, (b) for the absence of any vaporization of this water during the average temperature rise of 2°, and (c) for the small amount of water vapor condensed from the air initially in the bomb by the sulfuric acid produced. The sulfuric acid corresponded approximately to the concentration $H_2SO_4 \cdot 1.70H_2O$ and hence for comparative purposes our experimental combustions were always corrected to this exact composition by means of Table III in the paper of Huffman and Ellis.

Because of their volatility all these compounds, save the dodecylcyclohexane, were sealed into thin-walled capsules of soft glass, which in general had volumes of 0.5 to 0.8 ml. and weighed 0.065 to 0.085 g. empty. These capsules were flattened or collapsed on opposite sides so that, when practically filled with the sample to be burned, they would withstand the deformation produced by the oxygen pressure within the bomb. The capsules were made so light because it was found that when they weighed more than 0.100 g. they tended to explode on ignition and the liquid therein was thrown about the bomb with incomplete combustion as a result. Under our conditions the thin glass fused quietly to allow smooth combustion from the liquid surface. As a "promoter" in these combustions about 0.02 g. of *n*-hexadecane was placed within the combustion crucible and always in part on an upturned flat side of the glass capsule so that the ignition took place mainly from above. Hexadecane was chosen for this purpose because of its very small volatility at room temperature and its high, precisely known heat of combustion (11,283 cal. $g.^{-1}$ in air[2]). Its preliminary ignition was always accomplished with the platinum wire and cotton string system described by Richardson and Parks.

Units.—The unit of energy used throughout this paper is the defined conventional calorie which has been derived from the international joule by multiplying by the factor 1.0004/4.185. The unit of mass is the gram true mass which is derived from the weight in air against brass weights by use of a suitable correction factor for buoyancy. The molecular weights are based on the 1939 table of atomic weights.[4]

Materials

The various substances studied had been prepared and purified with great care and were exceptionally high grade. After due allowance is made for the effect of dissolved air in these liquids, the impurities, except possibly in the case of the heptylcyclohexane, should produce no error in the combustion results greater than 0.01%.

Methylnonanes.—The samples of 2-methylnonane and 5-methylnonane were prepared in the Research Laboratory of the Ethyl Gasoline Corporation. Their preparation and properties have been fully described by Calingaert and Soroos.[5]

***n*-Heptylcyclohexane and *n*-Dodecylcyclohexane.**—These substances were prepared in the Chemical Laboratory of Stanford University by Dr. Simon Kinsman, working with Prof. C. R. Noller. The preparations were made

(1) Du Pont Fellow, 1939–1940.
(2) Richardson and Parks, THIS JOURNAL, **61**, 3543 (1939).
(3) Huffman and Ellis, *ibid.*, **57**, 41 (1935).
(4) Baxter, Guichard, Hönigschmid and Whytlaw-Gray, **61**, 223 (1939).
(5) Calingaert and Soroos, *ibid.*, **58**, 635 (1936).

from highly purified intermediates by Grignard syntheses, followed by careful drying and fractional distillations under reduced pressure. Part of these samples were first used in heat capacity measurements at low temperatures and in this connection their fusion behavior was carefully noted.

The *n*-dodecylcyclohexane melted sharply at 12.5° and from its fusion curve we have estimated its purity at 98.8 mole %. Undoubtedly the remaining 1.2% represents for the most part closely related hydrocarbons which produce no appreciable error in the heat of combustion. The *n*-heptylcyclohexane melted at −41.2° but with considerable premelting. Our estimate of its purity was 97.1 mole %. In view of this rather low figure the material was carefully tested for impurities, such as halogens, which might produce an appreciable error in our combustion value. These tests indicated not more than 0.003% chlorine (by weight). Moreover, microanalyses on these two compounds yielded results for carbon and hydrogen corresponding to the theoretical compositions within the limits of experimental error (about 0.1%).

Methyl Ethyl Ketone.—This material was specially prepared for our low temperature specific heat measurements by the Shell Development Company. The fusion behavior indicated a purity of 99.74 mole %. As several months elapsed after our specific heat studies, we again dried and redistilled this material in two batches, just before the combustions, using as drying agents calcium sulfate and calcium oxide, respectively. These two samples yielded identical combustion results within the limits of experimental error.

Methylcyclopentane, Ethylcyclopentane, Cyclohexane, Methylcyclohexane and Thiophene.—All five compounds were specially prepared for this study in the Research Laboratory of the Shell Development Co. Three purity requirements were set up for these preparations: first, that the sample should be free of any elements not present in the molecular formula of the compound; second, that its only permissible impurities should be isomers or closely related homologs; and third, that its absolute purity should be greater than 98 mole %. Careful syntheses and extensive chemical purifications were relied on to meet these first and second requirements and repeated fractional distillations in a Podbielniak column to meet the third. The final criterion of purity adopted was that all portions of the distillate, on refractionation of a "pure" sample, should be of the same refractive index (within ±0.00003) as the charge to the still.

In the case of the ethylcyclopentane three different syntheses were employed before all these requirements were completely met. The second of these preparations, however, contained only 0.012% chlorine and we made a number of combustions with this as well as with the "pure" third sample. Counting this small chlorine content as inert material, we obtained practically identical heats of combustion for these two samples.

For cyclohexane three fractional crystallizations were employed in addition to the foregoing purification methods. The final product melted very sharply at 6.35°.

Table I contains the refractive indices and densities at 20° of the "pure" samples of these five compounds.

TABLE I

REFRACTIVE INDICES AND DENSITIES

Substance	$n^{20}D$	d^{20}_4
Methylcyclopentane	1.4095	0.7482
Ethylcyclopentane	1.4196	.7665
Cyclohexane	1.4262	.7785
Methylcyclohexane	1.4230	.7694
Thiophene	1.5283	1.0638

The Heats of Combustion and Derived Data

After considerable preliminary work on the method of burning with the glass capsules, about sixty precise combustion determinations were made upon these ten compounds. These combustions ordinarily involved gaseous carbon dioxide and liquid water as end-products but in the special case of thiophene the water was replaced by sulfuric acid at the concentration $H_2SO_4 \cdot 1.7H_2O$.

Table II contains a summary of our experimental combustion data together with some important thermal data calculated therefrom. The number of combustions made on each particular compound is given in the fifth column. The resulting mean values for the energy evolved in the isothermal bomb process per g. at 25.0°, represented by the term $-\Delta U_B/m$, and the mean deviations of the individual combustions from these mean values, represented by Δ, appear in the succeeding column. The values of the bomb process were then calculated per mole and corrected to the standard constant-volume process where the reactants and products are each at 1 atmosphere by means of the equations of Washburn.[6] The energy evolved in this hypothetical standard process is designated in the table by the symbol $-\Delta U_R$. From this quantity $-\Delta H_R$, the heat evolved in the isobaric process at 1 atm., was obtained by addition of the proper work term. Finally, $-\Delta H_f^\circ$, the heat of formation of the compounds from the elements (gaseous hydrogen, graphitic carbon and rhombic sulfur) was then calculated from $-\Delta H_R$ by use of 68,318 cal.[7] and 94,030 cal.[8] for the heats of formation of water and carbon dioxide, respectively, and in the case of thiophene by the value $\Delta H = -135{,}010$ cal.[3] for the process

$$S(\text{rhombic}) + 2.7H_2O(l) + 3/2O_2(g) = H_2SO_4 \cdot 1.7H_2O\ (l)$$

In the calculation of the quantity $-\Delta U_R$ from the tabulated $-\Delta U_B/m$ values a correction of +0.02% was made in all cases for the air dis-

(6) Washburn, *Bur. Standards J. Research*, **10**, 525 (1933).
(7) Rossini, *J. Research Nat. Bur. Standards*, **22**, 407 (1939).
(8) Rossini and Jessup, *ibid.*, **21**, 491 (1938).

TABLE II

SUMMARY OF EXPERIMENTAL AND DERIVED DATA

All substances are liquid and all weights are reduced to a vacuum basis

Substance	Formula	Mol. wt.	Density	No. of combns.	$-\Delta U_B/m$ and Δ cal. $g.^{-1}$	$-\Delta U_R$ kcal. $mole^{-1}$	$-\Delta H_R$ kcal. $mole^{-1}$	$-\Delta H_f^\circ$ kcal. $mole^{-1}$
2-Methylnonane	$C_{10}H_{22}$	142.278	0.725	5	11,344.6±2.4	1614.00±0.56	1617.26	74.54
5-Methylnonane	$C_{10}H_{22}$	142.278	.729	5	11,347.9±1.8	1614.46±0.38	1617.72	74.08
Methylcyclopentane	C_6H_{12}	84.157	.745	6	11,153.8±3.3	938.58±0.40	940.36	33.73
Ethylcyclopentane	C_7H_{14}	98.183	.763	10	11,147.6±2.7	1094.40±0.37	1096.47	39.97
Cyclohexane	C_6H_{12}	84.157	.775	5	11,106.8±1.5	934.62±0.31	936.40	37.69
Methylcyclohexane	C_7H_{14}	98.183	.766	5	11,086.0±2.9	1088.35±0.45	1090.42	46.02
n-Heptylcyclohexane	$C_{13}H_{26}$	182.341	.810	5	11,088.6±0.8	2021.71±0.55	2025.56	84.96
n-Dodecylcyclohexane	$C_{18}H_{36}$	252.472	.822	5	11,108.5±1.7	2804.30±0.84	2809.63	112.63
Methyl ethyl ketone	C_4H_8O	72.105	.805	9	8,068.6±2.3[a]	581.70±0.20	582.59	66.80
Thiophene	C_4H_4S	84.132	1.060	3	7,915.1±2.5	665.91±0.60	667.39	−19.62

[a] This is the mean of the six combustions made on the unboiled samples.

solved in the liquid sample when weighed. This is the correction worked out from the available solubility data by Richardson and Parks to allow for the air dissolved in other liquid hydrocarbons. Whether the same figure should be applied to methyl ethyl ketone, which is considerably more polar, seemed perhaps questionable. Accordingly, we first made six combustions on the two preparations of this substance containing dissolved air and then three more combustions on samples of the same materials which, just prior to weighing, had been boiled under reduced pressure. For $-\Delta U_B/m$ the mean value for these first six combustions, corrected by +0.02%, was 8070.2 (±2.3) cal., while the last three air-free samples yielded a mean of 8071.1 (±0.9) cal. This agreement is highly satisfactory, and therefore we have used 8070.6 cal. as a final mean for this substance in computing $-\Delta U_R$.

The uncertainties attached to the tabulated values of $-\Delta U_R$ have been calculated by use of the "precision error" described by Rossini.[9] This includes not only the "reaction error" for the combustion of the particular compound but also our "calibration error" averaging 0.014%, an "assigned error" of 0.023% on the standardizing substance, and an arbitrary allowance for a 10% uncertainty in the Washburn correction.

Previous Work.—The literature contains no earlier combustion values for five of these compounds. Zubow made determinations on methylcyclopentane, cyclohexane, methylcyclohexane and methyl ethyl ketone. His values, as revised by Swietoslawski,[10] differ from our present data by −0.23%, +0.01%, +0.16% and −0.04%, respectively. More modern combustion results for cyclohexane, obtained by Richards and Barry (revision by Swietoslawski and Bobinska[11]) and by Roth and von Auwers,[12] exceed our present value by 0.41 and 0.10%, respectively. Berthelot's very early result[12] for thiophene apparently differs from ours by +0.54% and that of Thomsen by −0.68%.

Acknowledgment.—Before concluding, we wish to thank Dr. George Calingaert for the gift of the methylnonane samples and the Shell Development Co. for the preparation of six of these ten compounds as well as for financial assistance in this research during the summer of 1939.

Summary

1. A bomb calorimeter has been calibrated and then used for precise measurements of the heats of combustion of the following ten substances at 25° and constant volume: 2-methylnonane, 5-methylnonane, methylcyclopentane, ethylcyclopentane, cyclohexane, methylcyclohexane, *n*-heptylcyclohexane, *n*-dodecylcyclohexane, methyl ethyl ketone and thiophene.

2. From these experimental results the corresponding heats of combustion and heats of formation at constant pressure have been calculated.

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RECEIVED MARCH 11, 1940

(9) Rossini, *Chem. Rev.*, **18**, 252 (1936).

(10) Swietoslawski, THIS JOURNAL, **42**, 1092 (1920).

(11) Swietoslawski and Bobinska, *ibid.*, **49**, 2476 (1927).

(12) Landolt-Börnstein-Roth-Scheel, "Tabellen," Julius Springer, Berlin, 1923, p. 1587.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NEW YORK UNIVERSITY]

Acid-Polymerized Dipinene. I. Dehydrogenation[1]

BY JOHN J. RITTER AND JACOB G. SHAREFKIN[2]

Dipinene, $C_{20}H_{32}$, resulting from the action of acids on alpha- or beta-pinene has been studied by various investigators since its discovery a century ago by Deville,[3] who obtained the substance from turpentine oil and sulfuric acid.[4]

The delayed revival of active interest in the diterpene group is probably due in part to the fact that the diterpenes are comparatively few and their acids quite common, while the converse is true of the sesquiterpenes. Recent workers have made use of sulfur dehydrogenation with inconclusive results in most instances, particularly with the acid-polymerized diterpenes. Up to the present no definite facts bearing upon their structure have appeared. Of the naturally occurring diterpenes alpha-camphorene, distilled from camphor oil[5] and also resulting from myrcene by polymerization,[6] dehydrogenated with sulfur to a product which failed to yield a picrate. Careful fractionation of the unsaponifiable portion of rosin oil[7] gave colophene and diterpenes which were believed to be identical with those prepared by heat and acid polymerization of monoterpenes. Although retene was obtained in the Vesterberg reaction from the colophene fraction, the diterpenes were reported unchanged after this treatment. Neither Aitken[8] nor Blackie[9] obtained an aromatic on sulfur dehydrogenation of the solid diterpene dacrene. The first instance of successful dehydrogenation of a naturally occurring diterpene is Beath's[10] isolation of isoretene from a diterpene which he considered identical with rimunene.

Among the synthetic diterpenes the only reported dehydrogenation resulting in an isolable aromatic is that of dipinene by Dulou,[4] after Kondakow and Saprikin[11] found no aromatic on sulfur dehydrogenation of this substance. Carter, Smith and Read[12] were unable to isolate an aromatic after sulfur dehydrogenation of the closely similar acid-polymerized di-alpha-phellandrene. Dulou's picrate melted at 132° and the hydrocarbon at 64–65°. The latter he stated to be di-isopropyldiphenyl although this compound does not appear in the literature and no proof of structure is given by the author.

We have now reinvestigated the dehydrogenation of dipinene with the immediate view to isolation and identification of a pure aromatic and ultimately arriving at significant facts bearing upon the nature of the carbon skeleton of dipinene. The conditions for most satisfactory dehydrogenation were studied first. High temperature (280°) resulted in complete carbonization while lower temperature (150°) gave no aromatic isolable as picrate. Slow sulfur addition to dipinene at intermediate temperatures (200°) proved most effective in minimizing carbonization; however, the yield of pure aromatic even under the most favorable conditions was of the order of 1.0%. Dilimonene, practically identical with dipinene in physical characteristics, dehydrogenated under the same conditions to the same product. The same product, in yields of the same order, was obtained by the use of diphenyl ether as solvent in the dehydrogenation as well as by slow selenium addition[13] and by the pressure-tube procedure of Ruzicka.[14]

All of the picrates prepared melted at 169.5–170° and showed no depression in mixed melts. From these a solid hydrocarbon was obtained melting at a higher temperature (78.2–78.4°) than that reported by Dulou. This hydrocarbon is not reported in the literature; its analysis and general characteristics indicated a phenanthrene of molecular formula $C_{17}H_{16}$, and its synthesis by an independent method[15] proves it to be 2,6,9-trimethylphenanthrene.

Experimental

Dipinene.—alpha-Pinene was purified by repeated distillation through a 20-cm. column: b. p. 155–156°;

(1) Based upon a portion of the dissertation submitted by Jacob G. Sharefkin to the Graduate Faculty of New York University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1937.

(2) Present address Brooklyn College, Brooklyn, New York.

(3) Deville, *Ann. chim. phys.*, [2] **75**, 66 (1840); *Ann. Chir.*, **37**, 192 (1840).

(4) See Dulou, *Chimie et Industrie*, **27**, (Spec. No.) 651 (1932), for a review of the literature of synthetic dipinenes.

(5) Semmler and Rosenberg, *Ber.*, **46**, 771 (1913).

(6) Semmler and Jonas, *ibid.*, **46**, 1566 (1913).

(7) Knecht and Maurice, *J. Soc. Dyers Colorists*, **41**, 356 (1925).

(8) Aitken, *J. Soc. Chem. Ind.*, **47**, 223T (1928).

(9) Blackie, *ibid.*, **49**, 26T (1930).

(10) Beath, *ibid.*, **52**, 338T (1933).

(11) Kondakow and Saprikin, *Bull. soc. chim.*, **37**, 918, 1415 (1925).

(12) Carter, Smith and Read, *J. Soc. Chem. Ind.*, **44**, 543T (1925).

(13) Diels and Karstens, *Ber.*, **60B**, 2323 (1927).

(14) Ruzicka, *et al.*, *Helv. Chim. Acta*, **16**, 216, 812 (1933); **17**, 200 (1934); **18**, 676 (1935); **19**, 424 (1934).

(15) See the succeeding paper, THIS JOURNAL, **62**, 1509 (1940).

d^{20}_{20} 0.8613; $n^{23}D$ 1.4682; $[\alpha]^{25}D$ +28.12°. Limonene prepared in the same manner gave the constants: b. p. 175.5–175.8°; d^{25}_{25} 0.8395; $n^{23}D$ 1.4710. Phosphoric acid (85%, 500 cc.) is placed in a three-neck flask fitted with a mechanical stirrer, dropping funnel and thermometer; an equal volume of monoterpene is added dropwise with rapid stirring during eight hours while the temperature is held below 30°. After the addition is completed the stirring is continued at room temperature for one hundred and twenty hours. The mixture is then allowed to stand until the layers separate, and the upper layer neutralized with potassium carbonate solution, dried over anhydrous potassium carbonate and distilled. Dipinene, a colorless viscous liquid, is obtained in 71% yield: b. p. 127–128° (1 mm.); d^{25}_{25} 0.9316; $n^{25}D$ 1.5149; $[\alpha]^{25}D$ ±0. *Anal.* Calcd. for $C_{20}H_{32}$: C, 88.15; H, 11.85. Found: C, 87.44; H, 11.71. Dilimonene, prepared in the same way, gave the constants: b. p. 128° (1 mm.); d^{25}_{25} 0.9313; $n^{25}D$ 1.5170; $[\alpha]^{25}D$ ±0. The procedure is that of Carter, Smith and Read[12]; the yields and constants of our products are in agreement with theirs.

Dehydrogenation.—Sulfur (80 g., 2.5 moles) is added to dipinene (136 g., 0.5 mole) in 2–3 g. portions at uniform intervals over a ten-day period, the temperature remaining close to 200° throughout. The resulting black tarry mass is distilled with superheated steam to yield an oil which is extracted from the distillate with ether and distilled at 1 mm. after drying the extract with anhydrous potassium carbonate and removing the ether on the steam-bath. Three fractions are cut: to 140°, 3.7 g.; 140–160°, 36.3 g.; 160° until no further distillation, 32.2 g. Addition of hot saturated alcoholic picric acid to these fractions shows picrate formation only with the latter two.

By the same procedure, 1760 g. of dipinene gave 980 g. of steam-distilled oil which yielded for the three fractions 60, 390, and 375 g., respectively. Redistillation of these through a 20-cm. column at 1 mm. resulted in a fraction of 472 g. at 160–185° which yielded a solid picrate. The crude picrate melted at 137°; after three recrystallizations from alcohol 19.7 g. of pure product, m. p. 169.5–170°, was obtained. *Anal.* Calcd. for $C_{23}H_{19}N_3O_7$: N, 9.35. Found: N, 9.25. The picrate from dilimonene dehydrogenation, m. p. 169–170°, showed no depression in a mixed melting point with that from dipinene. *Anal.* Calcd. for $C_{23}H_{19}N_3O_7$: N, 9.35. Found: N, 9.29. Attempts to increase the yield of the picrate-producing hydrocarbon by re-treatment of the low-boiling fraction from the dehydrogenation with sulfur resulted in failure.

Hydrocarbon $C_{17}H_{16}$.—The picrate from the previous section (23.5 g.) was decomposed in a Soxhlet thimble by refluxing with water for fifteen hours; the 10.5 g. of yellowish solid remaining in the thimble after drying at 40° was extracted with benzene in the Soxhlet apparatus. The extract on evaporation left a solid residue, m. p. 75–75.5°; after three recrystallizations from 95% alcohol colorless tablets, m. p. 78.2–78.4°, were obtained. *Anal.* Calcd. for $C_{17}H_{16}$: C, 92.68; H, 7.32. Found: C, 92.61; H, 7.53.

Summary

A modified Vesterberg reaction was found most suitable for dipinene dehydrogenation.

All dehydrogenation methods tested with dipinene and dilimonene yielded the same hydrocarbon, which has a higher melting point than that previously reported.

Analysis of the hydrocarbon and its picrate rules out the proposed di-isopropyldiphenyl structure of Dulou.

The hydrocarbon has the composition and general characteristics of a phenanthrene.

WASHINGTON SQUARE COLLEGE,
NEW YORK, N. Y. RECEIVED MARCH 27, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NEW YORK UNIVERSITY]

Acid-Polymerized Dipinene. II. Identification of the Dehydrogenate

BY JOHN J. RITTER AND VIRGIL BOGERT[1]

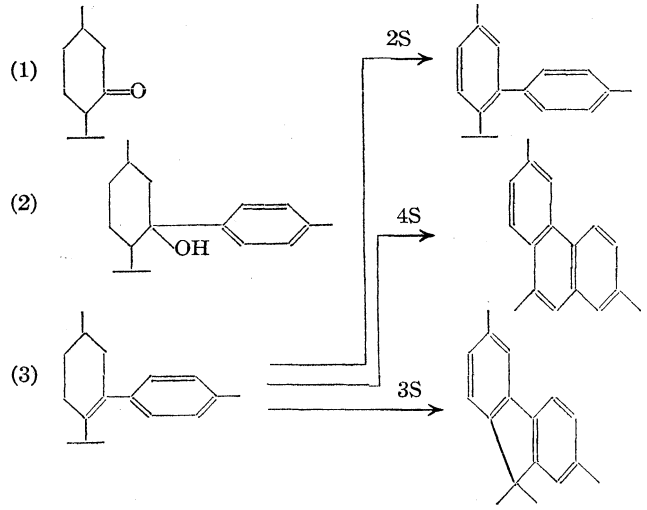
In the preceding paper the isolation of a pure crystalline aromatic hydrocarbon $C_{17}H_{16}$ from the sulfur dehydrogenation of acid-polymerized dipinene $C_{20}H_{32}$ is reported. While the limited amount of this substance at hand curtailed rather severely any extended studies of structure by oxidative or other means, its general characteristics indicated the structure of a phenanthrene. Our inability on repeated attempts to isolate a phenanthraquinone on oxidation was ascribed to the presence of a methyl group on carbon atom 9 or 10. Consideration of antecedent literature dealing with dipinene and the action of acids on alpha-pinene led us to the postulation of a carbon skeleton for the dimer which pointed specifically to 2,6,9-trimethylphenanthrene as the most probable substance resulting from its dehydrogenation. This has now been verified by synthesis and the demonstrated identity of the synthetic product with the dehydrogenate.

We proceeded from *l*-menthone (1) which was condensed with *p*-tolylmagnesium bromide to 3-*p*-tolylmenthol (2); the latter was dehydrated to 3-*p*-tolylmenthene-3 (3), which was dehydrogenated with sulfur to 3,4[1]-dimethyl-6-isopropyl-

(1) Based upon a portion of the dissertation submitted by Virgil Bogert to the Graduate Faculty of New York University in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1940.

diphenyl (4) and also to 2,6,9-trimethylphenanthrene (5). The yield of the phenanthrene was low, the major portion of the product consisting of a liquid aromatic $C_{17}H_{18}$ which appears to be tetramethylfluorene (6). We hope to furnish unequivocal proof of the structure of the latter in a later publication. The tentative assignment of structure to (6) gains added confirmation from the fact that it, like fluorenes generally, forms no crystalline picrate.

The facts here presented serve not only to establish the structure of the dipinene dehydro-



genate but seem also to offer an explanation of the principal difficulty of structure determination by dehydrogenation in the acid-polymerized diterpene group, *i. e.*, the formation, principally, of a non-picrating fluorene along with very small quantities of the more easily recognizable phenanthrene. The synthetic trimethylphenanthrene is formed ultimately by dehydrogenative ring-closure of an *o*-isopropyldiphenyl; in spite of the homogeneity of the latter the yield of phenanthrene is of the same order as that resulting from dipinene dehydrogenation under the same conditions. Previous investigators[2] have uniformly disregarded the non-picrating liquid fractions from dipinene dehydrogenation.

We are at present engaged in further studies of the partial and complete dehydrogenation of dipinene with a view to isolation of diphenyls or fluorenes, as well as the more general problem of dehydrogenative ring-closure of *o*-alkyl diphenyls with sulfur. The results of these investigations will appear shortly in THIS JOURNAL.

(2) Dulou, *Chim. & Ind.*, **27**, 651 (Spec. No.) March (1932); Kondakow and Saprikin, *Bull. soc. chim.*, **37**, 918, 1415 (1925).

Experimental

3-*p*-Tolylmenthol.—*p*-Bromotoluene (129 g., 0.75 mole) is added slowly with mechanical stirring to magnesium (18 g., 0.75 mole) and 400 cc. of absolute ether after the reaction has been started with only 50 cc. of ether. After completion of the reaction on the water-bath the mixture is cooled in an ice-bath; ordinary (1) menthone (80 g., 0.52 mole) in 100 cc. of absolute ether is added slowly with continuous stirring. The reaction product is allowed to stand overnight at room temperature, heated on the water-bath for one hour, and then hydrolyzed with 25% aqueous ammonium chloride solution. The ether layer is separated, dried over sodium sulfate, and the ether removed. Distillation of the residue at 2 mm. yields 28–37 g. of menthone and 64–71 g. of the carbinol: b. p. 127–128° (2 mm.); 140–142° (4 mm.); m. p. 39.5°; d^{25}_4 0.9745; $n^{25}D$ 1.5150; $[\alpha]^{25}D$ −14.49°. *Anal.* Calcd. for $C_{17}H_{26}O$: C, 82.93; H, 10.57. Found: C, 82.81; H, 10.26.

3-*p*-Tolylmenthene-3.—3-*p*-Tolylmenthol-3 (50 g.) is mixed with twice its weight of anhydrous oxalic acid and the mixture heated in an oil-bath at 150° for six to eight hours. Water is added to dissolve the oxalic acid and the upper layer of hydrocarbon separated. Distillation of the product yields 37–40 g. (80–87%) of 3-*p*-tolylmenthene: b. p. 118–120° (2 mm.); 145–147° (10–11 mm.); d^{25}_4 0.9269; $n^{25}D$ 1.5218; $[\alpha]^{25}D$ +49.45. *Anal.* Calcd. for $C_{17}H_{24}$: C, 89.47; H, 10.53. Found: C, 89.59; H, 10.26.

3,4[1]-Dimethyl-6-isopropyldiphenyl.—3-*p*-Tolylmenthene-3 (22.8 g., 0.1 mole) is placed in a 50-cc. round-bottom flask sealed to an air-cooled reflux condenser which is in turn connected with a potassium hydroxide trap to collect the evolved hydrogen sulfide. Sulfur (6.4 g., 0.2 mole) is added in portions of 1–2 g. over a twelve-hour period at 220–230°. The heating is continued for an additional sixty hours or until 6.3–6.7 g. of hydrogen sulfide (93–99% of calcd.) has been collected in the trap: yield, 19 g. (85%); b. p. 108–110° (2 mm.); 130–132° (4–5 mm.); d^{25}_4 0.9619; $n^{25}D$ 1.5579. *Anal.* Calcd. for $C_{17}H_{20}$: C, 91.07; H, 8.93. Found: C, 91.11; H, 9.09.

Trinitro Derivative.—3,4[1]-Dimethyl-6-isopropyldiphenyl is heated for one-half hour on the steam-bath with concentrated nitric–sulfuric acid mixture: m. p. (from alcohol) 164–165°. *Anal.* Calcd. for $C_{17}H_{17}N_3O_6$: N, 11.70. Found: N, 11.76.

Total Dehydrogenation of 3-*p*-Tolylmenthene-3 with Sulfur.—3-*p*-Tolylmenthene-3 (22.8 g., 0.1 mole) is dehydrogenated as in the preceding paragraph with sulfur (12.8 g., 0.4 mole) added in portions of 1–2 g. over a twenty-four hour period. After addition of one-half of the sulfur the temperature is raised from 220–230° to 280–300° and finally to 320–340°, where it is held for thirty-six hours. The total time of dehydrogenation is ninety-six hours, and the weight of hydrogen sulfide collected 12.2 g. Distillation at 2 mm. yields: dimethylisopropyldiphenyl, b. p. 110°, 1.3 g.; 2,6,9,9-tetramethylfluorene, b. p. 123–125°, 5 g.; high-boiling fraction, 130–210°, 1.4 g. The latter yields the picrate of 2,6,9-trimethylphenanthrene; a further quantity of picrate is obtained by alcohol extraction

of the distillation residue and treatment of the extract with alcoholic picric acid. The total yield of picrate is 0.3 g. (0.66%).

Total Dehydrogenation with Selenium.—3-*p*-Tolylmenthene-3 (22.8 g., 0.1 mole) is dehydrogenated with 32 g. of selenium added over thirty-six hours. Heating for an additional seventy-two hours with gradual increase of the temperature from 290 to 360° gives a product which on ether extraction and distillation yields: 3,4¹-dimethyl-6-isopropyldiphenyl, 3.0 g.; 2,6,9,9-tetramethylfluorene, 4.0 g.; fraction 130–210°, 1.5 g. From the latter and also the distillation residue 0.9 g. of picrate, m. p. 169–170°, is obtained (yield, 2%).

2,6,9-Trimethylphenanthrene.—The hydrocarbon is obtained from its picrate by the method described in the previous paper: yield, 1.4% of calculated from 3-*p*-tolylmenthene-3; m. p. 78.5°. Both the picrate and the hydrocarbon show no depression in mixed melts with the corresponding products from dipinene dehydrogenation.

2,6,9,9-Tetramethylfluorene.—B. p. 123–125° (2 mm.); d^{25}_4 0.9893; $n^{25}D$ 1.5811; mol. wt. (Rast, camphor) 225, calcd. 222. *Anal.* Calcd. for $C_{17}H_{18}$: C, 91.89; H, 8.11. Found: C, 91.80; H, 8.20. Monobromo derivative, m. p. 94.5°. *Anal.* Calcd. for $C_{17}H_{17}Br$: C, 67.77; H, 5.64. Found: C, 67.75; H, 5.15. Dinitro derivative (mixed acid at room temperature), m. p. 218° (from alcohol). *Anal.* Calcd. for $C_{17}H_{16}N_2O_4$: N, 8.97. Found: N, 9.15.

Summary

2,6,9-Trimethylphenanthrene has been synthesized, characterized, and shown to be identical with the product of dipinene dehydrogenation.

WASHINGTON SQUARE COLLEGE
NEW YORK, N. Y. RECEIVED MARCH 27, 1940

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY]

Mono- and Di-α-furfuryl Glycines

BY J. E. ZANETTI AND J. T. BASHOUR

We have shown the pronounced reactivity of furfuryl bromide in ether solution on the amino group[1] and it appeared of interest to investigate whether the neighboring presence of a carbethoxy group would influence the reaction. Accordingly we have studied its action on the amino group of α-aminoacetic ethyl ester and found it to proceed quite satisfactorily. The free α-furfurylamino acid can be obtained readily from the ester by hydrolysis. We have found that excess of the ethyl aminoacetate to liberate the furfuryl addition compound from its hydro bromide gave better results than the use of sodium or potassium hydroxides for similar purposes. The reaction may then be written as

$$C_4H_3OCH_2Br + 2NH_2CH_2COOC_2H_5 \longrightarrow C_4H_3OCH_2NHCH_2COOC_2H_5 + NH_2HBrCH_2COOC_2H_5$$

The glycine ester hydrobromide precipitates out of the ether, leaving in solution the furfuryl glycine ethyl ester.

As explained in the experimental part, both the mono- and di-α-furfurylglycines can be obtained in one operation by using varying ratios of α-furfuryl bromide to the amino acetate, a procedure which we found unsatisfactory when working with free amines.

Experimental

The general procedure was similar to that already described for the preparation of furfurylalkyl amines.[1] The hydrobromide precipitated and was filtered off in the usual manner. It was also found that the difurfurylaminoacetic ester could be obtained in one operation by slightly increasing the ratio of furfuryl bromide to amine. Two and one-half cc. of ethyl aminoacetate per cc. of furfuryl alcohol used in the bromide synthesis, gives a product consisting of 80% monofurfuryl derivative and 20% difurfuryl derivative. Two cc. of amine per cc. of furfuryl alcohol resulted in approximately equivalent quantities of secondary and tertiary products. Yields were over 80% on the basis of 70% yield of furfuryl bromide.

Ethyl aminoacetate was prepared from glycine through the ester hydrochloride by the methods of Curtius[2] and Fischer.[3] Over-all yields of 65% were readily obtained.

Ethyl Furfurylaminoacetate.—In contrast to glycine ester, this product is quite stable, long standing causing only a slight yellowing with very slight decomposition as determined by redistillation. No diketopiperazine formation was observed. It is soluble in most organic solvents: b. p. 99–101° at 3 mm.; $n^{25}D$ 1.4735; d^{25}_{20} 1.096. The hydrochloride melted at 68–70°. It was recrystallized from absolute alcohol by addition of absolute ether to incipient cloudiness.

Anal. Calcd. for $C_9H_{13}O_3N$: N, 7.65. Found: N, 7.70.

Ethyl Benzofurfurylaminoacetate.—Three cc. of ethyl furfurylaminoacetate was dissolved in 4.2 cc. of benzoyl chloride with cooling in an ice-bath. Thirty cc. of 2.5 *N* sodium hydroxide, ice-cold, was added at once and the mixture shaken for twenty minutes. Ether was added and the aqueous layer discarded. The ether layer was washed with dilute hydrochloric acid and water, and dried overnight with sodium sulfate. After removal of the ether, the product was collected at 157–162° at approximately 1 mm.

(1) Zanetti and Bashour, THIS JOURNAL, **61**, 3133 (1939); **62**, 742 (1940).

(2) Curtius and Goebel, *J. prakt. Chem., N. F.*, **37**, 159 (1888).

(3) Fischer, *Ber.*, **34B**, 436 (1901).

The compound is highly viscous, quite soluble in ether, insoluble in water and petroleum ether. It crystallizes from ether–petroleum ether solution in a dry-ice bath, remelting at once on removal from the bath, $n^{25}D$ 1.5072.

Anal. Calcd. for $C_{16}H_{17}O_4N$: C, 66.9; H, 5.9. Found: C, 66.5; H, 6.1.

Furfurylaminoacetic Acid.—Ethyl furfurylaminoacetate was boiled with ten times the quantity of water until solution was complete (about two and one-half hours). The solution was evaporated to incipient dryness, the residue dissolved in a minimal quantity of water and precipitated in the form of fine needles by the addition of ten volumes of dioxane. It may be recrystallized from boiling alcohol or from four parts of hot water, the latter producing thick, transparent prisms: m. p. 210–212° (corr.) in preheated baths. Slow heating results in much decomposition starting at about 180°.

Anal. Calcd. for $C_7H_9O_3N$: C, 53.8; H, 5.80; N, 9.03. Found: C, 53.7; H, 5.72; N, 8.94.

Ethyl Difurfurylaminoacetate.—B. p. 154–157° at 3 mm.; $n^{25}D$ 1.4691; d^{25}_{20} 1.135; m. p. of hydrochloride, 94–96° (corr.) (recrystallized from absolute ethanol and ether). The ester is soluble in most organic solvents.

Anal. Calcd. for $C_{14}H_{17}O_4N$: N, 5.3. Found: N, 5.6.

Difurfurylaminoacetic Acid.—The preceding ester was hydrolyzed by two methods: (A) 1 g. of ester was boiled for fifteen minutes with 3 g. of barium hydroxide octahydrate and 5 cc. of water. The barium was removed in the usual manner and the filtrate evaporated nearly to dryness; (B) 1 g. of ester was boiled with 5 cc. of 24% sodium hydroxide until solution was complete (ten minutes). It was cooled at once and an equivalent quantity of sulfuric acid was added. After evaporation to dryness the product was extracted with hot ethanol, from which it crystallizes on cooling. It may be recrystallized from hot water, or more conveniently from 10 parts of ethanol and decolorizing with bone black. It is insoluble in ether and benzene; m. p. 140–141° (corr.).

Anal. Calcd. for $C_{12}H_{13}O_4N$: C, 61.3; H, 5.53; N, 5.95. Found: C, 61.3; H, 5.60; N, 6.04.

The authors are indebted to Mr. Saul Gottlieb for the microanalyses of these compounds.

Summary

The following derivatives of glycine have been synthesized by the use of furfuryl bromide, and their properties reported: ethyl furfurylaminoacetate, ethyl benzoylfurfurylaminoacetate, furfurylaminoacetic acid, ethyl difurfurylaminoacetate and difurfurylaminoacetic acid.

NEW YORK, N. Y. RECEIVED APRIL 15, 1940

[CONTRIBUTION FROM THE WILLIAM H. CHANDLER CHEMISTRY LABORATORY, LEHIGH UNIVERSITY]

The Preparation of 2-Furanacetic Acid

BY JULIUS PLUCKER, III, AND E. D. AMSTUTZ

In the course of other work to be reported shortly, it became necessary to prepare considerable quantities of 2-furanacetic acid. This compound is not accessible by the usual avenues of approach[1] and, although it has been prepared in several ways,[2] either the methods are inconvenient or the yields are low.[3] It was therefore thought to be of interest to investigate the applicability of the rhodanine method.

Julian and Sturgis[4] have repeated some of the elegant work of Gränacher[5] on the aldehyde-rhodanine condensation products and have shown that the rhodanine method offers a valuable way of preparing the acids of one more carbon atom. Gränacher condensed furfural with rhodanine[5] and cleaved the resulting product with alkali to give β-2-furyl-α-thioketopropionic acid (II) which in turn was converted to the oximino acid (IV). In order to prove the applicability of this method therefore it was necessary only to determine whether the oximino acid could be satisfactorily decarboxylated and dehydrated to furanacetonitrile (V). This has been done and it was found that the desired nitrile is obtained in yields consistently above 80% of the theoretical. In this connection it is interesting to note that furanacetaldoxime (VII) is reported to yield only a small amount (12–15%) of the same nitrile on dehydration under essentially the same conditions.[2b] Following is a summary of the reactions involved in the rhodanine method

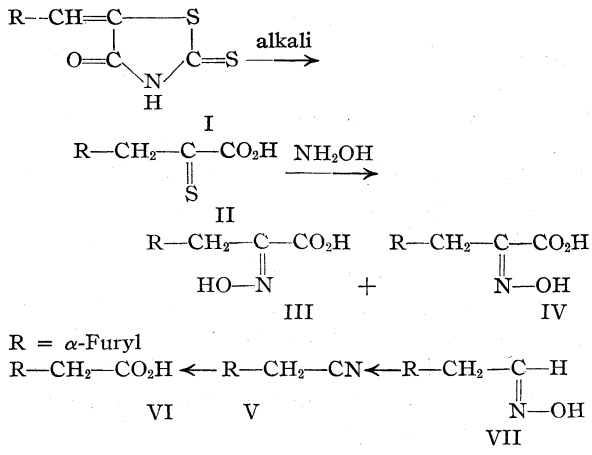
(1) (a) Johnson and co-workers, THIS JOURNAL, **52**, 1284 (1930), and Reichstein, *Ber.*, **63B**, 749 (1930), have shown that when furfuryl chloride is treated with aqueous potassium cyanide the product is composed mainly of 5-methyl-2-furonitrile instead of the expected 2-furanacetonitrile. (b) Gilman, *Rec. trav. chim.*, **51**, 93 (1932), has found that furfuryl chloride could not be made to undergo a smooth reaction leading to the Grignard reagent which, if formed, would be expected to yield the desired acid on carbonation.

(2) By the following reaction sequences: (a) Reichstein, ref. 1a; furoyl chloride → furoyl cyanide → furoyl formic acid → furanacetic acid. Sodium furylglycidate → furanacetaldehyde → furanacetic acid. (b) Johnson, ref. 1a; furfural → furyl nitro ethylene → furanacetaldoxime → furanacetonitrile → furanacetic acid.

(3) R. Robinson, *J. Chem. Soc.*, 718 (1937), mentions the lack of a satisfactory method of preparation of 2-furanacetic acid.

(4) THIS JOURNAL, **57**, 1126 (1935).

(5) *Helv. Chim. Acta*, **5**, 610 (1922).



The oxime of 2-furanpyruvic acid was obtained in two forms, both light yellow microcrystalline powders, m. p. 127–128° dec.[6] and m. p. 143.8–144° dec., tentatively designated[7] as compounds III and IV, respectively. The lower melting form is the more soluble and reacts the less vigorously with acetic anhydride but gives essentially the same yield of the nitrile as the higher melting form. They were not investigated further.

Experimental[8]

Fufuralrhodanine (m. p. 229–231° dec.; yield, 94%) was prepared and cleaved with alkali to 3-α-furyl-2-thioketopropionic acid (m. p. 114.6–115°; yield, 99%) according to the directions of Julian and Sturgis.[4]

3-α-Furyl-2-oximinopropionic Acid.—A solution of 26.6 g. of thioketo acid and 16 g. of hydroxylamine (from 33.8 g. of the hydrochloride and 11.3 g. of sodium) in 325 cc. of absolute ethyl alcohol was refluxed for one-half hour and distilled under diminished pressure till all the alcohol was removed. The brown solid remaining was dissolved in 80 cc. of 5% sodium hydroxide solution and filtered free of sulfur. Cautious acidification of the cooled filtrate with 75 cc. of 10% hydrochloric acid precipitated 8.5 g. (32%) of the acid as a light brown powder, m. p. 143.8–144° dec.; reported, m. p. 145°.[4] The filtrate was extracted with five 50-cc. portions of ether which were combined, dried over anhydrous magnesium sulfate and evaporated. There was obtained in this way an additional 13 g. (49.5%) of acid, m. p. 127–128° dec.; total yield, 21.5 g. or 81.5% of the theoretical.

In a run with twice the quantities used above the alkaline solution of the acid was acidified to congo red in the cold under ether. There was obtained a yield of 49.1 g. (93%) of acid, m. p. 121.5–122° dec.

2-Furanacetonitrile.—A mixture of 49.1 g. of oximino acid (m. p. 121.5–122.0°) and 237 g. of acetic anhydride was warmed till effervescence set in. Upon cessation of the vigorous reaction the dark reddish solution was rapidly steam distilled. The steam distillate was extracted with 300 cc. of ether in several portions which were combined, washed to neutrality with sodium carbonate solution, dried over anhydrous magnesium sulfate and distilled. There was obtained a yield of 27.3 g. (87.7%) of nitrile, b. p. (17 mm.) 84°, $n^{25}D$ 1.4691; reported,[1a] b. p. (20 mm.), 78–80°, $n^{25}D$ 1.4715.

The oximino acid (11.7 g.), m. p. 127–128°, gave 6.1 g. or an 82.5% yield of the nitrile and 7.3 g. of the acid, m. p. 143.8–144°, gave 3.5 g. or 76%. The use of a smaller quantity of the higher melting material is thought to explain the discrepancy in yields.

Hydrolysis of the nitrile in the customary way with 18% aq. potassium hydroxide gave 96% of the theoretical yield of 2-furanacetic acid, white leaflets, m. p. 66.8–67.5° (crude); m. p. authentic specimen,[9] 67–67.5°; mixed m. p. 66.5–67°.

The over-all yield of 2-furanacetic acid from furfural is about 73% of the amount required by theory.

Summary

It has been shown that 2-furanacetic acid may be conveniently prepared in very satisfactory yield from furfural by the rhodanine method.

BETHLEHEM, PA. RECEIVED APRIL 20, 1940

(6) All m. p.'s uncorrected.

(7) On the basis of Hantzsch's work on the configuration of oximes, *Ber.*, **25**, 2164 (1892). See also, "Organic Chemistry, An Advanced Treatise," H. Gilman, Ed., p. 391.

(8) The authors are indebted to Dr. F. N. Peters and the Quaker Oats Company for their generous donation of the furfural used in this work.

(9) Prepared by the reaction of α-furfuryl chloride with cuprous cyanide in acetonitrile; Johnson and Amstutz, unpublished data.

[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF IOWA STATE COLLEGE AND SOUTHWESTERN COLLEGE]

Benzylalkali Compounds[1]

BY HENRY GILMAN, HENRY A. PACEVITZ AND OGDEN BAINE

Benzylsodium was found to be the most effective organometallic compound of a series examined in the metalation of furan.[2] In extension of interconversion reactions of organometallic compounds, we have examined procedures which might make the highly effective benzylalkali compounds more accessible.

Rearrangement of Sodium in *p*-Tolylsodium.—Bachmann and Clarke[3] isolated benzoic acid (34%), *p*-toluic acid (30%) and phenylacetic acid (0.36%) after carbonation of a reaction mixture of di-*p*-tolylmercury, sodium and benzene which had been allowed to stand for one month. The formation of phenylacetic acid establishes a migration of sodium to benzylsodium, and is an interesting variation of the lateral metalation of toluene by ethylsodium which was first examined by Schorigin.[4] However, it is uncertain in the Bachmann–Clarke experiment whether migration took place directly or involved first the metalation of benzene, used as a medium, inasmuch as phenylsodium must have formed because of the high yield of benzoic acid. We have carried out the same reaction using as a medium petroleum ether, which is not metalated by organosodium compounds, and find that phenylsodium is no necessary intermediate, benzylsodium being formed in quite satisfactory yields.

Ziegler[5] prepared *p*-tolylsodium from *p*-chlorotoluene and found that by omitting strong heating a migration of the metal from the nucleus to the side-chain did not occur. This result is also consistent with the long time, room temperature experiment of Bachmann and Clarke. Apparently the migration of sodium is not only independent of the intermediate formation of phenylsodium, but also takes place very slowly at room temperature. Actually, as we have shown, the reaction can be carried out for a short time and without refluxing to give exclusively *p*-tolylsodium; and, with refluxing, to give exclusively benzylsodium. This is also strikingly illustrated with the reaction of *m*-chlorotoluene and sodium.[6]

Benzylpotassium.—The existence of benzylpotassium has been postulated reasonably in some reactions, but the compound has not hitherto been accessible. Marcus,[7] in some studies with Schlenk, mentioned that 1,1,1,2-tetraphenylethane was cleaved by potassium to triphenylmethylpotassium and benzylpotassium.

$$(C_6H_5)_3CCH_2C_6H_5 + 2K \longrightarrow (C_6H_5)_3CK + C_6H_5CH_2K$$

Subsequently, Ziegler and Thielmann,[8] in an orienting experiment, carried out a similar reaction with sodium–potassium alloy and isolated, subsequent to carbonation, triphenylacetic acid but no phenylacetic acid. Wooster and Mitchell[9] added one equivalent of benzyl bromide to two equivalents of potassium in liquid ammonia. A deep red color developed, and this faded gradually until the solution was colorless. They concluded that the red color was due to benzylpotassium.

We now find that it is possible to prepare benzylpotassium in workable quantities by two different procedures. First, di-*p*-tolylmercury and potassium are heated in petroleum ether.

$$(p\text{-}CH_3C_6H_4)_2Hg \xrightarrow{[K]} p\text{-}CH_3C_6H_4K \longrightarrow C_6H_5CH_2K \qquad [I]$$

Second, toluene is metalated laterally in essential accordance with Schorigin's procedure in which ethylsodium was used. In one of these syntheses phenylpotassium (prepared from benzene and *n*-butylpotassium) was used as the metalating agent.

$$C_6H_5CH_3 + C_6H_5K \longrightarrow C_6H_5CH_2K + C_6H_6 \qquad [II]$$

In the other synthesis, the transitorily formed phenylpotassium was used as the metalating agent.

$$C_6H_5Cl + 2K \longrightarrow [C_6H_5K]$$
$$[C_6H_5K] + C_6H_5CH_3 \longrightarrow C_6H_5CH_2K \qquad [III]$$

Phenylpotassium is most probably formed as an intermediate in reaction [III], although we have not as yet succeeded in interrupting the reaction to capture the phenylpotassium by carbonating to benzoic acid. Our present interpretation is that phenylpotassium is formed from chloro-

(1) This is paper XXXI in the series entitled: "Relative reactivities of organometallic compounds," and an account of the studies was presented at the Eighth National Organic Symposium, St. Louis, Dec. 30, 1939. The preceding paper is in THIS JOURNAL, **62**, 1243 (1940).

(2) Gilman and Breuer, *ibid.*, **56**, 1123 (1934).

(3) Bachmann and Clarke, *ibid.*, **49**, 2096 (1927).

(4) Schorigin, *Ber.*, **41**, 2723 (1908); **43**, 1931, 1938 (1910).

(5) Ziegler, *Angew. Chem.*, **49**, 455 (1936).

(6) Gilman and Pacevitz, THIS JOURNAL, **62**, 673 (1940).

(7) Marcus, Dissertation on "Triarylmethyls," Jena, 1914.

(8) Ziegler and Thielmann, *Ber.*, **56**, 1740, 2453 (1923).

(9) Wooster and Mitchell, THIS JOURNAL, **52**, 688 (1930).

benzene and potassium in toluene, and then rapidly metalates the toluene to give benzylpotassium. This reaction, by the way, is one of choice for the preparation of benzylpotassium inasmuch as the 82–84% yield of pure phenylacetic acid indicates an even higher yield of benzylpotassium.

In sharp contrast with the reaction of chlorobenzene and potassium is the related reaction with sodium. Bockmühl and Ehrhart[10] were probably the first to prepare phenylsodium (in 70–80% yields) from chlorobenzene and sodium. We have found that it is possible to prepare phenylsodium in at least an 87% yield, and in a few hours, by appropriately cooling a mixture of chlorobenzene and sodium in toluene. If, however, the mixture is refluxed then the phenylsodium metalates the toluene to give benzylsodium in an 80% yield. Morton and co-workers[11] have prepared benzylsodium by metalation of toluene with amylsodium directly, or with phenylsodium prepared by metalation of benzene by amylsodium.

An examination of the reaction of *p*-chlorotoluene with sodium in some solvents has shown that *p*-tolylsodium can be prepared in 80% yield in toluene. When the reaction mixture is refluxed, a migration of the sodium takes place and benzylsodium is formed in a 79% yield. This migration is not peculiar to *p*-tolylsodium, for we have observed that benzylsodium is also formed from *o*-tolylsodium (prepared from di-*o*-tolylmercury and sodium), and from *m*-tolylsodium (prepared from *m*-chlorotoluene and sodium,[6] as well as from di-*m*-tolylmercury and sodium). As illustrated in reaction [I], *p*-tolylpotassium also undergoes a thermal rearrangement to give benzylpotassium.

Benzyllithium.—Although benzylsodium and benzylpotassium can now be obtained very conveniently and in highly satisfactory yields, benzyllithium is relatively inaccessible. Hein and co-workers[12] have prepared benzyllithium from dibenzylmercury and ethyllithium.

$$(C_6H_5CH_2)_2Hg + 2C_2H_5Li \longrightarrow 2C_6H_5CH_2Li + (C_2H_5)_2Hg \quad [IV]$$

Ziegler and Dersch[13] have used two different reactions for the synthesis of benzyllithium. One of these is the interaction of benzylmagnesium chloride in ether with metallic lithium.

$$C_6H_5CH_2MgCl + Li \longrightarrow C_6H_5CH_2Li + Mg + LiCl \quad [V]$$

The other is probably a two-stage reaction between benzylmagnesium chloride and phenyllithium.

$$C_6H_5CH_2MgCl + C_6H_5Li \longrightarrow C_6H_5CH_2MgC_6H_5 + LiCl$$
$$C_6H_5CH_2MgC_6H_5 + C_6H_5Li \longrightarrow C_6H_5CH_2Li + (C_6H_5)_2Mg \quad [VI]$$

No one of these procedures is quite satisfactory. Reaction [IV] involves the relatively inaccessible dibenzylmercury, and may be incomplete; reaction [V] is quite slow and, if conditions are not followed rigorously, may be erratic; and reaction [VI] produces a mixture of two different but relatively reactive organometallic compounds.

Unfortunately, we have not succeeded as yet in effecting a rearrangement of *p*-tolyllithium to benzyllithium under conditions where *p*-tolylsodium and *p*-tolylpotassium (reaction [I]) rearrange to benzylsodium and benzylpotassium, respectively. It is possible to prepare benzyllithium by metalating toluene laterally with *n*-butyllithium. However, the yield is not much greater than that required to establish definitely that benzyllithium is formed. Interestingly enough, Mr. F. W. Moore has shown that benzene can be metalated by *n*-butyllithium under corresponding conditions to give a 15% yield of phenyllithium. In general, our experience is that alkylsodium and alkylpotassium compounds are distinctly more effective for lateral metalations than are alkyllithium compounds.

Lateral Metalations.—We have extended lateral metalations by organosodium and organopotassium compounds to mesitylene and to β-methylnaphthalene. In the absence of functional groups that would undergo secondary transformations, it is probable that lateral metalation will prove serviceable in effecting indirectly such reactions as oxidation. For example, there is no known procedure for oxidizing a methylcarbazole to a corresponding carbazolecarboxylic acid.[14] Lateral metalation followed by oxidation or carbonation would undoubtedly facilitate conversion of a methyl group to a carboxyl group. Occasional cases of oxidation-resistant methyl groups are

(10) Bockmühl and Ehrhart, French Patent 736,428 [*Chem. Zentr.*, **104**, II, 2193 (1933)]; see, also, Ziegler, ref. 5.

(11) (a) Morton and Hechenbleikner, THIS JOURNAL, **58**, 2599 (1936). (b) Morton and Fallwell, Jr., *ibid.*, **60**, 1429 (1938). (c) Morton, Fallwell, Jr., and Palmer, *ibid.*, **60**, 1426 (1938). It is interesting to note that Morton, LeFevre and Hechenbleikner, *ibid.*, **58**, 754 (1936), obtained a 95% yield of *p*-toluic acid from *p*-chlorotoluene, sodium and carbon dioxide at 50° and under 500 pounds pressure. See, also, Morton and Massengale, *ibid.*, **62**, 120 (1940).

(12) Hein, Petzchner, Wagler and Segitz, *Z. anorg. allgem. Chem.*, **141**, 204 (1924).

(13) Ziegler and Dersch, *Ber.*, **64**, 448 (1931).

(14) Dunlop and Tucker, *J. Chem. Soc.*, 1945 (1939).

found in other types, for example, dibenzofuran.[15]

Rates of Carbonation.—It has long been known that the kind and ratio of products obtained by carbonation of organometallic compounds are influenced markedly by the rate and temperature of carbonation,[16a] particularly with organolithium compounds.[16b] Low temperature together with a large excess of carbon dioxide, conditions realized by pouring RM compounds on crushed solid carbon dioxide, give predominantly the acid and little of the ketone or tertiary alcohol. Furthermore, carbonation by solid carbon dioxide depresses markedly the formation of malonic acids from benzylmetallic types.[16c] For example, benzylpotassium under such conditions gives an 82% yield of phenylacetic acid and no significant quantity of phenylmalonic acid. However, slow carbonation with gaseous carbon dioxide gives 55% of phenylacetic acid and 23% of phenylmalonic acid. Related observations were made in the carbonation of 3,5-dimethylbenzylpotassium. What probably happens predominantly in such cases is the metalation of the active methylene group formed after the initial carbonation. The following reactions were investigated in some detail by Ivanoff and Spassoff[17] with benzylmagnesium chloride.

$$C_6H_5CH_2MgCl + CO_2 \longrightarrow C_6H_5CH_2COOMgCl \quad [VII]$$

$$C_6H_5CH_2COOMgCl + C_6H_5CH_2MgCl \longrightarrow [C_6H_5CHCOOMgCl][MgCl] + C_6H_5CH_3 \quad [VIII]$$

$$[C_6H_5CHCOOMgCl][MgCl] + CO_2 \xrightarrow{[H_2O]} C_6H_5CH(COOH)_2 \quad [IX]$$

Slow carbonation undoubtedly would facilitate metalation of the methylene group by the RM compound in essential accordance with reaction [VIII]. This mechanism for the carbonation of benzylsodium has been established by Morton and co-workers.[11c]

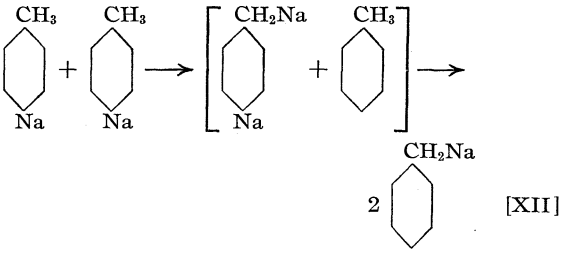
Reaction Mechanisms.—It is quite clear that there are at least two stages in the formation of benzylsodium from toluene, chlorobenzene and sodium.

$$C_6H_5Cl + 2Na \longrightarrow C_6H_5Na + NaCl \quad [X]$$

$$C_6H_5Na + C_6H_5CH_3 \longrightarrow C_6H_5CH_2Na + C_6H_6 \quad [XI]$$

The same reactions are probably the predominant ones when potassium is used in place of sodium, even though no direct evidence has been obtained as yet for the precursory formation of phenylpotassium. Reaction [XI] is apparently irreversible, for no benzoic acid has been isolated after carbonation of a reaction mixture of benzylsodium (free of toluene) and benzene which was stirred for fourteen hours at room temperature.

The migration of sodium in the transformation of *o*- and *p*-tolylsodiums to benzylsodium may be due to an allylic rearrangement of the type frequently observed with organometallic compounds. It is, however, difficult to account on such a basis for the conversion of *m*-tolylsodium to benzylsodium. Another possible mechanism that may involve all three isomeric tolylsodiums is the following



[XII]

That is, one molecule of *p*-tolylsodium may first metalate another molecule, and the resulting *p*-sodiobenzylsodium may then metalate the toluene formed in the first metalation to give benzylsodium. The apparent absence of any homoterephthalic acid, p-$HO_2CC_6H_4CH_2CO_2H$, suggests that reaction [XII] is either invalid or that *p*-sodiobenzylsodium metalates toluene with great ease.

It has been suggested that the difficulties of applying an allylic rearrangement for the tolylsodiums can be avoided by assuming the presence of traces of toluene, possibly formed by hydrolysis. This toluene would be metalated by the tolylsodium to give benzylsodium and toluene. Since the toluene is regenerated during the reaction, a small quantity would be adequate as a sort of catalyst. This sequence of reactions must be rapid because of the observed fairly prompt conversion of tolylsodium to benzylsodium.

Thermal Stabilities.—It has long been known that methylsodium, ethylsodium and methylpotassium are thermally labile, and that some decomposition occurs at room temperature,[18] particularly at initial stages.[19] Also, it appears that phenylalkali compounds are less thermally stable

(15) Gilman, Van Ess and Hayes, THIS JOURNAL, **61**, 643 (1939).

(16) (a) Some general references together with experimental work are given in the paper by Gilman and Parker, *ibid.*, **46**, 2816 (1924); (b) Gilman and Van Ess, *ibid.*, **55**, 1258 (1933); (c) Gilman and Pauvitz, *ibid.*, **62**, 1301 (1940).

(17) Ivanoff and Spassoff, *Bull. soc. chim.*, **49**, 19 (1931).

(18) Carothers and Coffman, THIS JOURNAL, **51**, 588 (1929); **52**, 1254 (1930).

(19) Gilman and Young, *J. Org. Chem.*, **1**, 315 (1936).

than benzylalkali types. In our lateral metalations by phenylsodium no benzoic acid was isolated. This is strikingly illustrated in the metalation of β-methylnaphthalene which gave an almost analytically pure β-naphthylacetic acid. The non-isolation of benzoic acid may not have been due to thermolysis of small amounts of phenylsodium, but rather to a rapid, irreversible metalation. However, the action of heat on *m*-tolylsodium in petroleum ether illustrates a marked difference in thermal stabilities of *m*-tolylsodium and benzylsodium. When *m*-tolylsodium is prepared from *m*-chlorotoluene and sodium in petroleum ether, and with no refluxing, there results an 85% yield of *m*-toluic acid unaccompanied by any phenylacetic acid. But with only a ten-minute period of refluxing, phenylacetic acid (6.4% yield) but no *m*-toluic acid was formed. The benzylsodium formed intermediately in such reactions is relatively little affected by prolonged refluxing. The products of thermolysis other than benzylsodium have not as yet been examined.

Organolithium compounds differ markedly from other organoalkali compounds in thermal stabilities. For example, *p*-tolyllithium was found neither to decompose nor to rearrange after relatively long periods of refluxing in petroleum ether.

Experimental Part

Reaction of Sodium with Di-*p*-tolylmercury.—In a three-necked flask provided with stirrer, condenser and nitrogen inlet, was placed a mixture of 10 g. (0.43 g. atom) of sodium, 7.7 g. (0.02 mole) of di-*p*-tolylmercury, and 160 cc. of petroleum ether (b. p. 85–115°). The di-*p*-tolylmercury is not totally soluble in the solvent, but apparently reacted completely inasmuch as none was recovered at the end of the reaction. A reaction set in after the mixture was refluxed for ten minutes. The yellow-brown reaction mixture, after nineteen hours of refluxing, was cooled, carbonated by solid carbon dioxide, and then hydrolyzed. The yield of phenylacetic acid (mixed melting point) was 3.1 g. or 57%. In addition, the mother liquor yielded 0.13 g. of an oily solid which appears to be mainly phenylacetic acid.

When toluene was substituted for the petroleum ether, the yield of phenylacetic acid was 3.6 g. or 66%.

A sealed tube experiment now in progress indicates that di-*p*-tolylmercury and sodium in petroleum ether react very slowly at room temperature if there be no shaking or stirring.

Reaction of Sodium with Di-*o*-tolylmercury and Di-*m*-tolylmercury.—The di-*o*-tolylmercury and di-*m*-tolylmercury were prepared by conventional procedures using the Grignard reagents. Parallel experiments were made with each isomer, using three-necked flasks, 7.7 g. (0.02 mole) of mercurial, 10 g. (0.43 g. atom) of sodium wire and 160 cc. dry, unsaturate-free petroleum ether (b. p. 85–100°). Each mixture was stirred and refluxed for eighteen hours; and before carbonation with solid carbon dioxide, the red color characteristic of benzylsodium was evident.

The yield of phenylacetic acid from the di-*o*-tolylmercury experiment was 0.95 g. or 17.5%; and the yield from the di-*m*-tolylmercury experiment was 2.02 g. or 37.2%. No phenylmalonic acid was isolated from either carbonation product. Also, no toluic acid (*o*- or *m*-) was isolated from either reaction mixture, although the slightly lower melting point of the phenylacetic acid from the di-*o*-tolylmercury experiment may indicate the possible presence of traces of *o*-toluic acid.

The approximate times noted for inception of reaction between the mercurials and sodium were: di-*o*-tolylmercury, twenty minutes; di-*m*-tolylmercury, fifteen minutes; and di-*p*-tolylmercury, ten minutes.

Preparation of Phenylsodium in Toluene.—In a 500 cc. three-necked flask, equipped with a nitrogen inlet, condenser, mercury-sealed stirrer and thermometer, was placed a mixture of 150 cc. of toluene, 11.5 g. (0.5 g. atom) of sodium sand, and 22.5 g. (0.2 mole) of chlorobenzene. After stirring at room temperature for about forty-five minutes, the temperature started to rise. By appropriate cooling, the temperature was not allowed to exceed 40° during the entire reaction period, which was about two hours. When the temperature started to fall, the mixture was immediately poured jet-wise upon crushed solid carbon dioxide. The yield of benzoic acid (mixed melting point) was 21.2 g. or 87%.

Apropos the thermal stability of phenylsodium, two parallel preparations were made in a customary manner from 5 g. (0.014 mole) of diphenylmercury, 2 g. of sodium wire and 100 cc. of benzene. One of these was refluxed for twenty-four hours and after carbonation yielded 2.13 g. (62%) of benzoic acid. The other, stirred at room temperature for twenty-four hours, yielded 2.96 g. (86%) of benzoic acid.

Attempt to Prepare Phenylpotassium in Toluene.—To a mixture of 7.4 g. (0.19 g. atom) of potassium sand in 100 cc. of toluene, cooled to 0°, was added 11.2 g. (0.1 mole) of chlorobenzene in 45 cc. of toluene at such a rate that the temperature at no time rose above 0°. The time required for the addition in this orienting experiment was four and one-half hours. Carbonation, at the end of this time, gave 7.3 g. or a 60% yield of phenylacetic acid. On concentration of the mother liquors from the crystallization of an aliquot of the total acidic material, no benzoic acid was isolated.

Preparation of *p*-Tolylsodium.—In each of the experiments, the results of which are given in Table I, 12.7 g. (0.1 mole) of *p*-chlorotoluene, 5.5 g. (0.23 g. atom) of sodium sand and 75 cc. of solvent were used. The sodium sand should be as fine as possible, inasmuch as the reaction starts more promptly and runs a smoother course when the sand is very fine. It is also recommended that the fine sodium be freshly prepared. The conventional procedure of heating sodium in xylene was used for the preparation of the fine sodium. Reaction sets in almost immediately when the *p*-chlorotoluene is added to the sodium in the organic medium, and is accompanied by a temperature rise and the formation of black specks on the sodium. The mixture is stirred rapidly, and the temperature is

held between 35–40°. After about one and one-half hours the temperature shows no further tendency to rise. Then the cooling-bath is removed, and stirring is continued until room temperature is reached. In carbonating by solid carbon dioxide it is desirable to add 100–200 cc. of dry ether when benzene is used as the medium, in order to reduce freezing of the benzene. The excess sodium is destroyed by the cautious dropwise addition of ethanol and water.

TABLE I

PREPARATION OF *p*-TOLYLSODIUM IN SOME SOLVENTS

[0.1 Mole of *p*-Chlorotoluene]

Solvent	Yield of *p*-toluic acid G.	%
Benzene	8.9	65.5
Benzene	9.5	70.0
Cyclohexane	7.8	57.3
Cyclohexane	7.6	56.0
Pet. ether (70–80°)	10.1	74.3
Pet. ether (70–80°)	9.7	71.3
Toluene	10.9	80.1
Toluene	10.8	80.0

Preparation of Benzylsodium

A. From Chlorobenzene, Sodium and Toluene.—The preliminary operations in the following experiment were those described in the preparation of phenylsodium in toluene. After the formation of phenylsodium the suspension was refluxed for three hours. As soon as refluxing started, the black suspension assumed a brick-red color, and at the end of three hours the color was typical of benzylsodium. Carbonation, in the usual manner by solid carbon dioxide, gave 20.9 g. or a 77% yield of phenylacetic acid (mixed melting point). Carbonation after refluxing for six hours gave an 80% yield of phenylacetic acid. There was no perceptible formation of phenylmalonic acid under either of these sets of experimental conditions.

B. From *p*-Tolylsodium by Heating.—In each of the experiments, the results of which are given in Table II, the *p*-tolylsodium was prepared in accordance with directions given earlier from 0.1 mole of *p*-chlorotoluene, 0.23 g. atom of sodium sand, and 75 cc. of the solvent designated. The yields of phenylacetic acid are based on the initial 0.1 mole of *p*-chlorotoluene, and not on the % of *p*-tolylsodium obtained from the *p*-chlorotoluene.

TABLE II

PREPARATION OF BENZYLSODIUM BY HEATING *p*-TOLYLSODIUM IN SOME SOLVENTS

Solvent	Reflux period, hours	Yield of phenylacetic acid G.	%
Benzene	24	7.1	52.2
Benzene	16	6.8	50.0
Benzene	12	6.6	48.5
Toluene	4	8.5	62.0
Toluene	14	10.75	79.0
Toluene	14	10.7	79.0
Cyclohexane	18	7.3	53.7
Cyclohexane	14	7.9	58.1
Pet. ether (70–80°)	18	8.5	62.5

Rapid and Slow Carbonation of Benzylsodium.—The general conclusions drawn from the results reported recently[16e] on the rapid and slow carbonation of amylsodium were substantiated with benzylsodium. Two parallel preparations of benzylsodium were made from 11.2 g. (0.1 mole) of chlorobenzene, 5.75 g. (0.25 g. atom) of sodium sand, and 75 cc. of toluene. One of these was carbonated by pouring on solid carbon dioxide (time, five seconds); yield of phenylacetic acid 9.9 g. (72.9%); and no phenylmalonic acid isolated. The other was carbonated by gaseous carbon dioxide (time, four to five hours); yield of phenylacetic acid, 2.4 g. (17.6%); and yield of phenylmalonic acid, 3.8 g. (42.2%).

The mode of formation of benzylsodium is without essential effect, for benzylsodium from dibenzylmercury, sodium wire and toluene gave on rapid carbonation (five seconds) 3.3 g. (61%) of phenylacetic acid, and 0.03 g. or less than 1% of phenylmalonic acid; on slow carbonation (five hours, gaseous carbon dioxide), 0.46 g. (8.5%) of phenylacetic acid and 0.81 g. (22.8%) of phenylmalonic acid.

Preparation of Benzylpotassium

A. From Chlorobenzene, Potassium and Toluene.—In a 500-cc. round-bottomed flask, provided with the customary appurtenances mentioned previously, was placed a mixture of 8.5 g. (0.22 g. atom) of potassium sand and 100 cc. of toluene. A solution of 11.2 g. (0.1 mole) of chlorobenzene in 50 cc. of toluene was added very slowly, the temperature being kept between 30–35°. Since there is no induction period, the temperature starts rising with the addition of the first few drops of chlorobenzene. Occasional cooling with an ice-bath is necessary. The average time necessary for the addition of the chlorobenzene is one and one-half hours. At the conclusion of this preliminary operation, the reaction mixture was refluxed for one hour, during which time the color changed from black to a brilliant brick-red. On completion of the refluxing, the mixture was cooled and poured jet-wise upon solid carbon dioxide. The yield of pure phenylacetic acid was 11.2 g. or 82%.

B. From Phenylpotassium and Toluene.—A mixture of 5 g. (0.016 mole) of di-*n*-butylmercury, 3 g. (0.077 g. atom) of potassium and 50 cc. of benzene was stirred for sixty hours at room temperature. At the end of this time an aliquot, which was removed and carbonated and then hydrolyzed and acidified, gave no odor of valeric acid, thereby establishing the absence of *n*-butylpotassium. Subsequent to the addition of 50 cc. of toluene to the main reaction mixture, refluxing was carried out for six hours. The mixture was then cooled, and carbonated by pouring on solid carbon dioxide. Large pieces of potassium were removed by filtration, and then the carbonation mixture was hydrolyzed carefully and in sequence with butanol, ethanol and water. The yield of phenylacetic acid was 1.9 g. or 44%.

C. From Di-*p*-tolylmercury and Potassium.—A mixture of 7.7 g. (0.02 mole) of di-*p*-tolylmercury, 7.8 g. (0.2 g. atom) of potassium and 160 cc. of petroleum ether (b. p., 85–115°) was refluxed for 18.5 hours. Subsequent to cooling and carbonation, hydrolysis was effected by ethanol and then by water. The yield of phenylacetic acid was 0.9 g. or 16.5%. In addition, there was obtained 0.17 g. of a water-insoluble acid which charred at about 300°.

Reaction of Benzylpotassium with Gaseous Carbon Dioxide.—A suspension of benzylpotassium was prepared in accordance with the directions given in the preparation from potassium, chlorobenzene and toluene. At the end of the refluxing period, the mixture was cooled and then carbonated by passing carbon dioxide over the surface of the well-stirred suspension. The temperature was kept between 35–40°, and a negative color test[20] was obtained in fifteen minutes. The weight of the total acids was 10.1 g., and this mixture was separated, on the basis of solubility differences in chloroform, to give 2.1 g. or a 23% yield of phenylmalonic acid and 7.5 g. or a 55% yield of phenylacetic acid.

Reaction of Benzylpotassium with Benzophenone.—To benzylpotassium prepared from potassium (0.1 g. atom), chlorobenzene and toluene, was added 18.2 g. (0.1 mole) of benzophenone in 50 cc. of toluene over a one and one-half hour period. The brick-red color slowly disappeared and the solution assumed a deep emerald-green color, possibly due (in part) to the formation of the potassium ketyl of benzophenone. The temperature was not allowed to exceed 40°, and the mixture was stirred for one hour after the temperature ceased rising. Subsequent to hydrolysis, there was isolated 22 g. or a 59% yield of diphenylbenzylcarbinol melting at 87–88°.

Preparation of 3,5-Dimethylbenzylpotassium.—To a mixture of 8.5 g. (0.22 g. atom) of potassium sand and 100 cc. of dry mesitylene, was added slowly a solution of 11.2 g. (0.1 mole) of chlorobenzene and 39 cc. of mesitylene. The time of addition was one and one-half hours, and the temperature was kept between 30–35°. The black suspension changed slowly to the characteristic brick-red color upon refluxing for one hour. After carbonation by solid carbon dioxide and hydrolysis, there was isolated 13 g. or a 79% yield of 3,5-dimethylphenylacetic acid melting at 99.5–101°.

Under corresponding conditions, when sodium sand was used in place of the potassium sand, 3.3 g. or a 20% yield of 3,5-dimethylphenylacetic acid was obtained, in addition to some as yet unidentified tarry oil.

Slow Carbonation of 3,5-Dimethylbenzylpotassium.—In an orienting experiment, 3,5-dimethylbenzylpotassium was carbonated by the slow addition of gaseous carbon dioxide. The yield of 3,5-dimethylphenylacetic acid was 30%. In addition, there was obtained a 15% yield of 3,5-dimethylphenylmalonic acid, which softened at 149–150° and melted with decomposition at 154–155°.

Anal. Calcd. for $C_{11}H_{12}O_4$: neut. equiv., 104; C, 63.46; H, 5.77. Found: neut. equiv., 106, 107; C, 63.55, 63.57; H, 5.85, 5.81.

β-Naphthylmethylsodium.—Phenylsodium was prepared from 5.7 g. (0.25 g. atom) of sodium sand and 11.2 g. (0.1 mole) of chlorobenzene in 100 cc. of benzene. To the phenylsodium was added 28.4 g. (0.2 mole) of β-methylnaphthalene. No reaction was evident after stirring at room temperature for one hour. The mixture was refluxed for twenty-one hours, carbonated by solid carbon dioxide and then worked up in a customary manner to yield 0.8 g. or 4.3% of β-naphthylacetic acid melting at 137–139°. The yield of acid was 31% when metalation was effected by *n*-butylsodium (from di-*n*-butylmercury) in petroleum ether (b. p. 85–100°) at room temperature for twenty-six hours.

Phenylisopropylsodium (By Richard V. Young).—A mixture of 2.6 g. (0.01 mole) of diethylmercury, 0.035 g. atom of sodium and 25 cc. of cumene was stirred for twelve hours. In the course of the reaction a red precipitate formed, and this gave a positive color test. Carbonation of the reaction mixture by solid carbon dioxide gave a 41% yield of phenyldimethylacetic acid (mixed melting point). This preparation was carried out some time ago, and in view of the other results reported at this time it is quite possible that the widely used phenylisopropylpotassium might be prepared readily by metalation of cumene by benzylpotassium.

Benzyllithium from Toluene and *n*-Butyllithium.—To a filtered ether solution of *n*-butyllithium, prepared from 27.4 g. (0.2 mole) of *n*-butyl bromide,[21] was added 180 cc. of toluene. Within five minutes of the application of heat, a heavy white precipitate (probably lithium bromide) formed. After refluxing for nineteen hours, carbonation was effected by solid carbon dioxide, and the yield of phenylacetic acid was 0.06 g. or 0.22%.

Experiment on Thermal Stability

Dangers in Handling Organopotassium Compounds and Potassium.—In our experiments, we have generally used the conventional three-necked flasks provided with a mercury-sealed stirrer, condenser, and inlet tube for dry nitrogen. Inasmuch as dry organopotassium compounds, like benzylpotassium, are spontaneously inflammable on atmospheric exposure, there are occasional fire risks when the apparatus is disconnected. At times some of the benzylpotassium splashes up into parts of the apparatus attached to the flask, and is dried there by the stream of nitrogen. This risk can be decreased by stirring the solution vigorously at the end of the reaction so that some of the solvent wets any benzylpotassium and thereby prevents premature ignition.

Potassium residues should not be allowed to accumulate, and should not be added to sodium residues. There are two cases, in different laboratories, where sodium residues under kerosene have ignited and exploded. The causes of these accidents are not known, but it is possible that potassium residues in the sodium residues may be responsible. Potassium peroxide appears to form readily, and in contact with fresh potassium surfaces may give rise to violent explosions. If this is one of several possible explanations, then shaking a container of potassium residues may increase the hazard by exposing fresh surfaces.

Acknowledgment.—The authors are grateful to F. W. Moore for assistance.

(20) Gilman and Schulze, THIS JOURNAL, **47**, 2002 (1925).

(21) Gilman, Zoellner and Selby, *ibid.*, **54**, 1957 (1932).

Summary

The pronounced effectiveness of benzylalkali compounds in some interconversion reactions of organometallic compounds made desirable improved and convenient directions for the preparation of benzyl types. Benzylpotassium, now available for the first time in workable quantities, is readily prepared in 82% yield from toluene, chlorobenzene and potassium. Benzylsodium can be obtained in 80% yield by heating *p*-tolylsodium (from *p*-chlorotoluene and sodium in 80% yield) in petroleum ether; and in 80% yield by heating phenylsodium (from chlorobenzene and sodium in 87% yield) with toluene.

There is a lateral migration of sodium to give benzylsodium when *o*-, *m*-, or *p*-tolylsodium is heated. *p*-Tolyllithium is stable under these conditions. However, *n*-butyllithium metalates toluene laterally to give benzyllithium (0.2% yield).

In addition to other lateral metalations, an account is given of rates of carbonation, thermal stabilities, reaction mechanisms and some hazards in manipulating organopotassium compounds and potassium.

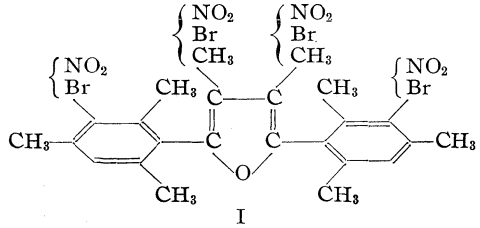
AMES, IOWA RECEIVED FEBRUARY 26, 1940

[CONTRIBUTION FROM THE COBB CHEMICAL LABORATORY, UNIVERSITY OF VIRGINIA]

Some Substituted 2,5-Dimesitylfurans

BY ROBERT E. LUTZ AND CHARLES J. KIBLER

This investigation has been made in order to study the effect of substitution of mesityl groups on the reactions of the furan nucleus, and also to test the possibility of stereoisomerism involving restricted rotation on the inter-nuclear bonds.

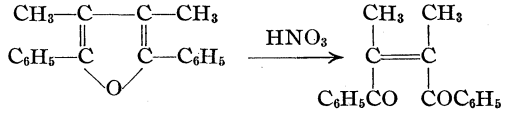


I

Five 2,5-dimesitylfurans of the type I have been prepared by methods in which the final step has completed the introduction of groups requisite for diastereoisomerism due to restricted rotation. In no case was there found any evidence of the existence of isomers. It would appear, therefore, that under the somewhat drastic preparative conditions involved in all but one case, stereoisomers are not stable enough for independent existence, as would be expected since interference effects in this type of compound should be small. It is, of course, possible that labile isomers, once formed, might be stable enough to exist under ordinary conditions; and further investigation should be made, including an attempt to resolve a suitable derivative which presumably would have the more stable *trans-dl* configuration.

In the preparation and study of the compounds mentioned above, it was found that the mesityl groups offer very little hindrance to nitration and bromination at the furan β-positions and that these β-positions are generally more reactive than the unsubstituted positions in the mesityl nuclei. The results parallel those obtained in the halogenation of 2,5-diphenylfuran.[1]

The most striking generalization arising from this investigation concerns oxidative ring fission, which is a reaction characteristic of 2,5-diarylfurans with no ortho substituents in the aryl nuclei. The *cis* unsaturated 1,4-diketone is produced whenever this stereoisomer is stable under the reaction conditions,[2] as is illustrated in the case of the oxidation of diphenyldimethylfuran (II) to the new *cis* unsaturated diketone, III. There are



II III

over 25 examples of this reaction among the 2,5-diaryl types alone, and there is now no authentic failure of the reaction when tried. Substituents in these compounds in the para position of the phenyls include chlorine and bromine, and in the furan β-positions, chlorine,[1,2] methyl,[3] chloromethyl,[3] phenyl,[1,2] and mesityl.[4] On the other

(1) Lutz and Wilder, THIS JOURNAL, **56**, 2145 (1934); Lutz, Tyson, Sanders and Fink, *ibid.*, **56**, 2679 (1934).

(2) Lutz and Wilder, *ibid.*, **56**, 978 (1934), and references cited; *cf.* also examples cited by Gilman and Wright, *Chem. Rev.*, **11**, 523 (1932).

(3) Lutz and McGinn, results to be published shortly.

(4) Lutz and Kibler, THIS JOURNAL, **61**, 3007 (1939).

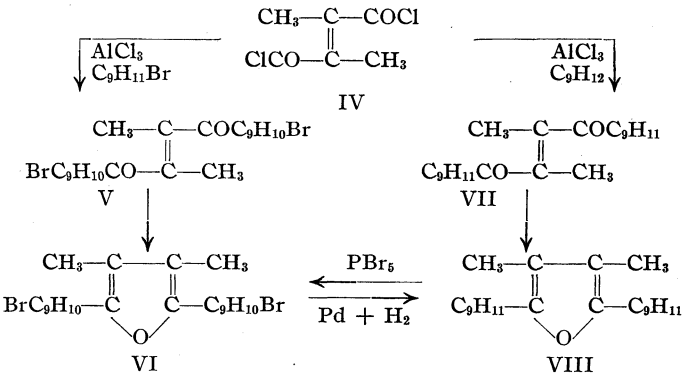
hand, 2,5-dimesitylfuran and a large number of derivatives are now known, including a number described in the experimental part of this paper. Among the substituents are bromine and nitro in the mesityl nuclei, and bromine, nitro, methyl, phenyl[5] and mesityl[6] in the furan β-positions. These compounds consistently have resisted oxidative ring fission under the usual conditions effective for the 2,5-diphenyl types. If they have reacted at all, they have undergone only nitration or decomposition; in no case was there any evidence of simple ring fission to the unsaturated 1,4-diketone.

These results are significant in connection with the mechanism of the oxidative ring fission. It has been suggested[2,7] that the reaction involves addition of nitric acid or its equivalent (an anhydride or a mixed anhydride) to the diene system of the furan, followed by break-up and loss of the equivalent of nitrous acid, the ethylene linkage being formed before the break in the oxygen bridge of the ring with the consequent production of a *cis* product whenever this isomer is stable under the conditions of the experiment. The failure consistently of 2,5-dimesitylfurans to undergo the oxidative ring fission is readily understandable if one assumes that the α-mesityl groups offer hindrance to addition at the ends of the diene system involved, and supports the hypothesis that α-substitution in general, including displacement of one group by another, involves 1,4-addition and elimination at the α-carbons. Since substitution in the β-positions is not hindered to any significant extent by α-mesityl groups, it might be supposed also that β-substitution proceeds either direct or by addition and elimination at the vinyl ether system, —C=C—O—, but without involving addition at the α-carbon.

Experimental Part

2,5 - Di - (bromomesityl) - 3,4 - dimethylfuran (VI).—The preparation of this furan, VI, was accomplished in two ways. One synthesis began with the Friedel–Crafts reaction between dimethylfumaryl chloride (IV) and bromomesitylene. The desired unsaturated diketone, di-(bromotrimethylbenzoyl)-ethylene (V), was obtained but in extremely poor yield. Zinc and acetic acid reduction of this and dehydration of the product with acetic anhydride and sulfuric acid gave di-(bromomesityl)-dimethylfuran (VI) in good yield.

The first step in the above synthesis was entirely impractical because under the necessary conditions of the Friedel–Crafts reaction bromomesitylene undergoes dismutation to mesitylene and di- and tribromomesitylene, a reaction for which there are many analogies[8] and one which proceeds more rapidly than the desired Friedel–Crafts reaction. Under the most favorable conditions a very difficultly separable mixture was obtained which contained large amounts of di-(trimethylbenzoyl)-ethylene and only a small amount of the desired di-(bromomesityl) derivative, V; laborious fractional crystallization was necessary for separation. This synthesis, however, in conjunction with the second preparation to be described below, shows the structure of the final product and the location of the bromine atoms in the mesityl nuclei. The two halogens of the furan, VI, are not removable by means of zinc dust and acetic acid but are eliminated by catalytic hydrogen.



The best preparation of di-(bromomesityl)-dimethylfuran (VI) was through direct bromination of dimesityldimethylfuran (VIII) with phosphorus pentabromide.

The Friedel–Crafts Reaction between Dimethylfumaryl Chloride and Bromomesitylene.—A series of reactions was run using aluminum chloride as catalyst and carbon

(5) Lutz and Kibler, THIS JOURNAL, **61**, 3010 (1939).
(6) Lutz and Kibler, *ibid.*, **62**, 360 (1940).
(7) Freure and Johnson, *ibid.*, **53**, 1142 (1931).

(8) α- and β-bromonaphthalenes with aluminum chloride and toluene at 100° give a mixture of bromotoluenes and naphthalene, and in carbon disulfide (refluxing) α-bromonaphthalene gives β-bromonaphthalene and 1,2-dibromonaphthalene [Roux, *Ann. chim. phys.*, [6] **12**, 345 (1887)]; bromobenzene and aluminum chloride at high temperature give benzene and dibromobenzene [Dumreicher, *Ber.*, **15**, 1867 (1882)]; and *o*-dichlorobenzene, methyl chloride, and aluminum chloride at 100° give trichloromesitylene [Friedel and Crafts, *Ann. chim. phys.*, [6] **10**, 418 (1887)].

disulfide as solvent, with variation in temperature, proportion of materials and time of reaction. The following compounds were isolated: dibromomesitylene, tribromomesitylene, di - (trimethylbenzoyl) - dimethylethylene (VII), the desired di - (bromotrimethylbenzoyl) - dimethylethylene (V), and 1 - bromomesityl - 2,3 - dimethyl - 4-mesityl-2-butenedione-1,4. The bromomesitylene used was carefully purified and had the b. p. 117° at 25 mm. and m. p. −0.1°. Three typical experiments were as follows:

(a) Bromomesitylene (69 g.) was added to 300 cc. of carbon disulfide and 136 g. of anhydrous aluminum chloride, followed quickly by 31 g. of dimethylfumaryl chloride, added dropwise with stirring, allowing the mixture to reflux gently for one hour. This gave 81 g. of a mixture of diketones. Tribromomesitylene (2.3 g.) was obtained from the residues (identified by m. p. 227–228° and analysis). The diketone mixture was fractionally crystallized from acetone, butanone, ethyl acetate, and other solvents until 10 mg. of nearly pure monobromo derivative remained, the melting point becoming constant.

(b) In another run, the temperature was held to 22°. From this all three diketones were isolated. At 0° to −5° no reaction occurred.

(c) With a large excess of bromomesitylene, the product was nearly pure di-(trimethylbenzoyl)-ethylene (yield, 78%). Steam distillation of the residues gave unchanged bromomesitylene, and then dibromomesitylene which solidified in the condenser; the yield was 68% based on disproportionation to mesitylene and dibromomesitylene. The dibromomesitylene was identified by m. p. 64° and b. p. 278–279°.

trans - **4 - Bromomesityl - 2,3 - dimethyl - 1 - mesityl-2-butenedione-1,4,** $BrC_9H_{10}COC(CH_3)=C(CH_3)COC_9H_{11}$. —This compound was obtained in only very small amounts by fractional crystallization of the mixtures of diketones, the best sample melting from 124–127° (rosets of blade-shaped plates).

Anal. Calcd. for $C_{24}H_{27}O_2Br$: C, 67.6; H, 6.4. Found: C, 65.3; H, 6.0.

trans - **1,4 - Di - (bromomesityl) - 2,3 - dimethyl - 2 - butenedione-1,4, V.**—The best sample obtained melted at 140–143°.

Anal. Calcd. for $C_{24}H_{26}O_2Br_2$: C, 56.9; H, 5.2. Found: C, 56.9; H, 5.0.

A mixture of 0.07 g. of V with 0.5 cc. of concd. acetic acid, 1 cc. of acetic anhydride and 0.5 g. of zinc dust was boiled for one minute and filtered. One drop of concd. sulfuric acid was added to the filtrate; then, when worked up in the usual way, the furan, VI, was obtained in good yield.

2,5-Dimesityl-3,4-dimethylfuran, VIII.—Attempts to oxidize the furan with concd. nitric acid in acetic or propionic acid gave only resinous products even at −10°.

2,5-Di-(bromomesityl)-3,4-dimethylfuran, VI.—A mixture of 0.2 g. of dimesityldimethylfuran, VIII, and 0.8 g. of phosphorus pentabromide (50% excess) was heated at 100° for three minutes and allowed to cool slowly (ten minutes). Decomposition in water gave an oil which solidified. Crystallization from isopropanol gave 0.28 g. of nearly pure product (rhomboids); m. p. 111.5–113°.

Anal. Calcd. for $C_{24}H_{26}OBr_2$: C, 58.8; H, 5.3. Found: C, 58.4, 58.9; H, 5.2, 5.5.

Runs on a large scale gave poorer yields ranging from 65–75%.

The furan was not appreciably affected by zinc dust and concd. acetic acid. Hydrogenation with palladium on barium sulfate catalyst proceeded with absorption of approximately two molecules of hydrogen, and 2,5-dimesityl-3,4-dimethylfuran, VIII, was isolated and identified.

3,4 - Dibromo - 2,5 - di - (bromomesityl)-furan (XVII).—This furan (XVII) was prepared in three ways. The best synthesis started with dimesitylfuran, XIV. Bromination directly[9] gives mixtures which are not easily handled, but the 3,4-dibromo derivative, XV, has actually been made in this way and isolated.[9] Using phosphorus pentabromide at 90°, the desired tetrabromo derivative, XVII, is produced in excellent yield; when an insufficient quantity of this reagent is used, a difficultly separable mixture of the tri- and tetrabromo compounds, XVIII and XVII, is obtained; but at a higher temperature with an excess of the reagent there is produced the pentabromo derivative, XVI.

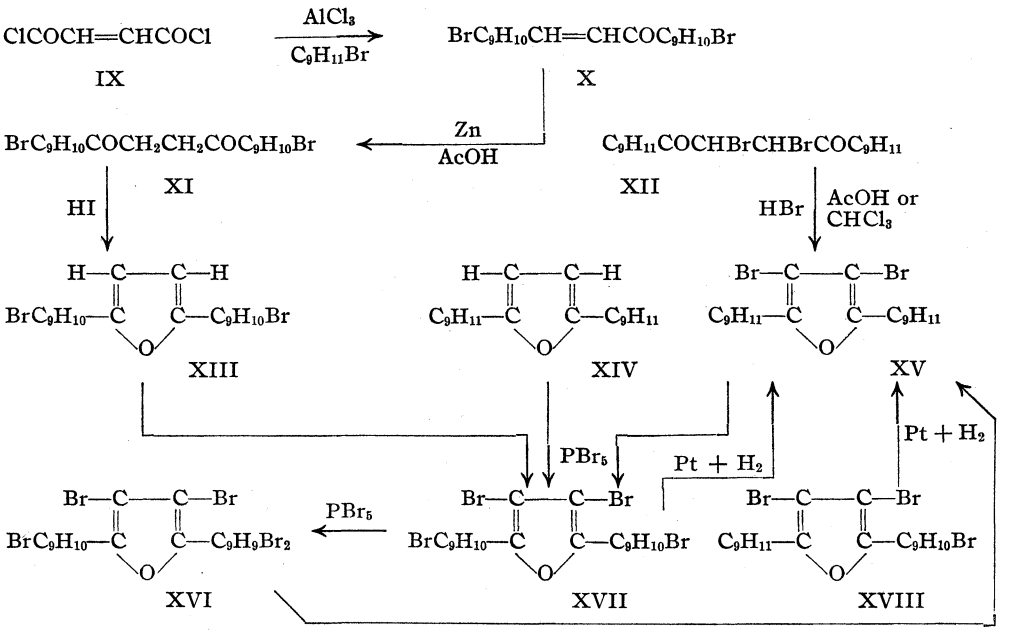
A second synthesis started with the Friedel–Crafts reaction between fumaryl chloride and bromomesitylene.[9] Here dismutation of bromomesitylene does not interfere seriously although it occurs to some extent. Reduction of the resulting unsaturated diketone to the saturated diketone, XI, was followed by dehydration to the furan, XIII, with hydriodic acid; and finally bromination with phosphorus pentabromide gave the tetrabromo derivative, XVII, in good yield.

The third synthesis utilized 3,4-dibromodimesitylfuran, XV, which was prepared by an improved method through the action of hydrogen bromide in acetic acid or chloroform on di-(trimethylbenzoyl)-dibromoethane, XII. The furan, XV, reacted with phosphorus pentabromide to give the tetrabromo derivative, XVII, in excellent yield.

Attempts to make the tetrabromo furan, XVII, by dehydration of the dibromide of di-(bromotrimethylbenzoyl)-ethylene (X) were unsuccessful.

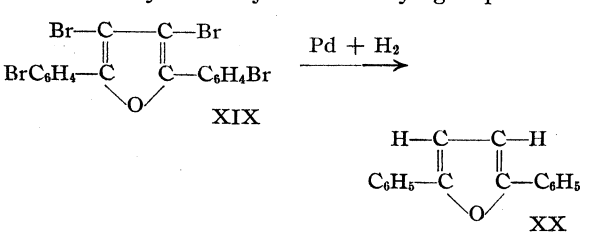
The positions of the halogens in the tetrabromo furan, XVII, are established by two of the syntheses described above involving different orders of introduction of halogens and starting from the dibromo derivatives, XI and XII, in which the location of the halogens is known, and by the reductions described below.

(9) Lutz, Johnson, and Wood, THIS JOURNAL, **60**, 716 (1938).



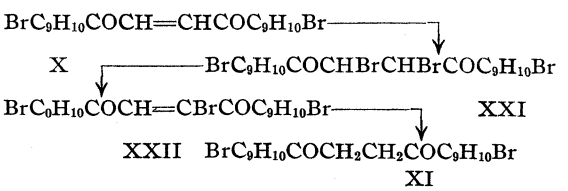
Reductive elimination of the halogens could not be brought about by means of zinc and acetic acid since no aliphatic halide groupings were involved. Hydrogenation with a palladium catalyst removed halogens from the mesityl nuclei in four compounds which were tested, namely, di-(bromomesityl)-dimethylfuran (VI), and the tri-, tetra- and pentabromo furans, XVIII, XVII and XVI. In the latter three cases the bromines in the β-positions of the furan nucleus resisted the catalytic reduction and remained untouched. Reduction, then, distinguishes between the two types of halogens, those in the mesityl nuclei being the more active and reducible.

The resistance of the halogens in the furan β-positions toward reduction was observed only in the 2,5-dimesitylfuran series, however; 3,4-dibromo-2,5-di-(bromophenyl)-furan, XIX, under comparable conditions is readily reduced by palladium and hydrogen to diphenylfuran, XX, with elimination of all four halogens including those in the furan β-positions. Probably the resistance to reduction of the β-halogens in the dimesitylfuran series is to be attributed to steric hindrance by the adjacent mesityl groups.



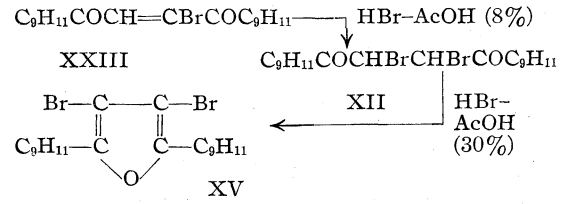
The various reactions described above show clearly that both in dimesityl- and diphenylfuran the β-positions in the furan nucleus are consistently more reactive toward bromination than the free positions in the aryl nuclei. Each mesityl or phenyl nucleus can subsequently be brominated once in each ring. The introduction finally of a second bromine into either mesityl nucleus meets with resistance, and disubstitution could be brought about in only one of the two rings under the most drastic conditions which were employed, the pentabromo derivative, XVI, being the result.

Some Halogen Derivatives of the Dimesityl 1,4-Diketones.—Incidental to this research, the following reactions were carried out. The dibromide of di-(bromotrimethylbenzoyl)-ethylene was made by direct addition of bromine to the unsaturated diketone, X. When a solution of the dibromide (XXI) in concd. acetic acid was refluxed, hydrogen bromide was quickly eliminated with formation of the bromo unsaturated diketone, XXII. The structure of this compound was proved by analysis and reduction to the saturated diketone, XI.

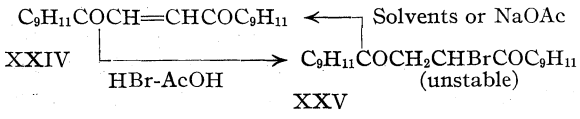


In the dimesityl series the dibromo diketone,

XII, was made by the action of 8% hydrogen bromide in concd. acetic acid on di-(trimethylbenzoyl)-bromoethylene, XXIII, the reaction proceeding quickly at room temperature. The conversion of the product by dehydration into the dibromo furan, XV, required longer standing under similar conditions with 30% hydrogen bromide in concd. acetic acid; while the yield was poor, no unchanged material was left to complicate the separation of the product.



Di-(trimethylbenzoyl)-ethylene, XXIV, itself reacts with hydrogen bromide in concd. acetic acid at 10° to give the addition compound, XXV, which was isolated and was moderately stable in the solid state. This product lost hydrogen bromide when treated with sodium acetate or upon standing in contact with solvents, particularly during crystallization, the unsaturated diketone, XXIV, being regenerated.



In connection with the relative stabilities of halides in the various saturated 1,4-diketones of the type under discussion, it is worthy of note that the chloro analog of XXV, namely, di-(trimethylbenzoyl)-chloroethane, also is unstable.[10] The dibenzoylchloro and bromoethanes require higher temperatures for decomposition, usually fusion temperature. The dihalides, both in the dimesityl and in the dibenzoyl series, decompose on melting or in boiling solvents with loss of halogen acid to give the halogeno unsaturated diketones. The dimesityl mono- and dihalogeno compounds in general, however, lose halogen acid with definitely greater ease than do the diphenyl analogs, perhaps due to the greater negativity of the mesityl groups as compared with phenyls.

Little is known about the corresponding halogeno compounds with an aryl group substituted on the ethylene linkage, but it should be pointed out that the two pairs of stereoisomers of the 1,2,4-trimesityl halogeno 1,4-diketones, $C_9H_{11}COCH(C_9H_{11})CH(X)COC_9H_{11}$, are known and are remarkably stable, resistant even to the action of sodium acetate in boiling ethanol.[6]

Meso - 1,4 - dimesityl - 2,3 - dibromobutanedione - 1,4, XII, was obtained when the unsaturated bromo diketone, XXIII, was dissolved at room temperature in 8% hydrobromic–concd. acetic acid, the dibromo diketone separating within two minutes.

1,4 - Dimesityl - 2 - bromobutanedione - 1,4 (Di-(trimethylbenzoyl)-bromoethane), XXV.—One gram of XXIV was added to 18 cc. of 13% hydrobromic acid in concd. acetic acid at 10°, the solid dissolving quickly. After standing for fifteen minutes and diluting with water, a gum was obtained which solidified. Crystallization from methanol gave a small amount of the dibromide, XII, formed by the brominating action of the bromo diketone, XXV, under these conditions.[11] The filtrate deposited 0.83 g. of the addition compound, XXV. It was difficult to purify any lost hydrogen bromide during crystallization. By careful manipulation and crystallization at moderate temperatures a sample of m. p. 81.5–82° was obtained. The analysis for bromine was low, indicating some loss of hydrogen bromide on standing, but it showed beyond question that one and only one bromine was present.

Anal. Calcd. for $C_{22}H_{25}O_2Br$: Br, 19.9. Found: Br, 18.9.

A small sample, when refluxed in ethanol for ten minutes with sodium acetate, gave di-(trimethylbenzoyl)-ethylene, XXIV, in quantitative yield.

***trans* - 1,4 - Di - (bromomesityl) - 2 - butenedione - 1,4, X,** was prepared by the Friedel–Crafts reaction[9] between fumaryl chloride and bromomesitylene. From the residues of the run, by steam distillation, dibromomesitylene of m. p. 63–64° was obtained and identified.

2,3 - Dibromo - 1,4 - di - (bromomesityl) - butanedione-1,4, XXI.—To a stirred suspension of 8 g. of X in 400 cc. of concd. acetic acid, heated to 60–65°, was added 2.68 g. of bromine in concd. acetic acid, the stirring being continued with heating for a short time after addition. The suspended solid went into solution as the bromine was added, and the difficultly soluble dibromide separated. On cooling and filtering 10 g. was obtained (82%). It crystallized from acetic acid or benzene as long flat rectangular prisms which melted with decomposition at about 250°.

Anal. Calcd. for $C_{22}H_{22}O_2Br_4$: C, 41.4; H, 3.5. Found: C, 41.2; H, 3.3.

Attempts to furanize this compound with 30% hydrobromic acid in concd. acetic acid failed, and only unchanged material was obtained after standing for five months in contact with the reagent. When refluxed with this reagent the hydrogen bromide was expelled and the bromo unsaturated diketone, XXII, was isolated. Reduction of the dibromide with zinc dust and concd. acetic acid in the usual way gave the saturated diketone, XI.

***trans* - 2 - Bromo - 1,4 - di - (bromomesityl) - 2 - butenedione-1,4, XXII.**—A suspension of the dibromide, XXI, in

(10) Lutz and Wood, THIS JOURNAL, **60**, 229 (1938).

(11) *Cf.* Lutz and Stuart, *ibid.*, **59**, 2324 (1937).

concd. acetic acid was refluxed for one hour and diluted with water. A good yield of the bromo unsaturated diketone, XXII, was obtained and crystallized from isopropanol; light yellow needles of m. p. 154–155°.

Anal. Calcd. for $C_{22}H_{21}O_2Br_3$: C, 47.4; H, 3.8. Found: C, 47.1; H, 3.8.

Reduction with zinc dust and concd. acetic acid in the usual way gave the saturated diketone, XI.

2,5-Dimesitylfuran, XIV.—Attempts to dehydrate the saturated diketone with dry hydrogen chloride in boiling concd. acetic acid (twenty-seven hours) or chloroform at room temperature (standing for six months), were not successful as preparative methods for the furan because the reactions were not complete. The hydriodic acid method was used.[9]

Oxidation with potassium permanganate in acetone, water or concd. acetic acid gave only small amounts of mesityl carboxylic acid.

2,5-Di-(bromomesityl)-furan, XIII, was made by hydroiodic acid dehydration of XI.

3,4-Dibromo-2,5-dimesitylfuran, XV, was prepared[9] by stepwise bromination of dimesitylfuran, XIV, but the yields were poor and uncertain. The dehydration of the dibromo diketone, XII, was studied in order to find effective conditions. Acetic anhydride and 30% hydrobromic acid in concd. acetic acid had no effect. With chloroform or concd. acetic acid, saturated with dry hydrogen chloride and allowed to stand, respectively, for one and six months, there were obtained impure mixtures that were difficult to purify. The following two experiments were highly successful, the latter being of advantage only when the material was needed quickly.

(a) A solution of 5 g. of the dibromo diketone, XII, in 50 cc. of dry chloroform, saturated with dry hydrogen bromide, was allowed to stand at room temperature for six months. The progress of the reaction was followed by withdrawing samples at intervals, evaporating the solvent under an air blast, and determining the melting point. The entire product was worked up in this way, 3.6 g. being obtained (m. p. 130–137°). Crystallization from ethanol gave 3.1 g. melting at 139–142°. The yield of dibromofuran (60%) does not take into account the material withdrawn for tests.

(b) A suspension of 10 g. of XII in 80 cc. of 30% hydrogen bromide–concd. acetic acid was allowed to stand at room temperature, the reaction being complete in two weeks. The resinous product obtained by diluting the mixture with water was crystallized three times from ethanol giving a 37% yield of nearly pure furan. A large amount of resinous material was formed in this reaction.

Attempts to hydrogenate the furan with platinum oxide or palladium on barium sulfate as catalysts were without result, the bulk of the furan being recovered unchanged.

3,4-Dibromo-2,5-di-(bromomesityl)-furan, XVII.—This furan was prepared by the bromination of the furans, XIV, XV, XIII and XVIII, by the same procedure described below, using phosphorus pentabromide. A large excess of reagent was necessary due to loss of bromine. With an insufficient amount a difficultly separable mixture of tri- and tetrabromo furans was obtained. The temperature was not allowed to go above 90° in order to avoid formation of the pentabromo derivative. 2,5-Dimesitylfuran was used in large scale preparations because it was the most easily obtained of the starting materials.

A mixture of 0.2 g. of dimesitylfuran and 1.5 g. of phosphorus pentabromide was ground together thoroughly and heated at 88–90° for forty-five minutes. The red melt was then hydrolyzed in water, the oily product coagulating on standing. The yield of crude but nearly pure material was 0.41 g. (m. p. 170–172.5°). It crystallized from ethanol, isopropanol, and ethyl acetate; long rectangular plates; m. p. 177°.

Anal. Calcd. for $C_{22}H_{20}OBr_4$: C, 42.6; H, 3.25; Br, 51.55. Found: C, 42.34; H, 3.6; Br, 51.2.

The furan occurs in two distinct modifications. As usually obtained it was in the form of long rectangular plates melting at 175–177°, but these were usually contaminated by traces of the second form (rhombic). The presence of the rhombic form, visible under the microscope, probably accounted for the unsharp melting point. The rhombic form was obtained free from the other modification only once, after filtration of a hot solution of the compound in isopropanol. It melted sharply at 166° and, after solidifying in the capillary tube, remelted sharply at 177°.

Reduction of 0.4 g. of XVII with hydrogen and palladium on barium sulfate as catalyst (0.5 g.) in 25 cc. of ethanol involved absorption of two molecules in nine hours and 0.29 g. of 3,4-dibromo-2,5-dimesitylfuran, XV, was isolated and identified.

2-Bromomesityl-3,4-dibromo-5-mesitylfuran, XVIII.—In the first brominations carried out under somewhat milder conditions than those described above, a mixture of this furan, XVIII, and the tetrabromo derivative, XVII, was obtained and separated by laborious fractional crystallization and by sublimation under reduced pressure.

A mixture of 4 g. of XIV and 25 g. of phosphorus pentabromide was heated for thirty minutes at 70°, giving 8 g. of product. It was repeatedly crystallized from ethyl acetate and isopropanol, giving the tetrabromo compound pure. The residues were subjected to fractional sublimation in the vacuum oven at 150°. The tribromo compound distilled first and was finally purified by crystallization from isopropanol, the sample obtained melting at 125.5–126.5° (blade-shaped scales).

Anal. Calcd. for $C_{22}H_{21}OBr_3$: Br, 44.4. Found: Br, 41.3.

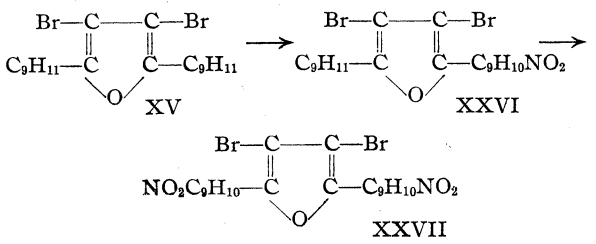
From analyses it was evident that the sample still contained some impurity, probably the dibromo derivative, but not enough material was left for further purification.

2-Bromomesityl-3,4-dibromo-5-dibromomesitylfuran,[9] XVI.—Nine grams of bromine (7 moles) in 10 cc. of carbon disulfide was added slowly to a mixture of 2 g. of dimesitylfuran, 5 cc. of carbon disulfide, and 0.5 g. of iron filings; the mixture was then refluxed gently for four hours. A quantitative yield of the pentabromo derivative was obtained; m. p. 280–282.5°.

Zinc dust and concd. acetic acid had no effect on this compound. Hydrogenation using palladium on barium sulfate gave 3,4-dibromo-2,5-dimesitylfuran (XV).

The pentabromide was prepared also by the action of phosphorus pentabromide at 100° on the tetrabromo compound, XVII.

3,4 - Dibromo - 2,5 - di - (nitromesityl) - furan (XXVII).—This furan was prepared by the action of a 1–3 mixture of concd. nitric and acetic acids at refluxing temperature on 3,4-dibromodimesitylfuran (XV). The mononitro derivative, XXVI, was obtained under similar conditions when a lower concentration of nitric acid was used.



3,4 - Dibromo - 2 - mesityl - 5 - nitromesitylfuran, XXVI.—Dimesityldibromofuran, XV, did not react with 1–10 mixture (by vol.) of concd. nitric and acetic acids at 100°. Nitration was brought about as follows: a solution of 0.38 g. of XV in 20 cc. of concd. acetic acid and 3.8 cc. of concd. nitric acid was refluxed for thirty minutes and diluted with water. Crystallization of the product from ethanol gave 0.28 g. of nearly pure mononitro derivative; needles of m. p. 121.5–122.5°.

Anal. Calcd. for $C_{22}H_{21}O_3NBr_2$: C, 52.1; H, 4.2; N, 2.75. Found: C, 52.5; H, 4.0; N, 2.3.

Nitration further with 1–4 (by vol.) concd. nitric-acetic acid mixture (refluxed) gave the dinitro derivative, XXVII.

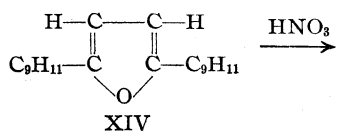
Zinc dust and concd. acetic acid (refluxed) gave a solid of m. p. 150–153° which has not been investigated further.

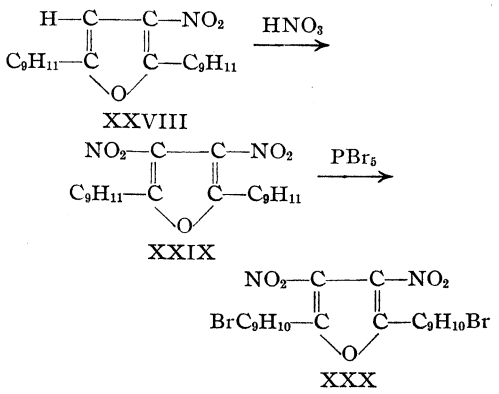
3,4 - Dibromo - 2,5 - di - (nitromesityl) - furan, XXVII.—A mixture of 0.8 g. of dibromodimesitylfuran (XV), 5 cc. of concd. nitric acid and 15 cc. of concd. acetic acid was refluxed for five minutes and diluted with water. The product was crystallized from ethanol; yield 0.57 g. It crystallized from ethanol and isopropanol as tapered needles melting at 204–205°.

Anal. Calcd. for $C_{22}H_{20}O_5N_2Br_2$: C, 47.85; H, 3.65; N, 5.1. Found: C, 47.5; H, 3.8; N, 5.2.

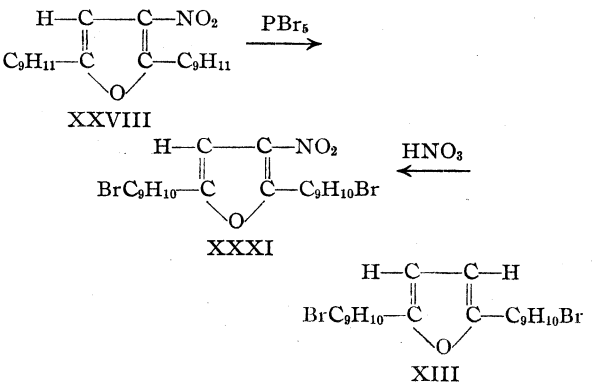
A thorough examination of the residues from this preparation failed to reveal any trace of another compound.

2,5 - Di - (bromomesityl) - 3,4 - dinitrofuran (XXX).—The logical synthesis of this furan by nitration of di-(bromomesityl)-furan (XIII) was unsuccessful because of the surprising resistance to the substitution of the second nitro group. The desired furan was prepared from dimesitylfuran (XIV) by successive substitutions of two nitro groups in the β-positions in the furan nucleus, followed by bromination with phosphorus pentabromide.





The first step in the above synthesis involved introduction of one nitro group into a β-position in the furan nucleus to give XXVIII; this is evident from the following facts. Bromination of the mononitro product, XXVIII, gave di-(bromomesityl)-nitrofuran (XXXI) which was made in a second way by nitration of di-(bromomesityl)-furan (XIII). The positions of the bromine atoms in XXXI are demonstrated conclusively by this second synthesis. The position of the nitro group of both XXVIII and XXXI in the furan β-position is evident from the following considerations: it has been shown that the nitro groups in dinitrodi-(nitromesityl)-furan (XXXII) effectively block bromination in the remaining vacant positions in the mesityl nuclei; therefore, bromination of XXVIII could not have involved both mesityl groups if one of them already carried the nitro group as a substituent; instead, bromination in only one (the unsubstituted) mesityl nucleus or/and the two β-positions in the furan ring would have occurred, whereas actually the bromines are known to have gone one to each mesityl group.



From these facts, then, it is evident that the first nitro group enters a furan β-position. The presence of this nitro group blocks substitution of

bromine in the remaining furan β-position and halogens then enter the two mesityl nuclei.

Unfortunately, further nitration of the 2,5-di-(bromomesityl)-3-nitrofuran (XXXI) could not be controlled successfully to give the desired dinitro derivative, XXX; when the reaction was forced it went too far and there was produced a compound which apparently contained five nitro groups. Thus, a simple proof of structure for XXX could not be obtained and it was necessary to be content with indirect evidence.

In nitration of dimesitylnitrofuran (XXVIII) it might be supposed that the second nitro group would not be able to enter the remaining furan β-position, but would, like bromine, enter a mesityl nucleus. However, from the fact that only one more nitro group (the second) entered, it is to be presumed that it went to the second furan β-position since, otherwise, substitution in both and not just one mesityl group would be expected. Furthermore, the formula XXIX for the dimesityldinitrofuran best explains the introduction subsequently of two bromines by the action of phosphorus pentabromide; if the alternative structure with the second nitro group in a mesityl nucleus were assumed, then bromination of the dinitro compound could have introduced only one bromine atom and this in the unsubstituted mesityl nucleus, because, as has just been shown, a nitro group in one furan β-position blocks bromination at the other β-position, and because, as will be shown below, a nitro group in a mesityl group hinders further substitution in this nucleus. Since this reasoning is involved, the evidence is not as conclusive as could be desired.

2,5-Dimesityl-3-nitrofuran, XXVIII,[9] reacts with 1–4 (by vol.) concd. nitric–acetic acid mixture (boiling for two minutes) to give the dinitro derivative, XXIX.

2,5-Dimesityl-3,4-dinitrofuran, XXIX.—A solution of 1 g. of dimesitylfuran, XIV, in 15 cc. of concd. acetic acid and 5 cc. of concd. nitric acid was refluxed for five minutes and cooled, the dinitro derivative, XXIX, crystallizing; yield 0.5 g. A crystalline impurity, visible under the microscope, was removed by repeated crystallization from isopropanol and from concd. acetic acid. The dinitrofuran crystallized as hexagonal plates of m. p. 213°. It is difficultly soluble in the alcohols.

Anal. Calcd. for $C_{22}H_{22}O_5N_2$: C, 67.0; H, 5.6; N, 7.1. Found: C, 66.7, 67.1; H, 5.4, 5.6; N, 7.0.

From the mother liquors 0.2 g. of mesityl carboxylic acid was isolated.

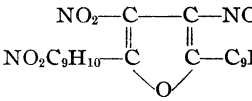
2,5-Di-(bromomesityl)-3,4-dinitrofuran, XXX.—A mixture of 0.28 g. of dimesityldinitrofuran, XXIX, and 0.7 g. of phosphorus pentabromide was heated at 90° for thirty minutes, then 0.3 g. more of the reagent was added and heating continued for fifteen minutes at the same temperature. Hydrolysis gave an oil which solidified. Washing with methanol several times on the filter left 0.36 g. (92%) of nearly pure dibromo compound, XXX. It crystallized from isopropanol or concd. acetic acid as colorless rhombic plates melting at 200.5–201.5°.

Anal. Calcd. for $C_{22}H_{20}O_5N_2Br_2$: C, 47.8; H, 3.65. Found: C, 47.7; H, 3.8.

2,5-Di-(bromomesityl)-3-nitrofuran, XXXI.—A solution of 0.1 g. of di-(bromomesityl)-furan (XIII) in a 1–3 mixture (by vol.) of concd. nitric and acetic acids was refluxed for five minutes. On cooling 0.06 g. of the nitro derivative, XXXI, separated and was purified from isopropanol; m. p. 130–130.5°.

Anal. Calcd. for $C_{22}H_{21}O_3NBr_2$: C, 52.1; H, 4.2. Found: C, 51.7, 51.6; H, 4.0, 4.2. (Carbon analyses on known compounds were running consistently 0.3% low when these were made.)

This furan, XXXI, was obtained in a second way as follows: a mixture of 0.1 g. of 2,5-dimesityl-3-nitrofuran, XXVIII, and 0.3 g. of phosphorus pentabromide was heated at 90–93° for fifteen minutes and hydrolyzed. The product was crystallized from isopropanol giving 0.05 g. of pure XXXI.



3,4-Dinitro-2,5-di-(nitromesityl)-furan, XXXII.—This tetranitro derivative was made by nitration of dimesityldinitrofuran, XXIX, using a stronger nitric–acetic acid mixture. The symmetrical structure, XXXII, has been assigned because the only alternative would be one in which at least one of the mesityl nuclei carried two nitro groups, an unlikely possibility. Further substitution of nitro groups was not accomplished, and phosphorus pentabromide at 100° was without action on the compound.

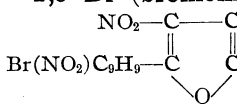
A suspension of 0.15 g. of dimesityldinitrofuran, XXIX, in 4 cc. of a 1–1 (by vol.) mixture of concd. nitric and acetic acids, was refluxed for five minutes and diluted with water, the product crystallizing. Recrystallizing from ethyl acetate gave 0.1 g. of nearly pure product; m. p. 266–267°.

Anal. Calcd. for $C_{22}H_{20}O_9N_4$: N, 11.56. Found: N, 11.8.

Nitration of 2,5-Di-(bromomesityl)-furan and the 3-Nitro Derivative.—When the furans, XIII and XXXI, were treated with a 1–1 mixture (by vol.) of fuming nitric and concd. acetic acids at 90–94° for five minutes, a product was obtained which crystallized from isopropanol or concd. acetic acid as long rectangular plates of m. p. 287–288°. It gave no mixture melting point depression with XXXIII of m. p. 251–252°. But in view of the analysis and this difference in melting point, there is little doubt of non-identity with XXXIII.

Anal. Calcd. for $C_{22}H_{17}O_{11}N_5Br_2$: C, 38.45; H, 2.5. Found: C, 38.7, 38.14; H, 3.1, 3.14.

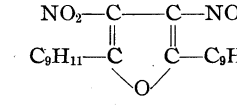
2,5-Di-(bromonitromesityl)-3,4-dinitrofuran,



XXXIII.—This furan could not be made by bromination of the tetranitro compound, XXXII; but it was obtained through a different order of introducing the groups, namely, by nitration of dinitro-di-(bromomesityl)-furan (XXX) with a 1–1 fuming nitric–concd. acetic acid mixture, as follows:

A solution of 0.3 g. of di-(bromomesityl)-dinitrofuran, XXX, in 6 cc. of a 1–1 (by vol.) mixture of fuming nitric and concd. acetic acids was allowed to stand for thirty minutes at 90°. On cooling 0.18 g. of nearly pure material separated. From the filtrate 0.23 g. of partly reacted material was obtained, which was nitrated again by the same procedure, giving 0.17 g. of product. It crystallized from concd. acetic acid as colorless rhombic plates which melted with decomposition at 245° (at 251–252° in an evacuated tube).

Anal. Calcd. for $C_{22}H_{18}O_9N_4Br_2$: C, 41.1; H, 2.8; N, 8.7. Found: C, 40.8, 40.7; H, 2.8, 2.7; N, 8.6.



Trinitro-2,5-dimesitylfuran.—A suspension of 0.3 g. of dimesitylfuran (XIV) was allowed to stand in 8 cc. of a 1–1 (by vol.) mixture of concd. nitric and acetic acids at room temperature until a thick paste formed. The mixture was then refluxed for three minutes and diluted with water. The amorphous product on standing overnight in ethanol became crystalline and was recrystallized from ethanol; tapered needles of m. p. 158–160°.

Anal. Calcd. for $C_{22}H_{21}O_7N_3$: C, 60.1; H, 4.8. Found: C, 60.3; H, 4.95.

After standing for several days the first filtrate deposited 0.03 g. of nitromesityl carboxylic acid which was identified by mixture melting point with a sample prepared by nitration of mesityl carboxylic acid.

***cis*-2,3-Dimethyl-1,4-diphenyl-2-butenedione-1,4 (*cis*-Dibenzoyldimethylethylene), III.**—A suspension of dimethyldiphenylfuran (II) in 4 cc. of propionic acid was made by dissolving the furan in the hot solvent and chilling to obtain fine crystals free from lumps; this mixture was maintained at −10° and treated with 0.2 cc. of concd. nitric acid in 0.6 cc. of propionic acid, also at −10°. The crystals dissolved quickly. On standing for fifteen minutes at −10° and diluting with water, the diketone, III, separated crystalline in practically quantitative yield. It crystallized from isopropanol or acetic acid–water mixtures as slender needles melting at 86.5–87°.

Anal. Calcd. for $C_{18}H_{16}O_2$: C, 81.8; H, 6.1. Found: C, 81.4; H, 5.8.

The structure of this compound was demonstrated by reduction with zinc dust and concd. acetic acid (boiling one minute) followed by treatment of the filtrate directly with acetic anhydride and a trace of concd. sulfuric acid to give the furan, II, in 90% yield.

3,4-Dibromo-2,5-di-(4-bromophenyl)-furan, XIX.—Catalytic reduction of 0.4 g. with 0.5 g. of palladium on barium sulfate in ethanol was complete in three hours, 4 molecules of hydrogen being absorbed; 0.16 g. of diphenylfuran, XX, was isolated, purified and identified.

Summary

1. In a study of five suitably substituted compounds, no evidence of diastereoisomerism due to restricted rotation on the internuclear 2,5-dimesitylfuran bonds has been found.

2. 2,5-Dimesityl groups prevent the oxidative fission of the furan nucleus by nitric and acetic acids, a reaction which is shown to be general for furans with 2,5-diaryl groups carrying no ortho substituents. The bearing of these results on the mechanism of furan reactions is considered.

3. The reactions involved in the synthesis and proof of structure of the various substituted 2,5-dimesitylfurans are described and discussed.

4. Catalytic hydrogen eliminates the bromines from the mesityl nuclei of four substituted 2,5-dimesitylfurans, but is without effect on bromines substituted in the β-positions. In the case of 2,5-di-(*p*-bromophenyl)-3,4-dibromofuran all four bromines are eliminated by catalytic reduction.

5. Some new halogeno saturated 1,4-diketones of the dimesityl series are described, and the relative ease of elimination of halogen acid is considered.

6. 3,4-Dibromo-2,5-dimesitylfuran is nitrated stepwise in the mesityl nuclei.

7. 2,5-Di-(bromomesityl)-3-nitro- and -3,4-dinitrofurans have been prepared by stepwise nitration and bromination of dimesitylfuran. Evidence for the structures is discussed.

8. Disubstitution in the 2,5-dimesityl groups was accomplished only in the nitration of 2,5-di-(bromomesityl)-3,4-dinitrofuran to the di-(bromonitromesityl) derivative.

CHARLOTTESVILLE, VIRGINIA
RECEIVED DECEMBER 23, 1939

[CONTRIBUTION FROM THE FRICK CHEMICAL LABORATORY, PRINCETON UNIVERSITY]

The Dipole Moments and Structures of the Esters of Some Fatty and Some Inorganic Acids

BY GEORGE L. LEWIS AND CHARLES P. SMYTH

This paper is a report of measurements of dipole moment made some time ago upon three groups of substances, all of which were esters. The moments of the ethyl esters of three long-chain fatty acids were determined with the object of confirming the expectation that the long chain would have little effect upon the moment. The moments of three alkyl borates were measured with the object of studying the structures of their molecules, in particular, the possibility of rotation around the B–O bonds. The moments of triphenyl phosphite, phosphate and thiophosphate were determined in the hope of obtaining further evidence as to the values of the moments of the semipolar bonds, $P^+–O^-$ and $P^+–S^-$. The moments were obtained in the usual manner from measurements of the dielectric constants and densities of solutions in benzene or heptane. The dielectric constants were measured at a frequency of 520 kilocycles with a crystal-controlled heterodyne beat apparatus previously described,[1] and the densities were determined with an Ostwald–Sprengel pycnometer in a manner described elsewhere.[2]

Purification of Materials

Benzene and heptane were purified as in previous work.[3] The ethyl undecylate, palmitate, and stearate were portions of the materials which had been carefully purified by Dr. W. O. Baker in this Laboratory for use in studying the dielectric constants in the solid state.[4]

The three alkyl borates were prepared by Dr. Allen Scattergood by fractionating a mixture of two moles of boric acid and nine moles of the corresponding alcohol according to the method given in "Organic Syntheses."[5] The liquids had the following values of the boiling point, the density d, the refractive index for the sodium D line n_D, and the dielectric constant ϵ at 25°: *n*-propyl borate, b. p. 177–178°, d 0.85448, n_D 1.39227, ϵ 2.239; *i*-butyl borate, b. p. 208.0–208.5°, d 0.84033, n_D 1.40101, ϵ 2.213; *s*-butyl borate, b. p. 193–194°, d 0.82902, n_D 1.39444, ϵ 2.194.

Triphenyl Phosphite.—Material from the Eastman Kodak Company was washed with dilute sodium carbonate solution and then with water, dried over calcium chloride, filtered, and vacuum distilled at 200° and 6 mm.; $n^{25}D$ 1.58801.

Triphenyl Phosphate.—Material from the Eastman Kodak Company was recrystallized from distilled ether three times; m. p. 46°.

Triphenyl Thiophosphate.—Material from the Eastman Kodak Company was recrystallized from distilled ether three times; m. p. 53°.

Experimental Results

The dielectric constants, ϵ, and the densities, d, of benzene or heptane solutions containing mole fraction c_2 of solute are given in Table I, the polarizations P_2 being listed in the last column. The polarization of the pure solvent is given as P_1. Table II lists in the second column the values of MR_D, the molar refraction for the D sodium line, obtained directly from the experimental data for the long chain esters and the borates, and calculated for the phosphite, phosphate and thiophosphate from the refractions of the corresponding alkyl compounds,[6] the refraction of benzene, and atomic refractions given in Landolt–Börnstein. The third column gives the polarizations P_2 for the pure liquids at 25°, the fourth column the polarizations P_∞ obtained by extrapolation to $c_2 = 0$ of the values of P_2 in Table I, and the fifth column gives the dipole moments calculated in the usual manner.

Discussion of Results

For the long-chain esters of the fatty acids in Table II the difference between the polarization of the pure liquid and that of the substance at infinite dilution decreases with increasing length of the carbon chain, the difference being 25.0 for ethyl undecylate, 17.8 for ethyl palmitate, and 15 for the stearate, for which the difference is obtained by a rough extrapolation of the polarization of the pure liquid down to 25°. Increase in the length of the chain effectively dilutes the dipoles and thereby reduces the intermolecular action, which is responsible for the difference between P_2 and P_∞. This difference is very small in the three alkyl borates as it is in ethyl ether[7] and for the same reason. The three ethyl groups form a shield around the three C–O moments, while, as will be seen presently, the three B–O dipoles radiating from the center of the molecule presumably cancel one another. The variation of P_2 with concentration for triphenyl phosphite in Table I is much less than that in the cases of the

(1) Lewis and Smyth, *J. Chem. Phys.*, **7**, 1085 (1939).
(2) Lewis and Smyth, THIS JOURNAL, **61**, 3063 (1939).
(3) Smyth and Walls, *ibid.*, **54**, 1854 (1932).
(4) Baker and Smyth, *ibid.*, **60**, 1229 (1938).
(5) "Organic Syntheses," W. H. Carothers, Ed., Vol. XIII, John Wiley and Sons, New York, N. Y., 1933, p. 16.
(6) Jones, Davies and Dyke, *J. Phys. Chem.*, **37**, 583 (1933).
(7) *Trans. Faraday Soc.*, **30**, Appendix (1934).

TABLE I

DIELECTRIC CONSTANTS, DENSITIES AND POLARIZATIONS AT 25°

c_2	ϵ	d	P_2
	Heptane–Ethyl Undecylate		
0.00000	1.917	0.67958	(34.49 = P_1)
.02389	1.984	.68696	135.5
.05707	2.063	.69705	131.3
.07051	2.093	.70098	129.6
.08980	2.132	.70558	127.8
	Heptane–Ethyl Palmitate		
0.00659	1.936	.68250	160
.01883	1.966	.68736	157
.02863	1.997	.69091	156
.03106	1.999	.69196	155
.04063	2.024	.69566	155
.06051	2.073	.70307	153.4
.08181	2.121	.71070	151.7
.11265	2.191	.72068	149.8
.15184	2.259	.73206	147.9
	Heptane–Ethyl Stearate		
0.02063	1.974	.68833	166
.04154	2.028	.69724	163.5
.06501	2.082	.70642	161.2
.08909	2.128	.71518	159.4
.11978	2.177	.72329	157.4
	Benzene–*n*-Propyl Borate		
0.00000	2.276	.87344	(26.67 = P_1)
.04864	2.273	.87091	64.9
.08467	2.272	.86918	65.0
.13320	2.266	.86709	64.6
	Benzene–*i*-Butyl Borate		
0.03237	2.275	.86990	81.2
.07196	2.273	.86554	80.9
.10729	2.267	.86235	80.9
	Benzene–*s*-Butyl Borate		
0.03860	2.273	.86851	81.4
.06912	2.270	.86453	81.5
.09238	2.265	.86115	81.3
	Benzene–Triphenyl Phosphite		
0.01423	2.359	.88568	170.8
.02988	2.461	.89905	170.6
.04001	2.525	.90773	170.5
.05302	2.605	.91887	170.1
.06389	2.674	.92819	169.6
	Benzene–Triphenyl Phosphate		
0.02098	2.517	.89341	246.9
.03210	2.645	.90389	245.4
.05142	2.867	.92226	242.7
.06831	3.061	.93830	239.7
.08354	3.236	.95276	237.3
	Benzene–Triphenyl Thiophosphate		
0.01035	2.378	.88425	227.4
.02770	2.544	.90238	223.8
.03372	2.598	.90866	222.9
.04010	2.657	.91533	220.7
.05328	2.779	.92910	218.8

TABLE II

MOLAR REFRACTIONS, POLARIZATIONS (AT 25°) AND DIPOLE MOMENTS

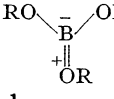
Substance	MR_D	P_2	P_∞	$\mu \times 10^{18}$
$C_{10}H_{21}COOC_2H_5$	63.8	113.1	138.1	1.89
$C_{15}H_{31}COOC_2H_5$	87.08	141.6	159.4	1.87
$C_{17}H_{35}COOC_2H_5$	95.91	146.6 (42°)	168.8	1.88
$(n\text{-}C_3H_7)_3BO_3$	52.55	64.30	65.0	0.77
$(i\text{-}C_4H_9)_3BO_3$	66.44	78.81	81.5	.85
$(s\text{-}C_4H_9)_3BO_3$	66.44	78.95	81.4	.85
$(C_6H_5)_3PO_3$	87.2		171.7	2.02
$(C_6H_5)_3PO_4$	86.1		250	2.81
$(C_6H_5)_3PO_3S$	93.3		231	2.58

phosphate and thiophosphate, which indicates that the P–O and C–O moments are well screened by the phenyl groups in the former, while the large $P^+–O^-$ and $P^+–S^-$ dipoles in the latter two give rise to strong intermolecular action.

The moments of ethyl undecylate, palmitate and stearate in Table II may be regarded as identical. They are also identical with the value 1.86 found in this Laboratory for ethyl acetate in benzene solution[8] but lower than the value 1.98 for ethyl acetate in heptane.[9] In general, the moments of a large number of esters in the literature show an increase in value from the methyl to the ethyl, presumably because of induction, with little change produced by further lengthening of this part of the molecule. On the other side of the molecule, addition of carbon to go from formate to acetate to propionate lowers the moment slightly as it lowers the dissociation constant, the latter to a much greater extent. The moments of these three long-chain ethyl esters are only 0.05 higher than the values for ethyl propionate[8,10] and butyrate[10] in benzene solution, a difference to be expected from the difference in solvent effect. It may, therefore, be concluded that the long chains in these molecules do not affect the dipole moment of the molecule or hinder its free orientation in externally applied electric fields of frequencies up to those employed in the present measurements.

The moment of propyl borate in Table II fits well into the series of values 0.75, 0.77 and 0.79 previously found for ethyl borate,[11] butyl borate,[12] and amyl borate,[12] respectively. The branching of the carbon chain seems to raise the moment slightly, the isobutyl and *s*-butyl borate moments in Table II being 0.85. In view of the zero mo-

(8) Smyth and Walls, THIS JOURNAL, **53**, 527 (1931).
(9) Smyth, Dornte and Wilson, *ibid.*, **53**, 4242 (1931).
(10) Wolf and Gross, *Z. physik. Chem.*, **B14**, 305 (1931).
(11) Cowley and Partington, *Nature*, **136**, 643 (1935).
(12) Otto, THIS JOURNAL, **57**, 1476 (1935).

ment found for boron trichloride[7] and the symmetrical, triangular planar structures found by electron diffraction for the boron halides and boron trimethyl[13] and the analogous symmetrical structure found by X-ray analysis for the BO_3 group in crystalline boric acid and metallic metaborates[14] it seems almost certain that, in these alkyl borates, the boron lies at the center of an equilateral triangle with the oxygens at the three apices. As the resultant of the three B–O moments would thus be zero, any moment of the molecule as a whole must be due to the H–C and C–O bond moments. The total R–O moment may be taken as approximately 1.2 acting in the C–O direction.[15] If all positions of rotation around the B–O bonds were equally probable and if the oxygen valence angle were 110°, the resultant moment of the trialkyl borates should be[16] $1.2\sqrt{3}\sin 110° = 1.95$. However, the borates should have structures which through resonance are mainly the resultant of contributions from three structures such as  . Consequently, the B–O should have approximately one-third double-bond character, which would tend to make the three carbons attached to the three oxygens coplanar with the boron and the oxygens and give oxygen valence angles of about 120°. If steric repulsion between the alkyl groups were negligible, there would be eight possible coplanar arrangements of the three alkyl groups, six of them equivalent to one another and having a moment 2.1 and the remaining two being equivalent to one another and having zero moment. The resultant observed moment should then be $2.1\sqrt{6/8} = 1.8$. Increase of the oxygen valence angles to a rather probable value of 125° would decrease this calculated value by 0.1. The observed values in Table II are less than half of these calculated values.

Examination of the bond and kinetic theory radii of the atoms in these molecules shows that neglect of steric repulsion in calculating moments for the molecules is quite unjustifiable. In the hypothetical structure in which free rotation is supposed, the positions in which the alkyl groups turn on to the same side of the molecule, thereby giving the maximum resultant moment, are rendered much less probable by repulsion between the groups. The resulting tendency to occupy positions giving lower resultant moment could account for the difference between the low observed and the high calculated moment values. In the more probable structure in which partial double-bond character hinders or prevents rotation around the B–O bonds, steric repulsion renders the six equivalent, unsymmetrical, planar structures impossible or highly improbable without distortion. The distortion and greatly decreased probability of these structures of large moment and the greatly increased probability of the two symmetrical structures of zero moment, in which steric repulsion is small or negligible, can easily account for the smallness of the observed moments.

The conclusion that steric repulsion is the cause of the low moments of the alkyl borates is borne out by examination of the moment values, 1.85 and 1.90, found by Otto[12] for butylboric and amylboric acids, respectively. If the H–O moment is taken[15] as 1.5, the moment calculated as before for the hypothetical structure having freedom of rotation around the B–O bonds is 2.35 and the value calculated for the planar structure without rotation around the B–O bonds is about 2.1. As there is only one alkyl group in these molecules, steric repulsion should be very much less than that in the trialkyl borates. Indeed, of the eight possible arrangements in the planar structure, the two equivalent ones having largest moment should have almost as little steric repulsion as the two with smallest moment, only the dipole–dipole interactions reducing somewhat the probabilities of the former two. The observed value 1.9 is thus reduced but slightly below the roughly calculated value 2.1. The observed moments of the trialkyl borates and the monoalkyl boric acids are evidently consistent with the planar structure in which the three B–O bonds making angles of 120° with one another have sufficient double-bond character to prevent rotation around the bonds, although, in the so-called unsymmetrical planar structure, steric effects would tend to twist the carbons attached to the oxygens out of the plane of the boron and the oxygens. The moment values alone do not, however, preclude the possibility of rotation around the B–O bonds.

The triphenyl phosphite molecule looks some-

(13) Pauling, "The Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1939, pp. 88, 220.

(14) Ref. 13, pp. 195, 291.

(15) Smyth, *J. Phys. Chem.*, **41**, 209 (1937).

(16) See Eyring, *Phys. Rev.*, **39**, 746 (1932); Smyth and Walls, THIS JOURNAL, **54**, 2261 (1932).

what analogous to those of the alkyl borates, but the moment observed for it is more than twice as large. If all positions of rotation around the C–O and P–O moments were equally probable, its mean square moment could be written[16] $\mu_1^2 = 3m_1^2(1 + 2\cos^2\theta\cos\varphi) + (3m_2^2 + 6m_1m_2\cos\theta)(1 + 2\cos\varphi)$, in which m_1 is the sum of the H–C and C–O bond moments, m_2 is the P–O bond moment, θ is the oxygen valence angle, and φ is the phosphorus valence angle. The same equation was used to calculate the moment of the alkyl borates, for which the fact that φ was 120° caused all the terms containing m_2, the B–O moment, to drop out. m_1 is calculated[15] from the moment of diphenyl ether 1.14 as 1.0, and m_2 is calculated as the difference 1.2 between the H–O and H–P bond moments.[15] The oxygen valence angle θ is taken as 110° as in the borates. The phosphorus valence angle is 100° in trimethylphosphine and varies from 98° to 104° in the phosphorus trihalides.[17] If it is taken as 100° in triphenyl phosphite, the moment calculated by the above equation is 2.0, in exact agreement with the observed value in Table II. Increase of the angle φ to 110° reduces the calculated value to 1.8 and further increase to 120° reduces it to 1.6. In spite of the excellent agreement between the observed and calculated moment values, examination of the atomic dimensions shows that certain positions of rotation around the P–O bonds are impossible because of interference of the benzene rings with one another. There is, however, no general exclusion of the positions of highest moment like that which lowers the moment so much in the case of the borates. A sufficiently wide variety of positions appears to be possible to permit of a distribution of moment values close to the random one given by the equation. If, instead of using the estimated value 1.2 for the single P–O bond moment to calculate the resultant moment of the triphenyl phosphite molecule, the observed moment of the molecule is used to calculate the P–O moment, the value obtained is 1.2, which may therefore be regarded as an approximate experimental value for the normal P–O bond.

The moments of the phosphate and thiophosphate molecules are changed from that of the phosphite by the presence of the semipolar bond $P^+–O^-$ or $P^+–S^-$ and the calculated mean square moment should be

$$\mu_2^2 = \mu_1^2 + m_3^2 + 6m_2m_3\cos\chi + 6m_1m_3\cos\theta\cos\chi$$

where μ_1 is the moment of the phosphite as given by the previous equation for it, m_2 is the semipolar bond moment, χ is the angle which the semipolar bond makes with the three P–O bonds, and the other quantities are the same as those used in the previous equation. In the case of the phosphite, the most probable value of the O–P–O angle, $\varphi = 100°$, gives exact agreement between the observed and calculated moments. If $\varphi = 100°$ in the phosphate and thiophosphate, then the $O–P^+–O^-$ angle χ may be calculated as 118°, since the $P^+–O^-$ or $P^+–S^-$ bond should lie symmetrically with respect to the three P–O bonds. When μ_2 is set equal to the observed moment for the phosphate or thiophosphate in Table II and μ_1 is taken as the observed phosphite moment, which agrees with the calculated value, the moment m_3 of the semipolar $P^+–O^-$ bond is given by the equation as 3.5 and that of the $P^+–S^-$ bond as 3.2. If all the phosphorus valence angles were identical so that $\chi = \varphi = 110°$, μ_1 would have the calculated value 1.83, and the values of m_3 calculated would be 3.2 for the $P^+–O^-$ bond and 2.9 for the $P^+–S^-$ bond. As the first structure, in which $\varphi = 100°$ and $\chi = 118°$, seems to be the most probable approximation, the values 3.5 for $P^+–O^-$ and 3.2 for $P^+–S^-$ should be most nearly correct. It should be borne in mind, however, that, as in the previously considered[18] case of the same bonds in $POCl_3$ and $PSCl_3$, neither bond is a pure semipolar structure, as other resonating forms, particularly double-bonded structures, contribute to the structures of the molecules. The values must, in any event, be regarded as approximate because of possible errors in the assumed bond moments and valence angles. The $P^+–O^-$ moment value 3.5 is identical with that found for this bond in $POCl_3$, while the value 3.2 for the $P^+–S^-$ bond is considerably higher than the apparent value 2.5 found for it in $PSCl_3$, which was thought to be too low because of the inductive action of the P–Cl dipoles. The small difference 0.3 here found between the $P^+–O^-$ and $P^+–S^-$ moments justifies the conclusion previously reached[18] that the two moments are not very different from one another, the two lying in the neighborhood of 3.5, where most of the more or less hybrid semipolar bonds seem to lie. It would appear that the $P^+–S^-$ is actually some-

(17) See ref. 13, p. 80.

(18) Smyth, Lewis, Grossman and Jennings, THIS JOURNAL, **62**, 1219 (1940).

what lower than the P^+-O^- moment in contrast to the fact that the C=S moment is 0.3 higher than the C=O, which latter bonds contain large contributions from semipolar forms.[19]

Summary

The dielectric constants and densities of solutions of ethyl undecylate, palmitate and stearate in heptane, of *n*-propyl, *i*-butyl and *s*-butyl borate in benzene, and of triphenyl phosphite, phosphate and thiophosphate in benzene have been measured at 25° and used to calculate the dipole moments of the molecules of the solutes.

The small variation of polarization with concentration shows the intermolecular action to be very small in the three trialkyl borates and in triphenyl phosphite and to decrease with increasing molecular size in the long-chain fatty acid esters. The small intermolecular action is due to effective screening of the dipoles from one another by the hydrocarbon groups, while the large intermolecular action in the phosphate and thiophosphate is due to the presence of an imperfectly screened semipolar bond.

Ethyl undecylate, palmitate and stearate have dipole moments indistinguishable from one another and from those of ethyl propionate and butyrate, which shows that the long chains in these molecules do not affect the dipole moment of the molecule or hinder its free orientation at 25° in an alternating electric field of frequency as high as 520 kc. Equations are derived for the calculation of the resultant moments of the trialkyl borates and of triphenyl phosphite, phosphate and thiophosphate on the assumption of equal probabilities of all the positions of rotation around the B–O and P–O bonds. Strong steric repulsion between the alkyl groups in the borates lowers their moments to less than half of the values calculated on the basis of free rotation as well as on that of B–O bonds stiffened by double-bond character. Excellent agreement is obtained between the observed and the calculated values for triphenyl phosphite, where steric hindrance plays a minor role. The equations are used to calculate approximate moment values for three bonds as follows: P–O, 1.2; P^+-O^-, 3.5; P^+-S^-, 3.2.

(19) Smyth, THIS JOURNAL, **60**, 183 (1938).

PRINCETON, NEW JERSEY RECEIVED APRIL 12, 1940

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 762]

A Redetermination of the Parameters in Ammonium Bifluoride

BY M. T. ROGERS AND L. HELMHOLZ

Introduction

The structure of ammonium bifluoride has been determined by Pauling,[1] who gave approximate values of the parameters obtained with the use of the data of Hassel and Luzanski.[2] He found a hydrogen-bonded structure with each nitrogen atom surrounded by four fluorine atoms at tetrahedral corners, the mean N–F distance being 2.76 ± 0.06 Å. and the F–F distance 2.37 ± 0.10 Å. The value we have found[3] for the F–F distance in KHF_2, 2.26 ± 0.01 Å., is equal to Pauling's value of the distance in NH_4HF_2 to within its limits of error, so it is not possible to say whether or not the distance has been increased by the formation of two additional hydrogen bonds in NH_4HF_2. For this reason a more accurate determination of this distance has been made.

(1) L. Pauling, *Z. Krist.*, (A) **85**, 380 (1933).
(2) O. Hassel and N. Luzanski, *Z. Krist.*, **83**, 448 (1932).
(3) L. Helmholz and M. T. Rogers, THIS JOURNAL, **61**, 2590 (1939).

The unit translations found by Hassel and Luzanski[2] and the parameters given by Pauling[1] have been revised and the limits of error reduced. From these new values the F–F and N–F distances have been calculated to be F–F = 2.32 ± 0.03 Å. and N–F = 2.82 ± 0.03 Å. The weakening of the F–F bond in the formation of two hydrogen bonds in passing from KHF_2 to NH_4HF_2 is thus shown to exist; the increase in bond length amounts to 0.06 ± 0.04 Å. The space group D_{2h}^7 used by Pauling has been confirmed by the absence of reflections of the type $(h0l)$, h odd, observed by Hassel and Luzanski.

Experimental Method and Results

Oscillation photographs about the c and a axes were taken of crystals of orthorhombic NH_4HF_2 prepared by evaporation of solutions of NH_4HF_2 in glacial acetic acid.

The space group was shown to be D_{2h}^7 by the

absence of reflections of type $(h0l)$, h odd, and $(hk0)$, h and k odd. The reflection (102) reported by Hassel and Luzanski, which would eliminate this group, was sought but not observed on any photographs. This justifies the choice made by Pauling. The unit cell contains four molecules and the dimensions of the unit were found to be

$a_0 = 8.426 \pm 0.020$ Å.; $b_0 = 8.180 \pm 0.020$ Å.; $c_0 = 3.69 \pm 0.05$ Å.

The first two are from oscillation photographs, the third from layer line measurements. Data giving a_0 and b_0 are shown in Table I. These correspond to axial ratios $1:0.971:0.438 = a_0:b_0:c_0$ compared by goniometric values $1:0.977:0.444 = a_0:b_0:c_0$ (Groth).

TABLE I

EQUATORIAL MEASUREMENTS

(hkl)	$d_{obsd.}$ Å.	a_0 obsd. Å.
400	2.105	8.421
600	1.405	8.434
800	1.053	8.424
1000	0.0842	8.423
	Average a_0	8.426
020	4.097	8.195
040	2.045	8.180
060	1.362	8.172
080	1.022	8.177
	Average b_0	8.180

The relative intensities of all observed reflections were estimated visually using a calibrated scale.

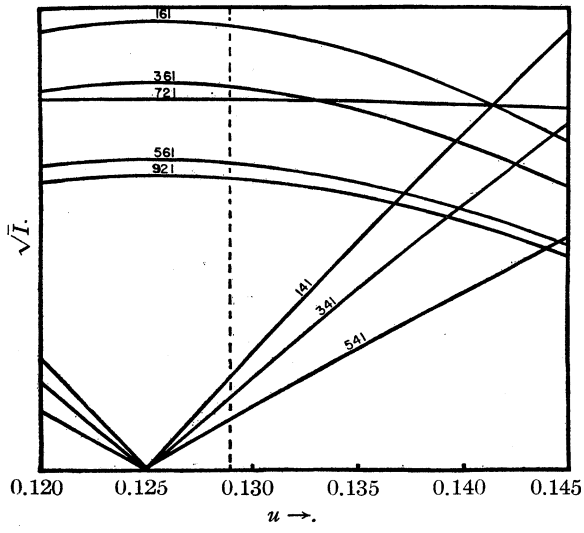


Fig. 1

Theoretical values for the relative intensities were calculated using the formula

$$I = C \frac{1 + \cos^2 2\theta}{\sin 2\theta} F^2 \exp -3.0 \left(\frac{\sin\theta}{\lambda}\right)^2$$

where F is the structure factor and $\exp -3.0 \left(\frac{\lambda}{\sin\theta}\right)^2$ the temperature factor. The structure factors for the four classes of planes are

I $F = 4f_F \sin 2\pi ku \sin 2\pi lv$ for h odd, k even

II $F = 4f_{NH_4} \cos 2\pi \left(\frac{h+k}{4} + lz\right) - 4f_F \sin 2\pi ku \sin 2\pi lv$ for h even, k odd

III $F = 4f_F(\cos 2\pi hw - \cos 2\pi ku \cos 2\pi lv)$ for h odd, k odd

IV $F = 4f_{NH_4} \cos 2\pi \left(\frac{h+k}{4} + lz\right) + 4f_F(\cos 2\pi kw + \cos 2\pi ku \cos 2\pi lv)$ for h even, k even

The f values used were those of Pauling and Sherman.[4] The intensities of reflections $(h00)$ depend only on parameter w, and of reflections $(0k0)$ only on parameter u, and a rough determination of these parameters might have been made using the observed $(h00)$ and $(0k0)$ intensities. The intensities of these reflections, however, are so sensitive to the choice of f values for F^- and NH_4^+ that little confidence was felt in the determination carried out from this starting point, and, indeed, the parameters thus obtained led to marked discrepancies between calculated and observed intensities for planes of different types.

To overcome this difficulty the determination was carried out in the following manner. The parameter u was determined first using observed intensities for planes of class I with $l = 1$. The factor $\sin v$ is known closely enough from Pauling's determination of $v = 0.135 \pm 0.01$ since it enters only as a common factor. The calculated intensities are plotted as functions of u in Fig. 1. The value $u = 0.131 \pm 0.002$ is found.

Accepting this value of u it is now possible to choose the f values for NH_4^+ which will account for the observed intensities of $(0k0)$ planes. The appropriate f_{NH_4} values were found to be close to the values used by Pauling.[1] Experimental values of f_{NH_4} have been obtained by Wyckoff and Armstrong[5]; a comparison of these values with those we have used is shown in Table II.

TABLE II

Sin θ/λ	0.1	0.2	0.3	0.4	0.5	0.6	0.7
f_{NH_4} (Pauling)	8.11	6.01	3.96	2.65	1.99	1.68	1.55
f_{NH_4} (Hartree)	6.7	4.4	3.1	2.50	2.0	1.65	1.65
f_{NH_4} (used)	7.7	5.64	3.70	2.43	2.00	1.68	1.55
f_{NH_4} (Wyckoff)	8.8	5.5	3.1	1.8	1.2		

We next obtained an approximate value of w, 0.137 ± 0.004, from reflections $(h00)$. The value of v was obtained by comparing intensities of

(4) L. Pauling and J. Sherman, *Z. Krist.*, **81**, 1 (1932).
(5) Wyckoff and Armstrong, *ibid.*, **72**, 319 (1930).

planes of Class I with varying values of l, using the value found for u. The calculated intensities plotted as functions of v are shown in Fig. 2. Planes with $k = 2, 6, 10$ were used since these vary negligibly with u in the allowed range for that parameter.

The value $v = 0.131 \pm 0.003$ was obtained in this way. A more accurate value of w was then found using intensities of reflections of type III with $l = 0$, which depend only on u and w. Plots were made of the calculated intensities as functions of both u and w for these planes and values of these parameters giving the best agreement with observed intensities were taken. To account for the observed intensity ratios of 910:930:350:530 it was found necessary to use the lower limit for u ($u = 0.129$). The value of w chosen was $w = 0.137 \pm 0.002$. This choice was confirmed by plotting calculated intensities for reflections of type III with $l = 1$ as functions of w using previously obtained values of u and v.

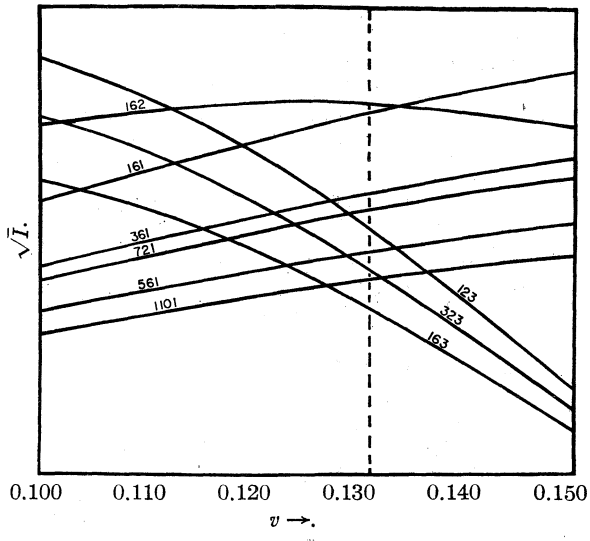


Fig. 2

TABLE III

TYPE I PLANES

hkl	Calcd.	Obsd.	*hkl*	Calcd.	Obsd.
121	32	33	921	5.4	4.5
141	1.9	2.3	122	20.5	14
161	8.4	7.4	142	1.4	1.2
181	1.2	abs.	162	8.5	6.7
1,10,1	5.0	4.1	322	12.5	14
321	20.5	20	342	1.1	abs.
341	1.4	1.8	362	7.8	4.0
361	6.8	6.6	123	7.0	5.4
521	11.2	14	143	0.8	1.0
541	1.0	abs.	163	4.7	4.1
561	5.6	4.5	323	5.6	4.4
721	6.4	5.7	343	0.5	abs.
741	0.6	abs.	363	4.6	2.5
761	5.3	4.0			

TABLE IV

TYPE II PLANES

hkl	Calcd.	Obsd.	*hkl*	Calcd.	Obsd.
011	20.4	18.7	012	27.7	30
031	22	26.5	032	7.9	7.9
051	12.6	10	052	4.6	4.2
071	2.2	abs.	072	7.5	8.2
211	31	36	092	9.2	10
231	9	11	212	7.8	6.1
251	5.7	7.1	232	15.6	17.8
271	5.2	6.3	252	11.7	11.6
291	6.1	4.4	272	1.4	abs.
411	8.9	7.1	013	0.2	abs.
431	11.3	14.1	033	8.5	10
451	8.1	9.2	053	7.9	8.5
471	1.8	2.0	073	1.1	5
611	8.5	10.0	213	9.7	11
631	3.3	3.1	233	0	abs.
651	3.2	3.1	253	0.8	abs.
671	4.6	3.6	273	6.6	7.1
811	2.8	1.1	014	4.1	7.5
831	5.2	5.1	034	5.2	4.1
851	6.2	3.4	054	5.5	5.4
10,1,1	5.3	5.0	214	4.4	1.4
			234	4.1	5.2

TABLE V

TYPE III PLANES

hkl	Calcd.	Obsd.	*hkl*	Calcd.	Obsd.
110	3.7	4.2	931	4.6	4.9
310	67	61	151	17.7	23
510	22.5	30	351	5.6	7.7
710	2.6	3.3	551	0.2	abs.
910	4.4	3.3	751	10.5	8.6
130	63	61	171	0.2	abs.
330	2.6	4.0	371	12.4	11
530	5.5	5.8	571	8.3	8.1
730	15.2	17	771	2.0	abs.
930	6.6	7.3	191	1.6	3.6
150	25	37	391	9.6	7.4
350	3.6	4.3	112	16.8	16.7
550	2.0	abs.	312	13.9	14
750	11.7	11.5	132	10.6	14
950	5.2	5.0	332	11.0	7.5
170	1.6	abs.	152	6.7	5.8
370	14.5	15.3	352	6.7	5.8
570	9.4	10.2	172	5.4	2.5
770	0.3	abs.	372	5.7	5.8
190	0.9	abs.	113	12.8	13
390	10.3	8.4	313	2.8	4
590	w+	6.0	133	0.6	2.5
111	10.4	14.0	333	11.7	7
311	42.5	45	153	1.5	abs.
511	12.6	14	173	9.5	3.5
711	4.6	5.9	114	10.2	5.8
911	3.4	2.5	314	1.2	2
131	37	43	134	0.6	abs.
331	7.3	7	334	10.5	6
531	1.5	abs.	552	3.4	vvw
731	12.3	15	553	6.5	vvw

The reflections of type II, h even and k even, with different values of l were used to obtain a value of z. Intensities which were very sensitive to u, v, or w were not used. As before, calculated intensities were plotted as a function of z and the best value chosen; $z = 0.540 \pm 0.005$ was found.

Comparison of calculated and observed intensities for reflections of type II (Table III) served as a check on all these parameters. The calculated and observed intensities for all reflections observed are listed in Tables III to VI. Intensities of reflections observed by Hassel and Luzanski[2] and not by us are designated by letters rather than numbers.

TABLE VI

TYPE IV PLANES

hkl	Calcd.	Obsd.	*hkl*	Calcd.	Obsd.
020	7.3	7.9	081	7.2	8.6
040	25.9	19.4	082	13	12
060	6.7	8.1	0,10,1	11.4	14.1
080	22	15.8	201	61	70
0,10,0	0	abs.	202	14.1	14.1
200	0	abs.	203	4.1	abs.
220	35.8	40	204	12.5	w
240	27.0	43	221	30	44
260	9.1	8.6	222	13.5	10.6
280	1.0	abs.	223	6.0	6.1
400	27	27	224	2.5	3.3
420	42	31.5	241	4.4	4.5
440	20.2	19	242	10.5	12.3
460	14.6	13	243	7.9	7.2
480	5.5	3.4	261	7.4	5.9
600	10.8	13	262	4.0	8
620	16	14	263	5.9	4.4
640	12.8	12	281	9.7	8.2
660	9.6	7.7	282	5.5	5
680	4.4	2.6	401	21.2	28
800	20.8	20	421	6.8	10.5
820	1.4	2.2	441	12.4	19.4
840	4.7	5.3	461	1.4	3.6
860	1.9	2.0	481	7.6	5.2
10,0,0	3.3	2.5	601	22.4	20
003	0	abs.	621	2.7	3.8
004	3.0	vvw	641	3.4	5.5
021	78	75	661	1.1	abs.
022	9.7	9.3	801	7.0	8.3
023	15.7	14.7	821	11.8	10
024	5	3.3	841	4.9	3.3
041	7.1	10.5	404	11.5	w
042	21.7	21	402	6.3	vw
043	10.4	8.3	403	18.9	m
044	17.8	10	802	10.7	m
061	21.3	16.4	442	2.7	vw(w)
062	3.3	5.6	443	5.5	vw(m^-) (m^+)
063	10.8	10.5	662	8.1	m^{++}

Conclusions.—The values of the F–F distance calculated using these parameters are

$$F_1\text{–}F_1 = 2.31 \pm 0.035 \text{ Å.}$$
$$F_2\text{–}F_2 = 2.320 \begin{matrix} +0.03 \\ -0.02 \end{matrix} \text{ Å.}$$

The lower limit is less in the latter case since the value chosen for u was the lower limit (0.129) given it in the determination above; probably u cannot be less than 0.129.

Comparing these values with the value F–F 2.26 ± 0.01 Å. for KHF_2 it is seen that there is a slight increase in the distance in NH_4HF_2, amounting to between 0.03 and 0.08 Å., due to the weakening of the bond by the two extra hydrogen bonds formed in NH_4HF_2.

The N–F distances found are $N\text{–}F_1 = 2.80 \pm 0.02$ Å., and $N\text{–}F_2 = 2.80 \pm 0.03$ Å. This value is larger than the average found by Pauling (2.76 Å.) and is 8% larger than the value N–F = 2.63 Å. for NH_4F. We thus confirm the observation of Pauling that the hydrogen bond in NH_4HF_2 is weaker than that in NH_4F. The longer ammonium ion to fluorine contacts are: $N\text{–}F_I = 3.02$ Å. and $N\text{–}F_{II} = 3.40$ Å.

Summary

The unit translations for the orthorhombic crystal NH_4HF_2 have been revised to $a_0 = 8.426$ Å., $b_0 = 8.180$ Å., $c_0 = 3.69$ Å. The space group and structure given by Pauling have been confirmed and the parameters redetermined:

$$z = 0.540 \pm 0.005 \text{ Å.} \qquad u = 0.129 \begin{matrix} +0.003 \\ -0.001 \end{matrix} \text{ Å.}$$
$$w = 0.137 \pm 0.002 \text{ Å.} \qquad v = 0.131 \pm 0.003 \text{ Å.}$$

The four smallest N–F distances are all equal to 2.80 ± 0.025 Å. and the F–F distances in the two non-equivalent HF_2^- ions are found to be 2.32 ± 0.03 Å.

PASADENA, CALIFORNIA RECEIVED MARCH 13, 1940

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, No. 771]

The Crystal Structure of Potassium Fluoroiodate, KIO_2F_2

BY LINDSAY HELMHOLZ AND M. T. ROGERS

Introduction

A complete knowledge of the crystal structure of potassium fluoroiodate should afford considerable evidence concerning the steric effect of unshared electron pairs in molecules and ions and concerning the influence of relative electronegativity on the interatomic distances. The structure determination has been carried out to investigate these questions. Unfortunately it has turned out that the number of parameters to be determined is so great that, although the general characteristics of the structure are certain, the accuracy of the determination permits us to make only qualitative remarks about the effects mentioned above.

It has been found that the $IO_2F_2^-$ group approximates an octahedral group with two of the positions unoccupied. A tetrahedral configuration for the ion, which might have been anticipated from the similarity of the unit dimensions of this crystal and those of KIO_4, is clearly impossible.

A distinction between oxygen and fluorine atoms or ions in the structure is suggested by the intensities and the interatomic distances, but it is impossible for us to insist on our assignment and so to give any detailed discussion of the influence of electronegativity on bond distance.

The observation that potassium iodate, formed by the hydrolysis of the compound in moist air, is oriented to a considerable extent on the surface of the fluoroiodate suggests (as is borne out by the structure) that the crystal resembles KIO_3 much more than KIO_4.

Procedure.—Potassium fluoroiodate was prepared by dissolving potassium iodate in concentrated hydrofluoric acid and allowing the resulting solution to stand until, after a few days, tabular crystals were precipitated. Some smaller crystals were formed for which the principal direction of growth was normal to the plate. Goniometric measurements showed the crystals to be identical with those described by Groth.[1] In order to prevent reaction of the crystals with atmospheric moisture they were coated with a layer of lacquer.

(1) Groth, "Chemische Krystallographie," Teil II, Leipzig, 1908, p. 94.

Oscillation photographs were taken with CuK_α and MoK_α radiations and Laue photographs with continuous radiation ($\lambda_{min.} = 0.24$ Å.) from a tungsten target. Intensities were estimated visually using a calibrated scale and photographs of different exposure times. For the CuK_α pictures the influence of absorption was considered; for the Mo pictures the crystals were small enough so that the absorption correction was shown to be negligibly small.

Space Group and Unit Cell.—Laue photographs taken with the X-ray beam normal to the plates showed the Laue symmetry D_{2h}. The regular absences $h0l$, $h \neq 2n$ and $0kl$, $l \neq 2n$ were observed giving C_{2v}^5 and D_{2h}^{11} as possible space groups. A pyroelectric experiment which gave a positive result eliminated D_{2h} and established $C_{2v}^5 - Pca$ as the correct space group for the crystal.

The dimensions of the unit cell were found, from oscillation photographs, to be $a_0 = 8.38 \pm 0.02$ Å.; $b_0 = 5.97 \pm 0.02$ Å.; $c_0 = 8.41 \pm 0.02$ Å. The data from which these values were obtained are listed in Table I. The X-ray data give the axial ratios $a:b:c = 0.996:0.7098:1$ to be compared with the crystallographic axial ratios $a:b:c = 0.9925:2 \times 0.7074:1$ given by Groth.[1]

Assuming the density of the fluoroiodate to have a value close to the densities of potassium iodate (3.89 g./cm.^{3}) and periodate (3.61 g./cm.^{3}) the number of molecules in the orthorhombic unit was found to be four. The density calculated for four molecules per unit cell is 3.71 g./cm.^{3} Numerous Laue photographs of long exposure time showed no reflections requiring a large unit.

Determination of the Structure.—For the space group $C_{2v}^5 - Pca$ there exists only one set of positions, the general four-fold positions $4a$):[2] x, y, z; $\bar{x}, \bar{y}, \frac{1}{2} + z$; $\frac{1}{2} - x, y, \frac{1}{2} + z$; $\frac{1}{2} + x, \bar{y}, z$.

There are then three parameters to be determined for iodine and three for potassium. The eight fluorine atoms in the unit are to be placed in two sets of positions $4a$, and the eight oxygen atoms also in two sets of the four-fold positions.

The first step in the structure analysis was the determination of the iodine parameters. For this

(2) "Int. Tab. z. Bestimmung v. Kriststrukturen."

TABLE I

a_0			b_0			c_0		
(h00)	a_0 (obsd.)	a_0 (calcd.)	0k0	b_0 (obsd.)	b_0 (calcd.)	00l	c_0 (obsd.)	c_0 (calcd.)
(200)	8.346	8.38	010	5.963	5.97	(002)	8.30	8.41
(400)	8.376		020	5.974		(004)	8.37	
(600)	8.382		030	5.990		(006)	8.47	
(800)	8.368		050	5.960		(008)	8.408	
(10,00) α_1	8.381		060	5.984		(00,10) α_1	8.412	
α_2	8.378		070 α_1	5.978		α_2	8.409	
			α_2	5.974				

purpose a Patterson projection on the x–z plane was made using $h0l$ data. This projection (Fig. 1) shows strong peaks, corresponding to iodine–iodine interactions, at $x = \frac{1}{2}$, $z = 0$; $x = 0$, $z = \frac{1}{2}$; and $x = z = \frac{1}{2}$. This distribution can be accounted for only if the iodine parameters $x_1 = z_1 = 0$, or an arrangement equivalent to this. This assignment of parameters may be checked by a qualitative consideration of the intensities. The intensities of reflection from planes (hkl), with $h + l \neq 2n$ were observed to be very much weaker than the reflections with $h + l = 2n$ even for large values of h, k and l. For the iodine parameters $x_1 = z_1 = 0$ the iodine contribution to the intensities of the type of planes first mentioned is zero.

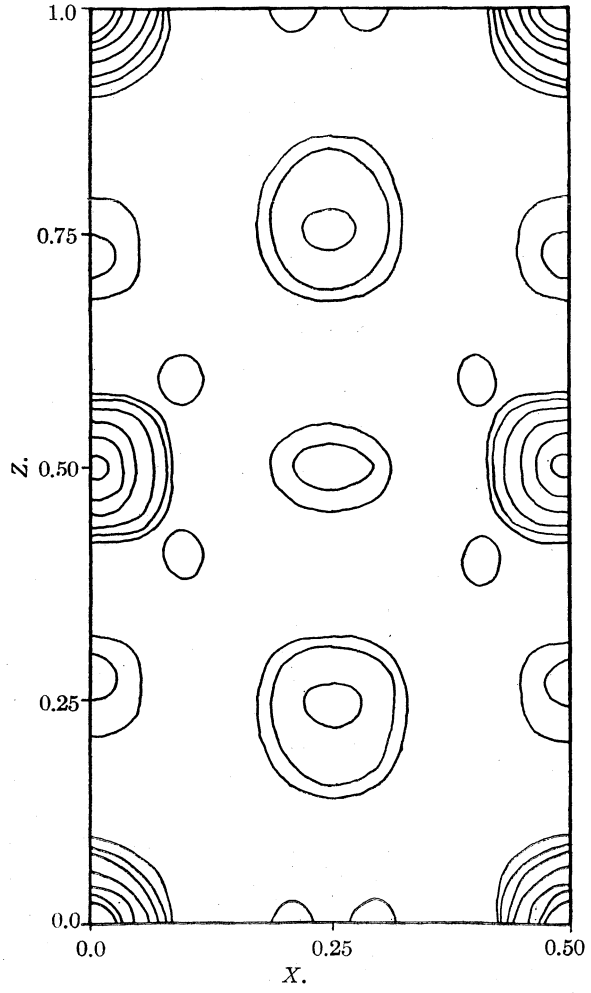


Fig. 1.—Patterson projection, $P(x,z)$, on x–z plane.

A Harker projection, $H(xy\frac{1}{2})$, making use of the two-fold screw axis parallel to z, was calculated as the next step in the determination. This gave a value for the y-parameter for iodine, $2y = 0.135$. Complete data were not used in preparing this projection but the final structure indicates that the 200 important reflections which were used gave a very reliable value for the parameter. No other use was made of the projection.

Since the projection of the scattering matter in the cell on the x–y plane contains a center of symmetry it was profitable next to make a Fourier projection on this plane using the (hk0) data. The signs of the F's for all strong reflections are unambiguously determined by the iodine contribution, so that, starting with these reflections, a complete Fourier projection could be made by a process of successive approximations. From the first of these the potassium ions were found to have $x \approx 0.25$, $y \approx 0.50$.

As long as only reflections to which iodine contributes were used, a plane of symmetry, not present in the crystal, persists along a line $x = 0$. The strongest F to which iodine does not contribute, F_{310}, was next introduced arbitrarily with positive sign. The introduction of this single F_{310} destroys the plane of symmetry and permits the assignment of approximate x and y parameters for potassium ions, fluorine and oxygen atoms. The final projection, shown in Fig. 2, was obtained by including all the $F_{(hk0)}$'s in the Fourier series. The letters refer to the atoms with parameter z, the primed letters to equivalent atoms at $z + \frac{1}{2}$. The c-glide planes are indicated by dotted lines, the a-glide plane by the dashed line. Contour lines have been drawn at 20, 30, 40, 50, 100, 150, 250, and 350 on an arbitrary scale.

Figure 2 shows clearly the iodine atoms at I and

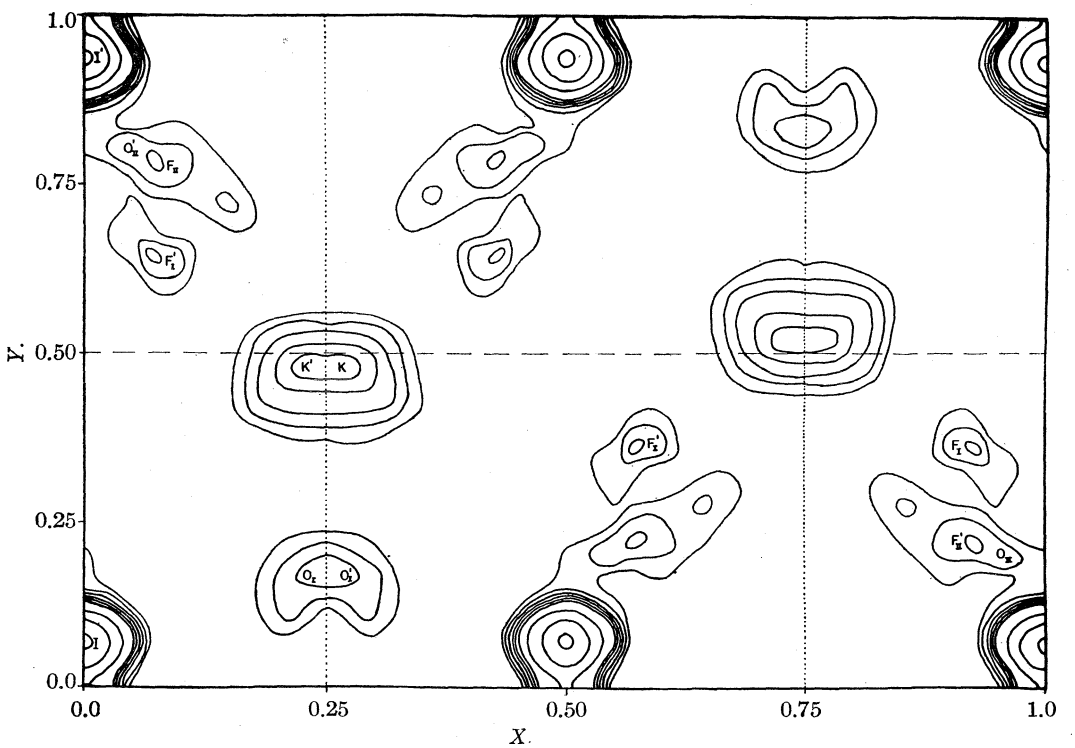


Fig. 2.—Fourier projection of scattering matter on (001) face.

I′. The peak K (and K′) is unresolved and due to equivalent potassium ions at xyz and $\frac{1}{2} - x, y, z + \frac{1}{2}$. The differentiation of oxygen and fluorine atoms cannot be made on the basis of the projection, and evidence for the distinction finally made is not entirely conclusive but the discussion will be continued on the basis of the final assignment and it will be borne in mind that an exchange of oxygen atoms for fluorine in the structure is possible within the limits of error of the X-ray data. The unresolved peak at O_I (O_I') is due to oxygen atoms and the clearly defined maximum at F_I can be identified as a fluorine atom. The remaining somewhat diffuse maximum in the neighborhood of F_{II} and O_{II} is believed to be due to the superposition of two maxima.

The atoms were given x- and y-parameters as indicated by the lettering of the maxima and as seem reasonably definite from the size of the maxima for all cases except that of O_{II}. Two possible positions for this atom are compatible with the projection; (1) the maximum corresponding to O_{II} lies so close to I that it is not observed, or (2) the maximum for O_{II} is part of the O_{II}–F_{II} maximum which is unresolved. A decision in favor of the second alternative was made with reasonable certainty on the basis of the intensities of reflection which are independent of the iodine atoms.

The evaluation of the z parameter was carried out by making use of the general characteristics of the X-ray spectra, the Patterson projection, and structural arguments as outlined below. It is seen (most clearly on Laue photographs) that, for all pairs of reflections (hkl) and (lkh) having the same type of structure factor, the intensities are very nearly equal for all values of h and l. This fact together with the evidence of the Patterson projection indicates that a projection of the scattering matter on the x–z plane has approximately tetragonal symmetry.

If F_I is associated with any iodine atom it must be bonded to I and not to I′ since the projection of the distance I′ − F_I on the x–y plane (see Fig. 2) is greater than could correspond to an iodine–oxygen bond. The projection places another fluorine atom at F_{II}, which might be bonded to I′ as far as the projection is concerned. If this were the case and if I − F_I were equal to I′ − F_{II} then the projection of the interatomic distance on the x–z plane should show up on the Patterson projection where no maximum is observed. Since F_{II} is the same distance from I as F_I and lies on a straight line through I and F_I (in the projection)

it is suggested that these two atoms form opposed bonds with iodine and by referring to the argument in the previous paragraph the values of x_{FI} and x_{FII} will be approximately ± 0.08. This assignment of parameters is made more probable by the small maximum at $z = 0.40$, $x = 0.10$ on the Patterson projection.

The oxygen atom O_I may be assigned fairly definite parameters, the Patterson projection indicating that z_{O_I} cannot be very large. From the projection x has two possible values $\approx 0.25 \pm 0.025$. This choice must be made on the basis of structural arguments and intensities of *hkl* planes. If $IO_2F_2^-$ groups are postulated then certainly x must be less than 0.25. The possibility that x is larger than 0.25 is not altogether unreasonable and was considered seriously but no fit between experimental and calculated intensities could be obtained on this basis. With F_I, F_{II} and O_I placed the choice of parameters for O_{II} was made by concluding from the Patterson projection that it must have a position relative to the z-axis similar to that of O_I relative to the x-axis. In trying to find the proper parameters the iodine to fluorine distances were considered to be equal, as were the iodine to oxygen distances.

The potassium parameters were determined roughly from the projections and then refined by comparison of observed and calculated intensities. The parameters were varied subject to the condition that distances from potassium to oxygen and fluorine be larger than 2.60 Å.

The atomic positions fixed by the means described in the previous paragraphs were finally varied by small amounts (0.005 to 0.01) to obtain the best fit between experimental and observed intensities. The resulting parameters are given below:

	x	y	z
I	0.00	0.067 ± 0.001	0.00
K	.215 ± 0.005	.465 ± .005	.29 ± 0.005
F_I	− .08 ± .01	.355 ± .01	.09 ± .01
F_{II}	.08 ± .01	− .22 ± .01	− .09 ± .01
O_I	.215 ± .01	.175 ± .01	.035 ± .01
O_{II}	− .02 ± .01	.19 ± .01	.210 ± .01

The atoms occupying the positions F_I and F_{II} it was felt must be the same, either oxygen or fluorine. The position of these atoms is fairly well fixed and it is found that the agreement is considerably better for some of the weak reflections if fluorine atoms are placed in positions F_I and F_{II}. The fact that the I–O distance for this assignment is so closely equal to the same interatomic distance in $(NH_4)_2H_3IO_6$ also lends support to this arrangement.

Tables II and III give the calculated and observed F_{hkl}'s. Pauling–Sherman f-values were used in calculating the F's.

TABLE II

VALUES OF F_{hkl}

(*hkl*)	Obsd.	Calcd.	(*hkl*)	Obsd.	Calcd.	(*hkl*)	Obsd.	Calcd.
(010)	70	100	(310)	54	68	(600)	64	56
(020)	81	79	(320)	abs	10	(610)	82	89
(030)	14	17	(330)	abs	4	(620)	50	52
(040)	abs	6	(340)	18	26	(630)	23	19
(050)	30	24	(350)	abs	6	(640)	abs	7
(060)	35	30	(360)	abs	2	(650)	28	24
(070)	46	50	(370)	abs	12	(660)	23	30
(080)	28	35				(670)	abs	25
						(680)	28	30
(110)	abs	6	(400)	112	152			
(120)	abs	3	(410)	81	94	(710)	abs	1
(130)	20	24	(420)	92	80	(720)	abs	5
(140)	26	28	(430)	abs	0.0	(730)	abs	1
(150)	14	15	(440)	abs	1.0	(740)	abs	4
(160)	15	20	(450)	23	27	(750)	abs	1
(170)	abs	16	(460)	24	28			
			(470)	27	32	(800)	35	42
(200)	94	136	(480)	31	31	(810)	50	54
(210)	129	169				(820)	31	32
(220)	45	35	(510)	abs	14			
(230)	69	61	(520)	abs	2	(10,00)	36	50
(240)	15	20	(530)	abs	10	(10,10)	31	28
(250)	16	19	(540)	abs	5	(10,20)	28	27
(260)	38	43	(550)	abs	8			
(270)	37	43				(12,00)	abs	22
(280)	33	27				(12,10)	23	34

TABLE III

VALUES OF F_{hkl}

(*hkl*)	Obsd.	Calcd.	(*hkl*)	Obsd.	Calcd.	(*hkl*)	Obsd.	Calcd.
002	87	145	(801)	abs	9	(211)	30	30
004	98	148	(802)	63	55	(212)	85	94
006	68	70				(213)	23	24
008	56	49				(214)	100	126
00,10	29	61	(111)	71	78	(215)	abs	3
			(112)	abs	10	(216)	69	80
(201)	10	8	(113)	55	76	(217)	abs	14
(202)	130	172	(114)	abs	29	(218)	50	50
(203)	53	65	(115)	52	57			
(204)	88	89	(116)	abs	12	(221)	25	33
(205)	abs	14				(222)	102	134
(206)	73	68	(121)	83	98	(223)	abs	13
			(122)	37	46	(224)	49	64
(208)	50	62	(123)	70	89	(226)	49	64
			(124)	abs	5	(228)	38	45
(401)	33	47	(125)	78	96			
(402)	84	91	(126)	abs	16	(231)	23	25
(403)	abs	31	(127)	39	50	(232)	32	33
(404)	119	128	(128)	abs				
(405)	25	22						
(406)	74	80	(131)	98	131			
			(132)	12	28			
			(133)	106	105			
(601)	22	33						
(602)	80	73						
(603)	27	32	(141)	125	103			
(604)	65	83	(142)	abs	9			
(605)	abs	22	(143)	101	83			
(606)	65	68						
(608)	45	45						

As an additional check on the parameters the ratio of intensities I_{hkl}/I_{lkh} were compared with the calculated intensity ratio. Since the inter-

planar distances d_{hkl} and d_{lkh} are so nearly equal quantitative use could be made of the Laue intensities for such pairs of reflections. Reflections with $n\lambda$ in the neighborhood of the critical absorption limit for iodine were not used in these comparisons. The intensities were estimated visually with the use of a calibrated scale. Table IV gives the results.

TABLE IV

	hkl	I_{hkl}/I_{lkh} obsd.	I_{hkl}/I_{lkh} calcd.
1	(415)	15.0	13.10
2	(611)	5.5	4.22
3	(613)	2.4	2.02
4	(614)	1.0	0.98
5	(615)	7.5	6.30
6	(617)	7.5	10.8
7	(811)	4.5	4.5
8	(813)	3.5	4.9
9	837	2.0	30.0[a]
10	429	8.0	6.2

[a] The calculated F's for both reflections are so small for this case 5.7 and 1.0 that a very small error in parameters makes a very large error in the calculated intensities.

Discussion of the Structure.—The crystal structure derived from the above parameters is shown in Fig. 3. The fluoroiodate ion, as shown in the figure, consists of a central iodine atom forming bonds to two fluorine and two oxygen atoms. The fluorine atoms lie on a straight line through the iodine atom and may be thought of as forming opposed bonds. The oxygen atoms lie in a plane perpendicular to the I–F bonds and form bonds with the iodine atom at about 100°. This arrangement gives the group as a whole the appearance of an octahedron with two of the corners removed. It may perhaps better be thought of as a trigonal bipyramid in which one of the three equivalent orbitals is occupied by an unshared pair and the angle between the remaining two decreased from 120 to approximately 100°. The interatomic distances are: $I–O_I = 1.93 \pm 0.05$ Å.; $I–O_{II} = 1.92 \pm 0.05$ Å.; $I–F_I = 2.00 \pm 0.05$ Å.; $I–F_{II} = 1.99 \pm 0.05$ Å.; $O_I–O_{II} = 2.85 \pm 0.10$ Å.; and the angle $O_I–I–O_{II} = 100 \pm 7°$. The fluorine–oxygen contacts are the same within the limits of error and equal to 2.75 ± 0.10 Å.

This configuration of the $IO_2F_2^-$ group is the same, within the limits of error, as that reported by Stevenson and Schomaker[3] for $TeCl_4$ in which the unshared pair of electrons has apparently the same steric effect as in the $IO_2F_2^-$ ion.

(3) D. P. Stevenson and Verner Schomaker, THIS JOURNAL, **62**, 1267 (1940).

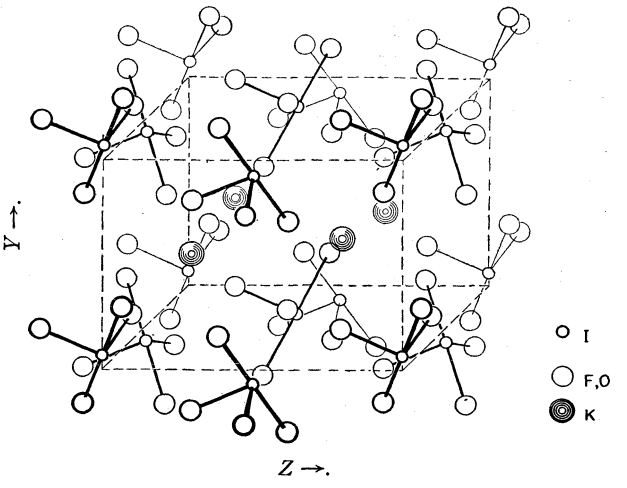


Fig. 3.—Structure of potassium fluoroiodate.

The effect of the unshared pair of electrons on the bond distances may be discussed by comparing the effective iodine radius in this compound with the iodine radii in other related compounds. The data for a number of these compounds are shown in Table V. The table shows that a considerable decrease in the effective iodine radius can be correlated with an increase in formal charge. Since the unshared pair in $IO_2F_2^-$ contributes the same number to the formal charge of iodine as the two additional electron pair bonds in IO_6^{5-} the I–O distances in the two ions might be expected to be nearly the same. The iodine radii for the cases of the iodates and of IF_5 seem to be much too large to be accounted for on the assumption that the radius is a simple function of the formal charge. It is true, however, that the determinations of these two distances are not completely reliable, and satisfactory answer has not yet been given to the question of the existence of discrete IO_3^- ions in iodate crystals.

TABLE V

Compd.	I – X, Å.	Configuration	Formal charge	I-radius
KIO_4[a]	2.23	Octahedral	+3	1.18
$(NH_4)_2H_3IO_6$[b]	1.93	Octahedral	+1	1.27
KIO_2F_2	1.93 (O)	Octahedral or	+1	1.27
	2.00 (F)	trig. bipyr.	+1	1.36
IF_5[c]	2.56	Trig. bipyr.	0	1.90
$KICl_4$[d]	2.34	Octahedral	−1	1.35
KIO_3[e]	2.23	Octahedral	−1	1.58

[a] E. A. Hazelwood, *Z. Krist.*, **98**, 439 (1938).
[b] L. Helmholz, THIS JOURNAL, **59**, 2036 (1937).
[c] Braune and Pinnow, *Z. physik. Chem.*, **35**, 239 (1937).
[d] R. C. L. Mooney, *Z. Krist.*, **98**, 377 (1938).
[e] Zachariasen, *Phys. Rev.*, **37**, 1626 (1931).

If the iodine–oxygen and iodine–fluorine dis-

tances in potassium iodate and iodine pentafluoride are assumed to be even approximately correct then it would seem evident that two cases must be distinguished. If a vacant orbital exists in the coördination polyhedron, the unshared pair may occupy that orbital and its effect on the iodine radius will be small and may be correlated with the formal charge on the central atom. If no such vacant orbital exists, then the extra electrons become an "inert pair" having no steric effect, but causing a relatively large increase in the iodine radius.

The Structure.—The coördination of oxygen and fluorine atoms about potassium is irregular but it is probable that the packing of the $IO_2F_2^-$ groups is the determining factor in the structure. The K–O and K–F contacts are: O_I-K = 2.75, 2.76 Å.; $O_{II}-K$ = 2.63, 3.03 Å.; F_I-K = 2.64, 3.06 Å.; $F_{II}-K$ = 2.74, 3.04 Å.

The interatomic distances which are less than 3.50 Å. between oxygen and fluorine atoms of different anion groups are: F_I-F_{II} = 2.77, 3.23 Å.; F_I-O_{II} = 3.40 Å.; $F_{II}-O_I$ = 3.24 Å.

There are, in addition, two distances between iodine atoms and oxygen atoms in different $IO_2F_2^-$ groups that are shorter than three Ångströms: $I-O_I$ = 2.82 Å.; $I-O_{II}$ = 2.88 Å.

The similarity between this structure and that reported for potassium iodate may be seen if one considers an altered KIO_2F_2 in which the I–O contacts just mentioned are made real bonds so that each oxygen atom is shared between two iodine atoms. If, then, the iodine atoms and bonds to oxygen atoms are placed in the x–z plane, then this plane will be identical with a plane $z = 0$ for the potassium iodate structure. In this altered structure the I–F bonds will be in a vertical position along the lines $x = z = 0$, etc. If now one atom of oxygen is substituted for two atoms of fluorine and this atom shared between two iodine atoms the structure would become the cubic structure attributed to potassium iodate. It is suggested that the similarity, although not very great, is sufficient to cause the orientation effects observed on photographs of KIO_2F_2 in which some of the salt had hydrolyzed. The powder lines had quite definite maxima at positions corresponding to the equator and layer lines for potassium iodate oriented with the cube edges parallel to the orthorhombic axes of KIO_2F_2.

Summary

From a determination of the crystal structure of KIO_2F_2 it has been found that the $IO_2F_2^-$ group is composed of an iodine atom forming bonds at approximately 100° with two oxygen atoms, and perpendicular to the plane of these three atoms, two opposed bonds at 180° to fluorine. The configuration may perhaps best be thought of as that of a trigonal bipyramid in which one of the three equivalent orbitals is occupied by an unshared electron pair. The interatomic distances in the ion were found to be: I — O = 1.93 ± 0.05 Å.; I — F = 2.00 Å. ± 0.05 Å. The O–I–O bond angle = 100 ± 10°. The influence of the unshared pair on the bond distance is discussed.

PASADENA, CALIFORNIA RECEIVED APRIL 5, 1940

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE ETHYL GASOLINE CORPORATION]

The Redistribution Reaction. VIII. The Relative Affinity of Mercury and Lead for Methyl and Ethyl Radicals

BY GEORGE CALINGAERT, HAROLD SOROOS AND GEORGE W. THOMSON

Previous papers[1,2] of this series have described the redistribution reaction for the interchange of alkyl radicals in alkyl compounds of lead, tin, silicon, or mercury. Redistribution of alkyl groups is not confined to systems containing a single metal, but under suitable conditions can take place between compounds of more than one metal. This was illustrated in the first paper[1] of this series by an analytical distillation[3] curve for the reaction product of tetramethyltin with tetraethyllead, which indicated the presence of all ten possible R_4M compounds.

The fact that the equilibrium composition of a redistributed mixture corresponds to a random distribution of all the organic radicals present indicates that the relative affinity of a given radical for a given metal is independent of the

(1) Calingaert and Beatty, THIS JOURNAL, **61**, 2748 (1939).

(2) Calingaert, Beatty and Soroos, *ibid.*, **62**, 1099 (1940); Calingaert, Soroos and Hnizda, *ibid.*, **62**, 1107 (1940).

(3) Calingaert, Beatty and Neal, *ibid.*, **61**, 2755 (1939).

nature of the other radicals attached to the metal. When two metals, for example mercury and lead, are present in the system, the same should still hold true for each metal separately, but it does not follow that the different radicals, for example methyl and ethyl, should be divided equally between the two metals. If the affinity of the methyl radicals, relative to that of the ethyl radicals, is greater for mercury than for lead, then the R_2Hg compounds will contain a greater proportion of methyl than the R_4Pb compounds. Based on the law of mass action, this difference in relative affinity can be expressed by a "relative affinity constant," K, whose value is given by $K = [Me\text{-}Hg][Et\text{-}Pb]/[Et\text{-}Hg][Me\text{-}Pb]$, where the brackets denote the proportions of the four different R-M bonds in the total product.

The above example is particularly suitable for experimental study, first, since it includes two dissimilar metals of different valence, for each of which alone the redistribution reaction is known[2] to occur readily, giving random equilibrium mixtures, and, second, since its reaction product is of such nature as to facilitate an accurate analysis.[3] Accordingly, two tests were made, one with a mixture of tetramethyllead and diethylmercury, the other with tetraethyllead and dimethylmercury, each mixture containing equal proportions of methyl and ethyl radicals, and equivalent amounts of mercury and lead. Both mixtures, with aluminum chloride as the catalyst, underwent redistribution at 80° in five hours. The results are given in Tables I–III, and the distillation curves for the reaction products are shown in Fig. 1.

The data show that: (1) the recovery of each metal was quantitative, exclusive of handling losses resulting from filtration and transfer of

TABLE I

REDISTRIBUTION OF TETRAMETHYLLEAD AND DIETHYLMERCURY: DISTILLATION AND ANALYTICAL DATA

Fraction No.	Fraction Wt., g.	Fraction B. p. (50 mm.) up to	Lead Content Wt. %	Lead Content Wt., g.	Lead Content Mmoles.	Mercury Content Wt. %	Mercury Content Wt., g.	Mercury Content Mmoles.	Composition assumed from b. p.
1	91.72	31.5	0.315	0.288	1.39	85.51	78.430	390.96	Me_4Pb; Me_2Hg
2	9.27	50.5	4.06	0.376	1.81	78.05	7.235	36.07	Me_4Pb; MeEtHg
3	96.76	54.0	5.855	5.665	27.34	74.16	71.757	357.69	Me_3EtPb; MeEtHg
4	12.45	75.0	19.45	2.422	11.69	58.20	7.246	36.12	Me_2Et_2Pb; MeEtHg; Me_3EtPb; Et_2Hg[a]
5	53.83	78.5	45.95	24.735	119.37	26.62	14.330	71.43	Me_2Et_2Pb; Et_2Hg
6	43.58	94.0	65.34	28.475	137.42	2.02	0.880	4.39	Me_2Et_2Pb; $MeEt_3Pb$; Et_2Hg[b]
7	23.53	99.5	66.42	15.629	75.43	0.28	0.0659	0.33	$MeEt_3Pb$; Et_4Pb; Et_2Hg[b]
8	24.61	..	62.81	15.458	74.60	0.135	0.0332	0.16	Et_4Pb; Et_2Hg
9	Column washings			0.027	0.13				Et_4Pb
	Total				449.18			897.15	

[a] Estimated composition for each metal is 50% of each of the two alkyls present. [b] Composition determined assuming that the fraction is 100% metal alkyl.

TABLE II

REDISTRIBUTION OF TETRAETHYLLEAD AND DIMETHYLMERCURY: DISTILLATION AND ANALYTICAL DATA

Fraction No.	Fraction Wt., g.	Fraction B. p. (50 mm.) up to	Lead Content Wt. %	Lead Content Wt., g.	Lead Content Mmoles.	Mercury content Wt. %	Mercury content Wt., g.	Mercury content Mmoles.	Composition assumed from b. p.
1	92.20	21.0	0.14	0.129	0.62	83.283	76.787	382.77	Me_2Hg; Me_4Pb
2	19.80	49.0	1.81	0.358	1.73	82.83	16.400	81.75	Me_2Hg; MeEtHg; Me_4Pb; Me_3EtPb[a,b]
3	101.86	57.5	5.795	5.903	28.49	75.085	76.482	381.25	MeEtHg; Me_3EtPb
4	5.53	76.0	27.40	1.515	7.31	49.35	2.729	13.60	MeEtHg; Et_2Hg; Me_3EtPb; Me_2Et_2Pb[a,b]
5	55.19	80.4	43.17	23.826	114.98	30.087	16.605	82.77	Et_2Hg; Me_2Et_2Pb
6	5.34	93.0	61.63	3.291	15.88	7.775	0.415	2.07	Et_2Hg; Me_2Et_2Pb; $MeEt_3Pb$[b]
7	52.36	95.3	66.445	34.791	167.90	0.375	.196	0.98	Me_2Et_2Pb; $MeEt_3Pb$
8	36.22	109.0	64.525	23.371	112.79	0.15	.054	0.27	$MeEt_3Pb$; Et_4Pb
9	Column washings			2.16	10.42				Et_4Pb
	Total				460.12			945.46	

[a] Estimated composition for lead alkyl is 50% of each of the two present. [b] Composition determined assuming that the fraction is 100% metal alkyl.

TABLE III

COMPOSITION OF REACTION PRODUCTS

Compound	From Me_4Pb + Et_2Hg Milli-moles	Mole per cent. Found	Calcd.[a]	From Et_4Pb + Me_2Hg Milli-moles	Mole per cent. Found	Calcd.[a]
Me_4Pb	3.2	0.7	1.0	1.5	0.3	0.8
Me_3EtPb	33.2	7.4	8.9	33.0	7.2	7.8
Me_2Et_2Pb	130.7	29.1	28.3	126.4	27.5	26.8
$MeEt_3Pb$	199.8	44.5	40.3	199.7	43.4	41.0
Et_4Pb	82.3	18.3	21.5	99.5	21.6	23.6
Total	449.2	100.0	100.0	460.1	100.0	100.0
Me_2Hg	391.0	43.6	44.3	430.9	45.6	46.1
MeEtHg	411.8	45.9	44.5	422.0	44.6	43.6
Et_2Hg	94.4	10.5	11.2	92.6	9.8	10.3
Total	897.2	100.0	100.0	945.5	100.0	100.0
Methyl, %						
in R_4Pb		31.9			30.3	
in R_2Hg		66.5			67.9	
overall		49.2			49.3	
% R—Hg bonds		50.0			50.7	
Relative affinity constant K		4.2			4.9	

[a] Calculated[1] from % methyl found.

material, and there was no appreciable decomposition. Also, the over-all per cent. methyl in the product equalled that of the input, within experimental error. (2) The over-all equilibrium was completely attained, since the same product was obtained starting with either pair of metal alkyls. (3) Each metal yielded a random equilibrium mixture. (4) The per cent. methyl (67.2 ± 0.7) in the mercury alkyls was about twice that in the lead alkyls, corresponding to a marked difference in relative affinity of mercury and lead for methyl with respect to ethyl radicals. (5) The numerical values of K (as defined above) of 4.2 and 4.9 are in excellent agreement, in view of the sensitivity of the constant to slight differences in the composition of the product.

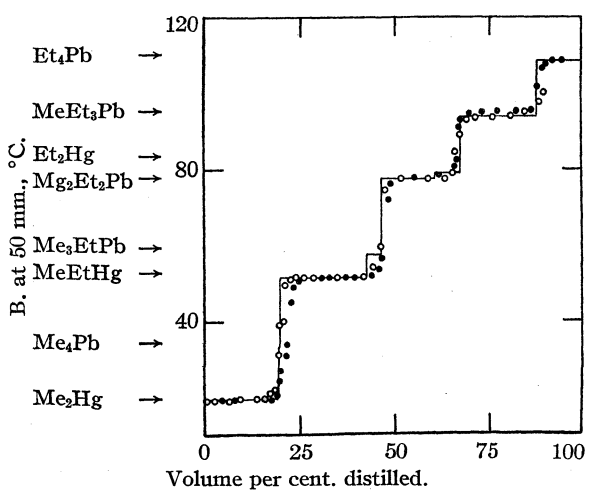


Fig. 1.—Distillation of reaction product from: ○—Me_4Pb + Et_2Hg; ●—Et_4Pb + Me_2Hg. Solid line calculated for random equilibrium mixtures, with 50.0% R-Hg and 50.0% R-Pb bonds, and with a total of 49.3% Me radicals, 33.3% Me-Hg and 16.0% Me-Pb.

Investigations of this kind obviously can be extended to other systems containing two or more metals or other central atoms or groups which, individually, are known to undergo redistribution under the conditions used. The reaction was shown to occur between the methyl and ethyl compounds of lead and tin,[1] and quantitative experiments are in progress to determine the value of K.

A few related observations of the interchange of radicals between different RM compounds have been reported, although the existence of equilibria has nowhere been recognized. Schlenk and Holtz[4] prepared methyllithium and phenyllithium by treating ethyllithium with methylmercury and phenylmercury, respectively. Challenger and Ridgway[5] isolated di-α-naphthylmercury, diphenyl-α-naphthylbismuth, and triphenylbismuth from the reaction product obtained by heating a mixture of tri-α-naphthylbismuth and diphenylmercury at 200° for two hours. Evidence has been reported[6] indicating similar reactions between diphenylselenium and *n*-butyllithium, diphenylmercury and *n*-butylsodium, and between triarylbismuth compounds and *n*-butyllithium or *n*-butylsodium.

Accordingly, it appears that redistribution reactions like the one described in the present study may be expected to occur, under suitable experimental conditions, in a variety of other analogous systems. It is evident that the analysis of such equilibria as these furnishes a useful method for the determination of relative bond energies, in which the comparison is obtained from a single reaction process, under strict equilibrium conditions, and is uncomplicated by side or consecutive reactions. Investigation of the temperature coefficient of these energies is also facilitated, inasmuch as the equilibria for each metal taken alone are not affected by temperature, so far as has been observed.

Experimental

Tetramethyllead and Diethylmercury.—To 1.83 g. (0.014 mole) of aluminum chloride contained in a small 3-

(4) Schlenk and Holtz, *Ber.*, **50**, 262 (1917).

(5) Challenger and Ridgway, *J. Chem. Soc.*, **121**, 104 (1922).

(6) Gilman and Bebb, THIS JOURNAL, **61**, 109 (1939); Gilman, Yablunky and Svigoon, *ibid.*, **61**, 1170 (1939).

neck flask fitted with a dropping funnel, reflux condenser, and thermometer, was added a mixture of 134.9 g. (0.502 mole) of tetramethyllead and 253.7 g. (0.973 mole) of diethylmercury, while cooling the flask in ice water. An atmosphere of nitrogen was maintained within the system during the addition and for the duration of the experiment. The mixture was kept at 78–83° for four hours, after which it was cooled and allowed to stand at room temperature overnight. The catalyst was extracted by shaking with water; the oily layer was separated and shaken twice with concentrated ammonia solution and finally with distilled water. After filtration through paper to remove traces of water, the product was fractionated[3] through a column packed with glass helices. The metal alkyls distilled readily and without decomposition. The various fractions were analyzed for lead and mercury. Figure 1 shows the distillation curve, Table I the analyses, and Table III the composition of the product.

Tetraethyllead and Dimethylmercury.—The above experiment was repeated, starting with 2.0 g. (0.015 mole) aluminum chloride, 233 g. (1.006 mole) dimethylmercury (which contained 0.001 mole tetramethyllead), and 162 g. (0.498 mole) tetraethyllead. The reaction time was five hours at 80°, and the product stood at room temperature over two nights. Subsequent handling was the same as above. The distillation curve, analyses, and composition of the product are given in Fig. 1 and Tables II and III, respectively.

Summary

Mixtures of diethylmercury with tetramethyllead, and of dimethylmercury with tetraethyllead, containing equal proportions of methyl and ethyl radicals and equivalent amounts of mercury and lead, undergo redistribution and yield the same random equilibrium mixture, in which the mercury shows a greater relative affinity than lead for methyl with respect to ethyl radicals.

DETROIT, MICHIGAN RECEIVED OCTOBER 13, 1939

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF THE ETHYL GASOLINE CORPORATION]

The Redistribution Reaction. IX. Redistribution of Halides and of Esters[1]

BY GEORGE CALINGAERT, HAROLD SOROOS, VINCENT HNIZDA AND HYMIN SHAPIRO

As stated in the first paper of this series,[2] the redistribution reaction is not confined to organometallic compounds, but also has been found to take place in two distinctly different fields, namely, aliphatic halides and esters. So far, the work in these and other fields has been merely exploratory, designed to furnish only a roughly quantitative measure of the occurrence or non-occurrence of redistribution. No attempt has been made to study the influence of the different reaction variables, such as the temperature and amount of catalyst, and no accurate material balances or measurements of the amount of side reaction with the catalyst have been obtained. Further experiments are in progress but, pending future publication of their results, the present paper completes the presentation of the experimental data previously cited.[2]

In the halides, redistribution was found to occur between ethylene dichloride and dibromide, between ethyl chloride and ethylene dibromide, and between ethyl bromide and ethylene dichloride, in each case using 1.5–3 mole per cent. aluminum chloride as the catalyst.

As shown in Fig. 1 and Table I, in the first of these reactions, between the two ethylene dihalides, the composition of the product corresponded within experimental error to a random distribution of the halogen atoms. In this one case, we found later that our result has been fully antici-

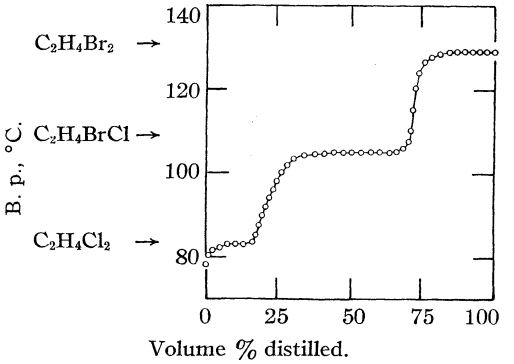


Fig. 1.—Distillation of the reaction product from $C_2H_4Br_2$ + $C_2H_4Cl_2$.

TABLE I

PRODUCTS FROM THE REDISTRIBUTION OF ETHYLENE DICHLORIDE WITH ETHYLENE DIBROMIDE

	Composition, mole per cent. Found	Calcd.[2] for r^a = 0.467
$C_2H_4Cl_2$	23.0	21.8
C_2H_4ClBr	47.4	49.8
$C_2H_4Br_2$	29.6	28.4

[a] r is the atomic fraction of chloride found in the product.

(1) For paper VIII, see Calingaert, Soroos and Thomson, THIS JOURNAL, **62**, 1542 (1940).

(2) Calingaert and Beatty, *ibid.*, **61**, 2748 (1939).

pated by Dougherty,[3] who stated that the reaction was reversible and that its product corresponded to "the laws of chance." The significance and generality of this statement apparently was not appreciated by either this author or his readers, since no subsequent reports on the subject appear in the literature.

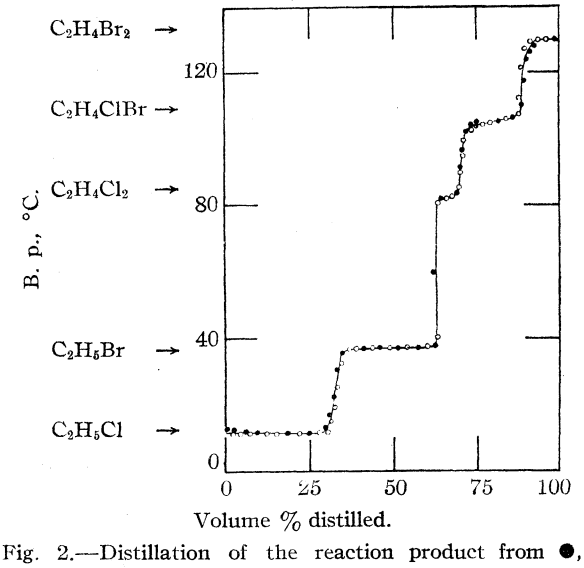


Fig. 2.—Distillation of the reaction product from ●, $C_2H_4Cl_2 + C_2H_5Br$; ○, $C_2H_4Br_2 + C_2H_5Cl$.

In the other two of these reactions, the products, which contained each of the expected five ethyl and ethylene halides, were identical, showing that equilibrium was attained from both sides. The analytical data are shown in Fig. 2 and Table II.

TABLE II

PRODUCTS FROM THE REDISTRIBUTION OF (1) ETHYL CHLORIDE WITH ETHYLENE DIBROMIDE AND (2) ETHYL BROMIDE WITH ETHYLENE DICHLORIDE

	Composition found, mole per cent. (1)	(2)
C_2H_5Cl	35	34
C_2H_5Br	30	29
$C_2H_4Cl_2$	7	9
C_2H_4ClBr	17	18
$C_2H_4Br_2$	11	10

In this case, the composition of the product is not fixed solely by the laws of probability, since it depends on the relative affinities of the two halogens for the ethyl and ethylene radicals, as was shown in paper VIII of this series[1] for the distribution of methyl and ethyl radicals between mercury and lead. Inspection of the data in Table II shows that the relative affinity factor departs slightly from unity, in the direction of a preponderance of ethyl chloride and of ethylene dibromide and chlorobromide. At the same time, the three ethylene dihalides as a group within themselves are, as before, present in proportions corresponding to a random equilibrium mixture.

In the ester field, redistribution of the alkoxy radicals was found between dimethyl and dibutyl oxalates, between methyl acetate and ethyl butyrate, and between furfuryl acetate and ethyl furoate, in each case using 3–5 mole per cent. aluminum ethylate as the catalyst and a heating time of five hours at about 100°. Blank experiments showed that, in the absence of the catalyst, no redistribution took place.

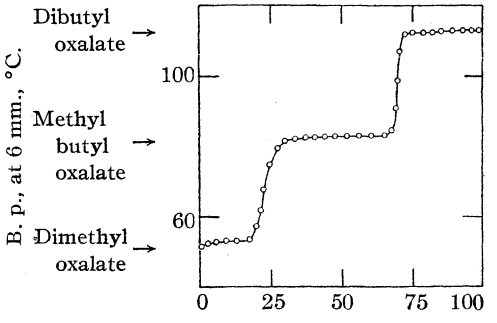


Fig. 3.—Distillation of the reaction product from dimethyl oxalate + dibutyl oxalate.

The first of these three systems, as seen from Fig. 3 and Table III, gave the expected three compounds in just the proportions of a random equilibrium mixture. Here, the accuracy of the analysis was facilitated by the relatively wide spread in the boiling points of the components.

TABLE III

PRODUCTS FROM THE REDISTRIBUTION OF DIMETHYL WITH DIBUTYL OXALATE

	Composition, mole per cent. Found	Calcd. for $r^a = 0.52$
$(COOMe)_2$	28	27
MeOOCCOOBu	48	50
$(COOBu)_2$	24	23

[a] r is the fraction of methoxyl radicals found in the product.

For the second of these ester systems, the composition of the product again is determined by relative affinities, in this case of the two alkoxy radicals for the two acyl radicals. Inspection of the results, given in Fig. 4 and Table IV, indicates that equilibrium was reached, and that the relative affinity factor in this case is close to unity, giving a symmetrical distribution of the radicals.

The third ester system—furfuryl acetate and ethyl furoate—gave quite similar results (Fig. 5

(3) Dougherty, THIS JOURNAL, **51**, 576 (1929).

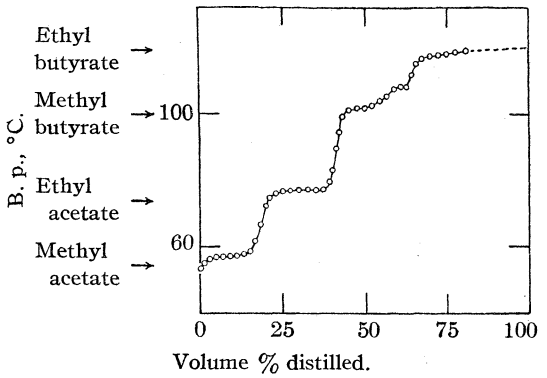


Fig. 4.—Distillation of the reaction product from ethyl acetate + methyl butyrate.

TABLE IV

PRODUCTS FROM THE REDISTRIBUTION OF ETHYL ACETATE WITH METHYL BUTYRATE

	Composition, mole per cent. Found	Calcd.[1] for $K = 1$, $[CH_3CO] = 0.50$ and $[OMe] = 0.45$[a]
CH_3COOMe	25.4	22.5
CH_3COOEt	23.4	27.5
C_3H_7COOMe	22.7	22.5
C_3H_7COOEt	28.5	27.5

[a] Concentrations are those taken in the reactants; the [OEt] was augmented by the $Al(OEt)_3$ used as catalyst.

and Table V), but the data suggest that either equilibrium was not completely attained or else there is a relative affinity factor greater than unity, in favor of the two original compounds.

TABLE V

PRODUCTS FROM THE REDISTRIBUTION OF FURFURYL ACETATE AND ETHYL FUROATE

	Composition found, mole per cent.
Ethyl acetate	23
Furfuryl acetate	24
Ethyl furoate	33
Furfuryl furoate	20

Altogether, it is evident that accurate determinations of equilibria such as these can furnish definite and specific information regarding some of the relative bond strengths in the compounds involved.

Experimental Part

Redistribution of Halides.—A mixture of 49.5 g. (0.5 mole) of ethylene dichloride, 98 g. (0.52 mole) of ethylene dibromide, and 2 g. (0.015 mole) of aluminum chloride was heated to refluxing for two hours. There was some decomposition and liberation of halogen acid. The reaction mixture, after cooling and extracting the catalyst with water, was analyzed by fractional distillation,[4] using a glass spiral packing in the column.

(4) Calingaert, Beatty and Neal, THIS JOURNAL, **61**, 2755 (1939).

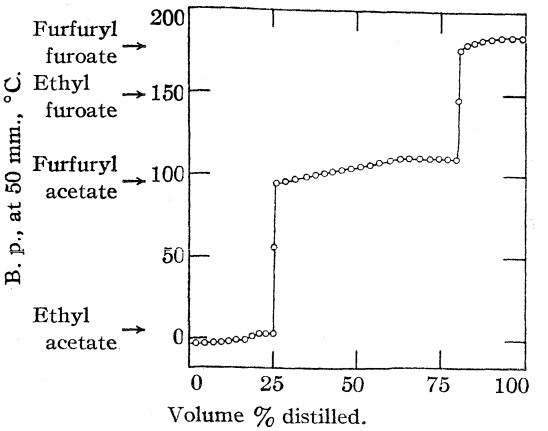


Fig. 5.—Distillation of the reaction product from furfuryl acetate and ethyl furoate.

The redistribution of a 2:1 mixture of ethyl chloride and ethylene dibromide, and of the corresponding mixture of ethyl bromide and ethylene dichloride, was carried out in steel bombs using about three mole per cent. aluminum chloride as catalyst. The mixtures were heated, respectively, to 25° for fourteen days and to 115° for twenty hours. After decomposing the catalyst with water, the products were distilled from the bomb and fractionated.

Redistribution of Esters.—A mixture of 47.2 g. (0.4 mole) of dimethyl oxalate, 80.8 g. (0.4 mole) of di-*n*-butyl oxalate and 5 g. (0.03 mole) of aluminum ethylate[5] was heated in a small flask to refluxing for five hours. The aluminum ethylate dissolved partially and later a voluminous flocculent white precipitate formed. After cooling in ice water, the reaction mixture was shaken twice with dilute hydrochloride acid. The ester layer was separated, washed with dilute sodium bicarbonate solution, and dried over anhydrous sodium sulfate. The aqueous layer and washings were extracted with several portions of ether, the extracts being combined and dried over sodium sulfate. The main product and ether extracts were subsequently fractionated.

The other ester systems were redistributed in essentially the same manner. The product from the redistribution of methyl butyrate with ethyl acetate was distilled directly from the catalyst, the distillate being subsequently fractionated.

Summary

Experimental data are presented for the redistribution reaction in the following six halide or ester systems: ethylene dibromide and ethylene dichloride, ethyl chloride and ethylene dibromide, ethyl bromide and ethylene dichloride, dimethyl oxalate and dibutyl oxalate, ethyl acetate and methyl butyrate, furfuryl acetate and ethyl furoate.

DETROIT, MICHIGAN RECEIVED DECEMBER 9, 1939

(5) The aluminum ethylate was prepared according to the method described in "Organic Syntheses," XV, 82.

[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF NORTHWESTERN UNIVERSITY]

Acetoacetyl Chloride

BY CHARLES D. HURD AND CHARLES D. KELSO

Since acetylketene, in conjunction with its resonance isomer β-crotonolactone, is the structure[1] of the dimer of ketene it seemed reasonable to think that acetoacetyl chloride could be synthesized from it by reaction with hydrogen chloride. Such proved to be the case.

$$CH_3COCH{=}CO + HCl \longrightarrow CH_3COCH_2COCl$$

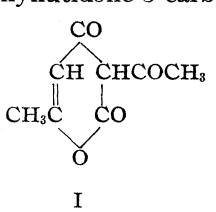
In the present synthesis low temperatures were found to be necessary because of the instability of acetoacetyl chloride at temperatures above −20°. A slight excess of hydrogen chloride was used in the synthesis and this excess remained in solution at the low temperature used. It was possible to remove this hydrogen chloride by vacuum treatment.

When acetoacetyl chloride was warmed to room temperature dehydroacetic acid (I) was formed

$$2CH_3COCH_2COCl \longrightarrow C_8H_8O_4 + 2HCl$$

Half of the hydrogen chloride was eliminated in three hours.

Low temperature (−60°) reactions of the acid chloride with alcohol or aniline gave rise to ethyl acetoacetate, $CH_3COCH_2COOC_2H_5$, and acetoacetanilide, $CH_3COCH_2CONHC_6H_5$, respectively. When acetoacetyl chloride was treated at room temperature with aniline there was formed 1-phenyllutidone-3-carboxylic acid (II).



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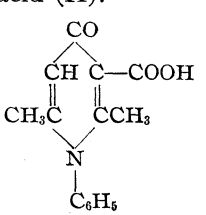


II

Another reaction investigated was that of acetoacetyl chloride and benzene in the presence of aluminum chloride. Benzoylacetone was produced.

$$C_6H_6 + CH_3COCH_2COCl \xrightarrow{AlCl_3} C_6H_5COCH_2COCH_3 + HCl$$

Acetylketene also formed benzoylacetone in a similar type of reaction but the yield was smaller.

$$C_6H_6 + CH_3COCH{=}CO \xrightarrow{AlCl_3} C_6H_5COCH_2COCH_3$$

(1) Hurd and Williams, THIS JOURNAL, **58**, 964 (1936); Hurd and Abernethy, *ibid.*, **62**, 1147 (1940).

The behavior of acetoacetyl chloride toward the Grignard reagent was studied also. A fair yield of benzoylacetone was formed with phenylmagnesium bromide at −50°.

$$C_6H_5MgBr + CH_3COCH_2COCl \longrightarrow C_6H_5COCH_2COCH_3 + MgBrCl$$

Several other β-diketones were synthesized to test the generality of this reaction. These included 2,4-octanedione from butylmagnesium bromide, 2,4-undecanedione from heptylmagnesium bromide, 2,4-dodecanedione from octylmagnesium bromide, and 5-methyl-2,4-undecanedione from 2-octylmagnesium bromide. This work will be reported in a subsequent article.

Experimental Part

Acetylketene, or "diketene," was generously donated for this study by the Carbide and Carbon Chemicals Corporation. We are very grateful for this assistance. This material was always redistilled before use: b. p. 42° (30 mm.).

Preparation of Acetoacetyl Chloride.—Dry hydrogen chloride was passed into 5 g. of cold acetylketene. At the outset the temperature was held near the freezing point of the acetylketene (−7°) but the temperature was changed to −50° or below as rapidly as the ability to withstand crystallization would permit. Usually this was only a few minutes. The cooling bath was solid carbon dioxide and acetone. When hydrogen chloride escaped through the outlet tube the reaction was stopped. The reaction mixture solidified on prolonged standing at −78°.

Analysis showed the presence of 107–109% of the theoretical amount of halogen, hence the product was contaminated with hydrogen chloride. It was kept at −70°, subjected to a vacuum of 20 mm. for five minutes and reanalyzed. The Cl-content was 104% of the theoretical. Another vacuum treatment for four minutes at −70° resulted in a solid which analyzed correctly (99.67, 99.20%) for halogen. This material was not stored but was used promptly for each experiment.

Method on Analysis.—A small dewar flask (7 cm. long by 1 cm. inside diameter) served as a weighing bottle. It was chilled to about −75° by rinsing it with butyl ether at −78°. Then 0.5 cc. of the cold butyl ether was added. The flask was stoppered and weighed, after which a 0.4-g. portion of the acetoacetyl chloride was introduced. The flask was reweighed and lowered carefully into a 500-cc. Erlenmeyer flask containing an excess of dilute base. Analysis for chloride ion followed the usual Volhard method.

Melting Point.—A three-junction copper–constantan thermocouple was calibrated at the melting points of ice, mercury and carbon tetrachloride. The acetoacetyl chloride, prepared as described above, analyzed for 99.3% of the theoretical amount of chlorine. This material melted sharply between −50 and −51°.

Behavior on Warming.—A 7-g. sample of acetoacetyl chloride which contained the equivalent of 1.9 g. of hydrogen chloride was allowed to come slowly to room temperature. The hydrogen chloride which was evolved was collected in standard alkali. At the end of three hours, 1.0 g. of hydrogen chloride was evolved. Only 0.15 g. was lost after another forty hours. Dehydroacetic acid crystals were deposited.

To this reaction product was added a slight excess of aniline. The reaction proceeded without warming, and much heat was evolved. Dehydroacetic acid reacts with aniline but heat is necessary to make the reaction take place. The product was treated with dilute hydrochloric acid to remove aniline and aniline hydrochloride. The solid was filtered off and recrystallized twice from alcohol. The melting point was 260–265° with decomposition. The neutral equivalent was found to be 235, which indicates that the product was 1-phenyllutidone-3-carboxylic acid.[2]

Reaction with Aniline at −60°.—Acetoacetyl chloride, prepared from 2.5 g. of acetylketene, was dissolved in 10 cc. of dry ether. Six grams of aniline in 20 cc. of dry ether was cooled to −60°. The acid chloride solution was poured into the aniline solution in small portions, both solutions being kept at −60° or below. This mixture was allowed to stand at −60° for three hours. The mixture was treated with water. The white solid dissolved completely. The layers were separated. The ether layer was dried and evaporated. The residue was a gummy mass which would not recrystallize from alcohol or ligroin. The residue was dissolved in ether and treated with 6 cc. of concentrated hydrochloric acid diluted with 20 cc. of water. This treatment removed the excess of aniline and removal of the ether yielded 2.3 g. of a solid which, when recrystallized from ligroin, melted at 84–85°, the melting point of acetoacetanilide. The yield was 44%.

Evaporation of the original aqueous layer yielded 3.8 g. of solid, presumably aniline hydrochloride, the theoretical amount being 3.85 g.

Reaction with Alcohol at −60°.—The reaction was run in the same manner as the previous reaction, using 2.5 g. of acetoacetyl chloride in 10 cc. of ether and 1.6 g. of absolute alcohol in the same volume of ether. The oil obtained from the aqueous layer yielded 1.6 g. (27% yield) of ethyl acetoacetate, b. p. 98° (65 mm.); semicarbazone, m. p. 120°.

Friedel–Crafts Reaction.—Thirty-six grams of benzene and 10.8 g. of acetoacetyl chloride, made by passing an excess of dry hydrogen chloride into 7.6 g. of acetylketene and then evacuating to 20 mm. at −70° until the weight of the product checked the calculated weight to 0.1 g., were placed in a flask and cooled to −50°. Twelve grams of aluminum chloride was added in portions with stirring over a period of two hours. Between additions the reaction mixture was allowed to warm up until the reaction appeared to be proceeding too vigorously. The dry-ice and acetone bath was then used to freeze out the reactants. This means of controlling the reaction was used until all the aluminum chloride was added. The mixture was allowed to warm up slowly. A sirupy layer settled to the bottom. The benzene was decanted and the sirupy layer was hydrolyzed with dilute hydrochloric acid. A semi-solid mass was obtained. On steam distillation of it, a little liquid was noted, then 3.6 g. (27% yield) of solid benzoylacetone was collected separately. It melted[3] at 59–60°. There was a non-volatile residue which was not characterized.

Friedel–Crafts Reaction with Acetylketene.—Thirty-nine grams of benzene and 8.4 g. of acetylketene were placed in a flask and cooled to −5°. Twenty-nine grams of aluminum chloride was added in portions as before and the reaction was controlled as above. The product was isolated by the same technique as above. The steam distillation yielded 1.7 g. of benzoylacetone melting at 59–60°. The yield is 10.5%.

In this reaction, 2.2 moles of aluminum chloride per mole of acetylketene was used, while in the preceding reaction, 1.1 moles of catalyst per mole of acid chloride was used.

Reactions of Acetoacetyl Chloride and Phenylmagnesium Bromide.—Phenylmagnesium bromide (0.2 mole in 250 cc. of ether) was prepared in the usual manner in an atmosphere of nitrogen. The reagent was filtered and transferred to a separatory funnel and dropped into 0.1 mole (12 g.) of acetoacetyl chloride in 150 cc. of dry ether at −60°, over a period of one and one-half hours in an atmosphere of nitrogen. The reaction mixture was allowed to stand overnight. The mixture was hydrolyzed with water and acetic acid after removal of most of the ether. The oil was removed from the aqueous layer by ether extraction. The extract was dried over sodium sulfate, the ether removed and the oil distilled at 20 mm. pressure. Two grams of an oil which partially soldified on standing was obtained in the boiling range 128–130° at 20 mm. The residue would not distil at a bath temperature of 250°. Recrystallization from ligroin gave a solid melting at 58–59°. This material and the products from the Friedel-Crafts reaction gave semicarbazones melting at 242–247° with decomposition. This is the melting point recorded for the disemicarbazone of benzoylacetone.[3]

The yield of benzoylacetone from this reaction is 12%.

Summary

Acetoacetyl chloride has been prepared from acetylketene and hydrogen chloride. It is unstable above −20°. Decomposition at room temperature yields dehydroacetic acid. Reactions with aniline, alcohol, and phenylmagnesium bromide are described.

Both acetoacetyl chloride and acetylketene undergo the Friedel–Crafts reaction with benzene and aluminum chloride.

EVANSTON, ILLINOIS RECEIVED APRIL 18, 1940

(2) Conrad and Guthzeit, *Ber.*, **20**, 161 (1887).

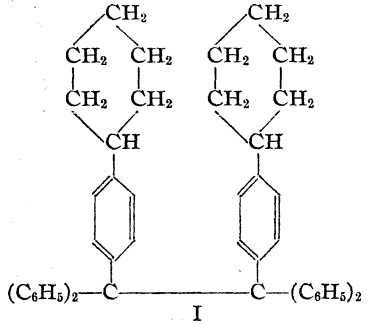
(3) Michael and Ross, THIS JOURNAL, **53**, 2394 (1931).

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

Hexa-*p*-alkylphenylethanes. X.[1] *p*-Cyclohexyl Derivatives of Hexaphenylethane

BY C. S. MARVEL AND CHESTER M. HIMEL

In connection with the study of the effect of alkyl groups on the dissociation of substituted hexaphenylethanes, di- (I), tetra- (II) and hexa- (III) -*p*-cyclohexylphenylethanes have been prepared and their dissociation measured by the magnetic susceptibility method.[2]



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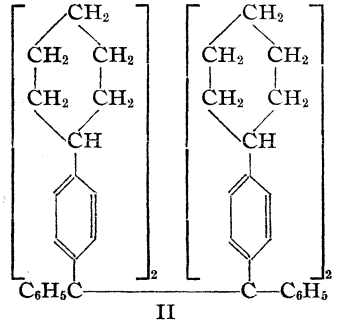

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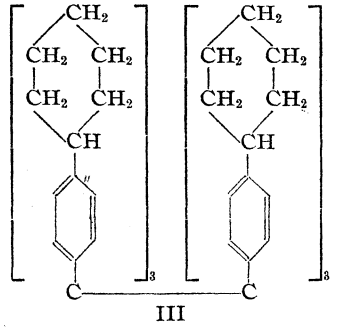
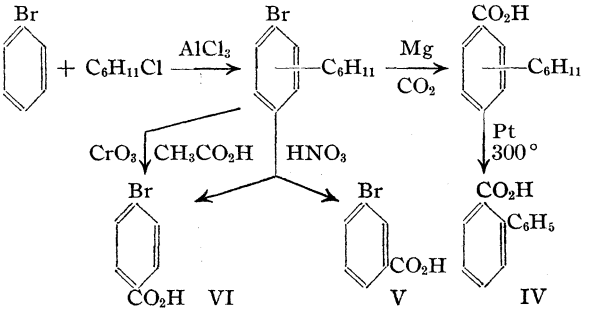


III

Zugrăvescu and Zugrăvescu[3] already have reported the preparation of di-*p*-cyclohexylphenyltetraphenylethane (I), and Brown and Marvel[4] have described a hexacyclohexylphenylethane which was believed to be the *para*-isomer (III). However, that product was prepared from a bromocyclohexylbenzene obtained by the action of cyclohexyl chloride on bromobenzene in the presence of aluminum chloride[5] and has been shown to be a mixture of isomers.

The bromocyclohexylbenzene obtained from the Friedel–Crafts reaction[4,5] has a fairly constant boiling point and its refractive index is very close to that of the product prepared by diazotization of *p*-aminocyclohexylbenzene and replacement of the diazonium group with bromine.[5] The product of the Friedel–Crafts reaction, however, contains the ortho-, meta- and para-isomers. The presence of the ortho-isomer has been demonstrated by carbonation of the Grignard reagent from the bromocyclohexylbenzene to give a mixture of acids which on dehydrogenation gave *o*-phenylbenzoic acid (IV). Meta- and para-isomers have been shown to be present by oxidation with nitric



acid to yield a mixture of bromobenzoic acids from which pure *m*-bromobenzoic acid (V) and pure *p*-bromobenzoic acid (VI) have been separated. The presence of the para-isomer also has been established by the oxidation of the bromocyclohexylbenzene in acetic acid solution by chromic acid to give pure *p*-bromobenzoic acid.

Bodroux and Thomassin[6] have described the bromination of cyclohexylbenzene to give *p*-bromocyclohexylbenzene. This reaction takes place readily and apparently yields the pure para-isomer since oxidation has given only *p*-bromobenzoic acid and conversion to the Grignard reagent followed by carbonation has produced *p*-cyclohexylbenzoic acid (VII) in yields of 80% of

(1) For the ninth communication in this series see THIS JOURNAL, **61**, 2771 (1939).

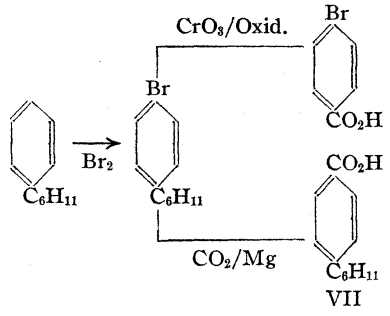
(2) (a) E. Müller and Müller-Rodloff, *Ann.* **520**, 235 (1935); (b) Roy and Marvel, THIS JOURNAL, **59**, 2622 (1937).

(3) Zugrăvescu and Zugrăvescu, *Bul. Soc. Chim. Romania*, **19A**, 85 (1937); *C. A.*, **33**, 4228 (1939).

(4) Brown and Marvel, THIS JOURNAL, **59**, 1175 (1937).

(5) Mayes and Turner, *J. Chem. Soc.*, 503 (1929).

(6) Bodroux and Thomassin, *Compt. rend.*, **205**, 991 (1937); *Bull. soc. chim.*, [5] **6**, 1411 (1939).



VII

the theoretical amount. As a further check on the purity of the *p*-bromocyclohexylbenzene obtained by this process, a sample has been made from *p*-aminocyclohexylbenzene and one of the carbinols described below has been made from each sample of the bromo compound. No difference in the properties of the carbinols thus obtained has been detected.

The three triarylcarbinols corresponding to the desired ethanes (I, II and III) have been prepared by treating the Grignard reagent from *p*-bromocyclohexylbenzene with benzophenone, ethyl benzoate and diethyl carbonate, respectively. All three carbinols thus prepared were obtained in crystalline form. The tri-*p*-cyclohexylphenylcarbinol melted at 180–181°, or twelve degrees higher than has been reported by Neunhoeffer.[7] It seems probable that Neunhoeffer may have had some ethyl ether of the carbinol mixed with the carbinol. We found that unless unusual care was taken to use alcohol-free ether in handling the carbinol, some ether formed and a low-melting product resulted. Our mono-*p*-cyclohexylphenyldiphenylchloromethane melted at 126–127°. Zugrăvescu and Zugrăvescu[3] report the melting point to be 123°. Our sample of the corresponding hexaarylethane peroxide melted at 158–159° whereas it has been reported[3] to melt at 164°.

The tri-*p*-cyclohexylphenylcarbinol, the corresponding chloromethane and peroxide obtained in this work did not have properties which agreed with those previously reported by Brown and Marvel.[4] It seems obvious that the products reported earlier as para-isomers are really mixtures of unknown composition.

The ethanes (I, II and III) were prepared from the carbinols by the usual procedures. The ethanes were not isolated but were characterized by conversion to the corresponding peroxides. Magnetic susceptibility measurements on benzene solutions of the ethanes showed that di-*p*-cyclohexylphenyltetraphenylethane (I) was dissociated to the extent of 9 ± 1% at 0.1 molar concentration and 25°. Its solution was an orange-yellow. This ethane, like other mono-*p*-alkylphenylethanes, decomposed very slowly. The tetra-*p*-cyclohexylphenyldiphenylethane gave a cherry-red solution and was dissociated to the extent of 10 ± 1% at 0.1 molar concentration and 25°. This ethane decomposed extensively in thirty-six hours. Hexa-*p*-cyclohexylphenylethane was quite insoluble and very unstable so that magnetic susceptibiliy measurements were not very satisfactory. The freshly prepared solutions had a Burgundy-red color and measurements at 0.01 molar and 25° indicated a dissociation of 50 ± 7%. Assuming that the mass law holds, this would indicate a dissociation of about 22% at 0.08 molar concentration. This value is very close to those found for other hexa-*p*-alkylphenylethanes.[1] The most remarkable fact concerning these dissociation measurements is that the disubstituted ethane is dissociated to almost the same extent as the tetra-substituted compound.

Experimental

***p*-Bromocyclohexylbenzene.**—**(a) Bromination of Cyclohexylbenzene.**—The method described by Bodroux and Thomassin[6] was used with the modification that iron was added as a bromination catalyst and the reaction mixture was stirred. The yield of bromo compound was 85%; b. p. 106–108° (1.5 mm.); $n^{20}D$ 1.5588; d^{25}_4 1.275.

(b) From *p*-Aminocyclohexylbenzene.—*p*-Nitrocyclohexylbenzene was prepared according to the method of Neunhoeffer[8] and reduced over Raney nickel to give a 97% yield of the amine. The amine hydrobromide was suspended in 40% hydrobromic acid and diazotized at 5°. The insoluble diazonium salt was decomposed with copper bronze powder. The material which separated from solution was a mixture of the phenol and the bromo compound. The phenol was removed with some difficulty by extraction with 10% potassium hydroxide solution. The yield of bromo compound was about 35%; b. p. 110° (1.5–2 mm.); $n^{20}D$ 1.5594; d^{25}_4 1.265.

(c) From Bromobenzene, Cyclohexyl Chloride and Aluminum Chloride.—This procedure previously described[4,5] gave a product of b. p. 93–95° (1 mm.); $n^{20}D$ 1.5605; d^{20}_4 1.300.

The ether solution of the Grignard reagent from 24 g. of this bromo compound was poured on solid carbon dioxide and the organic acids thus formed were isolated. The yield was 14.2 g. (70%) of product melting at 103–106°. A 0.3-g. sample of this acid was dehydrogenated by heating with a platinum on charcoal catalyst[9] at 300° for two hours. This treatment gave 0.02 g. of *o*-phenylbenzoic acid, m. p. 113°. This acid when mixed with an

(7) Neunhoeffer, *Ann.*, **526**, 61 (1936).

(8) Neunhoeffer, *J. prakt. Chem.*, **241**, 95 (1932).

(9) Linstead, Millidge, Thomas and Walpole, *J. Chem. Soc.*, 1146 (1937).

authentic specimen of *o*-phenylbenzoic acid (m. p. 114°) did not depress its melting point.

Oxidation of 9.5 g. of this bromocyclohexylbenzene in 100 cc. of boiling 50% acetic acid with 20 g. of chromic acid for twenty-four hours gave 0.3–0.5 g. of *p*-bromobenzoic acid, m. p. 252°.

By refluxing 2 g. of the bromo compound with 150 cc. of dilute nitric acid (sp. gr. 1.04) for four days, then adding 10 cc. of concentrated nitric acid (sp. gr. 1.42) and continuing the heating for three more days, some oxidation was obtained. The yield of acidic products was 0.6 g. The portion least soluble in hot water melted at 252° and was considered to be *p*-bromobenzoic acid. *m*-Bromobenzoic acid, m. p. 152–154°, was obtained from the remainder. This material did not depress the melting point of an authentic specimen of *m*-bromobenzoic acid whereas a mixture of it with *o*-bromobenzoic acid melted at 137–142°.

p-Cyclohexyl Derivatives of Triphenylcarbinol.—The Grignard reagent of *p*-bromocyclohexylbenzene (prepared by method (a)) was obtained in ether solution using a little ethylmagnesium bromide as a catalyst to start the reaction. Most of the ether was distilled from the reaction mixture and replaced by dry benzene. Then about 70% of the calculated amount of benzophenone, ethyl benzoate or diethyl carbonate, depending on the carbinol desired, was added. The reactions were carried out and the products isolated in the usual manner. The carbinols crystallized readily. Alcohol-free ether was used to avoid formation of some ether of the carbinol. Unless this precaution was taken the carbinols melted low.

From 86 g. of *p*-bromocyclohexylbenzene, 75 g. (65%) of *p*-cyclohexylphenyldiphenylcarbinol was obtained. The product was purified by recrystallization from petroleum ether (b. p. 90–100°) and then melted at 95–96°.

Anal.[10] Calcd. for $C_{25}H_{26}O$: C, 87.72; H, 7.60. Found: C, 87.55; H, 7.62.

From 239 g. of bromo compound, 65 g. (30%) of phenyldicyclohexylphenylcarbinol was obtained. This product first separated as an oil. A sample dissolved in low-boiling petroleum ether and held at the temperature of solid carbon dioxide for three days deposited a few crystals. When these were added to the main oil it crystallized completely. Recrystallization from petroleum ether (b. p. 90–100°) gave a product melting at 102–103°.

Anal. Calcd. for $C_{31}H_{36}O$: C, 87.73; H, 8.49. Found: C, 88.26; H, 8.66.

From 358 g. of the bromo compound, 80 g. (35%) of tri-*p*-cyclohexylphenylcarbinol was obtained. The first crop of crystals amounted to 65 g. The residual oil was distilled with steam and then washed with low-boiling petroleum ether to give an additional 15 g. of crystals. This second lot of crystals was recrystallized from reagent acetone. The first crop of crystals weighing 3–4 g. was *p,p'*-dicyclohexylbiphenyl.[7] The second crop of crystals was added to the 65 g. of crude product first obtained and all of this carbinol recrystallized from acetone. The pure carbinol thus obtained melted at 180–181°.

Anal. Calcd. for $C_{37}H_{46}O$: C, 87.75; H, 9.09. Found: C, 87.71; H, 9.18.

(10) The analyses reported in this paper are microanalyses and were done by Messrs. L. G. Fauble and W. H. Taylor.

From the acetone mother liquors 2–3 g. of *p,p'*-dicyclohexylbenzophenone, m. p. 136°,[7] was isolated.

A 3.58-g. sample of *p*-bromocyclohexylbenzene prepared by method (b) was converted to the Grignard reagent and treated with diethyl carbonate. The product was isolated as above. The carbinol thus prepared also melted at 180–181° and a mixture of this sample with a sample of carbinol prepared from *p*-bromocyclohexylbenzene obtained by method (a) also melted at 180–181°.

p-Cyclohexyl Derivatives of Triphenylchloromethane.—The carbinols were dissolved in dry benzene and acetyl chloride and heated for several hours at reflux temperature. The solutions were concentrated and cooled and then an excess of petroleum ether (b. p. 30–60°) was added. The chlorides thus precipitated were recrystallized from absolute ethyl acetate.

p-Cyclohexylphenyldiphenylchloromethane, m. p. 125–126°.

Anal. Calcd. for $C_{25}H_{25}Cl$: Cl, 9.83. Found: Cl, 9.70, 10.19.

Phenyldi-*p*-cyclohexylphenylchloromethane, m. p. 155–156°.

Anal. Calcd. for $C_{31}H_{35}Cl$: Cl, 8.01. Found: Cl, 7.95.

Tri-*p*-cyclohexylphenylchloromethane, m. p. 169–170°.

Anal. Calcd. for $C_{37}H_{45}Cl$: Cl, 6.76. Found: Cl, 6.73.

p-Cyclohexyl Derivatives of Triphenylmethyl Peroxide.—Solutions of the cyclohexylphenylethanes for use in the magnetic susceptibility measurements were prepared by treating solutions of the chloromethanes in benzene with silver and filtering the solutions. After the measurements were made the solutions were exposed to the air and evaporated to dryness. The solid residue thus obtained was dissolved in hot benzene, filtered and diluted with six to ten volumes of absolute alcohol. The peroxides crystallized from this mixture.

p-Cyclohexylphenyldiphenylmethyl peroxide, m. p. 158–159°, was obtained in 65–75% yields.

Anal. Calcd. for $C_{50}H_{50}O_2$: C, 87.98; H, 7.33. Found: C, 88.57; H, 7.47.

Phenyldi-*p*-cyclohexylphenylmethyl peroxide, m. p. 120–121°, was obtained in 55–60% yields.

Anal. Calcd. for $C_{62}H_{70}O_2$: C, 87.94; H, 8.27. Found: C, 88.47; H, 8.39.

Tri-*p*-cyclohexylphenylmethyl peroxide, m. p. 178–179°, was obtained by shaking a benzene solution of the chloromethane with silver in the air and recrystallizing as outlined above. The ethane decomposed so rapidly that by the time the magnetic susceptibility measurements were completed there were too many products in solution to give a peroxide which could be purified.

Anal. Calcd. for $C_{74}H_{90}O_2$: C, 87.92; H, 8.91. Found: C, 87.66; H, 9.26.

p-Cyclohexyl Derivatives of Triphenylcarbinol Ethyl Ether.—The respective carbinols were dissolved in ethyl alcohol, a drop of concentrated hydrochloric acid added, and the solutions boiled for a few minutes. On cooling the ethers crystallized.

p-Cyclohexylphenyldiphenylmethylcarbinol ethyl ether, m. p. 106–107°.

Anal. Calcd. for $C_{27}H_{30}O$: C, 87.57; H, 8.10. Found: C, 87.66; H, 8.14.

Phenyldi-*p*-cyclohexylphenylmethylcarbinol ethyl ether, m. p. 152–153°.

Anal. Calcd. for $C_{33}H_{40}O$: C, 87.61; H, 8.85. Found: C, 88.12; H, 8.94.

Tri-*p*-cyclohexylphenylmethylcarbinol ethyl ether, m. p. 189–190°.

Anal. Calcd. for $C_{39}H_{50}O$: C, 87.64; H, 9.36. Found: C, 87.97; H, 9.40.

Magnetic Susceptibility Measurements.—The magnetic susceptibility measurements were made as previously described.[2] Some difficulty was encountered due to the insolubility of the ethanes and for that reason it is necessary to report some of the details of the preparation of the ethane solutions which were used.

When a 0.2 molar solution of *p*-cyclohexylphenyldiphenylchloromethane (1.802 g. of chloride in 25 cc. of benzene) was shaken with silver, a heavy precipitate formed. This was obviously the ethane since on opening the tube to the air a 60–70% yield of peroxide was obtained and the orange-yellow color of the solution did not fade until the precipitate had completely disappeared. Similar results followed the first attempts to prepare 0.05 molar solutions of the ethane. It was then discovered that traces of undissolved chloromethane in the apparatus seemed to cause the rapid crystallization of ethane. A supersaturated solution of the ethane which could be used in the magnetic susceptibility measurements was obtained by putting 0.08 to 0.1 mole of the chloromethane in the apparatus with benzene, evacuating and sealing the outfit and then gently boiling the benzene until the vapor had condensed over the walls to remove stray crystals. After cooling, the silver was added and the mixture was shaken and filtered. Ethane began to crystallize from the solution in about three to six hours but the measurements could be completed before that happened. The values for dissociation of the ethane obtained on these supersaturated solutions checked well with those calculated from measurements made with a 0.025 molar solution of the ethane. After each measurement the apparatus was opened to the air and the peroxide which formed was isolated. The yields were usually about 70%, showing that the ethane had not undergone complete disproportionation.

No difficulties were encountered in preparing the solutions of the tetra-*p*-cyclohexyldiphenylethane. Measurements were made on both 0.1 and 0.05 molar benzene solutions. These solutions were cherry-red. Magnetic susceptibility measurements showed that this ethane had undergone extensive decomposition after thirty-six hours.

The ethane from tri-*p*-cyclohexylphenylchloromethane was very insoluble. By dissolving 0.305 g. of the chloride in 25 cc. of benzene, shaking with silver for fifteen minutes and filtering, a clear Burgundy-red solution of ethane was obtained. The magnetic susceptibility measurements were made at intervals until no free radical remained in solution. The values for $\chi_{sol.}$ obtained in these measurements were plotted and extrapolated to zero time[1] and this value used to calculate the degree of dissociation. The errors involved in this measurement may be large as no information is available as to the amount of ethane or radical held by the silver. Since the measured dissociation is 50% the exact concentration of ethane or radical is more important than it is in measurements of solutions which contain less radical. The calculations here are based on the assumption that the ethane in solution is 80% of the theoretical amount at zero time. The uncertainty in the value of 50% for the dissociation is thus about ±7%. The table gives the data on magnetic susceptibility.

MAGNETIC SUSCEPTIBILITY AND DEGREE OF DISSOCIATION OF *p*-CYCLOHEXYL DERIVATIVES OF HEXAPHENYLETHANE

Hexaphenylethane	*t*, °C.	% Ethane in benzene	$-\chi \times 10^6$ solution	α %	Molarity	$K \times 10^3$	α at 0.1 *M* %
Di-*p*-cyclohexyl (I)	27	3.0	0.6924	13.5	0.04	3.36	8.5
	26	3.0	.6931	13.0	.04	3.08	8.0
	26	3.7	.6908	12.0	.05	3.23	8.5
	28	1.84	.6938	19.5	.025	4.40	10.0
Tetra-*p*-cyclohexyl (II)	27	8.4	.6838	9.5	.1	4.0	9.5
	27	8.4	.6853	9.0	.1	3.76	9.0
	28	4.5	.6871	15.0	.05	5.28	11.0
	28	4.5	.6864	15.5	.05	5.68	11.0
Hexa-*p*-cyclohexyl (III)	26	1.1	.6938	50	.01		

Summary

The dissociation of di-*p*-cyclohexylphenyltetraphenylethane, tetra-*p*-cyclohexylphenyldiphenylethane and hexa-*p*-cyclohexylphenylethane into free radicals has been measured by the magnetic susceptibility method. The dissociation in benzene at 26–28° is 9 ± 1% in 0.1 *M* solution, 10 ± 1% in 0.1 *M* solution and 50 ± 7% in 0.01 *M* solution, respectively.

URBANA, ILLINOIS RECEIVED MARCH 29, 1940

[CONTRIBUTION FROM THE SQUIBB INSTITUTE FOR MEDICAL RESEARCH, DIVISION OF ORGANIC CHEMISTRY]

The Elimination of Hydrogen Bromide from Stigmasterol 22,23-Dibromide

BY ERHARD FERNHOLZ, WILLIAM L. RUIGH AND HOMER E. STAVELY

Under certain conditions the tetrabromides of stigmasteryl acetate[1] and brassicasteryl acetate[2] can be converted into dibromides containing the halogen in the side-chain on carbon atoms 22 and 23. In view of the fact that sterols with more than one double bond in the side-chain are not known, it seemed of interest to prepare such compounds from the new dibromides by the elimination of hydrogen bromide. The bromine atoms in the 22,23-dibromides of stigmasterol and brassicasterol are firmly bound and resist boiling methyl alcoholic alkali for several hours. While short boiling of stigmasteryl acetate 22,23-dibromide with 20% alcoholic potassium hydroxide removed only the acetyl group, prolonged boiling resulted in the formation of a mixture of halogen-free sterols from which only stigmasterol could be obtained in sufficiently pure form to assure its identity. This reducing action of alcoholic potassium hydroxide on the dibromide is somewhat analogous to its action on neopentyl iodide.[3]

Somewhat to our surprise the only product isolated in pure form from the action of boiling pyridine (116°) or quinoline (234°) on the dibromide was stigmasteryl acetate.

When the dibromide was refluxed in 2-ethylhexanol (b. p. 183°) in the presence of an excess of anhydrous potassium acetate the sole reaction product isolated was the acetate of a triene, m. p. 128–129°, which on hydrolysis yielded the triene alcohol, m. p. 125–126°. The new compound reacted with 3 moles of hydrogen yielding a saturated sterol which was identical with stigmastanol in melting point and rotation and gave an acetate and *m*-dinitrobenzoate with correct constants. This indicates that no rearrangement has occurred in the carbon skeleton of the side-chain.

The presence of a conjugated system of double bonds is indicated by the characteristic ultraviolet absorption spectrum[4] with a λ max. = 237.5 mμ, illustrated in Fig. 1. The shifting of the absorption maxima toward the longer wave length with the increase in the number of alkyl substituents, especially on the 1 and 4 position of a conjugated system, is illustrated by this compound. Butadiene has a λ max. = 217 mμ and, 2,3-dimethylbutadiene (see Fig. 1) has λ max. = 225.[5] The compound reacted with maleic anhydride, but resisted hydrogenation with sodium and alcohol.

In order to obtain information regarding the location of the two double bonds the substance was ozonized, and the volatile carbonyl compounds thus obtained transformed into *p*-nitrophenylhydrazones. By means of chromatographic adsorption the hydrazone of acetaldehyde was obtained in pure form, indicating that the ethyl group of the side-chain carries one of the double bonds.

Having fixed the position of one of the double bonds in the conjugated system the other must occupy the position between 22 and 23 or 25 and 26. The latter position seems most improbable since it would involve a shift of double bonds along four carbon atoms. Further, it is unlikely

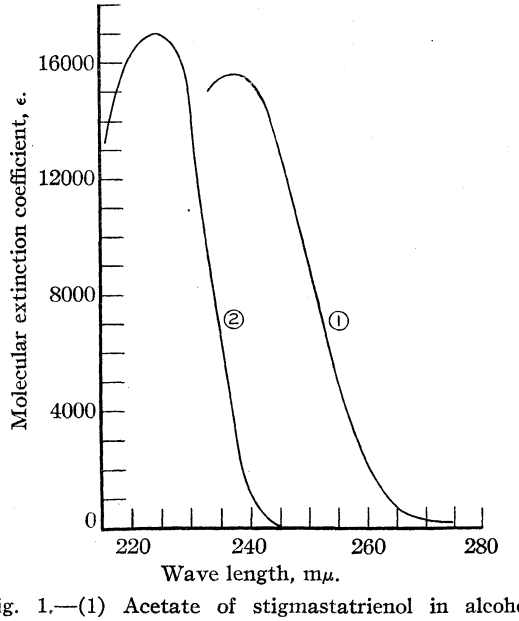
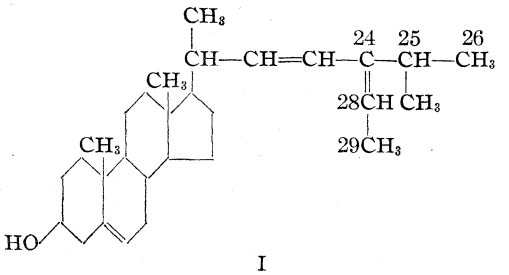


Fig. 1.—(1) Acetate of stigmastatrienol in alcohol, N. H. Coy; (2) 2,3-dimethylbutadiene in hexane, "I. C. T.," Vol. V, p. 364.

(1) E. Fernholz and H. E. Stavely, THIS JOURNAL, **61**, 2956 (1939).
(2) E. Fernholz and H. E. Stavely, *ibid.*, **62**, 428 (1940).
(3) F. C. Whitmore, E. L. Wittle and A. H. Popkin, *ibid.*, **61**, 1586 (1939).
(4) For the measurement of the absorption spectrum we are indebted to Dr. N. H. Coy of the Biological Laboratories of E. R. Squibb and Sons.
(5) Dimroth, *Angew. Chem.*, **52**, 545 (1939).

that formaldehyde *p*-nitrophenylhydrazone would remain undetected in the products from ozonolysis. The new stigmastatrienol is thus Δ-5,22,24:28-stigmastatrienol-(3) shown in formula I.



I

The compound autoxidized very readily, and showed peroxide reactions after short exposure to air. A sample took up 14% of a mole of oxygen within eighteen hours. The substance was definitely more sensitive to oxygen than ergosterol which has a conjugation in the ring system.

Experimental

Reactions of Stigmasteryl Acetate 22,23-Dibromide

(a) **Alcoholic Potassium Hydroxide.**—One gram of the acetoxydibromide was refluxed with 50 cc. of 20% ethyl alcoholic potassium hydroxide for twenty-one hours. Water was added and the mixture extracted with ether. The ether residue was crystallized from alcohol. A yield of 0.6 g. of material was obtained melting at 140–148°. Repeated crystallizations raised the melting point to 162°. This material was acetylated by means of acetic anhydride in the presence of pyridine at room temperature. The product melted at 139° and gave no depression with stigmasteryl acetate (141°). Also the rotation $[\alpha]_D$ −56° agreed with that of stigmasteryl acetate, and on bromination a tetrabromide of m. p. 205° was obtained. *Anal.* Calcd. for $C_{31}H_{50}O_2$: C, 81.88; H, 11.09. Found: C, 81.95; H, 10.93.

(b) **Pyridine.**—Three grams of stigmasteryl acetate 22,23-dibromide were refluxed with 20 cc. of dry pyridine for seven hours. After addition of water the mixture was extracted with ether, the ether washed with dilute acid, then with water, dried, and evaporated. The residue was recrystallized repeatedly from ethanol, and 1.5 g. of stigmasteryl acetate (m. p. 139°, $[\alpha]_D$ −54° in chloroform) was obtained; 1.0 g. of this acetate was dissolved in 15 cc. of ether and 25 cc. of 5% bromine in acetic acid was added. After two hours the precipitate was filtered and washed with ether; 1.2 g. of the characteristic stigmasteryl acetate tetrabromide of m. p. 205° was thus obtained.

A similar experiment in boiling quinoline (b. p. 234°) also yielded stigmasteryl acetate although in lower yield.

Preparation of the Acetate of Stigmastatrienol.—Fifty grams of fused potassium acetate was added to 550 cc. of 2-ethylhexanol, and 50 cc. of the alcohol was distilled off to remove traces of water; to the hot solution was rapidly added 50 g. of stigmasteryl acetate 22,23-dibromide and one gram of hydroquinone as anti-oxidant. The mixture was refluxed for one hour while a stream of dry carbon dioxide was passed in through a tube reaching the bottom of the flask. After cooling, water was added and the octyl alcohol layer washed several times with water. The solvent was then removed on the steam-bath in a stream of carbon dioxide in a good vacuum. The oily residue was dissolved in 75 cc. of hot *n*-butyl alcohol containing 0.1 g. of hydroquinone and the solution allowed to crystallize in the icebox. The solid was filtered off and washed with cold alcohol and recrystallized from a mixture of 50 cc. of butanol and 25 cc. of ethanol; yield 13.8 g., m. p. 123–125°. This material still contained traces of unchanged dibromide. This could be removed by sublimation in a high vacuum. The pure material forms shining leaflets from 95% alcohol, m. p. 128–129° (sealed capillary under CO_2), $[\alpha]^{24}_D$ −47° (26.0 mg. in 2 cc. chloroform solution, 1-dm. tube, α_D −0.61°).

Anal. Calcd. for $C_{31}H_{48}O_2$: C, 82.24; H, 10.69. Found: C, 81.74; H, 10.58. The carbon values are low because of rapid autoxidation.

Bromination of the Triene Acetate.—To a solution of 0.5 g. of the crude acetate m. p. 123–125° in 5 cc. of ether, 14 cc. of a 5% bromine solution in acetic acid was added. A small precipitate of stigmasteryl acetate tetrabromide (25 mg.) was obtained, largely due to the presence of some stigmasteryl acetate dibromide in the starting material. The acetate of the trienol does not form an insoluble bromide.

Reaction with Maleic Anhydride.—One gram of the acetate was refluxed with 0.5 g. of maleic anhydride in 10 cc. of dry toluene for ninety minutes. The solution was then evaporated to dryness, hydrolyzed with methyl alcoholic potassium hydroxide on the steam-bath, diluted with water and extracted with ether. Only 172 mg. of a neutral material was obtained probably from the oxidation of the substance before reaction with maleic anhydride. No attempt was made to purify the addition product.

Saponification.—To 0.618 g. of the triene acetate was added 15 cc. of 0.5 *N* KOH in 95% alcohol and this solution, as well as a blank, refluxed for one hour. The solutions were then titrated to determine the consumption of alkali. Calcd. for 1 acetyl: 1.35 cc. *N* KOH; found: 1.34 cc. The sterol was isolated by means of ether, crystallized from alcohol, and obtained in the form of leaflets, m. p. 125–126° (sealed capillary under CO_2).

Anal. Calcd. for $C_{29}H_{46}O$: C, 84.81; H, 11.29. Found: C, 84.33; H, 11.62.

Reduction with Sodium and Alcohol.—The trienol (3.5 g.) was dissolved in absolute alcohol (350 cc.) and heated with a flame. In the course of two hours 35 g. of sodium was added in portions. The hot solution was then poured into water and the sterol extracted with ether. It consisted largely of starting material of which 80% could be recovered. An examination of the mother liquors failed to disclose the presence of a dihydro derivative, particularly stigmasterol.

Catalytic Hydrogenation.—The acetate of stigmastatrienol (2.08 g.) was suspended in acetic acid (50 cc.) and hydrogenated with platinum oxide catalyst. An amount of hydrogen corresponding to three moles was taken up within a few hours. Shaking was continued for twenty-four hours and the hydrogenation product isolated. It

gave a faint Liebermann reaction and was therefore dissolved in 50 cc. of chloroform, 40 cc. of acetic anhydride, cooled and treated with 15 cc. of concentrated sulfuric acid. The acetate was then recrystallized from alcohol and melted at 130–131°, $[\alpha]^{24}D$ +17°. These are also the constants for stigmastyl acetate. The acetate was saponified and converted into the 3,5-dinitrobenzoate, m. p. 213–214°, $[\alpha]^{24}D$ +15°. This derivative yielded after saponification stigmastanol, m. p. 135–136°, $[\alpha]^{24}D$ +24°.

Ozonization.—Two grams of the acetate of stigmastatrienol suspended in 20 cc. of acetic acid was ozonized for one hour; 100 cc. of water was then added and the mixture distilled through a column. The receiver contained *p*-nitrophenylhydrazine in 50% acetic acid. The distillation was discontinued when about 20 cc. had come over. The yield of crude hydrazone was 341 mg. On digestion with benzene it left undissolved 81 mg. of an unknown orange-yellow compound, m. p. 204°. The benzene soluble fraction was chromatographed on aluminum oxide and developed with benzene. The lower, orange layer was eluted with ether, giving a crude hydrazone of m. p. 118–123°. This was recrystallized from hot water and also from benzene–petroleum ether and melted then at 128–129°. Its identity with acetaldehyde *p*-nitrophenylhydrazone was shown by a nitrogen determination and mixed melting point determination. *Anal.* Calcd. for $C_8H_9O_2N_3$: N, 23.47. Found: N, 23.65.

Summary

Stigmasteryl acetate 22,23-dibromide yields stigmasterol or its acetate when treated with alcoholic potassium hydroxide, pyridine or quinoline. With potassium acetate in a high boiling alcohol a new stigmastatrienol acetate is obtained. Observations are reported indicating that the new compound is Δ-5,23,24:28-stigmastatrienol.

NEW BRUNSWICK, N. J. RECEIVED MARCH 23, 1940

[CONTRIBUTION FROM THE WILLIAM H. CHANDLER CHEMISTRY LABORATORY OF LEHIGH UNIVERSITY]

The Saponification of Ethyl Esters of Aliphatic Acids

BY H. S. LEVENSON AND HILTON A. SMITH

In a previous paper it was demonstrated that the effect of chain length on the velocity of acid catalyzed esterification of normal acids was quite similar to its effect on the velocity of saponification of the ethyl esters of the same acids.[1] The purpose of the present paper is to supplement the work on the saponification of aliphatic esters which is already available in the literature[2] so that a complete comparison of the effect of an aliphatic radical on the velocity of saponification of ethyl esters may be made with the recently published material on the catalyzed esterification of their corresponding acids.[3]

Experimental

Ethyl laurate was obtained from Eastman Kodak Co. The ester was fractionated under reduced pressure in a 5 ft. (1.5 meter) Vigreux column, and constant-distilling fractions were used.

Ethyl β-methylvalerate and ethyl isocaproate were prepared by esterification of the corresponding acids[4] with ethanol using sulfuric acid as a catalyst. The preparation of these acids has already been described.[3,5] The esters were purified by fractionation in a small 2-foot (0.6 meter) Vigreux column.

The ethyl esters of diethylacetic acid, dipropylacetic acid, dibutylacetic acid and di-isobutylacetic acid were prepared by esterification of the acids. Diethylacetic acid was obtained from Eastman Kodak Co. and the other acids were prepared by malonic ester syntheses.[3] The diethyl and di-isobutylacetic acid esters were purified by fractionation in a 5 foot (1.5 meter) Vigreux column, while the 2-foot column was used for purification of the other two.

Each ester was analyzed by complete saponification of weighed samples with excess alkali, and back titration with standard acid. All of the esters gave analyses between 99.5 and 100.5%, the precision of this method being about 0.5%.

The velocity determinations were carried out in 85% aqueous ethanol, this medium being prepared in the manner already described.[1] The method of making velocity determinations was similar to that previously employed.

Experimental Calculations and Results

In general, the rate constants were calculated using the second order reaction rate equation

$$k = x/t(a - x)a \qquad (1)$$

where a is the initial concentration of each reactant, and x represents the concentration of each reactant at the time t. The results of a typical run are given in Table I.

The runs with the esters of diethyl, dipropyl, and dibutyl acetic acids were so slow that, at higher temperatures, the action of alcoholic sodium hydroxide on the Pyrex glass reaction flasks was appreciable. This was indicated by an

(1) Smith and Levenson, THIS JOURNAL, **61**, 1172 (1939).
(2) Evans, Gordon and Watson, *J. Chem. Soc.*, 1439 (1938).
(3) Smith, THIS JOURNAL, **62**, 1136 (1940).
(4) The authors are greatly indebted to Mr. A. S. Raff for his aid in the preparation of these acids.
(5) Smith, THIS JOURNAL, **61**, 1176 (1939).

TABLE I

SAPONIFICATION OF ETHYL LAURATE AT 55°
a = (ester) = (NaOH) = 0.0500 mole/liter

t, min.	x	10^3k (liters mole^{-1} sec.$^{-1}$)
3.08	0.00713	18.4
6	.01279	19.1
9	.01633	18.0
15	.02281	18.6
25	.02917	18.7
42	.03513	18.7
80	.04079	18.5
115	.04334	18.9

increase in the values of the velocity constant toward the latter portion of each run. An approximate correction was applied as follows.

The relation between the total amount of sodium hydroxide (x) reacting with ester plus glass to that (y) reacting with the ester only is given by the equation

$$x = y + 2.303 \frac{k_g}{k_s} \log \frac{a}{a - y} \qquad (2)$$

where a is the initial concentration of ester and alkali, k_s is the reaction velocity constant for the saponification reaction and k_g is the unimolecular reaction rate constant representing the action of the alkali on the glass bottle. The values of k_g at 45 and 55° were 1.4×10^{-7} and 9.6×10^{-7} sec.$^{-1}$, respectively. The corrected k values were found by determining y for each experimental x, using for k_s the uncorrected figure, and substituting in equation I. These corrections were applied for runs at temperatures of 45 and 55°. Table II gives a sample of such calculations.

TABLE II

SAPONIFICATION OF ETHYL DIPROPYLACETATE AT 55°
a = (ester) = (NaOH) = 0.05 mole/liter

t, min.	x	y	10^3k (liters mole^{-1} sec.$^{-1}$) Uncor.	Cor.
460	0.01028	0.0096	0.188	0.172
1230	.02052	.0184	.189	.157
1860	.02610	.0232	.196	.155
2820	.03237	.0282	.217	.153
4290	.03859	.0331	.263	.152

The values of k for each ester are given in Table III. These were calculated by averaging the individual rate constants over 20 to 80% reaction except where corrections were made for glass reaction. For these only, figures for 20–60% reaction were averaged since the corrections are approximate, and become relatively large after 60% reaction.

TABLE III

REACTION RATE CONSTANTS FOR THE SAPONIFICATION OF ETHYL ESTERS OF ALIPHATIC ACIDS IN 85% ETHANOL
For all esters, (NaOH) = (ester) = 0.05 mole/liter

Ethyl ester	$k \times 10^3$ (liters mole^{-1} sec.$^{-1}$) t = 25°	t = 35°	t = 45°	t = 55°
Butyrate[a]	1.83	4.25	9.18	19.0
Laurate	1.81	4.11	9.31	18.6
	1.86	4.10	9.23	18.8
Average	1.84	4.11	9.27	18.7
Isocaproate	1.85	4.34	9.01	18.9
	1.87	4.28	9.06	18.9
Average	1.86	4.31	9.04	18.9
β-Methylvalerate	0.414	0.968	2.20	4.67
	.407	.959	2.19	4.62
Average	.411	.963	2.20	4.65
Diethylacetate	.0151	.0385	0.0955	0.216
	.0152	.0387	.0966	.211
	.0159	.0381	.0981	.217
Average	.0154	.0384	.0968	.215
Dipropylacetate	.0105	.0283	.0644	.154
	.0107	.0280	.0669	.154
Average	.0106	.0282	.0656	.154
Dibutylacetate	.0101	.0254	.0629	.153
	.0099	.0256	.0640	
Average	.0100	.0255	.0635	.153

[a] The figures for the butyrate are given for comparison purposes, and are interpolated from the data of Smith and Levenson.[1]

The plot of log k against $1/T$ is shown in Fig. 1.

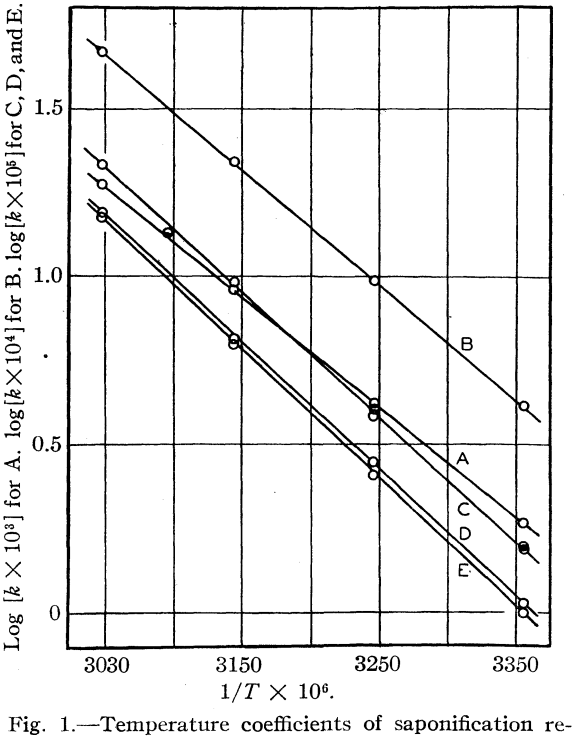


Fig. 1.—Temperature coefficients of saponification reactions: A, ethyl laurate and ethyl isocaproate; B, ethyl β-methylvalerate; C, ethyl diethylacetate; D, ethyl dipropylacetate; E, ethyl dibutylacetate; ○, points from data of Levenson and Smith; ◒, points for ethyl diethylacetate from data of Evans, Gordon and Watson.[2]

The saponification of ethyl diethylacetate in 85% ethanol was also studied by Evans, Gordon and Watson.[2] Figure 1 shows reasonable agreement with their data. The activation energies for these reactions are given in Table IV. They were calculated from the slopes of the lines in Fig. 1, and were checked by the method of least squares.

TABLE IV

ACTIVATION ENERGIES FOR THE SAPONIFICATION OF ALKYL SUBSTITUTED ALIPHATIC ETHYL ESTERS

Ethyl ester	E, cal./mole
Butyrate[a]	15,100
Laurate	15,100
Isocaproate	15,000
β-Methylvalerate	15,700
Diethylacetate	17,200 (17,400)[b]
Dipropylacetate	17,200
Dibutylacetate	17,700

[a] From the data of Smith and Levenson (ref. 1).
[b] The value obtained by Evans, Gordon, and Watson (ref. 2).

Discussion

The rate constants for ethyl laurate when compared with those for ethyl butyrate give additional confirmation to the fact that an increase of the chain length of an alkyl chain beyond four carbon atoms has no measurable effect on the velocity of saponification of esters under the conditions of the experiments here reported.

The results for β-methylvalerate and isocaproate combined with the earlier work of Smith and Levenson[1] and of Evans, Gordon and Watson[2] show the same effect for methyl substitution as was found for acid-catalyzed esterification in methanol.[5] The effect of substitution of a methyl group in the α, β, or γ position is the same in each process, as is shown in Table V.

TABLE V

EFFECT OF METHYL SUBSTITUTION ON REACTION VELOCITY

Position in which substitution takes place	Esterification	% Change saponification
α, (propionic ⟶ isobutyric)	62	78
β, (butyric ⟶ isovaleric)	76	77
γ, (valeric ⟶ isocaproic)	0	0

It is thus evident that in saponification as well as in esterification, only when substitution of a methyl group for a H atom in a normal alkyl chain takes place in the α or β position is the reaction velocity affected.

The effect of the simultaneous lengthening of two normal alkyl chains is shown in Table VI.

Just as in esterification, there is a much larger decrease in k when the chains are lengthened from the isobutyrate to the diethylacetate than was caused by the change from acetate to isobutyrate. Further lengthening of the carbon chain results in relatively smaller changes in saponification velocity. The changes in the activation energy also parallel those found for esterification.

TABLE VI

EFFECT OF CHAIN LENGTH OF ETHYL ESTERS OF DI-SUBSTITUTED ACETIC ACIDS ON THEIR VELOCITY OF SAPONIFICATION

Ethyl ester	$10^3 \times k_{25°}$	E
Acetate[a]	6.92	14,700
Isobutyrate[b]	0.801	15,000
Diethylacetate	.0154	17,200
Dipropylacetate	.0106	17,200
Dibutylacetate	.0100	17,700

[a] $k_{25°}$ and E for ethyl acetate are from the data of Smith and Levenson.[1] [b] $k_{25°}$ for ethyl isobutyrate was taken from the data of Evans, Gordon, and Watson, and E is a value recalculated from their data.[6]

The k values for the saponification of ethyl di-isobutylacetate are not included in Table III. This compound saponifies so slowly that the glass reaction correction becomes quite large. All that can be said with certainty is that this ester saponifies about one-third as fast as does dibutylacetic acid ester. ($k_{25°}$ for the di-isobutyl substituted ester is approximately 0.0031×10^{-3}.) A similar result was found in esterification studies.

The effect of increased methyl substitution in the α position also parallels that found for esterification, as is shown by the data of Evans and co-workers[2] for the saponification of esters of isobutyric and trimethylacetic acids.

In short, the processes of the acid catalyzed esterification of aliphatic acids and of the saponification of their ethyl esters are completely similar at least as far as the effect of the character of the alkyl chain upon reaction velocity is concerned.

Summary

The kinetics of the saponification in 85% ethanol of the following esters has been studied: ethyl laurate, ethyl isocaproate, ethyl β-methylvalerate, ethyl diethylacetate, ethyl dipropylacetate, ethyl dibutylacetate, and ethyl di-isobutyl acetate.

It is demonstrated that the effect of the character of the alkyl chain on reaction velocity is the same for the processes of acid-catalyzed esterification and saponification.

BETHLEHEM, PENNA. RECEIVED APRIL 23, 1940

(6) See Smith and McReynolds, THIS JOURNAL, **61**, 1963 (1939).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, INDIANA UNIVERSITY]

Kinetics of the Esterification of Substituted Benzoic Acids

BY R. J. HARTMAN AND A. G. GASSMANN[1]

The esterification of substituted benzoic acids has been studied by Hartman and Borders,[2] and by Hartman, Storms and Gassmann,[3] and others.[4,5] These investigations showed that in hydrion catalyzed esterifications, the reaction is facilitated by recession of electrons from the seat of the reaction and is therefore, according to Williams,[6] a Class B reaction. Both E and P of the Arrhenius equation

$$k = PZe^{-E/RT}$$

have been found to affect the reaction velocity. The effect of a meta or para substituent on the benzene nucleus on the reaction velocity is expressed by the equation[7]

$$\log k = \log k_0 + \rho\sigma$$

where k is the velocity constant of the substituted reactant, k_0 is the velocity constant of the unsubstituted reactant; ρ is a constant depending on the reaction, medium and temperature, and σ is a constant depending upon the substituent. Good agreement between observed and calculated values was found for the acids studied.

The object of this investigation was to determine the velocity constants of esterification of each of the three monosubstituted iodo-, fluoro-, methoxy-, and ethoxybenzoic acids with methyl alcohol and catalyzed by hydrions. Because *p*-iodobenzoic acid is only slightly soluble in methyl alcohol, its reaction rate was not studied. Using the data thus obtained, the energies of activation were determined in order to analyze the results in the light of the Arrhenius equation.

Experimental

Materials.—Absolute methanol was purified by the method of Bjerrum and Lund.[8] Water, aldehyde and ketone tests were negative. The acids were obtained either from Eastman Kodak Company or from Professor C. S. Marvel of the University of Illinois. The melting points of the purified acids agreed with those recorded in the literature. The acids were dried over phosphorus pentoxide, preceded in certain instances by drying in an oven at 105–110°.

Procedure.—The procedure followed was similar to that of Hartman and Borders.[2] The total acid concentration was determined at the beginning and at intervals throughout the course of the reaction by titrating 5-ml. samples against barium hydroxide solution using phenolphthalein as indicator. Correction was made for the expansion of solvent. The thermostats were maintained at 25.00, 40.00, 50.00 and 60.00 ± 0.02°.

Results and Discussions

The value of the velocity constant which accounts for the retardation of the reaction due to the water formed is given by the equation[9]

$$k = \frac{(r + a)\ln\left[\frac{a}{a - x}\right] - x}{crt}$$

where r is a constant which compensates for the water formed, a is the initial organic acid concentration, x is the quantity of acid esterified in time t, c is the concentration of the hydrion catalyst, and k is the velocity constant in g. moles/liter/sec. The values of r used were[2,10]

Temp., °C.	25	40	50	60
r	0.22	0.36	0.50	0.65

Table I shows a typical esterification reaction. The individual figures for $(a - x)$ and for k represent averages of several runs.

TABLE I

ESTERIFICATION OF m-FC_6H_4COOH AND CH_3OH AT 25°
$a = 0.1034$, $c = 0.0197$

Time, min.	$a - x$	$10^4 k$
1560	0.0820	1.32
2940	.0675	1.33
4320	.0572	1.29
5760	.0471	1.32
7200	.0410	1.28

No values of k were used which represent less than 20% or more than 80% reaction. This eliminates anomalies that might result from experimental errors and hydrolysis effect at the beginning and end of a reaction. Table II gives the velocity constants and energy of activation for benzoic acid and the eleven substituted benzoic acids studied in this investigation.

(1) This paper represents a part of a thesis to be presented by Albert George Gassmann to the Faculty of the Graduate School of Indiana University in partial fulfilment of the requirements for the degree of Doctor of Philosophy in Chemistry.

(2) Hartman and Borders, THIS JOURNAL, **59**, 2107 (1937).

(3) Hartman, Storms and Gassmann, *ibid.*, **61**, 2167 (1939).

(4) Kellas, *Z. physik. Chem.*, **24**, 221 (1897).

(5) Sudborough and Turner, *J. Chem. Soc.*, **101**, 237 (1912).

(6) Williams, *ibid.*, 37 (1930).

(7) Hammett, THIS JOURNAL, **59**, 96 (1937).

(8) Bjerrum and Lund, *Ber.*, **64B**, 210 (1931).

(9) Goldschmidt, *ibid.*, **39**, 711 (1906).

(10) Williamson and Hinshelwood, *Trans. Faraday Soc.*, **30**, 1145 (1934).

TABLE II

VELOCITY CONSTANTS AND ENERGIES OF ACTIVATION FOR HYDRION CATALYZED ESTERIFICATION OF AROMATIC ACIDS WITH METHYL ALCOHOL

Acid	$10^4 k$ 25°	40°	50°	60°	Energy of activation E
o-Iodobenzoic	0.331	1.13	2.27	4.21	14,300
p-Fluorobenzoic	.756	2.45	5.04	9.02	14,400
p-Methoxybenzoic	1.04	3.34	6.73	13.07	14,300
p-Ethoxybenzoic	1.13	3.22	6.52	14.25	13,400
m-Fluorobenzoic	1.31	3.90	8.63	16.51	14,300
m-Iodobenzoic	1.37	3.89	8.62	16.65	14,400
m-Methoxybenzoic	1.91	5.68	13.03	25.32	14,600
Benzoic	1.94	6.57	15.24	28.69	15,500
o-Fluorobenzoic	1.99	5.62	12.54	23.84	14,000
m-Ethoxybenzoic	2.11	6.50	13.61	26.55	14,300
o-Ethoxybenzoic	6.61	24.88	38.28	74.58	13,700
o-Methoxybenzoic	8.30	25.76	51.96	89.15	13,900

The values of E were obtained graphically from the slope of the line obtained by plotting log k against the reciprocal of the absolute temperatures. The energy of activation of benzoic acid was found to be 15,500 cal. The same value was reported by Hartman and Borders.[2] Hinshelwood and Legard[11] report 15,700 calories.

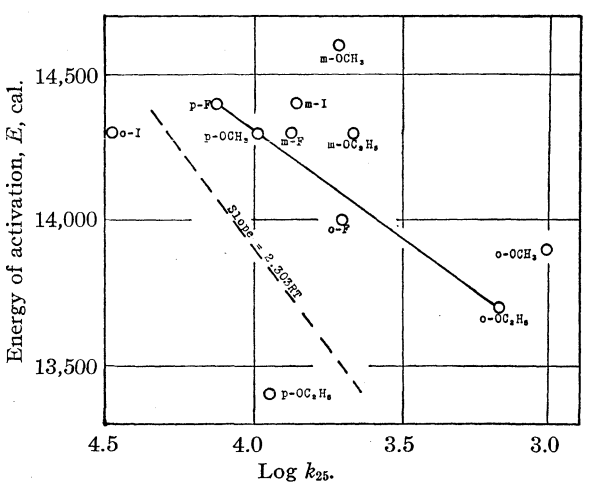


Fig. 1.—Relationship between speed of reaction and activation energy.

Table III gives the observed values of log k_{25} for meta and para substituted acids and the corresponding values as calculated from Hammett's equation.[7] The value of ρ was -0.54[2] and the values of σ were taken from Hammett.[7] The average error of log k is greater than the mean value of probable error by Hammett.[7] It is noticed in Table III that the error is greater for the *p*-methoxy-, *p*-ethoxy-, and *p*-fluorobenzoic acids than for the corresponding meta substituted acids. The average error of log k for the meta substituted acids is 0.056, which compares very favorably with that of Hartman and Borders[2] and Hammett.[7]

TABLE III

COMPARISON OF LOG k_{25} OBSERVED WITH LOG k CALCULATED FROM THE EQUATION: LOG $k = -3.712 + \sigma(-0.54)$

Acid	Log k, obsd.	Log k, calcd.	Error
m-Ethoxybenzoic	−3.676	−3.793	0.117
m-Methoxybenzoic	−3.719	−3.774	.055
m-Iodobenzoic	−3.863	−3.902	.039
m-Fluorobenzoic	−3.883	−3.894	.011
p-Ethoxybenzoic	−3.947	−3.577	.370
p-Methoxybenzoic	−3.983	−3.568	.415
p-Fluorobenzoic	−4.121	−3.745	.376
		Av.	.198

Because of the lack of close agreement between the observed and calculated values of log k for the *p*-methoxy-, *p*-ethoxy-, and *p*-fluorobenzoic acids, it appears that the Hammett equation fails in these instances.

To determine whether changes in velocity are due to changes in E or to changes in P of the equation $k = PZe^{-E/RT}$, log k was plotted against the measured value of E. Changes of E would be responsible alone if the resulting slope of the line were 2.303 RT. Figure 1 shows such a plot where the broken line represents the theoretical line having a slope of 2.303 RT and the solid line represents an approximate graphical average obtained from the data of this investigation. It is apparent that the two lines do not have the same slope and it may therefore be concluded that changes in E are not alone responsible for changes in reaction velocities. That the P term changes has been found to be true in the investigations of Hartman and Borders[2] and those of Hinshelwood and Legard.[11]

Summary

1. The study of the effect of polar groups has shown that the velocity of hydrion-catalyzed esterification of substituted benzoic acids is increased by displacement of electrons toward the carboxyl groups.

2. Comparison of experimental log k with that calculated from the Hammett equation shows good agreement for the meta substituted acids. Good agreement was not found, however, for the *p*-ethoxy-, *p*-methoxy-, and the *p*-fluorobenzoic acids.

3. Both the P factor and energy of activation have an effect on the velocity of esterification.

BLOOMINGTON, IND. RECEIVED APRIL 5, 1940

(11) Hinshelwood and Legard, *J. Chem. Soc.*, 587 (1935).

[CONTRIBUTION FROM THE BASIC SCIENCE RESEARCH LABORATORY OF THE UNIVERSITY OF CINCINNATI]

Molecular Size Distribution in Ethylene Oxide Polymers

BY PAUL J. FLORY

Little progress has been made toward the elucidation of the composition of high polymers by the two known experimental methods, fractionation[1] and ultracentrifugal analysis,[2] both of which yield at best only approximate results. In certain cases, however, it is possible to deduce theoretical relationships by means of which accurate size distributions can be calculated. Such relationships have been presented previously for linear condensation polymers.[3] In this paper size distribution equations will be derived for polymers formed by successive addition of *monomers* to a fixed number of chains. The bearing of the results on the interpretation of polymer viscosities will be discussed.

It has been known for a long time[4] that ethylene oxide reacts with ethylene glycol to form diethylene glycol and higher glycols by successive additions of ethylene oxide as follows

$$HOCH_2CH_2OH \xrightarrow{+CH_2CH_2O} HO[CH_2CH_2O]_2H \xrightarrow{+CH_2CH_2O} \text{etc.}$$

Ethylene oxide has been found to react similarly with alcohols, amines,[5] mercaptans, and acids, yielding, under proper conditions, polymers of considerable length.[6] In the patent literature there are described many technical processes in which polyoxyethylene glycol chains are built up through the reaction of ethylene oxide with a substance containing an appropriate functional group such as NH_2, NH, OH, SH or COOH. The available evidence indicates that these processes proceed exclusively by the reaction of monomer (ethylene oxide) with molecules possessing the propagating functional group (*e. g.*, OH); *reaction of polymer with polymer does not occur.* The process can be represented by

$$m_1 \xrightarrow{+m} m_2 \xrightarrow{+m} m_3, \text{ etc.}$$

where m_1 is the initial species which bears the propagating functional group, m represents ethylene oxide, and m_x is the product formed from m_1 plus $x - 1$ ethylene oxides.[7]

There are other types of polymers which, under certain conditions, may be formed by analogous mechanisms. It has been suggested that formaldehyde polymerization[8] initiated by traces of moisture proceeds as follows

$$HOCH_2OH \xrightarrow{+CH_2O} H[OCH_2]_2OH \xrightarrow{+CH_2O} \text{etc.}$$

Similar mechanisms may account for the conversion of cyclic anhydrides,[9] cyclic esters[10] (lactones) and cyclic acetals[11] to the corresponding linear polymers. Some of these reactions are sufficiently reversible to allow interchange to occur, and, as will be shown in another paper, interchange reactions may modify the molecular size distribution.[12]

The distribution of species obtained by the above mechanism of polymerization and the distribution resulting from condensation polymerization are strikingly different. Condensation polymerizations, *e. g.*, the polymerization of a hydroxy acid, proceed by the occurrence of reactions of the type

$$m_x + m_y = m_{x+y}$$

where m_x and m_y represent molecules composed of x and y units, respectively, x and y being integers from 1 to ∞. Not only do the polymer molecules react with monomers, but polymers of all sizes react with other polymers. In all of these reactions the same chemical process is involved, and it has been demonstrated in the case of polyesterification that all of them proceed with equal ease.[13]

(1) G. V. Schulz, *Z. physik. Chem.*, **B30**, 379–399 (1935) has determined the approximate distribution of species in polyisobutylene by fractionation.

(2) Concerning the use of the ultracentrifuge for determining size distributions, see W. D. Lansing and E. O. Kraemer, THIS JOURNAL, **57**, 1369 (1935).

(3) P. J. Flory, *ibid.*, **58**, 1877 (1936).

(4) Wurtz, *Ann. chim.*, (3) **69**, 330 (1863).

(5) H. Hibbert and S. Z. Perry, *Can. J. Research*, **8**, 102 (1933).

(6) H. Staudinger, "Die hochmolekularen organischen Verbindungen," Verlag Julius Springer, Berlin, 1932.

(7) Perhaps ethylene oxide polymerizes by other mechanisms under some conditions, as for example at high temperature in the absence of suitable propagating functional groups of the sort mentioned above (see ref. 6, p. 289). Only polymers formed by the above mechanism are considered here.

(8) H. Staudinger, ref. 6, p. 255; W. H. Carothers, *Trans. Faraday Soc.*, **32**, 39 (1936).

(9) J. W. Hill, THIS JOURNAL, **52**, 4110 (1930); J. W. Hill and W. H. Carothers, *ibid.*, **54**, 1569 (1932); **55**, 5023 (1933).

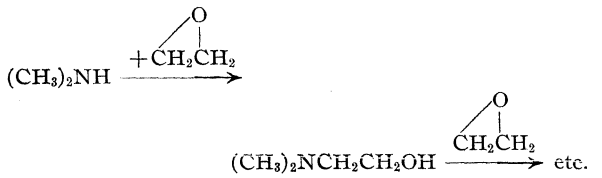
(10) W. H. Carothers, G. L. Dorough and F. J. Van Natta, *ibid.*, **54**, 761 (1932).

(11) J. W. Hill and W. H. Carothers, *ibid.*, **57**, 925 (1935).

(12) P. J. Flory, *ibid.*, **62**, 1064 (1940).

(13) P. J. Flory, *ibid.*, **61**, 3334 (1939).

The treatment presented below is applicable to polymerization processes which fulfill the following two conditions: (i) the total number of molecules possessing propagating functional groups (*e. g.*, the total number of glycol molecules) must remain constant throughout the reaction; (ii) the chains must be built up by a sequence of kinetically identical additions of monomer (ethylene oxide). In cases where the initial propagating molecules are neither glycols nor alcohols, *e. g.*, in the process[6]



condition (ii) will not be entirely satisfied. The rate of the first step will in general differ from the rates of subsequent steps, although the rates of the latter should not differ appreciably from one another. If the reaction is carried out under conditions such that reaction of the initial propagating molecules (*e. g.*, $(CH_3)_2NH$ above) with ethylene oxide is substantially complete before more than a small fraction of the ethylene oxide has been consumed, then the following treatment will serve as a satisfactory approximation. The first addition product ($(CH_3)_2NCH_2CH_2OH$, above) must then be considered the initial chain propagator. In cases where the initial step is extremely slow, the treatment of Dostal and Mark[14] may be approximately applicable.

The fundamental equations may be derived as follows. Letting N_1, N_2, N_3, etc., be the numbers of the species m_1, m_2, m_3, etc., which possess zero, one, two, etc., added ethylene oxides

$$dN_1/dt = -fN_1 \qquad (1)$$

where f is some function dependent upon the kinetics of the process and the manner in which it is carried out. Presumably, f (which includes the velocity constant) will be a function of the ethylene oxide concentration, but it may be a function of other variables also, such as t and the number of propagating molecules N^0. The solution of the present problem depends in no way upon the nature of f, so long as it is consistent with the above conditions. In view of condition (ii), the rate at which m_2 is converted into m_3 must be, similarly, fN_2. Hence

$$\begin{aligned} dN_2/dt &= fN_1 - fN_2 \\ dN_x/dt &= fN_{x-1} - fN_x \end{aligned} \qquad (2)$$

(14) H. Dostal and H. Mark, *Z. physik. Chem.*, **B29**, 299 (1935).

The rate of disappearance of ethylene oxide is

$$-dm/dt = fN^0 \qquad (3)$$

The ratio at time t of ethylene oxide consumed to N^0 is given by

$$\nu = \Delta m/N^0 = \int_0^t f\,dt \qquad (4)$$

Also

$$d\nu = f\,dt \qquad (4')$$

Substituting (4') in (1) and (2)

$$dN_1 = -N_1 d\nu \qquad (5)$$

$$dN_x = (N_{x-1} - N_x)d\nu \qquad (6)$$

Integrating (5)

$$N_1 = N^0 e^{-\nu}$$

Substituting this equation in (6) when $x = 2$ and integrating the resulting differential equation

$$N_2 = N^0 \nu e^{-\nu}$$

Substituting this equation in (6) with $x = 3$ and integrating

$$N_3 = N^0(\nu^2/2)e^{-\nu}$$

It is evident that continuation of this process yields

$$N_x/N^0 = e^{-\nu}\nu^{x-1}/(x-1)! \qquad (7)$$

This general expression (7) for the mole fraction of x-mer in the polymer (exclusive of unreacted ethylene oxide) is Poisson's distribution formula. From the nature of the problem dealt with here, it is obvious, without the above derivation, that the numbers of molecules of various sizes must be represented by Poisson's distribution.[15] A brief kinetic derivation has been included in order to point out the scope of applicability of (7) to size distribution problems.

The weight fraction distribution is usually of more interest than the mole fraction distribution. Since the molecular weight of the x-mer species is given by

$$M_x = xM + (M^0 - M)$$

where M is the molecular weight of one unit (ethylene oxide) and M^0 is the molecular weight of the initial molecule (*e. g.*, ethylene glycol) from which growth proceeded, the weight fraction of x-mer is

$$w_x = \frac{M_x N_x}{(\nu M + M^0)N^0} = \left[\frac{x + (M^0 - M)/M}{\nu + M^0/M}\right] e^{-\nu}\nu^{x-1}/(x-1)! \qquad (8)$$

The subsequent discussion will deal with the case in which $M^0 = M$. Hence

$$w_x = [\nu/(\nu+1)]e^{-\nu}x\nu^{x-2}/(x-1)! \qquad (9)$$

(15) See T. C. Fry, "Probability and its Engineering Applications," D. Van Nostrand Co., New York, N. Y., 1928.

Even when $M^0 \neq M$, (9) may be used for high polymers without significant error.

The number average molecular weight,[16] which equals the total weight of polymer in molecular weight units divided by the number of molecules, is given by

$$M_n = \nu M + M^0 \qquad (10)$$

or, when $M^0 = M$

$$M_n = M(\nu + 1) \qquad (10')$$

The degree of polymerization, *i. e.*, the *number average* value of x, is given by

$$DP = \nu + 1 \qquad (11)$$

For condensation polymers the weight fraction distribution is given by[17]

$$w_x = (1 - p)^2 x p^{x-1} \qquad (12)$$

where p is the fraction of the functional groups which have undergone condensation. Their degree of polymerization is given by

$$DP = 1/(1 - p) \qquad (13)$$

The solid curves in Figs. 1 and 2 represent weight fraction distributions, calculated from (9), for polyethylene oxides (or other polymers formed by reactions conforming with (i) and (ii)). The values of ν are included with each curve. For comparison, portions of two condensation polymer distributions have been included also (broken curves). The one shown in Fig. 1 has been calculated from (12) when $p = 0.9091$.

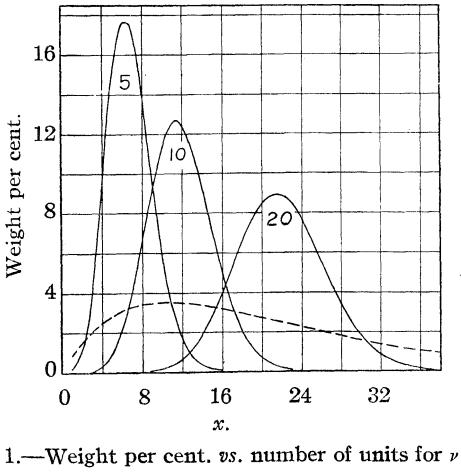


Fig. 1.—Weight per cent. *vs.* number of units for $\nu = 5$, 10 and 20. The broken curve represents a $DP = 11$ condensation polymer.

(16) The terms *number average* and *weight average* and their definitions were introduced by E. O. Kraemer and W. D. Lansing, *J. Phys. Chem.*, **39**, 153 (1935). The number average molecular weight, defined by $M_n = (1/N^0)\Sigma N_x M_x$, is the average obtained by end-group, osmotic, ebullioscopic or cryoscopic methods. The weight average is defined by equation (14), *cf. seq.*

(17) The symbol w_x is used here in place of the Π_x of an earlier paper, ref. (3).

This curve and the $\nu = 10$ polyethylene oxide curve possess the same number average, *i. e.*, $DP = 11$ for each. Both the $\nu = 100$ curve and the broken curve in Fig. 2 represent $DP = 101$.

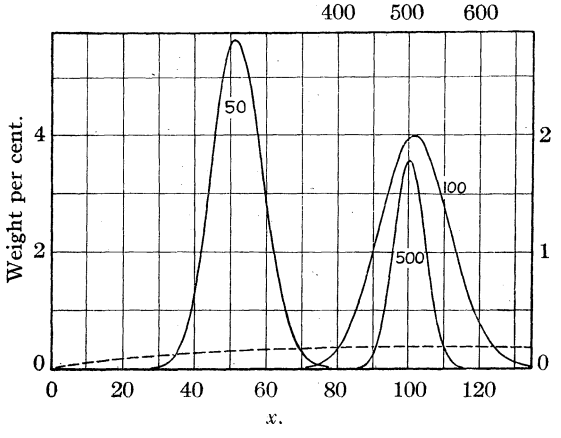


Fig. 2.—Weight per cent. *vs.* number of units for $\nu = 50$, 100 and 500. The broken curve represents a $DP = 101$ condensation polymer. The $\nu = 500$ curve is drawn to the scales along the upper and right margins; scales for the other curves are given along the lower and left margins.

The much greater homogeneity of the polyethylene oxide distribution compared with the condensation polymer distribution is apparent in these graphs. For example, in the range $x =$ 8–16, inclusive, there is included 79.6% of the $DP = 11$ ($\nu = 10$) polyethylene oxide; only 27.3% of the $DP = 11$ condensation polymer lies in the same range of sizes. The weight percentages of monomer in these two polymers are 0.041 (exclusive of unreacted ethylene oxide) and 0.826, respectively. At $DP = 101$ (Fig. 2) the difference is even more pronounced: in the range 90–112, inclusive, one finds 74.8% of the polyethylene oxide, but only 8.35% of the condensation polymer; the calculated weight percentages of monomer are 4×10^{-42} and 10^{-2}, respectively.

The other feature of the polyethylene oxide distribution which should be mentioned is the dependence of the heterogeneity on ν. Suppose the breadth of the curve midway between the maximum and the x-axis be adopted as the measure of heterogeneity. The number of species included in such a range increases as ν increases. However, the ratio of this breadth to $\nu + 1$, the distance of the maximum from the ordinate axis, decreases as ν increases. From this point of view the *relative* heterogeneity decreases as ν increases. Comparison of the $\nu = 100$ and 500 curves in Fig. 2 demonstrates this feature.

Kraemer and Lansing[16] have called attention to the necessity of using the weight average molecular weight M_w, defined by

$$M_w = \Sigma w_x M_x \qquad (14)$$

in the Staudinger relationship between the viscosity of a dilute solution of a polymer and its molecular weight. Recently the author[18] has found that the weight average molecular weight of linear polyesters can be expressed as a simple function of their viscosity in the liquid state. Whereas molecular weight determinations by cryoscopic, osmotic, and end-group methods yield number averages, viscosity methods yield weight averages when applied to heterogeneous polymers. It is important, therefore, to know the relationship between these two averages for a given distribution.

Substituting (9) in (14) and placing $M_x = xM$

$$M_w = M\left(\frac{\nu e^{-\nu}}{\nu + 1}\right)\sum_1^\infty \frac{x^2\nu^{x-2}}{(x-1)!} \qquad (15)$$

The summation rearranges to

$$\sum_2^\infty \frac{(x^2-1)\nu^{x-2}}{(x-1)!} + \sum_1^\infty \frac{\nu^{x-2}}{(x-1)!}$$

$$= \sum_3^\infty \frac{\nu^{x-2}}{(x-3)!} + 3\sum_2^\infty \frac{\nu^{x-2}}{(x-2)!} + \sum_1^\infty \frac{\nu^{x-2}}{(x-1)!}$$

$$= (\nu + 3 + 1/\nu)\sum_0^\infty \nu^x/x!$$

$$= (\nu + 3 + 1/\nu)e^\nu$$

Substituting this expression for the summation in (15)

$$M_w = M(\nu^2 + 3\nu + 1)/(\nu + 1) \qquad (16)$$

Dividing (16) by (10′)

$$M_w/M_n = 1 + \nu/(\nu + 1)^2 \qquad (17)$$

This ratio of weight average to number average is plotted as a function of DP in Fig. 3 (lower curve). The ratio approaches unity asymptotically as ν increases. For condensation polymers this ratio, which has been shown[3] to be equal to $1 + p$, approaches two as a limit with increasing DP (upper curve in Fig. 3).

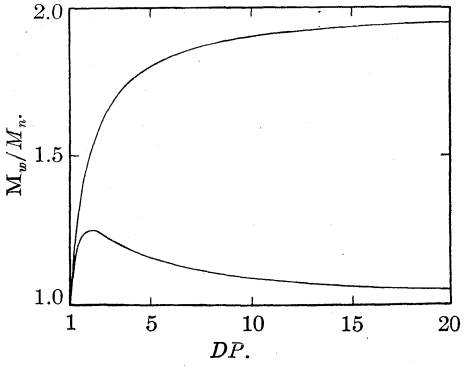


Fig. 3.—Ratio of weight average to number average as a function of DP. Upper curve, condensation polymers; lower curve, polyethylene oxides.

(18) P. J. Flory, THIS JOURNAL, **62**, 1057 (1940).

The ratio M_w/M_n may be regarded as a measure of the non-uniformity of the size distribution,[2] a value of unity representing complete homogeneity. On this basis polyethylene oxide heterogeneity must disappear as the average molecular weight becomes infinite. This does not mean that an extremely high molecular weight polymer would be composed essentially of a single species. Rather, it is the *relative* heterogeneity discussed above which disappears as the molecular weight becomes indefinitely large. However, when a high molecular weight polyethylene oxide is subjected to the types of experiments frequently applied to polymeric substances, *e. g.*, to viscosity measurements, ultracentrifugal analysis, and diffusion experiments, it may be expected to behave essentially as if it were a single species. This is in sharp contrast to condensation polymers which approach a constant degree of non-uniformity (M_w/M_n) as the average molecular weight approaches infinity.

Hibbert and co-workers[19] have prepared polyoxyethylene glycols by the reaction of the dihalide of a lower polyoxyethylene glycol with the mono-sodium alcoholate of another polyoxyethylene glycol. The polymers so prepared have been shown to be structurally identical[20] with polyethylene oxides. It should be possible to prepare heterogeneous polyoxyethylene glycols by the reaction

$$ClCH_2CH_2Cl + NaOCH_2CH_2ONa \longrightarrow Cl[CH_2CH_2OCH_2CH_2O]_xNa + x\,NaCl$$

which, being a condensation polymerization, should yield the typical condensation polymer distribution. After conversion of the end-groups to OH, the polymer should be identical, except in size distribution, with a polymer prepared from ethylene oxide and a small amount of ethylene glycol under conditions such that (i) and (ii) above are fulfilled. Comparison of their number average and weight average molecular weights, the latter determined viscometrically, would provide an experimental test of the size distribution equations.

(19) S. Z. Perry and H. Hibbert, *Can. J. Research*, **B14**, 77 (1936); R. Fordyce, E. L. Lovell and H. Hibbert, THIS JOURNAL, **61**, 1905 (1939).

(20) W. Barnes and S. Ross, *ibid.*, **58**, 1129 (1936).

Summary

It has been shown that in a polymer formed exclusively by the addition of monomers to a fixed number of polymer molecules, the numbers of species of various sizes are represented by Poisson's distribution law. Equations representing weight fraction distributions have been derived, and the calculated weight per cents. of various species in several polymers having average sizes of 6 to 500 units are shown graphically.

The distribution for these polymers, typified by the polyethylene oxides, has been contrasted with the distribution in condensation polymers. The former are much more homogeneous. Whereas the ratio of weight average to the number average molecular weight of condensation polymers approaches two as the degree of polymerization increases, for the polyethylene oxide distribution this ratio approaches unity.

CINCINNATI, OHIO RECEIVED MARCH 18, 1940

[A CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF WISCONSIN]

The Nature of the Thiocyanate Complex of Molybdenum

BY C. F. HISKEY* AND V. W. MELOCHE

In the determination of small amounts of molybdenum, the molybdenum as molybdate is reduced with stannous chloride in the presence of an alkali thiocyanate. The red coloration which is formed under these circumstances, is used in a wide variety of colorimetric procedures.[1] The earliest observations of this reaction were made concurrently by Braun and by Skey.[2] About forty years later, Chilesotti[3] electrolyzed acid solutions of molybdates from which he presumably obtained trivalent molybdenum. He reported that when these solutions were treated with potassium chloride or potassium thiocyanate, red salts were formed with a composition of $K_3Mo(SCN)_6 \cdot 4H_2O$ and K_3MoCl_6. Somewhat later Sand[4] and Rosenheim[5] carried out detailed investigations of the complexes which molybdenum formed in the trivalent and pentavalent states. They performed their reductions electrolytically, treating the solutions with an alkali thiocyanate and then extracting the red colored forms with ether. From the ethereal extracts complexes were precipitated with pyridine or quinoline, and, from an analysis of the complexes, these workers attempted to deduce its structure. The complex was variously reported at that time as $MoO(SCN)_3$, $Mo(OH)_2(SCN)_3$ and as $R_2MoO(SCN)_5$ where the R was an alkali atom. In addition to these structures they also were successful in isolating other series of thiocyanate complexes which were formed under nearly identical conditions. In some of these structures the molybdenum was trivalent and the complexes possessed different degrees of hydration. Other compounds differed only in the amount of alkali chloride bound into this complex. In view of the wide variety of structures observed, it becomes extremely difficult to decide which of these formulas should be assigned to the compound under question. Barbieri considered the thiocyanate complex to be $MoO(SCN)_3 \cdot H_2O$. In 1926, Krauskopf and Schwartz[6] reported $Mo(SCN)_3$ on the basis of a simple analysis of the ether extract. However, Wm. Wardlaw and his students[7] reinvestigated the problem of the thiocyanate complex formation and, as a result of a number of experiments decided that the structure of the complex could be either ($H_2MoO_2(SCN)_3$) or $H_2(MoO(SCN)_5)$ although he also isolated a large number of different salts series of the type $H_2(Mo_2O_3(SCN)_6)$. Thus, again no positive identification of the desired structure could be made.

In considering these variously proposed structures, it seemed somewhat doubtful to us that one could assume that the compounds isolated from the dark colored oily mixtures which these workers obtained were identical with the red thiocyanate used in the analytical determination of molybdenum. In view of the more drastic conditions

(*) Present address: University of Tennessee, Knoxville, Tenn.

(1) Kedesdy, *Mitt. kgl. Materialprüfungesamt*, **31**, 173 (1913); Maag and McCollam, *Ind. Eng. Chem.*, **17**, 524 (1925); James, *Ind. & Eng. Chem., Anal. Ed.*, **4**, 89 (1932); Hurd and Allen, *ibid.*, **7**, 396 (1935).

(2) Braun, *Z. anal. Chem.*, **6**, 86 (1867); Skey, *Chem. News, Am. Reprint*, **I**, 296 (1867).

(3) Chilesotti, *Atti. accad. Lincei*, **12**, ii, 22, 67 (1903).

(4) Sand and Burger, *Ber.*, **38**, 3384 (1905); also Maas and Sand, *ibid.*, **41**, 1500, 1861, 3367 (1908); **42**, 2642 (1909).

(5) Rosenheim and Koss, *Z. anorg. Chem.*, **49**, 148 (1906).

(6) Krauskopf and Schwartz, THIS JOURNAL, **48**, 3021 (1926).

(7) James and Wardlaw, *J. Chem. Soc.*, 2726–2739 (1928).

which these workers used, it seemed desirable to us to conduct a study in order to establish some of the limiting conditions governing proposals for structure of the complex. To that end, an investigation was begun to determine (1) whether the complex formed in the usual analytical procedure was identical with that formed between quinquevalent molybdenum and thiocyanate and whether it was at all possible for the trivalent molybdenum to form a red colored thiocyanate, (2) whether an equilibrium study of the reaction between the quinquevalent molybdenum and the thiocyanate ion would give some evidence as to the structure of the complex and (3) whether the pronounced color changes, which have been observed in quinquevalent molybdenum solutions, could be correlated with a previous observation of Hurd and Hiskey[8] that varying the acid concentrations resulted in a bleaching effect on the molybdenum thiocyanate complex.

1. The Valence State of the Molybdenum in the Complex.—It is recalled that when a molybdate solution, 2 *N* with hydrochloric acid is reduced with such reducing agents as stannous chloride,[9] the silver reductor,[10] or metallic mercury[11] quinquevalent molybdenum is formed. With all three of these agents the procedures have been made quantitative.

The solution of quinquevalent molybdenum, 2 *N* in hydrochloric acid, is amber-red in color. When the solution is in 8 *N* hydrochloric acid, it is emerald-green. These two colored forms of the molybdenum exist in equilibrium with each other. This equilibrium can be shifted from one form to the other simply by varying the hydrochloric acid concentration.

When the amber-colored form of the quinquevalent molybdenum is treated with an alkali thiocyanate solution, an interaction will begin proceeding at an appreciable speed to form a red complex which in appearance and properties seems to be identical with that formed when molybdenum is reduced with stannous chloride in the presence of thiocyanate. If the green colored form is treated with an alkali thiocyanate, no such reaction is observed. On the other hand, if the molybdenum is reduced under more drastic conditions, it can be brought to the trivalent state. Thus, when molybdenum is reduced in the Jones reductor (Zn) in 1–2 *N* sulfuric acid, it forms a green colored trivalent molybdenum compound. If the trivalent compound is treated with an alkali thiocyanate, meanwhile protecting the solution from atmospheric oxidation by blanketing with carbon dioxide or nitrogen, no red colored thiocyanate complex will be formed with the molybdenum even after a half-hour interval. Nor is it possible under these same conditions to extract any red colored complex from this solution with ether or butyl acetate. However, if some oxidant like hydrogen peroxide is added in such amounts as to bring the molybdenum to the five-valent state, the red compound will then be observed.

It is felt that evidence such as this definitely implies that there is no red trivalent complex of molybdenum but that the molybdenum in this complex must be approximately five-valent. In a more striking way, it can be shown that this is so, simply by taking an acid solution of molybdate and alkali thiocyanate and passing it through the Jones reductor. At first, as the solution comes in contact with the zinc, the red molybdenum thiocyanate complex appears but, as it moves down the tube, the solution loses its red color and when reduction is complete it has the blue-green color characteristic of trivalent molybdenum in dilute acid solutions.

The significance of these observations seems to be that as the molybdate passes down the reductor, the action of the zinc brings the molybdenum first to the five-valent state. At this point it reacts with the thiocyanate ion present to form the characteristic red color but, as the reducing action of the zinc is prolonged, the molybdenum is reduced to the trivalent state with the destruction of the red complex.

Besides the green trivalent form of molybdenum there is also a pink form of the trivalent state. It was thought that perhaps this substance reacted with the thiocyanate ion to give red trivalent complex and so it also was studied. This pink modification can be formed in a variety of ways. The essential element of the methods is that the molybdate must be reduced in fairly high concentrations of hydrochloric acid. Foerster[12] formed this pink trivalent molybdenum by electrolytic reduction while in a recent paper Hiskey, Springer and Meloche[13] show that this compound

(8) Hurd and Hiskey, *Ind. Eng. Chem., Anal. Ed.*, **10**, 623 (1938).
(9) Stéhlik, *Collection Czechoslov. Chem. Commun.*, **4**, 418 (1932).
(10) Birnbaum and Walden, THIS JOURNAL, **60**, 64 (1938).
(11) Furman and Murray, *ibid.*, **58**, 1689 (1936).
(12) Foerster, Fricke and Hausswald, *Z. physik. Chem.*, **146**, 81 (1929).
(13) Hiskey, Springer and Meloche, THIS JOURNAL, **61**, 3125 (1939).

can be formed by reduction in the silver reductor in hydrochloric acid concentrations above 4 *N*. Despite a wide variety of attempts to combine this substance with thiocyanate to form an ether soluble extract, our results were uniformly negative. Consequently it seems reasonable to conclude that trivalent molybdenum does not form any red colored thiocyanate complex.

In an attempt to establish more definitely that molybdenum in the thiocyanate complex is quinquevalent in character, it was decided to obtain the light absorption curves of this complex formed in two different ways. In one case, the complex was formed by reducing molybdate in the presence of an alkali thiocyanate with stannous chloride solution. In the other, the thiocyanate complex was formed by permitting an equivalent amount of a pure quinquevalent molybdenum solution to react with the thiocyanate ion until equilibrium was attained and then to determine its light absorption characteristics. In these experiments the concentration of the molybdenum and the thiocyanate ion in the final solution which were compared were exactly the same. The comparisons were made with the aid of special spectrophotometric equipment. A description has been given by James and Birge.[14]

The absorption curves for the two solutions are plotted in Fig. 1. For the purpose of comparison one of the curves is lowered in relationship to the other, but, on examination, it is apparent that they are practically identical. In addition to studying the absorption characteristics of the aqueous solutions of the thiocyanate complex formed in these two ways, similar studies were made of the butyl acetate extracts of these two solutions. By extracting the two solutions studied in Fig. 1 with butyl acetate, extracts containing approximately the same concentration of molybdenum and thiocyanic acid were obtained. The absorption spectra of these two extracts is given in Fig. 2. From this evidence it seems clear that the color characteristics are the same whether the complex is formed in the conventional manner or by the interaction of thiocyanate and quinquevalent molybdenum.

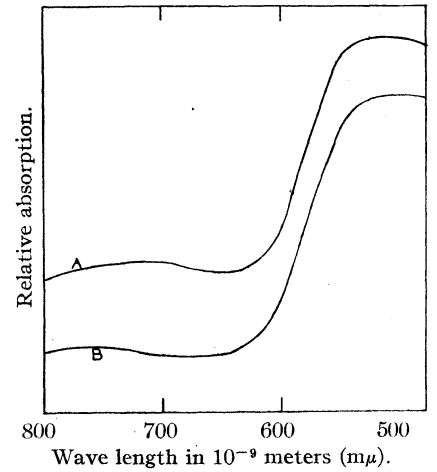


Fig. 1.—A = Mo^{+6} + SCN^- + $SnCl_2$; B = Mo^{+5} + SCN^-.

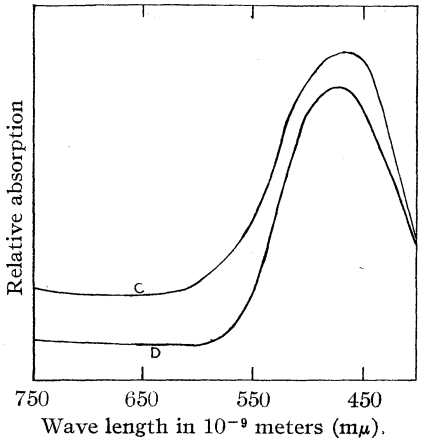


Fig. 2.—Butyl acetate extracts: C, extract of A; D, extract of B.

Therefore, it seems reasonable to conclude that trivalent formulas can be completely eliminated and that one of the limiting conditions concerning the structure of the thiocyanate complex of molybdenum must be a quinquevalent character for the molybdenum.

2. The Reaction between Quinquevalent Molybdenum and the Thiocyanate Ion. General Discussion.—At the outset of these studies it was recognized that the reaction between the thiocyanate ion and quinquevalent molybdenum did not lend itself to the most exact thermodynamical studies because certain difficulties are regularly encountered in the exact measurement of the molybdenum thiocyanate formed. Among those difficulties may be listed the interference due to the pink complex formation of the thiocyanate ion, as well as a fading effect of the molybdenum complex once it has formed.

A characteristic phenomenon of the acidified thiocyanate solutions is the tendency to form a pink colored substance. This pink colored substance is formed under conditions nearly the same

(14) James and Birge, *Trans. Wisconsin. Acad. Sci.*, **31**, 1 (1938).

as those which might be expected to prevail during the study of the reaction. It has often been observed in this Laboratory that it can be formed by placing a few drops of hydrochloric acid in a 20% solution of potassium thiocyanate. Once formed it can be extracted with any of the usual solvents employed in the molybdenum extraction. Many workers have thought that this pink compound is the ferric thiocyanate, but, even though it does possess a great similarity, it should be emphasized that it can also be formed in carefully distilled thiocyanic acid solutions where no iron could be present. In our particular studies we observed that invariably on mixing hydrochloric acid with a thiocyanate solution, followed by addition of quinquevalent molybdenum, the slow formation of a pure pink color would first be observed. After this color had developed for about ten minutes, the amber tint of the molybdenum complex would appear and reach a maximum while the pink color slowly would fade out. In an approximate fashion the course of these reactions might be represented graphically by the series in Fig. 3.

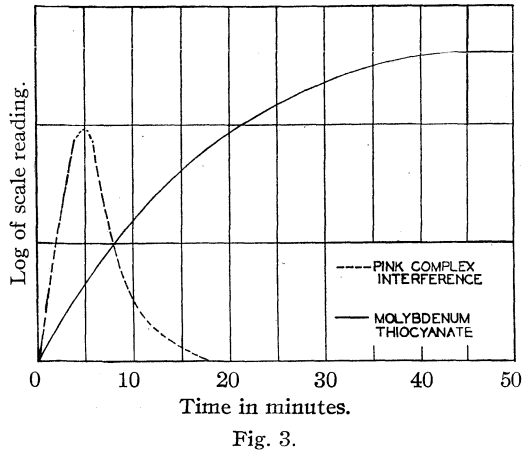


Fig. 3.

A second difficulty encountered in the study of this reaction is one due to an erratic and seemingly unpredictable fading which often occurs during these studies. When solutions of thiocyanate and quinquevalent molybdenum are mixed together and the concentrations are about 0.08 molar and 4.01×10^{-5} molar, respectively, the readings obtained from the colorimeter often will show that the color in some of the tubes has faded almost completely while others give perfectly reproducible values. Attempts to find out whether such phenomena were due to the catalyzing influence of traces of impurities seemed to give a negative answer. It did seem, however, that this type of phenomenon occurred with greater frequency in solutions of high hydrochloric acid concentration. Thus, in the four hydrochloric acid concentrations studied, 1.0, 1.5, 2.0, 2.5 *N*, the frequency of this type of fading was greatest in the 2.5 *N* and least in the 1.0 *N* solutions It also was observed that small amounts of stannous chloride solutions hastened the fading of all the solutions to which it was added.

Apart from these erratic fadings, all solutions of the complex showed a very slow fading after the maximum was attained. Thus a typical time *vs.* intensity curve when the hydrochloric acid concentration in the system was about 2.0 *N* appears in Fig. 4. At higher concentrations, the fading was more rapid and at lower concentrations it was much slower.

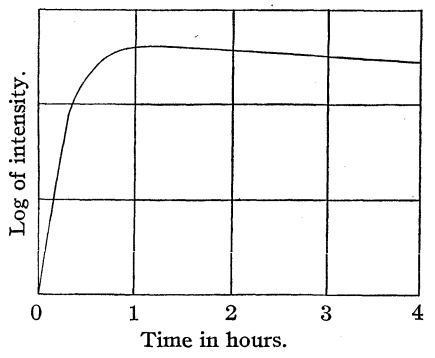


Fig. 4.—Molybdenum thiocyanate intensity as a function of time.

Despite this consecutive fading effect, we felt that we could profitably study the thiocyanate–molybdenum reaction because fading was generally extremely slow and the slight drift was scarcely detectable in the regions where data were of most significance.

Preparation of Materials

A. Approximately 1 Molar Thiocyanic Acid Solution.—This solution was prepared by taking 1 molar alkali thiocyanate, adding 30 ml. of concentrated sulfuric acid per liter and distilling the solution formed in an all glass distilling apparatus. The distillation was carried out at 20 mm. of mercury pressure. Whenever the thiocyanic acid came into contact with certain kinds of organic matter such as the skin, filter paper, cloth, stopcock grease, etc., a pink coloration would be induced. Apparently traces of organic matter or dust would also produce this color effect. In order to obtain a colorless thiocyanic acid solution and keep it so, all apparatus with which it came into contact had to be washed with a small amount of it until a pink coloration no longer formed. Standardization was effected by titration with alkali using phenolphthalein as in-

dicator. This was followed by a Volhard titration as an additional check on the purity of the solution. All of the thiocyanic acid prepared was used within twelve hours or less because, by that time, traces of its decomposition products could already be detected.

B. Quinquevalent Molybdenum Solutions.—This solution was prepared by taking 20.10 ml. of a 0.02495 molar molybdate solution, diluting with an equal amount of 4 *M* hydrochloric acid, heating to 80° and reducing in a silver reductor according to the method of Birnbaum and Walden.[10] The reduced solution was then diluted to one liter with additional 2 *M* acid. The solution was thus 5.01×10^{-4} molar with respect to the molybdenum and 2 *M* with hydrochloric acid. It was always prepared just before an experiment was to be performed.

C.—All other reagents used such as the thiocyanate salts and chlorides of lithium, sodium and potassium were C. P. analyzed and were used without further purification.

Experiments and Results

(1) The Reversible Character of the Reaction.—In this study the attempt was made to demonstrate whether or not the reaction was truly a reversible one. In most cases the usual procedure would be to demonstrate that from whatever side the reaction was begun, the final concentrations of the various components would be the same. But in this instance such an experiment could not be made directly because it was not possible to get pure molybdenum thiocyanate. Therefore, it became necessary to prepare molybdenum thiocyanate solutions of higher concentrations, and then, by proper dilution, to cause the molybdenum thiocyanate to decompose until equilibrium was attained. Then comparing these solutions to others which contained the same total concentration of quinquevalent molybdenum and thiocyanate acid but in which the formation of the molybdenum thiocyanate was performed directly, it became possible to see whether the equilibrium position was the same for the forward and the reverse reaction. In testing this reaction experimentally, two series of solutions were prepared. In one series, which we may designate as the A series, the solutions were prepared in the following manner.

To a 100-ml. volumetric flask, 8 ml. of 5.015×10^{-4} molar solution of quinquevalent molybdenum 2 molar with hydrochloric acid is added followed by 16 ml. of concentrated C. P. hydrochloric acid and varying amounts of water and thiocyanate solution to make up the remaining 100 ml. The solutions were then thoroughly shaken and set aside.

The other series, B was prepared by mixing the same amounts of quinquevalent molybdenum and hydrochloric acid plus 26 ml. of distilled water. To those solutions various amounts of the potassium thiocyanate solution were added and, after mixing, the solutions were permitted to stand until the color density was more than twice that of the corresponding solution in the series A. Then the appropriate amount of distilled water was added to bring the volumes of the solutions to 100 ml. and thus to bring the gross concentration of molybdenum and the thiocyanic acid to the same value as that in the A series. The solutions were permitted to stand while the molybdenum thiocyanate complex slowly decomposed until equilibrium was obtained. The amount of the complex was then determined by measurements in the Evelyn colorimeter using the no. 420 filter manufactured by the Rubicon Company. The results obtained as well as all of the data pertinent to this determination are listed in Table I.

TABLE I

0.9355 *M* KSCN soln., ml.	H_2O[a] added, ml.	Final concn. of KSCN in both series	Log galvanometer deflection Series A	Series B
10	40	0.0835	0.303	0.290
12	38	.1002	.465	.456
14	36	.1169	.523	.520
16	34	.1336	.557	.553
18	32	.1504	.553	.557
20	30	.1671	.569	.565
22	28	.1838	.561	.569
24	26	.2005	.581	.581
26	24	.2172	.581	.581
24	22	.2339	.581	.585

[a] This was the water withheld in series B.

A comparison of the results for the two solutions reveals that there is little difference in the equilibrium concentrations obtained under a given set of conditions even though the reaction is carried out in widely different manners and from opposite sides of the equation. This is a true test of reversibility and consequently established such a character for the reaction under discussion.

(2) Effect of Electrolyte Concentration on Equilibrium of the Reaction.—During the course of these investigations, it was observed that apparently the equilibrium of the reaction was affected by the character of the cations present. For example, it was observed in several instances that when a given concentration of thiocyanate solutions reacted with a fixed amount of quinquevalent molybdenum, apparently the density of the molybdenum thiocyanate color was greater when the sodium salt of thiocyanic acid was used instead of the potassium salt. Although such effects were known especially from the work of LaMer and others, it was thought worth while to investigate this effect more fully. Besides, any attempt to make equilibrium studies with the end in view of attempting to evaluate the thiocyanate–molybdenum ratio necessitated some knowl-

edge of the degree of these effects so that they could be accounted for properly in any later work.

With this objective in view, another series of solutions was prepared in which the concentration of the molybdenum, as well as the concentration of the free thiocyanate acid, was fixed. To these solutions variable amounts of four different electrolytes were added. These electrolytes were hydrochloric acid and the chlorides of lithium, sodium and potassium. The equilibria for these various systems were established at a temperature of 24.5°, and were attained after two hours. Stock solutions of hydrochloric acid and salts were 2 *M*. Suitable amounts of them were made up with water to a volume of 62 ml. and to this was added 38 ml. of quinquevalent molybdenum and thiocyanic acid mixtures so that their final molarities and that of the hydrochloric acid were 8.018×10^{-5}, 0.305 and 0.167 *M*, respectively. The data obtained are plotted in Fig. 5.

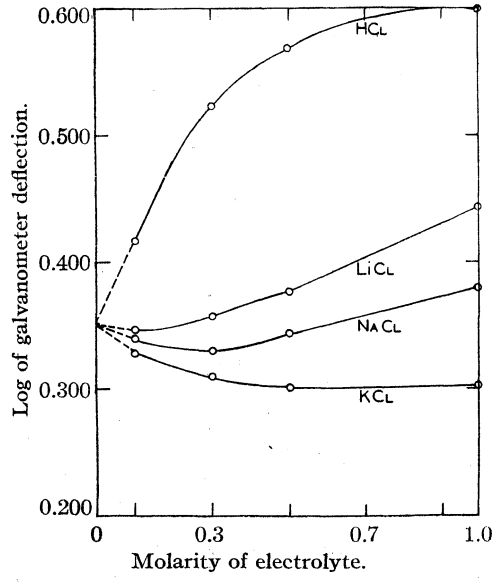


Fig. 5.—Effect of electrolyte concentration on equilibrium.

It is obvious from these data that not only does the ionic concentration of the system have a pronounced effect on the equilibrium of the reaction but that the degree of this effect is specific for the different cations used. It is also apparent that when the concentration of the added electrolytes is at zero (excepting the 0.167 *M* hydrochloric acid in all solutions), the color density indicates that little more than one-half of the quinquevalent molybdenum has reacted with the thiocyanate. The addition of more hydrochloric acid is sufficient to shift the equilibrium of the reaction to completion when its concentration is one molar. With the salts, however, the effect on the equilibrium is much less striking. It is apparent that in order to demonstrate this effect to best advantage it is necessary to choose such a concentration of the thiocyanate that the limiting color density is reached not because of a high thiocyanic acid concentration but rather because of the effect of the added electrolytes. Thus, it would be possible, if more than enough thiocyanate were added to drive the reaction to completion, to observe no effect from small amounts of added electrolytes.

The interpretation of this evidence leads one to believe that the structure of the complex in aqueous solution is not closely related to these salt effects but rather that what is being observed is some change of the apparent activities of the various components of this system due to salting-out or salting-in effects. However, more work would have to be done before any good explanation could be advanced.

Evaluation of the Thiocyanate–Molybdenum Ratio for the Complex.—Throughout this paper it has been postulated that the reaction between quinquevalent molybdenum and the thiocyanate can, in the most general way, be represented by the reaction

$$[Mo^{5+}R]^{n+} + n(SCN^-) \longleftrightarrow [Mo^{5+}R]^{n+}(SCN^-)n \quad (1)$$

It was generally apparent that the most likely value for n in this reaction was three, although as had been pointed out in the earlier discussion it had not been established conclusively by any of the previous investigators. In view of this fact, it seemed desirable to attempt an estimation of this ratio from a consideration of the effect which varying concentrations of the thiocyanate would have on the equilibrium of the reaction. Since these studies were to be made by means of colorimetric measurements, certain special details had to be considered. These details were largely associated with the need for exact measurements of all the substances participating in the reaction. Some of these difficulties were resolved by the mathematical treatment which was made of this problem. If we consider the reaction listed by equation 1, it is clear that this formulation does not consider the very pronounced effect of the hydrochloric acid observed in the preceding experiment. It seems better to represent the equation in a modified form such as equation 2.

$$[Mo^{5+}R]^{n+} + n(SCN^-) \longleftrightarrow [Mo^{5+}R](SCN)_n + X(OH^-) \quad (2)$$

The equilibrium constant of this reaction would then be

$$K' = \frac{C[Mo^{5+}R](SCN)_n C^x(OH)}{C[Mo^{5+}R]^{n+} C^n(SCN)} \quad (3)$$

Since the concentrations involved in these studies were to be low, one need not express K' in terms of activities. If the hydrochloric acid concentration is held constant for a series of studies, it then becomes possible to incorporate it in some new constant K and obtain

$$K = \frac{C[Mo^{5+}R](SCN)_n}{C[Mo^{5+}R]^{n+} C^n(SCN)} \text{ where } K = \frac{K'}{C^x(OH)} \quad (4)$$

Now let A = concentration of complex formed, B = total concentration of quinquevalent molybdenum, and C = total concentration of thiocyanate. Then the equilibrium constant can be expressed

$$K = \frac{A}{(B - A)(C - nA)^n} \quad (5)$$

Since A is small in comparison with C, it may be omitted from $(C - nA)^n$ term. Then

$$K = \frac{A}{(B - A)C^n} \quad (6)$$

Rearranging, $A = KBC^n - KAC^n$, $A + AKC^n = KBC^n$

$$\frac{A}{B} = \frac{KC^n}{(1 + KC^n)} \quad (7)$$

Setting $A/B = {}^1/_2$ and writing that value of C where $A/B = {}^1/_2$ as $C_{1/2}$, we have $KC_{1/2}^n = 1$ and $K = (1/C_{1/2})^n$. Substituting this value of K into equation 7, and rearranging we have

$$A = B\left(\frac{\left(\frac{C}{C_{1/2}}\right)^n}{1 + \left(\frac{C}{C_{1/2}}\right)^n}\right) \quad (8)$$

It is this equation which is used in the evaluation of the thiocyanate molybdenum ratio. By setting up a table in which the values for the term

$$\left(\frac{C}{C_{1/2}}\right)^n \Big/ 1 + \left(\frac{C}{C_{1/2}}\right)^n$$

are expressed as a function of the ratio $C/C_{1/2}$, it becomes extremely easy to calculate the value of A for any value of n and for any value of B. In using equation 8 for the experimental determination of the thiocyanate–molybdenum ratio, the theoretical curves for a plot of the log galvanometer deflection as a function of the thiocyanate concentration were calculated for various values of n. This could be done quite easily given the term for any particular value of B. In order to illustrate the use of the equation, a discussion of the method employed in evaluating the various terms is given.

(a) **Evaluation of A.**—Since A represents the amount of the complex which has formed under a given set of conditions, it can be determined by measuring the density of its color. In the usual colorimetric process, one simply calibrates the galvanometer deflection for these solutions. When monochromatic light is used and when Beer's law holds for the particular system under study, it will be found that the logarithm of the galvanometer deflection equals (kC), the product of the concentration and some constant.

In the process under discussion, this calibration was effected by taking a known amount of quinquevalent molybdenum and adding such an excess of thiocyanate that the reaction was driven to completion. Consequently the concentration of the complex becomes identical with that of quinquevalent molybdenum taken. It was in this way that the calibration curve illustrated in Fig. 6 was obtained.

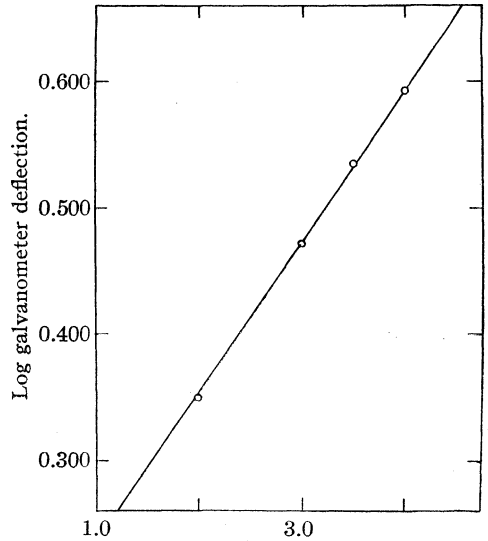


Fig. 6.

(b) **Evaluation of B.**—B was known because the solutions of quinquevalent molybdenum were prepared by quantitative reduction of analyzed molybdate solutions.

(c) **Evaluation of $C_{1/2}$.**—This concentration is determined by plotting the color density of a series of solutions as a function of the thiocyanate concentration. For any fixed amount of quinquevalent molybdenum, this plot will approach a limiting value of the color density. The concentration of the thiocyanate at the half-way point is the $C_{1/2}$ term wanted. In the actual determina-

tion of the thiocyanate–molybdenum ratio, a large number of series of solutions were prepared and their color densities determined. In each series the hydrochloric acid concentration and the quinquevalent molybdenum concentration were held constant while the concentration of the thiocyanate was varied. In Figs. 7, 8, and 9 some of the data are plotted.

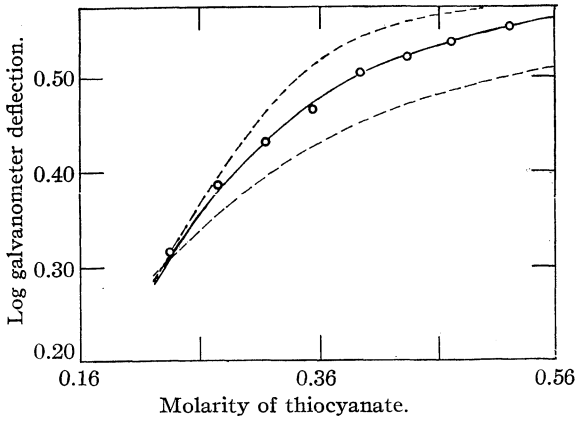


Fig. 7.—Theoretical curves: - - - - $N = 2$ and 4; ——— $N = 3$; ○, experimental points; 1.0 molar HCl concentration.

It should be remembered that in the mathematical treatment the hydrochloric acid concentration was incorporated into the special equilibrium constant K; therefore, at any given hydrochloric acid concentration, the $C_{1/2}$ term must be evaluated from the data. After $C_{1/2}$ is evaluated, it then becomes possible to calculate the theoretical curves observed in the figures.

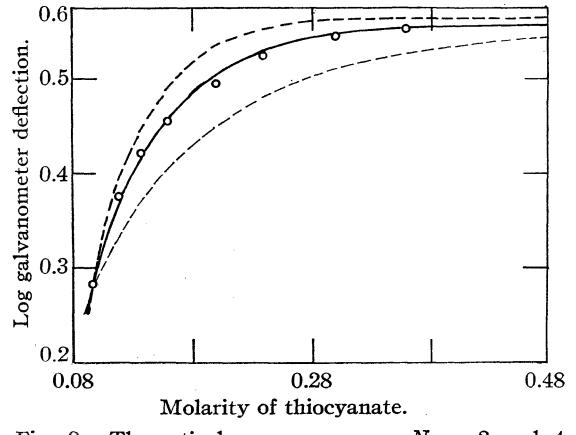


Fig. 8.—Theoretical curves: - - - - $N = 2$ and 4; ——— $N = 3$; ○, experimental points; 1.5 molar HCl concentration.

In the above figures only the experimental points are listed. All of the lines drawn represent

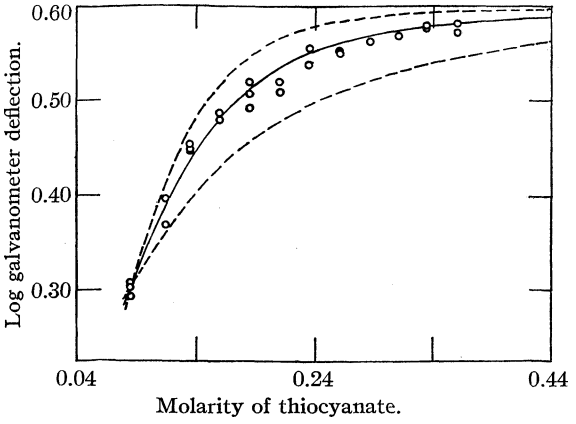


Fig. 9.—Theoretical curves: - - - - $N = 2$ and 4; ——— $N = 3$; ○, experimental points; 2.0 molar HCl concentration.

theoretical lines calculated with aid of equation 8. Experiments were also run in hydrochloric acid concentrations above 2.5 N but, since it became virtually impossible to get any semblance of reproducibility at this concentration, those experiments were discontinued. In fact, it can be observed that the results obtained at 2.0 M leave something to be desired. Examination of the data and the plots of these data reveals a close similarity between the theoretical values calculated for a thiocyanate ratio of three and the experimental points observed. It seemed reasonable to conclude that such a close agreement clearly establishes this ratio in a not too ambiguous manner. While one must admit that this ratio has not been established with stoichiometrical exactness from the data presented herein, nevertheless it is important to recognize that no matter how strict the interpretation of the results, a possible deviation greater than 6 or 7% from the value of 3 is not permitted.

If one attempts to solve equation 8 directly for the value of n, a much too rigorous testing of data is obtained. This is due to the fact that we obtain such a term as

$$n = \frac{\log \frac{A}{B - A}}{\log \frac{C}{C_{1/2}}}$$

As A approaches B the value of the $\log A/(B - A)$ term becomes extremely uncertain because a small variation in the value of the $(B - A)$ term causes large variations in $\log A/(B - A)$. As A approaches $B/2$ the expression becomes indeterminate and for values of A greater than $B/2$ it becomes impossible to obtain suitable experimental data.

Despite these general limitations, however, one thing remains clear; these experiments establish this ratio of 3 as a property of the colored substances in solution and not as a property of some dry compound isolated from tarry mixtures of many different substances.

Along with these general observations several other points may be made concerning the character of the reaction. Of these, perhaps the most important is the fact that from the slowness with which equilibrium is attained, one may conclude that this is not an ionic reaction. Additional evidence that the molybdenum complex is not ionic may be surmised from its extreme solubility in a large number of organic solvents. Consequently a representation of the reaction which involves only an exchange of the thiocyanate ion with the chloride ions of quinquevalent molybdenyl chloride must be considered as an over simplification.

3. Fading Effect Induced by Hydrochloric and Sulfuric Acids.—The next problem considered in this study was one associated with the very pronounced fading of the molybdenum thiocyanate observed in high acid concentrations. This effect was used to bleach the molybdenum thiocyanate color and thus prevent the molybdenum from interfering in the colorimetric determination of the rhenium. In view of similar striking color changes observed in pure quinquevalent molybdenum solutions, it was thought desirable to make a study of these two processes in order to determine whether any analogy existed between them.

Experimental

A. Quinquevalent Molybdenum Color Transition.—On taking a solution of quinquevalent molybdenum whose hydrochloric acid concentration is slowly increased, one may observe the series of color changes listed in Table II. This color transition may also be observed by starting with 8 *N* hydrochloric acid and progressively diluting with water whereby the same colors will appear in reverse order.

TABLE II

Molarity HCl	Color of solution	Molarity HCl	Color of solution
0.0–0.5	Faint amber	6.3–7.3	Brown changes to dark olive color
0.5–5.5	Amber color becomes more intense	7.7	Light olive
3.5–5.5	Amber changing to dark brown	8.0	Chrome-green
5.5–6.3	Brown color darkens appreciably	8.0	Above color becomes a pure emerald-green

For the purpose of this discussion, it will only be necessary to consider the color effects at the lower acid concentrations for which the color densities were measured. The measurements were made in the Evelyn colorimeter using the no. 420 filter.

The stock quinquevalent molybdenum solution used was 0.0107 and 2 molar with hydrochloric acid. Solutions of hydrochloric acid prepared by mixing various amounts of water with 5 molar hydrochloric acid had a total volume of 20 ml. To these solutions 5 ml. of the quinquevalent molybdenum solution was added, and the resulting solutions thoroughly mixed. The solutions were transferred to the colorimeter and the galvanometer deflection observed. Data obtained in this manner are plotted in Fig. 10.

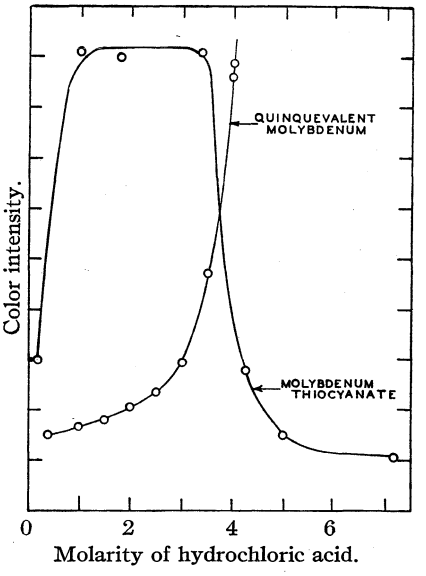


Fig. 10.

In studying the transition caused by the sulfuric acid, small amounts of hydrochloric acid added as a constituent of the stock solution of quinquevalent molybdenum exerted a profound effect upon the action of the sulfuric acid. In order to make the experiments comparable, it was neces-

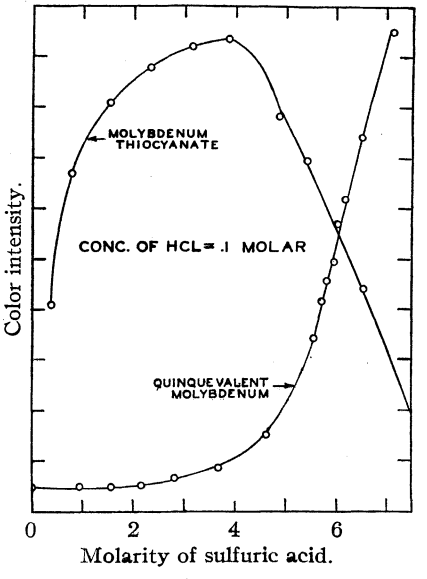


Fig. 11.

sary to adjust the hydrochloric acid concentration in the final solution to 0.1 molar. In these experiments our stock molybdenum solution was 0.015 molar with respect to molybdenum and 1.0 molar with hydrochloric acid. Five ml. of the stock solution was diluted to 50 ml. with a solution whose sulfuric acid concentration was known. After thoroughly mixing the readings of the color density were taken. These data are plotted in Fig. 11.

B. Fading Effect of the Thiocyanate Complex of Molybdenum.—The determination of the fading effect of these acids upon the molybdenum thiocyanate complex was done about five years ago, and for those experiments an Eastman Universal colorimeter was used. The principle of the instrument was based on a comparison of the color density of a solution with a standard glass wedge whose color density changed regularly from one end to the other. While the results obtained using such an instrument are not particularly quantitative, they still are sufficiently so to indicate the qualitative aspects of the process we are discussing. In those series, the molybdenum thiocyanate complex was formed by the reduction of alkali molybdate solution with stannous chloride in the presence of potassium thiocyanate while the concentrations of the hydrochloric and sulfuric acids were varied.

The solution, whose color density was to be studied, was prepared by taking 60.5 ml. of an acid solution whose concentration was known and adding to it 2 ml. of the molybdate solution (200 micrograms per ml.) and 2.5 ml. of a 10% potassium thiocyanate solution. Then, 7.5 ml. of 10% stannous chloride was added. The readings were taken after the solution had reached an equilibrium condition showing only a very slight fading effect as a function of time. They are plotted in Figs. 10 and 11.

In plotting these two sets of data, it was necessary to adjust the ordinates in order to properly compare the two curves. When this is done it will be observed how nearly identical the threshold acid concentrations are for these two effects.

It seems clear, therefore, that these two reactions are related to each other in no indirect manner. We feel, therefore, that a possible interpretation of these results is that the two effects are due to similar reactions: that in the case of the quinquevalent molybdenum, a colorless form, which we call "W," is progressively transformed into the amber colored form which we shall refer to as "X." In the case of the molybdenum thiocyanate complex, there is a red colored form W′ corresponding to the W form of the quinquevalent molybdenum and a colorless form of the thiocyanate complex X′ corresponding to the X form of the quinquevalent molybdenum.

If this interpretation is correct, then it is quite logical to agree that whatever the formula for the thiocyanate complex, it must contain within itself the possibility of explaining the fading effect observed.

With the information available from this research it is not possible for us to make any thoroughgoing prediction of what it should be like. Whether the color transitions observed are due to complex formation or to hydration cannot be adequately treated now but the correlation of these two phenomena make it seem likely that a study of the simpler system (*i. e.*, quinquevalent molybdenum without thiocyanate) will give information which has a direct bearing on the structure of the thiocyanate complex.

Acknowledgment.—The authors would like to express their indebtedness to the generous financial support of the Works Projects Administration and to the Brittingham Foundation for the use of the special spectrometer provided by their funds. They would also like to express their appreciation to Messrs. Warren Olson, V. F. Springer and Max Wolfe for their aid in the execution of some of the laboratory work.

Conclusions

An examination of the literature reveals that there is no clear formulation for the structure of the thiocyanate complex of molybdenum. In this research, evidence has been advanced to show that whatever the structure of the molybdenum thiocyanate complex, the formula of it must: (1) indicate quinquevalency for the molybdenum in the complex, (2) show a thiocyanate–molybdenum ratio of three and (3) offer an explanation of the color transitions observed.

RECEIVED FEBRUARY 26, 1940

[CONTRIBUTION FROM THE BAKER LABORATORY OF CHEMISTRY AT CORNELL UNIVERSITY]

The Chlorinates. III. Temperature–Concentration Equilibria in the Systems Methylene Chloride–Chlorine and Methyl Chloride–Chlorine. The Perchlorides of Methylene and of Methyl[1,2]

BY J. ALLEN WHEAT, II, AND A. W. BROWNE

In determining temperature–concentration equilibria in the system methylene chloride–chlorine the experimental procedure was identical with that followed in the earlier work with chloroform and chlorine.[2] The data obtained are presented in Table I and are plotted in Fig. 1.

TABLE I

TEMPERATURE–CONCENTRATION OR SOLUBILITY DATA OF THE SYSTEM CH_2Cl_2–Cl_2

Temp., °C.	Concn., mole % Cl_2	Curve (Fig. 1)
− 97.0	0.0	A. (Solid CH_2Cl_2, liq., vapor)
− 98.0	1.5	
− 99.5	3.1	
−101.5	6.0	
−104.0	7.4	
−108.5	11.5	
−110.0	14.7	AB. (Solid CH_2Cl_2, satd. soln., vapor)
−113.0	16.8	
−116.5	20.5	
−119.5	22.9	
−120.5	23.8	
−122.5	25.1	
−124.5	26.5	
−128.0	27.7	B. (Eutectic: solid CH_2Cl_2, solid $(CH_2Cl_2)_2$·Cl_2, satd. soln., vapor)
−127.0	28.5	
−126.0	29.4	
−125.5	30.8	
−125.0	32.2	
−125.0	34.8	BCD. (Solid $(CH_2Cl_2)_2$·Cl_2, satd. soln., vapor)
−126.0	37.4	
−127.5	39.4	
−129.5	41.0	
−131.5	42.6	
−134.0	44.5	
−135.0	45.1	D. (Eutectic: solid $(CH_2Cl_2)_2$·Cl_2, solid CH_2Cl_2·Cl_2, satd. soln., vapor)
−130.5	46.6	
−127.0	48.9	
−126.5	50.5	DEF. (Solid CH_2Cl_2·Cl_2, satd. soln., vapor)
−127.0	51.3	
−128.0	53.0	
−130.5	55.0	
−132.0	55.5	F. (Eutectic: solid CH_2Cl_2·Cl_2, solid CH_2Cl_2·$2Cl_2$, satd. soln., vapor)
−129.5	56.3	
−125.5	59.1	
−123.0	61.1	
−121.5	63.2	
−119.0	65.6	FGH. (Solid CH_2Cl_2·$2Cl_2$, satd. soln., vapor)
−117.5	67.0	
−119.0	68.6	
−121.0	70.2	
−122.0	71.3	H. (Eutectic: solid CH_2Cl_2·$2Cl_2$, solid Cl_2, satd. soln., vapor)
−120.0	72.5	
−119.0	74.8	
−117.5	76.2	
−115.5	79.8	HI. (Solid Cl_2, satd. soln., vapor)
−110.5	85.6	
−106.0	92.3	
−104.0	95.9	
−102.0	100.0	I. (Solid Cl_2, liquid, vapor)

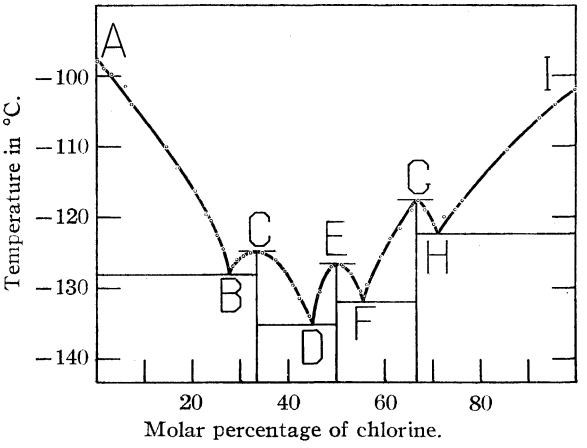


Fig. 1.—Freezing point *vs.* composition for system of methylene chloride–chlorine.

For the investigation of the system methyl chloride–chlorine, in which both components are vapors at ordinary temperatures, a special apparatus, shown in Fig. 3, was used. This consisted essentially of a closed reaction cell immersed in a pentane bath, the temperature of which could readily be controlled between −150° and +20° by means of liquid air. Accessory devices facilitated the introduction of measured amounts of either component into the cell. For

(1) This article is based upon the thesis presented to the Faculty of the Graduate School of Cornell University by J. Allen Wheat, II, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) For the preceding articles in the current series, see Wheat and Browne, THIS JOURNAL, **58**, 2410 (1936); **60**, 371 (1938).

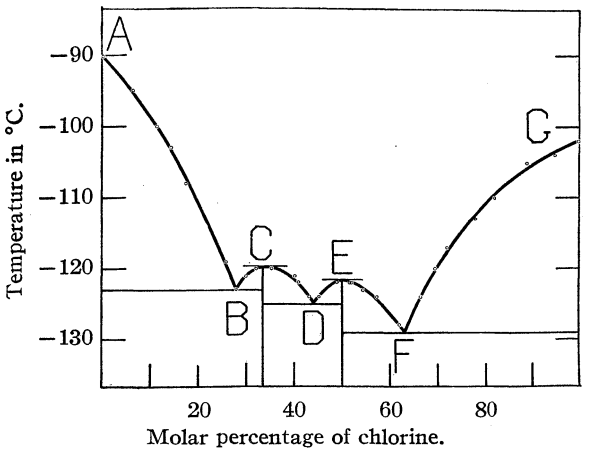


Fig. 2.—Freezing point *vs.* composition for system of methyl chloride–chlorine.

each concentration studied, the system was cooled well below the freezing point, with constant agitation, until solidification occurred. The bath was then allowed to warm slowly, with constant stirring, and the temperature of the bath at which the last trace of the solid phase disappeared, was taken as the freezing point. Possible error due to temperature lag between bath and cell was elimi-

TABLE II

TEMPERATURE–CONCENTRATION OR SOLUBILITY DATA OF THE SYSTEM CH_3Cl–Cl_2

Temp., °C.	Concn., mole % Cl_2	Curve (Fig. 2)
− 90	0.0	A. (Solid CH_3Cl, liq., vapor)
− 95	6.5	
−100	11.2	
−103	14.2	AB. (Solid CH_3Cl, satd. soln., vapor)
−108	17.5	
−114	21.6	
−119	25.8	
−124	27.8	B. (Eutectic: solid CH_3Cl, solid $(CH_3Cl)_2{\cdot}Cl_2$, satd. soln., vapor)
−123	28.3	
−121	30.0	
−120	34.6	
−120	35.1	BCD. (Solid $(CH_3Cl)_2{\cdot}Cl_2$, satd. soln., vapor)
−121	40.1	
−122	41.0	
−124	43.2	
−125	44.1	D. (Eutectic: solid $(CH_3Cl)_2{\cdot}Cl_2$, solid $CH_3Cl{\cdot}Cl_2$, satd. soln., vapor)
−124	45.2	
−122	49.0	
−122	51.6	DEF. (Solid $CH_3Cl{\cdot}Cl_2$, satd. soln., vapor)
−123	54.5	
−124	57.4	
−128	62.0	
−129	63.3	F. (Eutectic: solid $CH_3Cl{\cdot}Cl_2$, solid Cl_2, satd. soln., vapor)
−124	66.5	
−120	69.5	
−117	72.0	FG. (Solid Cl_2, satd. soln., vapor)
−113	78.0	
−110	82.0	
−105	89.6	
−104	95.0	
−102	100.0	G. (Solid Cl_2, liq., vapor)

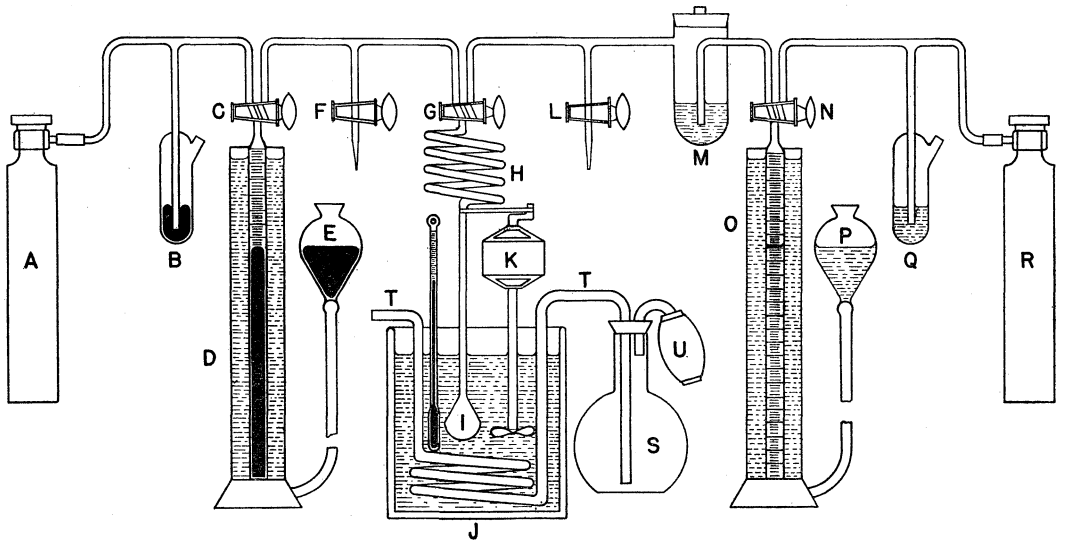


Fig. 3.—A, Cylinder of CH_3Cl; B, gas trap (mercury); C, double stopcock; D, E, water-jacketed gas buret and leveling bulb (mercury); F, exhaust stopcock; G, double stopcock; H, glass spiral; I, reaction cell; J, pentane-bath; K, electric motor; L, exhaust stopcock; M, gas drying bottle (concentrated sulfuric acid); N, double stopcock; O, P, water-jacketed gas buret and leveling bulb (saturated NaCl in water); Q, gas trap (saturated aqueous solution of sodium chloride); R, cylinder of chlorine; S, liquid air supply; T, copper tubing; U, aspirator pump.

nated by special calibration of the pentane thermometer with the aid of several pure gases whose (known) melting points were determined in the same way. The data are submitted in Table II, and are plotted in Fig. 2.

The data in the foregoing tables clearly indicate the formation of three chlorinates of methylene chloride, and two chlorinates of methyl chloride, all with congruent melting points, as follows

(1) methylene chloride hemichlorinate, $(CH_2Cl_2)_2 \cdot Cl_2$, −124.5°
(2) methylene chloride monochlorinate, $CH_2Cl_2 \cdot Cl_2$, −126.5°
(3) methylene chloride dichlorinate, $CH_2Cl_2 \cdot 2Cl_2$, −117.5°
(4) methyl chloride hemichlorinate, $(CH_3Cl)_2 \cdot Cl_2$, −120°
(5) methyl chloride monochlorinate, $CH_3Cl \cdot Cl_2$, −122°

While no evidence concerning the structure of these compounds has been obtained as yet, it is possible to write their formulas in the manner tentatively suggested for the chlorinates of chloroform and of carbon tetrachloride in the earlier articles of the current series. The fact that the maximum number of chlorine molecules held in combination by any of the chloromethanes is equal to the number of chlorine atoms in the chloromethane molecule tends, in the opinion of the authors, to confirm the idea that the solvates under investigation are coördination compounds.

In conformity with the definition of perchlorides proposed in the second article of this series, the three chlorinates of methylene chloride and the two of methyl chloride may be regarded as perchlorides of methylene, and of methyl, respectively. Their empirical composition could therefore be expressed by the formulas $(CH_2)_2Cl_6$, CH_2Cl_4, CH_2Cl_6, $(CH_3)_2Cl_4$ and CH_3Cl_3.

Summary

Two chlorinates of methyl chloride, or perchlorides of methyl, and three chlorinates of methylene chloride, or perchlorides of methylene, have been identified and their congruent melting points determined.

ITHACA, N. Y. RECEIVED APRIL 5, 1940

[CONTRIBUTION FROM THE BAKER LABORATORY OF CHEMISTRY AT CORNELL UNIVERSITY]

The Chlorinates. IV. Temperature–Concentration Equilibria in the System Hydrogen Chloride–Chlorine. The Hydrogen Perchlorides[1,2]

BY J. ALLEN WHEAT, II, AND A. W. BROWNE

Since chlorine readily forms solvates with the chloromethanes[2] it has been suggested tentatively

TABLE I

TEMPERATURE–CONCENTRATION OR SOLUBILITY DATA OF THE SYSTEM HCl–Cl_2

Temp., °C.	Concn., mole % Cl_2	Curve (Fig. 1)
−112	0.0	A. (Solid HCl, liquid, vapor)
−114	6.7	AB. (Solid HCl, saturated solution, vapor)
−117	12.5	
−120	17.0	
−122	19.6	
−125	23.0	
−128	25.6	
−129	26.3	B. (Eutectic: Solid HCl, solid $(HCl)_2$:Cl_2, saturated solution, vapor)
−123	30.6	BCD. (Solid $(HCl)_2$:Cl_2, saturated solution, vapor)
−122	32.2	
−122	35.0	
−124	37.6	
−125	38.0	D. (Eutectic: Solid $(HCl)_2$:Cl_2, solid HCl:Cl_2, saturated solution, vapor)
−120	40.4	DEF. (Solid HCl:Cl_2, saturated solution, vapor)
−116	44.8	
−115	49.4	
−116	54.0	
−117	57.3	
−120	60.0	
−124	63.5	
−128	66.0	F. (Eutectic: Solid HCl:Cl_2, solid Cl_2, saturated solution, vapor)
−122	68.7	FG. (Solid Cl_2, saturated solution, vapor)
−117	72.6	
−112	77.5	
−109	82.5	
−106	88.9	
−103	95.0	
−102	100.0	G. (Solid Cl_2, liquid, vapor)

(1) This article is based upon the thesis presented to the Faculty of the Graduate School of Cornell University by J. Allen Wheat, II, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) For the preceding articles in the current series, see Wheat and Browne, THIS JOURNAL, **58**, 2410 (1936); **60**, 371 (1938); **62**, 1575 (1940).

that chlorine attached to carbon will denote a pair of electrons to free chlorine. The purpose of the current investigation was to determine whether or not chlorides, in which the chlorine was attached to a more electropositive element than carbon, would also form solvates with free chlorine.

In the present investigation of the freezing point *vs.* concentration equilibria in the system of hydrogen chloride–chlorine, the experimental procedure was substantially identical with that employed in the study of the system of methyl chloride–chlorine.[2] The data obtained are presented in Table I and are plotted in Fig. 1.

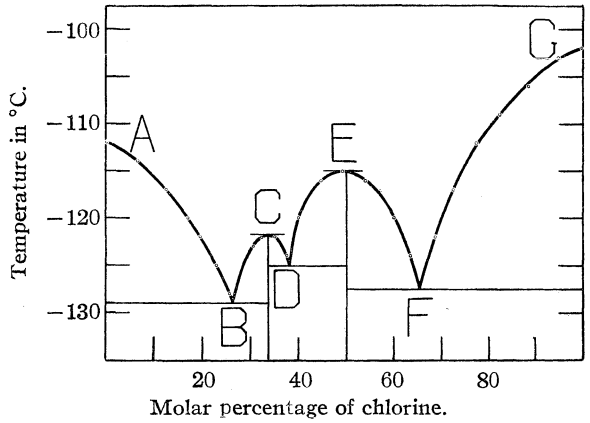


Fig. 1.—Freezing point *vs.* composition in system of hydrogen chloride–chlorine.

From the foregoing data it may be concluded that chlorine forms two solvates (chlorinates) with hydrogen chloride, whose empirical formulas and congruent melting points are as follows: (1) hydrogen chloride hemichlorinate, $(HCl)_2:Cl_2$, −121°; (2) hydrogen chloride monochlorinate, $HCl:Cl_2$, −115°.

Nothing concerning the structure of these compounds can be deduced from these data, but the authors venture the statement that it seems probable that hydrogen chloride should be combined with free chlorine by a coördinate covalent link. Since the hydrogen–chlorine link in hydrogen chloride is more polar than the chlorine–chlorine link in the free chlorine, the chlorine attached to hydrogen probably donates a pair of electrons which is accepted by the free chlorine. The structural formulas would therefore be

(1) H—Cl ⟶ Cl—Cl ⟵ Cl—H
(2) H—Cl ⟶ Cl—Cl

In conformity with the definition of perchlorides proposed in the second article of the current series,[2] the compounds identified during this investigation may be considered as perchlorides of hydrogen whose empirical formulas are H_2Cl_4 and HCl_3.

Summary

Two chlorinates of hydrogen chloride or perchlorides of hydrogen, have been identified and their congruent melting points determined.

ITHACA, N. Y. RECEIVED APRIL 5, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF CORNELL UNIVERSITY]

The Chlorides of Gallium

BY A. W. LAUBENGAYER AND F. B. SCHIRMER

The formation of compounds by gallium has been shown to present numerous interesting problems, both of valence state and of molecular configuration. While trivalency, which is to be expected for this atom, is well established, the molecular species and configuration of the compounds in this state have not been well understood. Gallium also has been reported[1] to show divalence, a condition which cannot be reconciled with its atomic structure, and univalence, which should be possible due to the use of only the $4p$ electron for bonding purposes. Very little work is available about these lower valence states.

(1) L. de Boisbaudran, *Compt. rend.*, **93**, 294 (1881).

The system gallium–chlorine is a favorable one to study because gallium–chlorine bonds are strong enough to ensure reasonably stable molecules and the volatility of the chlorides makes it possible to investigate them in the vapor phase.

Gallium trichloride has been shown[1] to resemble aluminum chloride closely, being associated at lower temperatures. While a recent vapor pressure and density investigation[2] of this compound has given considerable data, this work does not agree on a number of points with the reports of earlier investigators, the temperature range cov-

(2) Fischer and Jubermann, *Z. anorg. allgem. Chem.*, **227**, 227 (1936).

ered is not extensive enough to afford all the desired information, and the interpretation of the data is incomplete.

Gallium dichloride was prepared by de Boisbaudran[1] and other workers[3] by the reduction of gallium trichloride with hot gallium, but the conditions for preparation have not been well established, the purity of the product seems to have been considerably in doubt, and its properties have not been completely surveyed.

No reduction of gallium dichloride to a monochloride has been demonstrated, although Nilson and Pettersson suggested that a brownish colored film which remained on the walls of the glass reaction tube after reduction of the trichloride with excess gallium might have been the monochloride.

In the present investigation vapor phase studies of gallium trichloride over an extended temperature range have been undertaken. Pure gallium dichloride has been prepared and its properties, especially its behavior in the vapor phase, have been investigated. The possibility of obtaining gallium monochloride has been examined.

Apparatus and Procedure for Vapor Studies.—Because the system gallium–chlorine is very reactive, especially toward water and oxygen, the apparatus shown in Fig. 1, constructed completely of Pyrex glass, was used for vapor pressure and density measurements. This apparatus employed the vapor pressure cell A which had a glass manometer of the "sickle" type,[4] similar to a Bourdon gage. The cell could be connected by means of an interchangeable ground glass joint to the chain equipped with a mercury manometer, a McLeod gage, a vacuum pump, and drying tubes through which air could be admitted. The volume of the cell was determined by weighing it empty and then filled with water to the points on tubes B and C where they later would be sealed off. Corrections for change of volume with temperature were calculated.

The glass ampule containing the sample was scratched with a file, weighed, and introduced into the cell through tube B, which then was sealed off. The cell was attached to the chain, C was connected to D by glass and rubber tubing, and the cell was completely evacuated simultaneously on both sides of the sickle. C was sealed off and the zero positions of the pointers E and F were noted by means of a telescope. S_1 was closed, the cell was taken from the chain and shaken to break the sample tube, and then was reattached, and the chain beyond S_1 was evacuated. The temperature of the sample was controlled by immersing the cell to its side arm in a suitable thermostat. As the pressure in the cell rose the pointers were balanced approximately by admitting air through S_5 and S_1. When equilibrium at a given temperature was attained the pointers E and F were brought to their zero positions by manipulating the pressure of air, and this pressure was then read on the mercury manometer and corrected to give the pressure of the sample. To be sure that equilibrium was realized, the pressures corresponding to given temperatures were determined, both as the temperature was progressively raised and as it was lowered. By varying the size of the cell and the weights of sample used, accurate vapor pressure and density data could be secured over a wide temperature range. The apparatus and method were shown to be satisfactory by making measurements on pure aluminum chloride.

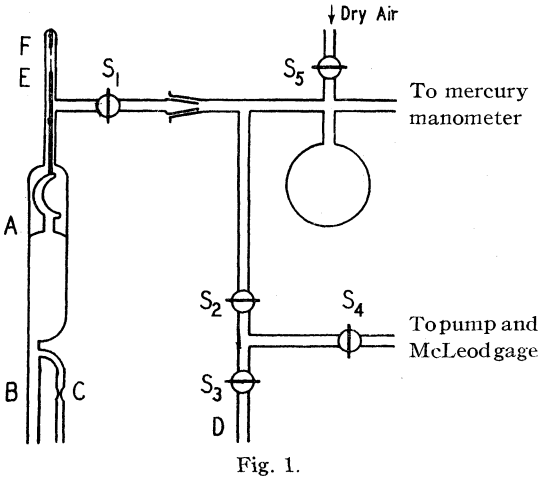


Fig. 1.

Study of Gallium Trichloride

Preparation and Analysis.—Gallium trichloride was prepared by the action of chlorine diluted with nitrogen on hot gallium. The product was distilled in a stream of nitrogen to remove the excess chlorine and further purified by sublimation *in vacuo*. It was analyzed by putting it into solution in 1% nitric acid and determining the gallium as the oxide and the chlorine as silver chloride.[5]

Anal. Calcd. for $GaCl_3$: Ga, 39.59; Cl, 60.41. Found: Ga, 39.55; Cl, 60.35.

Vapor Pressure of Gallium Trichloride.—Measurements were made in the temperature range 50 to 200°. The data for duplicate runs agree satisfactorily and are summarized in Table I. They check those reported by Fischer and Jubermann[2] but also cover a lower temperature range and thus give more information about the solid–vapor equilibrium.

The values of log p plotted against $1/T$ give solid–vapor and liquid–vapor lines which intersect at 77°, the melting point. The points for the liquid–vapor equilibria give a smooth slightly curved line, indicating a small change in the heat of vaporization with temperature. The thermal data for gallium trichloride calculated on the basis of these measurements are summarized in Table II and are compared with the values previously reported.

Vapor Density of Gallium Trichloride.—To determine the maximum association possible in

(3) (a) Nilson and Pettersson, *Z. physik. Chem.*, **2**, 668 (1888); (b) Muscher and Wehrli, *Helv. Phys. Acta*, **7**, 332 (1934).

(4) Phipps, Spealman and Cooke, *J. Chem. Education*, **12**, 321 (1935).

(5) Hillebrand and Lundell, "Applied Inorganic Analysis," John Wiley and Sons, New York, 1929.

TABLE I

VAPOR PRESSURES OF GALLIUM TRICHLORIDE

Temp., °C. (±0.1°)	$1/T \times 10^3$	p, mm. Hg (±0.1)	Log p
50.0	3.095	1.2	0.079
55.1	3.047	1.9	.279
60.1	3.001	2.8	.447
65.1	2.957	4.3	.633
70.2	2.913	6.0	.778
75.1	2.872	8.5	.929
80.1	2.831	11.8	1.072
90.1	2.753	19.1	1.281
100.1	2.680	28.9	1.461
109.9	2.611	44.4	1.647
120.1	2.543	65.5	1.816
130.4	2.478	94.5	1.975
140.6	2.417	134.6	2.129
151.0	2.375	189.3	2.277
161.3	2.302	260.4	2.416
171.3	2.250	351.4	2.546
181.4	2.200	465.9	2.668
191.2	2.154	608.5	2.784
200.8	2.110	771.7	2.888

TABLE II

THERMAL DATA FOR GALLIUM TRICHLORIDE

	Other Investigators	The Authors
Melting point, °C.	75.5[1] 78.0[6] 76.65[7] 77.9[2] 76[9]	77.0
Boiling point, °C. (760 mm.)	215–220[1] 205[6] 199.6[7] 201.3[2]	200.0
Heat of vap. at b. p., kcal.	10.5[2]	11.4
Heat of vap. at m. p., kcal.	12.3[2]	11.8
Heat of subl. at m. p., kcal.	9.2[8]	17.0
Heat of fusion at m. p., kcal.		5.2

the vapor phase, measurements were made between 117 and 177°, as low a temperature range as was practical to use. No evidence was obtained for association beyond the dimer, Ga_2Cl_6.

To follow the dissociation of the dimeric molecule, further vapor density measurements were made between 177 and 498°, the highest temperature to which the glass sickle could be heated without undergoing permanent distortion. Establishment of equilibrium and absence of any decomposition of the sample was proved by rechecking the data as the cell cooled. The results for a sample weighing 0.5763 g., measured in a cell of 223.4 cc. capacity, are given in Table III. The apparent molecular weight, the fraction α of the dimeric molecules dissociated according to the equation $Ga_2Cl_6 \rightleftarrows 2\,GaCl_3$, and the logarithm of the equilibrium constant K_p are tabulated for each temperature.

Log K_p plotted against $1/T \times 10^3$ gives a very smooth curve which is not a straight line, the slight curvature being real and indicating a difference in the heat capacity of the two molecular species present. The heat of dissociation, calculated from the slope of the line at 365° where the dissociation is about 50%, is about 20 kilocalories. The dissociation of the saturated gallium trichloride vapor at its b. p., 200°, is only 1.5%. A second run on a sample of 0.7365 g. in the same cell gave temperature–log K_p values which check very closely with those listed in Table III. The data agree well with the results reported by Fischer and Jubermann[2] for the range above 258°. They reported a heat of dissociation of 21 kilocalories calculated from a straight line representing log K_p plotted against $1/T \times 10^3$, but when their data are replotted clear evidence for the slight curvature noted in the present investigation is apparent.

Electron diffraction studies of gallium trichloride vapor in the temperature range in which it has been shown to be at least 98% dimeric are in progress to determine the configuration of the molecule, Ga_2Cl_6.

TABLE III

EQUILIBRIUM OF Ga_2Cl_6 AND $GaCl_3$

Temp., °C. (±0.5)	$1/T \times 10^3$	Pressure, mm. (±0.2)	Obsd. mol. weight	α	Log K_p
177.5	2.219	206.7	351.2	0.0029	−2.155
205.5	2.089	226.4	340.5	.0344	+0.027
232.2	1.979	245.6	331.3	.0631	0.592
264.3	1.861	279.3	309.8	.1369	1.330
298.5	1.749	324.0	283.9	.2406	1.901
329.5	1.659	373.0	259.9	.3552	2.333
364.7	1.568	436.2	235.2	.4974	2.759
395.7	1.495	493.9	217.7	.6177	3.086
430.1	1.422	558.3	202.4	.7400	3.432
463.0	1.359	611.4	193.5	.8201	3.701
498.3	1.296	662.5	187.1	.8826	3.971

Study of Gallium Dichloride

Preparation and Analysis.—Gallium trichloride was held during a period of one hour at 175° with an excess of gallium in an evacuated Pyrex reaction tube. The dichloride which formed was heated to 225° and distilled away from the non-volatile impurities. During the distillation some decomposition occurred, gallium trichloride condensing with the dichloride in the cooler portions of the tube and gallium remaining behind. This decomposition, however, was not very serious and a good yield of dichloride was obtained. The section of the tube containing the chlorides was sealed off and placed in an-

(6) Klemm and Tilk, *Z. anorg. allgem. Chem.*, **207**, 163 (1932).
(7) Craig and Drake, THIS JOURNAL, **56**, 584 (1934).
(8) Klemm, *Z. physik. Chem.*, **B12**, 17 (1931).
(9) Johnson, "Inorganic Syntheses," Vol. I, McGraw-Hill Book Co., New York, 1939, p. 27.

other glass tube which was evacuated and sealed. The tube containing the mixed chlorides was broken and the dichloride was purified by holding it at 160° and distilling off the more volatile trichloride. When most of the trichloride had been removed, the tube was cooled and the dichloride, which cracks away from the glass on cooling when fairly pure, was powdered by shaking. This powder was heated to 160° and the last traces of trichloride were driven to the cool end of the tube and sealed off. The pure gallium dichloride remaining was transferred and subdivided *in vacuo*, either by pouring the loose powder or by carefully melting it and allowing the liquid to flow. If the temperature was not raised much above the melting point, 170°, no appreciable decomposition occurred.

For analysis a weighed tube containing gallium dichloride was broken under 2% nitric acid. When the sample reacted with the nitric acid a small amount of gallium always formed. The solution was filtered and the gallium and fragments of glass were collected. The gallium and chlorine in the filtrate were determined as in the analysis of gallium trichloride. The metallic gallium was dissolved in aqua regia and precipitated as the hydroxide, which was added to that obtained from the main precipitation. The weight of the glass was determined and the weight of sample used was obtained by difference.

Anal. Calcd. for $GaCl_2$: Ga, 49.58; Cl, 50.42. Found: Ga, 49.42; Cl, 50.41.

The analytical results show that a chloride having a gallium–chlorine atomic ratio of 1 to 2 is secured by reduction of gallium trichloride under the conditions outlined, and that this compound can be freed completely of contaminating trichloride. No evidence of the formation of a monochloride in the presence of a large excess of gallium was observed.

Properties of Gallium Dichloride.—Gallium dichloride forms colorless crystals which were found to melt at 170.5 ± 0.5°, considerably higher than the value 164° reported by de Boisbaudran.[1] It is very probable that he did not have the pure substance. Liquid gallium dichloride does not wet glass readily but forms small droplets in the tube. The density of the liquid is greater than that of Pyrex glass, since fragments of the sample tubes were observed to float on the melt. The transparent colorless crystals which formed when gallium dichloride froze became opaque on further cooling and, in some cases, the movement through the solid of what appeared to be a crystalline boundary was observed. Single transparent crystals, grown by sublimation just below the melting point, were chilled quickly and were observed under the microscope to slowly become opaque. The evidence indicates that the solid is dimorphic and that the inversion is reversible, but attempts to determine the transition point were not conclusive. This transition is, however, not at all the same phenomenon as that reported by de Boisbaudran[1] as evidence of dimorphism of gallium dichloride. As will be pointed out later, the formation of a colored product when the dichloride is heated, which he mentioned, is satisfactorily explained by the formation of tiny droplets of gallium due to thermal decomposition.

Gallium dichloride deliquesces to give a thick sirupy colorless solution when exposed to the air. If it is placed in water a dark chocolate-brown solid precipitates. This solid slowly reacts with the water to give a gas, probably hydrogen, and the solid turns white, presumably forming gallic hydroxide. The liberation of a gas with an offensive odor, reported by de Boisbaudran and thought by him to be gallium hydride, was not observed in this investigation.

Gallium dichloride was found to dissolve readily in benzene with no apparent chemical interaction. It reacted with carbon tetrachloride and a black solid formed. This solid was insoluble in water, hydrochloric acid, and aqua regia and appeared to be carbon. Gallium dichloride is a powerful reducing agent.

In order to study the thermal stability of gallium dichloride, a sample in one end of an evacuated tube was heated and the other end of the tube was kept cool. Heating at 180° for three hours caused no change in the sample. At 200° a few small crystals of gallium trichloride collected in the cool end of the tube during one hour and, when the dichloride was cooled, a slight grayish color due to the formation of gallium was apparent in the solid. At still higher temperatures the decomposition to gallium and gallium trichloride was more rapid and globules of gallium were observed to form. When the dichloride was heated in Pyrex glass for some time at 500° the surface of the glass very slowly turned brown. The brown film could not be removed by aqua regia nor a mixture of nitric and chromic acids. These reagents would have reacted with the film had it been gallium monochloride. It is probable that the brown film was produced by a slight reaction of hot gallium or gallium dichloride with the glass.

Vapor Pressure and Apparent Molecular Weight of Gallium Dichloride.—In order to gain information concerning the molecular state of gallium dichloride and the equilibrium between the dichloride, gallium, and the trichloride, samples of the dichloride were heated in glass cells and vapor pressure and density determinations were made. The data for four runs, in

which the weight of sample per cc. of cell volume was varied, are given in Table IV. In each run the pressures for several temperatures were remeasured as the cell cooled. Good checks were obtained, proving that equilibrium had been satisfactorily established. The curves obtained by plotting temperature against pressure are shown in Fig. 2. In the first two runs the liquid phase was present for all the measurements and the curves are for saturated vapor pressures. Curves 3 and 4 flatten out beyond the point where the chlorides were completely vaporized. The equilibrium vapor pressures were found to decrease with decrease in weight of sample per cc. of cell volume. The data prove that the pressure of the vapor at equilibrium with the liquid is not a function of the temperature alone, but also is dependent upon the total weight of sample per unit volume of cell, and the system is divariant.

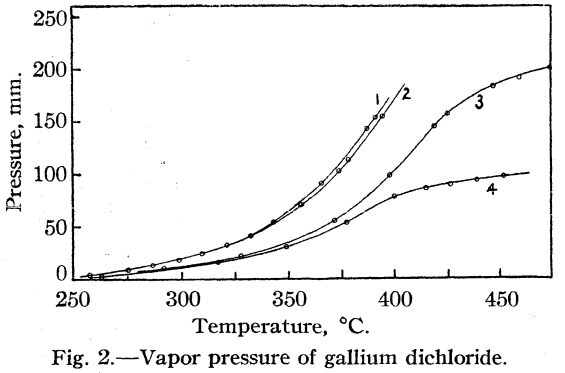


Fig. 2.—Vapor pressure of gallium dichloride.

Since the pressures were shown conclusively to be equilibrium values and the changes are easily reversible, the principle of the phase rule may be applied to the system. Experience with the dichloride has shown that above 200° it decomposes reversibly to gallium trichloride and gallium. Gallium trichloride in this temperature range has been shown to involve an equilibrium between the dimer and the monomer. Due to its high volatility the trichloride is probably completely in the vapor phase. Gallium is not volatile at the temperatures used and liquid gallium has been observed to exist as a separate phase in contact with liquid dichloride with no evidence of being soluble in the dichloride. Hence, in this system, when equilibrium prevails, there should be two liquid phases and one vapor phase. The system has two components and should be univariant. The authors are unable to suggest a satisfactory explanation of the observed divariancy. No reason for increasing the number of components or decreasing the number of phases can be suggested.

TABLE IV

VAPOR PRESSURE AND APPARENT MOLECULAR WEIGHT OF GALLIUM DICHLORIDE

Run	Cell volume, cc.	Sample, g.	Sample per cc. cell volume, g.	Temp., °C. (±0.5)	Pressure, mm. (±0.2)	Apparent mol. wt.
1	60	0.45	0.0075	239	2.4	
				258	4.9	
				276	8.8	
				299	17.9	
				321	31.9	
				343	53.8	
				367	93.6	
				387	141.4	
				391	152.8	
				425	284.6	
				449	431.1	
2	60	0.35	.00583	223	2.0	
				245	3.9	
				264	6.7	
				287	12.9	
				310	23.6	
				332	41.4	
				356	70.2	
				374	102.6	
				379	113.0	
				394	153.9	
3	225	0.1562	.000694	222	1.3	
				288	9.0	
				328	26.2	
				372	55.8	
				398	97.6	
				419	145.1	
				425	155.2	
				447	182.0	173
				460	190.4	167
				474	200.4	161
4	225	0.0754	.000335	220	1.3	
				263	3.8	
				317	16.3	
				349	31.1	
				365	44.6	
				377	54.3	
				400	78.3	180
				416	85.3	169
				427	89.6	163
				439	93.6	159
				452	97.3	156
				465	100.6	153

Molecular weights, calculated for the temperature ranges in Runs 3 and 4 where the chlorides were completely vaporized, are given in the last column in Table IV. These have been calculated on the assumption that the total weight of sample was in the vapor phase. Since some liquid gallium

undoubtedly was present, the actual average molecular weights for the vapor must be somewhat lower. The theoretical molecular weights for the molecules Ga_2Cl_6, $GaCl_3$, Ga_2Cl_4, and $GaCl_2$ are 352.2, 176.1, 281.2, and 140.6, respectively. The molecular weights in Table IV can be accounted for by postulating that the vapor was a mixture of molecules of $GaCl_2$ with heavier molecules, undoubtedly Ga_2Cl_6 and $GaCl_3$ and perhaps Ga_2Cl_4.

Klemm and Tilk found that solid gallium dichloride is diamagnetic and concluded that the solid is composed of Ga_2Cl_4 molecules and not $GaCl_2$. The present investigation indicates that considerable quantities of $GaCl_2$ molecules exist in the vapor above 400° under the conditions of the experiments. There seems to be no chance of determining the configuration of the gallium dichloride molecules by an electron diffraction study of its vapor because of the complex mixture of molecules present.

Summary

1. The equilibrium vapor pressures of gallium trichloride have been studied from 50 to 200° and its thermal properties have been determined. Vapor density studies from 117 to 498° give no evidence for association beyond the dimer. The saturated vapor is more than 98.5% dimeric up to 200°, and above this temperature reversible dissociation to the monomer becomes marked, the vapor being 88% dissociated at 498°.

2. Gallium dichloride has been prepared and a method for purifying it has been devised. The properties of the pure compound have been examined. Decomposition to gallium trichloride and gallium becomes appreciable at 200°. Vapor pressure measurements from 219 to 459° indicate that the system is divariant, although it apparently involves three phases and two components. Vapor density measurements in the range 400 to 470° indicate that the vapor contains some $GaCl_2$ molecules, in which gallium must show the anomalous valence of two.

3. No evidence for the existence of gallium monochloride was observed.

ITHACA, N. Y. RECEIVED APRIL 6, 1940

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, NO. 760]

A Theory of Chromatography

BY J. NORTON WILSON

The so-called chromatographic adsorption method of analysis was originated by the Russian botanist M. Tswett.[1] He discovered that if a solution containing a mixture of colored solutes is allowed to run through a vertical glass tube filled with a suitable powdered adsorbing material, the material adsorbed in the column appears as a series of colored bands, indicating that a partial separation of the components of the solution has taken place. This series of colored bands is known as a chromatogram. The separation can be completed by a procedure known as development of the chromatogram: there is poured through the column a suitable solvent which washes the colored bands down the tube at different rates, the lowest-lying band moving the fastest. If this process is carried out in a sufficiently long tube with the use of a sufficiently large volume of solvent it is possible to effect complete separation of the original components of the solution into a series of discrete bands separated by clear spaces of adsorbent.

The technique just outlined has become in recent years an important method for the separation, purification and identification of small amounts of complex naturally-occurring organic compounds; these developments have been described at length by Zechmeister and Cholnoky.[2] The method also has been applied to some extent in inorganic chemistry[3]; the most spectacular application in this field has been to the separation of lithium isotopes.[4]

Although the nature of the phenomenon seems to be roughly understood,[2] there has appeared so

(1) M. Tswett, *Ber. deut. botan. Ges.*, **24**, 234, 316, 384 (1906); *Ber.*, **41**, 1352 (1908); **43**, 3199 (1910); **44**, 1124 (1911).

(2) Zechmeister and Cholnoky, "Die chromatographische Adsorptionsmethode," Springer, Vienna, 1938; see also P. M. Jensen, "Die Bedeutung der chromatographischen Adsorptionsanalyse usw.," Dissertation, Technische Hochschule, Zurich, 1936; Zechmeister and Cholnoky, *Monatsh.*, **68**, 68–80 (1936).

(3) G. M. Schwab and co-workers, *Naturwiss.*, **25**, 44 (1937); *Angew. Chem.*, **50**, 546 (1937).

(4) T. I. Taylor and H. C. Urey, *J. Chem. Phys.*, **6**, 429 (1938).

far in the literature no quantitative treatment by means of which even an approximate prediction can be made of the width or rate of development of the bands to be expected in a given chromatogram. There is presented here a theoretical treatment which is based on the assumption of instantaneous equilibrium between the solution and the adsorbed material. The chromatography of a solution containing a single solute will be discussed first; it is evident that this simple problem must be solved before the more complicated problem of the chromatography of mixtures can be attacked successfully.

The Chromatography of a Solution Containing One Solute.—Let us consider a long column which contains M grams of adsorbent per centimeter of its length; we wish to calculate the distribution of adsorbed material in the column after a volume v of a solution containing solute at an initial concentration c_0 has passed through it. We shall assume that equilibrium between adsorbed material and the solution in contact with it is always maintained and that the volume of the interstices between the particles of adsorbent per unit length of the column is negligible. Let the isotherm which represents the adsorption of the given solute on the adsorbent be

$$q/m = f(c) \qquad (1)$$

where q is the number of millimoles of solute adsorbed on m grams of adsorbent in equilibrium with a solution whose concentration is c moles per liter. Then under equilibrium conditions at any point in the column where the concentration of solute is c there will be adsorbed Q millimoles of solute per centimeter length of the column, where

$$Q = Mf(c) \qquad (2)$$

Let the distance from the top of the column to any lower point in the column be x, and consider the changes in Q and c which occur at x when an element of volume dv of solution, whose concentration at x is c, passes through a thin cross-sectional layer of the column, of thickness dx, on which is adsorbed initially an amount $Q dx$ of solute. The number of millimoles of solute adsorbed on this layer will change by an amount $(\partial Q/\partial v)_x\, dv\, dx$, and the concentration of the solution will change by $(\partial c/\partial x)_v dx$. The number of millimoles of solute contained in the volume dv of solution will therefore change by an amount $(\partial c/\partial x)_v\, dx\, dv$. But since the total amount of solute is unchanged, we have

$$\left(\frac{\partial Q}{\partial v}\right)_x dv\, dx + \left(\frac{\partial c}{\partial x}\right)_v dv\, dx = 0 \qquad (3)$$

Substituting for Q from equation 2 we obtain as the differential equation for the chromatography of a single solute

$$\left[\frac{\partial}{\partial v}(Mf(c))\right]_x + \left(\frac{\partial c}{\partial x}\right)_v = 0 \qquad (4)$$

The general solution of this equation is

$$c = \varphi\{v - Mxf'(c)\} \qquad (5)$$

where φ is an arbitrary function and $f'(c)$ is the first derivative of $f(c)$. This equation will apply either to the process of formation of the chromatogram or the process of development. Different boundary conditions will apply to the two cases.

Let the chromatogram be formed by pouring a volume v of a solution whose initial concentration is c_0 through the column. The appropriate boundary conditions are:

$$\left.\begin{array}{ll} (1)\ \text{When } v = 0, & f(c) = 0 \text{ for } x \geqslant 0 \\ (2) \qquad v > 0, & f(c) = f(c_0) \text{ at } x = 0 \\ (3) \qquad vc_0 = \int_0^\infty Q dx = \int_0^\infty Mf(c) dx & \end{array}\right\} \qquad (6)$$

The last is a conservation condition.

It has been found that the first two boundary conditions are satisfied only by a discontinuous solution: $\varphi = const. = c_0$ up to a certain value of x; $\varphi = 0$ beyond that value. Application of conditions (2) and (3) leads to the solution:

$$\left.\begin{array}{l} \text{For } 0 \leqslant x < \frac{vc_0}{Mf(c_0)},\ Q = Mf(c_0) \\ \text{For } x > \frac{vc_0}{Mf(c_0)},\ Q = 0 \end{array}\right\} \qquad (7)$$

The discontinuous nature of the solution 7 accounts in a satisfactory way for the sharpness of the bands observed in chromatographic experiments; the result is also in accordance with the experimental observation that the intensity of color is approximately uniform throughout the band ($Q = Mf(c_0) = \text{const.}$).

We may now consider the case in which a band already formed is developed by passage through the column of a volume V of some solvent not necessarily the same as the solvent used in forming the band. Let the adsorption isotherm for the solute in the developing solvent be

$$q/m = F(c) \qquad (8)$$

We assume that the band was formed in accordance with equations 7, *i. e.*, that up to some point $x = x_1$, $Q = Q_0 = \text{const.}$; beyond x_1, $Q = 0$. We may also write

$$Q_0 = Mf(c_0) = MF(c_0') \qquad (9)$$

where c_0' is the concentration of solute which would be in equilibrium with Q_0 in the new solvent, and is not necessarily equal to c_0. The boundary conditions to be applied are

$$\left.\begin{array}{l}(1)\ \text{When } V = 0,\ 0 \leqslant x \leqslant x_1,\ Q = Q_0 = MF(c_0') = const. \\ (2)\ \text{When } V > 0,\ \text{at } x = 0,\ Q = MF(c) = 0 \\ (3)\ \text{For all values of } V,\ \int_0^\infty MF(c)dx = \int_0^\infty Q_0 dx = const.\end{array}\right\} \quad (10)$$

The solution of equation 4 for these conditions is

$$\left.\begin{array}{l}Q = 0 \text{ for } 0 \leqslant x < \frac{Vc_0'}{MF(c_0')} \text{ and for } x > x_1 + \frac{Vc_0'}{MF(c_0')} \\ Q = Q_0 \text{ for } \frac{Vc_0'}{MF(c_0)} < x < x_1 + \frac{Vc_0'}{MF(c_0')}\end{array}\right\} \quad (11)$$

The conclusion is thus reached that the band should remain sharp during the process of development and that its width should remain constant as it moves down the column. Experimentally these conclusions are found to hold only approximately.

The solutions 7 and 11 have been verified for the special case of the isotherm $f(c) = Kc$, where K is a constant, by an independent method in which the column was considered as being divided up into a large number of thin layers perpendicular to the wall of the tube. The process of formation or development of the chromatogram was treated as a succession of steps; in each step a small element of volume of solution was allowed to pass through the column layer by layer, coming into equilibrium with each layer in turn. The over-all effect was obtained by summing the effects of the individual steps in the process; a limiting value was then found for the summation by letting the thickness of the layers and the magnitude of the elements of volume become infinitesimal. The calculation will not be presented here in detail since it is tedious and treats only a special case. The method just outlined does, however, have the advantage of making clear the physical reason for the discontinuous nature of the bands: as an infinitesimal element of volume of solution passes over an infinitesimal element of length of the column just beyond the leading edge of the band, it deposits an infinitesimal amount of solute. The concentration of solute in the element of volume decreases in this process however by a *finite* amount, so that the concentration of the solution becomes zero in a small number of infinitesimal steps, *i. e.*, within an infinitesimal distance from the leading edge of the band.

In the development of equations 7 and 11 it has been assumed that the volume of the interstitial space between the particles of adsorbent is negligible, and that the volume v of solution or V of developing solvent is passed completely through the column before the measurement of the width and position of the band is made. In actual practice the interstitial volume is not negligible, and the developing solvent is added as soon as all of the original solution has entered the column, and is added continuously until the development has been carried to a convenient stage. If these facts are taken into account, the treatment of the problem is little altered.

Let the volume of interstitial space per centimeter length of the column be α cc. Then it is seen readily that the initial width of the band when a volume v of solution has entered the column is $vc^0/(\alpha c^0 + Mf(c^0))$. The edges of the band are sharp, as before, and the amount of solute per centimeter length of the band has the uniform value $\alpha c^0 + Mf(c^0)$ millimoles.

Let us now consider in detail the development of this band, assuming that the same solvent as was used in forming the band is added as soon as the solution has all entered the column. When a small volume ΔV of solvent enters the column, the liquid within the column will be displaced a distance $\Delta V/\alpha$. A volume ΔV of solution whose concentration is c^0 will leave the lower edge of the band and will form an extension to the band of width $\Delta Vc^0/(\alpha c^0 + Mf(c^0))$. Suppose the upper edge of the band meanwhile has migrated a distance Δx. Since the liquid between this point and the point $x = 0$ has not passed through any part of the band, the volume of solvent which has been used to dissolve the solute formerly adsorbed between $x = 0$ and $x = \Delta x$ is $\Delta V - \alpha\Delta x$. If the concentration of solute in this volume of solvent has reached the value c^0, then

$$(\Delta V - \alpha\Delta x)c^0 = Mf(c^0)\Delta x$$

Whence

$$\Delta x = \frac{\Delta Vc^0}{\alpha c^0 + Mf(c^0)}$$

We conclude that the band should maintain the constant width $vc^0/(\alpha c^0 + Mf(c^0))$, and should migrate at a rate $c^0/(\alpha c^0 + Mf(c^0))$ cm. per cc. of developing solvent added to the column, provided the same solvent is used in developing the band as was used in forming it. A similar analysis

may be used to discuss the case in which a new solvent is used for development, whose adsorption isotherm is $q/m = F(c)$. As in the previous treatment (equation 9) let $f(c^0) = F(c^{0\prime})$. Then it is shown readily that the width of the band will change to $vc^0/(\alpha c^{0\prime} + Mf(c^0))$; after it has reached this value the width will remain constant and the band will migrate at a rate $c^{0\prime}/(\alpha c^{0\prime} + Mf(c^0))$ cm. per cc. of developing solvent added to the column. In practice the width of the bands varies widely with changes in the nature of the developing solvent. A discussion will now be given of the formation and development of chromatograms formed from solutions containing several solutes. In this discussion the volume of the interstitial space between the particles of adsorbent will for convenience be neglected. The treatment can easily be extended to take the interstitial volume into account.

The Chromatography of Mixtures.—The treatment of the formation and development of a chromatogram containing a mixture of solutes is very simple if the solutes are independently adsorbed, *i. e.*, if the adsorption isotherm of each solute is a function of the concentration of that solute alone. In that case each of the solutes will form a uniform band of width $vc_i^0/Mf_i(c_i^0)$, where v is the initial volume of the solution, c_i^0 is the initial concentration of the i'th solute, and $f_i(c_i)$ is the corresponding adsorption isotherm. These bands, each of which has its origin at $x = 0$, will overlap; if the solutes are colored, the resulting chromatogram will appear as a series of contiguous color zones, throughout each of which the color is constant. On development with the original solvent, each of the bands will move independently of the others at a rate equal to $c_i^0(Mf(c_i^0)$ cm. per cc. of developing solvent drawn through the column. In general these rates will be different; after sufficient development the bands will be completely separated, and will have, according to the present treatment, their original width and intensity.

In most actual cases, however, the adsorption of one solute is affected by all other solutes present, so that the adsorption isotherm of the i'th solute in a solution containing n solutes is a function of the concentrations of all the solutes. We thus write for the i'th solute

$$q_i/m = f_i(c_1, c_2, c_3, \ldots c_n) \qquad (12)$$

There appear to exist no general rules for predicting the form of the functions f_i in terms of the adsorption isotherms which apply to pure solutions of the individual solutes.[5] It is usually true that the adsorption of one solute from a solution of given concentration is less when a second solute is present than when only the first solute is present, and that the decrease in the adsorption of the first solute is greater, the greater the adsorption tendency of the second solute. It is well known, however, that the reverse effect, co-precipitation, sometimes occurs, and that in other cases two solutes may adsorb independently of each other. The difficulty of finding an explicit expression for the f_i's will not affect our general considerations, however, and we shall see that the results obtained from the treatment of the chromatography of mixtures, with the interdependence of the adsorption isotherms taken into account, are qualitatively similar to the results for the case in which all solutes adsorb independently of one another.

The Formation of a Mixed Chromatogram.—Let a chromatogram be formed from a volume v of a solution containing n solutes whose initial concentrations are $c_1^0, c_2^0, \ldots c_n^0$. Let the adsorption isotherms be defined by equation 12. For the i'th solute the differential equation, its general solution, and the boundary conditions governing the formation of the chromatograms are, in analogy with equations 4, 5 and 6:

$$\left.\begin{aligned} &\left[\frac{\partial}{\partial v}\{Mf_i(c_1, c_2, \ldots c_n)\}\right]_x + \left[\frac{\partial c_i}{\partial x}\right]_v = 0 \\ &c_i = \varphi\left[v - xM\frac{\partial f_i(c_1, c_2, \ldots, c_n)}{\partial c_i}\right] \end{aligned}\right\} \quad (13)$$

Boundary conditions

$$\left.\begin{aligned} &(1)\ \text{When } v = 0,\ x \geqslant 0: f_i(c_1, c_2, \ldots, c_n) = 0 \\ &(2)\qquad v > 0,\ x = 0: f_i(c_1, c_2, \ldots, c_n) = f_i(c_1^0, c_2^0, \ldots, c_n^0) \\ &(3)\quad vc_i^0 = \int_0^\infty Qi\,dx = \int_0^\infty Mf_i(c_1, c_2, \ldots, c_n)dx \end{aligned}\right\} \quad (14)$$

The solution for a given value of v is similarly $Q_i = Mf_i(c_1^0, c_2^0, \ldots, c_n^0)$ between $x = 0$ and $x = x_j$ at which point one of the solutes, say the j'th solute, has become exhausted. At this point there will be a discontinuity. Evidently

$$x_j = \frac{vc_j^0}{Mf_j(c_1^0, c_2^0, \ldots, c_n^0)} \qquad (15)$$

The solute which is exhausted at the first discontinuity is thus the one for which the quantity on the right side of equation 15 is lower than that for any other component in the solution. It should be noted that each of the solutes is adsorbed to

(5) Freundlich, "Colloid and Capillary Chemistry," Methuen, London, 1926, p. 200 ff.

some extent between $x = 0$ and the first discontinuity at $x = x_j$.

The amount of the i'th solute adsorbed between 0 and x_j is

$$Mf_i(c_1^0, c_2^0, \ldots, c_n^0)x_j = \frac{f_i(c_1^0, c_2^0, \ldots, c_n^0)}{f_j(c_1^0, c_2^0, \ldots, c_n^0)} vc_j^0 \quad (16)$$

The amount of the i'th solute originally present in the solution was vc_i^0. Hence the concentration of the i'th constituent in the solution which traverses the column beyond the first discontinuity is

$$c_i' = c_i^0 - \frac{f_i(c_1^0, \ldots, c_n^0)}{f_j(c_1^0, \ldots, c_n^0)} c_j^0 \quad (17)$$

The concentrations of all constituents change in this way at the first discontinuity; beyond this point the adsorption of the i'th solute is given by the equation

$$Q_i = Mf_i(c_1', c_2', \ldots, c_n'); c_j = 0 \quad (18)$$

This solution will hold between x_j and the point x_k where the k'th constituent is exhausted and the next discontinuity occurs. The changes in concentration at this discontinuity can be calculated in a similar way, and the process continued until all the solutes are exhausted. The equations representing the formation of a chromatogram from a volume v of a solution containing a mixture of solutes may then be summarized thus:

$$\begin{aligned}
&\text{For } 0 \leq x < x_j, \quad Q_i = Mf_i(c_1^0, c_2^0, c_3^0, \ldots)\\
&\qquad x_j = \frac{vc_j^0}{Mf_j(c_1^0, c_2^0, \ldots)}\\
&\text{For } x_j < x < x_k, \quad Q_i = Mf_i(c_1', c_2', c_3', \ldots)\\
&\qquad c_i' = c_i^0 - \frac{f_i(c_1^0, c_2^0, c_3^0, \ldots)\, c_j^0}{f_j(c_1^0, c_2^0, c_3^0, \ldots)} \quad (19)\\
&\qquad x_k = x_j + \frac{vc_k'}{Mf_k(c_1', c_2', c_3', \ldots)}\\
&\qquad Q_j = 0\\
&\text{For } x_k < x < x_l \quad Q_i = Mf_i(c_1'', c_2'', c_3'', \ldots)\\
&\qquad c_i'' = c_i^0 - \frac{f_i(c_1^0, c^0, c^0, \ldots)c_j^0}{f_j(c_1^0, c_2^0, c_3 \ldots)} - \frac{f_i(c_1', c_2', c_3', \ldots)c_k'}{f_k(c_1', c_2', c_3', \ldots)}\\
&\qquad x_l = x_k + \frac{vc_l''}{Mf_j(c_1'', c_2'', c_3'', \ldots)}\\
&\qquad Q_j = Q_k = 0
\end{aligned}$$

In Fig. 1A is shown a graphical representation of the results obtained from the application of these equations to the hypothetical case of a chromatogram formed from 10 cc. of a solution containing three solutes, each at an initial concentration of 0.02 mole per liter. It has been assumed that the adsorption isotherms are of the type proposed by Langmuir[6] to account for the sorption of dilute gases on solid surfaces:

$$q_i/m = A \frac{a_i c_i}{1 + \sum_j a_j c_j} \quad (20)$$

where A is a constant characteristic of the adsorbent and a_i is a constant characteristic of the i'th solute. The summation is taken over all solutes. This isotherm was chosen because it affords a convenient representation of the effect of one solute in lowering the adsorption of another. For convenience A and M have been taken equal to unity. The value $a_1 = 40$ has been assigned to solute number 1, with $a_2 = 20$ and $a_3 = 5$. For comparison in Fig. 1B, 1C and 1D are shown the chromatograms which would be formed from 10 cc. of a solution containing only one of these solutes at a concentration of 0.02 mole per liter. In connection with Fig. 1A it should be noted that whether the adsorption of a given solute increases or not after passing a discontinuity in the chromatogram depends on the total amount of the given solute which has been adsorbed up to that point, as well as on the solute which is exhausted at the discontinuity.

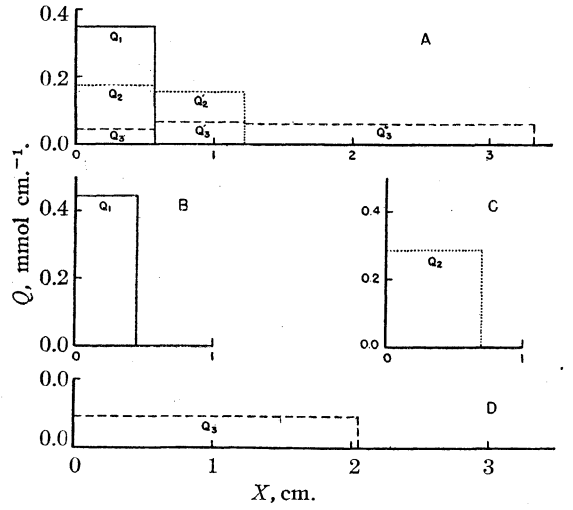


Fig. 1.—A: Chromatogram formed from a solution containing three solutes. B, C, D: Chromatograms formed from the same volume of solution containing only one solute (Solutes 1, 2 and 3, respectively). X is the vertical distance measured from the top of the column.

The Development of Mixed Chromatograms.—Since the discussion of the development of a mixed chromatogram becomes very complicated in the general case, the present treatment will be

(6) I. Langmuir, *Phys. Rev.*, **2**, 331 (1913); **6**, 79 (1915); THIS JOURNAL, **38**, 2221 (1916).

limited to the case of a chromatogram formed from a solution containing two solutes. Let the chromatogram formed from a volume v of a solution of initial concentrations c_1^0, c_2^0, be represented as follows:

$$\left.\begin{aligned} 0 < x < x_1\text{:}\quad & Q_1 = Mf_1(c_1^0, c_2^0);\ Q_2 = Mf_2(c_1^0, c_2^0) \\ & x_1 = \frac{vc_1^0}{Mf_1(c_1^0, c_2^0)} \end{aligned}\right\}\ \text{Band 1}$$

$$\left.\begin{aligned} x_1 < x < x_2\text{:}\quad & Q_1 = 0;\ Q_2 = Mf_2(c_2') \\ & x_2 = x_1 + \frac{vc'}{Mf_2(c_2')} \\ & c_2' = c_2^0 - \frac{f_2(c_1^0, c_2^0)\, c_1^0}{f_1(c_1^0, c_2^0)} \end{aligned}\right\}\ \text{Band 2} \qquad (21)$$

If this chromatogram is developed with a small volume V of the same solvent as was used in forming the chromatogram, the two solutes will migrate at different rates. The origin of the adsorbed solute 2 will migrate to a point $x_{20} = Vc_2^0/Mf_2(c_1^0, c_2^0)$. The solution as it reaches the point x_1 will have acquired the concentrations c_1^0, c_2^0; as it passes this point solute 1 will be completely, and solute 2 partially adsorbed. The discontinuity at x_1 will therefore migrate to a point $(v + V)c_1^0/Mf_1(c_1^0, c_2^0) = x_1' = (v + V)x_1/v$. The amount of solute 2 adsorbed between this point and $x = 0$ is then

$$\left\{\frac{(v + V)c_1^0}{Mf_1(c_1^0, c_2^0)} - \frac{Vc_2^0}{Mf_2(c_1^0, c_2^0)}\right\} Mf_2(c_1^0, c_2^0) = (v + V)c_1^0 \frac{f_2(c_1^0, c_2^0)}{f_1(c_1^0, c_2^0)} - Vc_2^0$$

The concentration c_2'' of solute 2 which passed the point x_1' is then given by the expression

$$Vc_2'' = vc_1^0 \frac{Mf_2(c_1^0, c_2^0)}{Mf_1(c_1^0, c_2^0)} - (v + V)c_1 \frac{f_2(c_1^0, c_2^0)}{f_1(c_1^0, c_2^0)} + Vc_2^0$$

Whence

$$c_2'' = c_2^0 - c_1^0 \frac{f_2(c_1^0, c_2^0)}{f_1(c_1^0, c_2^0)} = c_2' \qquad (22)$$

Thus the concentration of solute 2 in the solution traversing band 2 during this development is the same as went into the formation of the second band. The lower end of band 2 will therefore migrate to the point

$$x_2' = x_1' + \frac{(v + V)c_2'}{Mf(c_2')} = \frac{V + v}{v} x_2$$

The development will proceed in this way until the point x_{20}, the origin of solute 2, overtakes the point x_1', the discontinuity between bands 1 and 2. This will occur at a volume

$$V = v \left\{\frac{c_2^0 f_1(c_1, c_2^0)}{c_1^0 f_2(c_1^0, c_2^0)} - 1\right\}^{-1}$$

When V exceeds this value, the bands will separate. The solute 2 will all be contained in the second band which on further development will migrate at the rate $c_2'/Mf_2(c_2')$, and will maintain the constant width

$$\frac{vc'}{Mf_2(c_2')} \left\{\frac{c_2^0 f_1(c_1^0, c_2^0)}{c_2^0 f_1(c_1^0, c_2^0) - c_1^0 f_2(c_1^0, c_2^0)}\right\}$$

It should be noted that the volume V required for separation of the bands is infinite if the ratio $c_2^0 f_1(c_1^0, c_2^0)/c_1^0 f_2(c_1^0, c_2^0)$ is equal to unity. The departure of this ratio from unity is thus a measure of the ease of separation of two substances by chromatography on a given adsorbent. If the ratio is equal to unity the separation is impossible unless a different adsorbent is used or the value of the ratio is changed by altering the concentration of the initial solution.

The development of solute 1 is somewhat more complicated. As the origin of solute 2 moves through the first band, it will be accompanied by a discontinuity in the adsorption of solute 1. Suppose the adsorption of solute 1 between the beginning of the first band and the origin of solute 2 in the first band is given by $Q_1 = Mf_1(c_1')$. When the volume V of developing solvent has passed through the system, the origin of solute 1 will have moved to $x_{10} = Vc_1'/Mf_1(c_1')$. Between x_{20} and x_1' the adsorption of solute 1 is given by $Q_1 = Mf_1(c_1^0, c_2^0)$. Application of the conservation condition gives

$$vc_1^0 = Mf_1(c_1')(x_{20} - x_{10}) + Mf_1(c_1^0, c_2^0)\,(x_1' - x_{20}) \qquad (23)$$

Substituting the expressions previously derived for x_{20}, x_{10} and x_1', we obtain

$$c_2^0\{f_1(c_1') - f_1(c_1^0, c_2^0)\} = f_2(c_1^0, c_2^0)\{c_1' - c_1^0\} \qquad (24)$$

This equation can be solved for c_1' if the initial concentrations and the adsorption isotherms are known. When the two bands have separated, the solute 1 will be all contained within the first band, whose rate of migration will then be $c_1'/Mf_1(c_1')$, and whose width will maintain the constant value $vc_1^0/Mf_1(c_1')$. In Fig. 2 there is shown a graphical representation of several stages in the development of a hypothetical chromatogram which is assumed to have been formed from 10 cc. of a solution in which $c_1^0 = c_2^0 = 0.02$ mole liter^{-1}. The adsorption isotherms have been assumed to be of the Langmuir type, with

$$Q_1 = MA \frac{a_1 c_1}{1 + a_1 c_1 + a_2 c_2};\quad Q_2 = MA \frac{a_2 c_2}{1 + a_1 c_1 + a_2 c_2}$$

For convenience M and A have been given the value unity, and the values $a_1 = 40$, $a_2 = 10$ have

been assumed. Q_1, Q_2 are in units of millimoles per centimeter.

The treatment evidently can be extended to more complex situations involving a greater number of solutes, but the computations become much more involved. The development of such a complex chromatogram may take place in any one of a number of ways depending on the initial concentrations and the adsorption isotherms. The initial development will lead to broadening of the bands. At some point in the development the initial band system of contiguous bands will split into two sub-systems, each of which may later split again. This process will continue until each of the solutes initially present occupies a separate band, provided that the condition for separability of the solutes is fulfilled.

Discussion of the Theory

The theory presented here is in essence a very simple one. Since the processes of diffusion, adsorption and desorption proceed at finite rates, however, the present theory, in which it is assumed that the effects of diffusion can be neglected and that equilibrium between solute and adsorbed material is instantaneously reached, can provide only an approximate description of the phenomena of chromatography. The theory does account for the qualitative features of chromatography in a satisfactory way and provides a convenient basis from which a more precise theory may be developed.

The theory predicts that a chromatogram formed from a solution containing only one solute should form a single sharp band, and that if this chromatogram is developed with the same solvent as was used in its formation, the band should maintain a constant width and sharply defined edges. Experimentally none of these predictions is quantitatively verified. Solutes which adsorb strongly do in many cases form surprisingly sharp bands whose width does not vary rapidly on development and whose edges become diffuse only slowly. On the other hand, a solute which is not strongly adsorbed often forms a band whose lower edge is somewhat diffuse when the chromatogram is formed. The width of such a band and the diffuseness of its edges may increase quite rapidly as development proceeds. These observations are readily explained when the factors which have been neglected in the present treatment are taken into account. The width of a band may increase

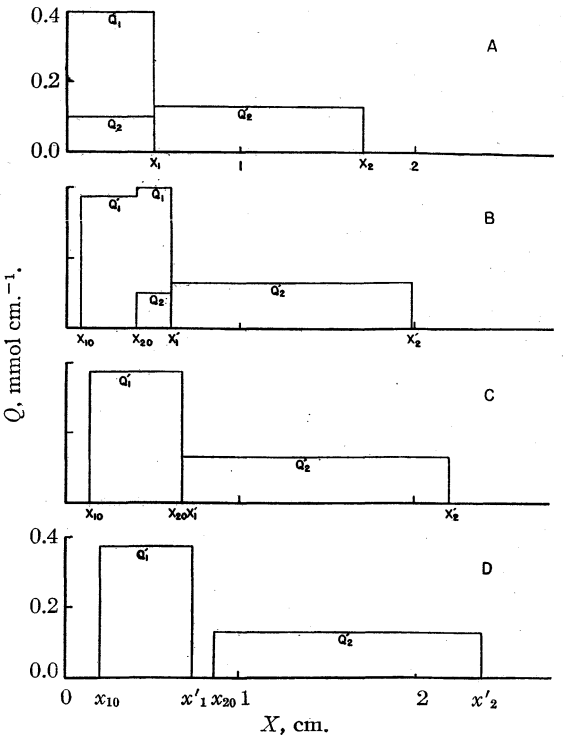


Fig. 2.—Stages in the development of a two-solute chromatogram, after various volumes V of developing solvent have passed through the column: A, $V = 0$; B, $V = 2.00$ cc.; C, $V = 3.33$ cc.; D, $V = 5.00$ cc. X is the vertical distance measured from the top of the column.

because of diffusion, or because the leading edge of the band migrates too rapidly on account of a low rate of adsorption, or because the trailing edge of the band migrates too slowly on account of a low rate of desorption. All these effects will lead the edges of the band to become diffuse. The process of diffusion is probably the least important of the factors leading to broadening of the bands since its effects are automatically corrected to a considerable extent as development proceeds. It is likely that in many cases a solute which is adsorbed but slightly will also have a low rate of adsorption, so that the leading edge of its chromatogram should migrate too rapidly and become more and more diffuse. The effects arising from low rates of adsorption and desorption can be diminished by decreasing the rate at which liquid flows through the column, but as the rate of flow decreases the importance of diffusion effects increases.

A further complication is introduced by the fact that the flow of liquid through the column is not uniform. The liquid usually flows more slowly at

the center of the column than near the walls of the tube. It is difficult to eliminate this effect completely, though its importance can be reduced somewhat by careful packing of the column. As a result of the varying rate of flow the development of a chromatogram proceeds more rapidly near the wall of the tube than at the center, so that an initially uniform and approximately horizontal band becomes dome-shaped (concave downward). Diffusion can then occur in a radial direction in the column, and the effect of this diffusion is not corrected for in the process of development. As a consequence the colored band as it is observed through the wall of tube appears to become wider and both edges to become diffuse. When the column is removed from the tube and carefully sliced it is often found that the band is narrower and more sharply defined near the center of the column than near the periphery.

Some preliminary experiments have shown that the band widths and rates of development predicted by means of the theory from adsorption measurements are correct as to order of magnitude. In these experiments all adsorption data used were determined directly with the same adsorbent as was used in the chromatographic experiments. The value of α, the volume of voids per centimeter length of the column, was determined by measuring the length of the packed column filled by a measured volume of liquid. The experiments will not be described in detail because of the wide variation in adsorbent properties among samples of a given adsorbent obtained from different sources. The experiments were moreover of only an exploratory nature; a systematic study of the extent to which the predictions of the theory approximate the results of experiment has yet to be made.

The following results were obtained. The initial width of a band formed on alumina from a solution of picric acid in benzene was 10% greater than the width predicted from adsorption measurements; on the other hand, a band formed on alumina from an aqueous solution of methylene blue had a width three times the predicted value. In a test of the relation between the width of the band and its rate of migration on development, the observed rate of development was found to be about 80% of the predicted rate. In this experiment a solution of lycopene in a mixture of benzene and petroleum ether was used; the adsorbent was calcium carbonate. The width of the lycopene band did not remain constant, but increased from 2 mm. to 4 mm. while the band was migrating 15 mm.

The theory presented here differs qualitatively from earlier ideas about the subject in one important respect. The belief has been expressed by some authors that the first color zone of a mixed chromatogram contains, before development occurs, essentially only the most strongly adsorbed solute. According to the present treatment, on the other hand, the first color zone should contain some of each solute initially present, in proportions determined by the initial concentrations and the adsorption isotherms. That the latter conclusion is correct was verified by the following experiment. A chromatogram was prepared by pouring a large volume of an extract of dried grass in a mixture of petroleum ether and benzene into a large column packed with powdered sugar. Seven bands of various widths and colors were formed; the first was quite wide. The liquid was forced completely through the column, which was then dried and removed from the tube. The first color zone was cut from the column and repacked on top of a second narrower column freshly packed with powdered sugar. When the same solvent as was used in preparing the first chromatogram was poured through this new column, the same sequence of six color zones appeared below the top band as occurred below the top band in the original chromatogram; the intensities of color and the relative widths of the bands were moreover roughly the same as in the original band system, in accordance with the present theory.

The present theory is also applicable to capillary analysis. In capillary analysis the lower end of a vertical strip of porous paper is allowed to dip into a solution of colored solutes. The solution rises in the paper strip because of capillarity; if the solutes are adsorbed by the paper a chromatogram is formed at the lower end of the paper in accordance with equations 19. This chromatogram may then be developed by dipping the lower end of the strip of paper into pure solvent and allowing solvent to rise in the paper through the initial chromatogram.[7]

The present treatment also may be applied to the chromatographic technique developed by W. G. Brown.[8] In this technique the chromatogram is formed on a sheet of blotting paper pressed be-

(7) Schwab and Jockers, *Angew. Chem.*, **50**, 546 (1937).
(8) W. G. Brown, *Nature*, **143**, 377 (1939).

tween glass plates, the upper one of which has a small hole bored through the center. The solution is allowed to run into the blotting paper from a glass tube whose fine capillary tip passes through the hole in the upper plate and presses against the paper. The chromatogram spreads radially from the point of contact as center. If M' is the mass of blotting paper per square centimeter, Q' the number of millimoles adsorbed per square centimeter, and r the radius measured from the point of contact, the equations analogous to equation 7 and 11 become, for formation of the chromatogram

$$\left.\begin{aligned} 0 \leqslant r_2 < \frac{vc^0}{\pi M'f(c^0)} \quad & Q' = M'f(c^0) \\ r^2 > \frac{vc^0}{\pi M'f(c^0)} \quad & Q' = 0 \end{aligned}\right\} \qquad (25)$$

and for development of the chromatogram with a volume V of the same solvent

$$\left.\begin{aligned} 0 < r^2 < \frac{Vc^0}{\pi M'f(c^0)}, \quad & Q' = 0 \\ \frac{Vc^0}{\pi M'f(c^0)} < r^2 < \frac{(V+v)c^0}{\pi M'f(c^0)}, \quad & Q' = M'f(c^0) \\ r^2 > \frac{(V+v)c^0}{\pi M'f(c^0)}, \quad & Q' = 0 \end{aligned}\right\} \qquad (26)$$

Thus it is predicted that the area of the ring will remain constant, and that the band will become narrower as development proceeds. This prediction is usually not verified experimentally because of diffusion and the finite rates of adsorption and desorption. The equations 25 and 26 may be readily corrected to take into account the interstitial volume between the fibers of the paper, or extended to the case of a mixed chromatogram. If the interstitial volume is taken into account it readily can be shown that the area of the band should remain constant if the same solvent is used for development as was used in forming the chromatogram, but should change if a different solvent is used for development.

It remains to discuss the possibility of using the present theory to predict on the basis of known sorption isotherms whether or not a given adsorbent may be used for the chromatographic separation of a given set of solutes. In view of the approximation involved in the neglect of diffusion and of rates of adsorption and desorption, it is evident that only an approximate prediction can be made; the complete application of the theory requires moreover a knowledge of the dependence of the sorption isotherms on the concentrations of all solutes present. In most cases it is more difficult and tedious to acquire this knowledge than to determine empirically which adsorbents are useful for the separation. In case adsorption isotherms for solutions containing only single solutes are available, a rough prediction can be made by assuming that the solutes are independently adsorbed; the separations actually obtained will in general be better than those predicted on the basis of this assumption. A better approximation may be made by fitting the adsorption isotherm for each solute, using measurements made on solutions containing that solute alone, to a curve of the Langmuir type: $q_i/m = Ka_ic_i/(1 + a_ic_i)$. It is usually possible to fit adsorption data to such a curve over small ranges of concentration, especially at low concentrations, say from 0 to 0.01 mole per liter. A very rough approximation to the adsorption isotherms which apply to a solution containing a mixture of solutes may then be obtained by using the a_i's obtained in this way, assuming that in mixed solutions $q_i/m = Ka_ic_i/(1 + \Sigma_i a_ic_i)$. Calculations made in this way, in spite of their approximate nature, might be useful for instance in deciding on a suitable adsorbent with which to attempt the separation of amino acids resulting from protein hydrolysis.

Summary

A theory of chromatographic analysis has been developed on the basis of the assumption that equilibrium between solution and adsorbent is instantaneously established and that the effects of diffusion can be neglected. The theory accounts qualitatively for the separations effected in chromatographic analysis, for the uniformity of color in the adsorption bands, and for the sharpness of the edges of the bands. Some experimental evidence is presented to show that the theory provides a semi-quantitative description of chromatographic adsorption. A brief discussion is given of the factors which make quantitative agreement between the theory and experiment unlikely.

PASADENA, CALIFORNIA RECEIVED FEBRUARY 12, 1940

[CONTRIBUTION FROM COATES CHEMICAL LABORATORY, LOUISIANA STATE UNIVERSITY]

The Kinetic Decomposition of Ethyl Chlorocarbonate II. Foreign Gas Effects

BY A. R. CHOPPIN AND G. F. KIRBY, JR.

A study of the kinetics of decomposition of pure ethyl chlorocarbonate was published recently and the present report constitutes the second in this series. The effects of foreign materials on the rate constant have been considered in specific relation to their normal decomposition described in the previous report. The techniques employed were chosen to coincide as nearly as possible with those of the original investigation, thus minimizing errors of comparison.

The thermoregulation and reaction system were essentially as described in the previous article.[1] The reaction was investigated by a static method in an all-glass system. A glass diaphragm and an automatic pressure regulating device were used in following the rate of reaction.

Experimental

Before the first run with any gas each reaction cell was thoroughly cleaned and flamed. A small bulb containing ethyl chlorocarbonate was first sealed into the cell and the foreign gas supply attached to the cell through a small side arm. The cell was then alternately evacuated and rinsed with the gas to displace adsorbed molecules of air and water vapor. The gas was next admitted to the desired pressure and the reaction vessel sealed. The vessel was finally brought to the temperature of the bath and the reactant bulb broken with the glass enclosed hammer.

When liquids of high vapor pressure were used as foreign materials a similar procedure was followed. However, when the vapor pressure was too low for the effective utilization of this method solutions of the liquid in ethyl chlorocarbonate were prepared. These solutions were chosen by composition to give approximately the desired partial pressure of each component, introduced into bulbs, and discharged in the cell in the usual way. The substances were tested thoroughly for chemical interaction before this procedure was employed.

In some cases the foreign substance was admitted at room temperature and the gas laws used to predict its partial pressure at reaction temperature. In other cases the foreign gas was allowed to come to temperature equilibrium before breaking the reactant bulb. Checks between the two methods showed the error to be negligible.

Oxygen, carbon dioxide, hydrogen and nitrogen were purified in conventional washing procedures for certain runs. They were not refractionated, however. Commercial carbon tetrachloride, hexane and benzene were subjected to careful fractionation. Nitric oxide was prepared according to the method of Johnston and Giauque[2] and stored in a five-liter container. Because of the difficulty of separating nitric oxide from certain other oxides of nitrogen, particularly nitrous oxide, the effect of the latter compound on the reaction was investigated. For this purpose a cylinder of the commercial product was used without further purification.

(1) Choppin, Frediani and Kirby, THIS JOURNAL, **61**, 3176 (1939).
(2) Johnston and Giauque, *ibid.*, **51**, 3194 (1929).

Experimental Results

As previously reported[1] the temperature 175° is approximately in the middle of the measurable range and gives rate constants of a convenient magnitude. This temperature was used for the greater number of runs on foreign gas effects. The effects of foreign materials on the rate were catalogued by comparison with the values for the specific rate constant k obtained in the previous research, and checked by controls during the present investigation. Where low pressure runs were made this effect was taken into account in tabulating the effect of foreign materials.

Runs were first made in the presence of an excess of carbon dioxide for the purpose of testing the reaction for reversibility. No measurable equilibrium effect could be detected. However, the carbon dioxide molecules seemed quite effective in maintaining the rate. No appreciable decrease in the value of k was detected as long as the total initial pressure remained above 175 mm.

Nitrogen and oxygen were also quite effective in maintaining the high pressure energy distribution. Curves showing typical rates of decomposition in the presence of these gases are shown in Fig. 1. Curves also have been included to show the effects of benzene, carbon tetrachloride and hexane. As may be seen from Table I, hexane increases the rate slightly while benzene and carbon tetrachloride show slight depressions. The effect is so slight that they may be regarded as relatively inert.

For many reactions hydrogen has been found quite effective in maintaining the rate at low pressures of reactant. In the case of ethyl chlorocarbonate, however, hydrogen fails to fulfill this function. It is less effective than any of the previously mentioned gases.

Chlorine exhibits a positive catalytic effect which does not seem to be directly proportional to the amount of chlorine present. Analyses of the products indicated no change in the nature of

TABLE I

P_i (total)	$P_{for.\ gas}$	$K_{obsd.}$	$K_{pure\ reac.}$
	Nitrogen		
124	30	0.040	0.034
148	120	.043	.037
200	65	.047	.045
236	25	.041	.045
175[a]	51	.180	.183
	Oxygen		
24	15	0.015	0.015
200	98	.043	.045
280	251	.041	.045
322	80	.047	.045
	Carbon Dioxide		
102	45	0.030	0.030
285	178	.048	.045
286	206	.050	.045
83[a]	25	.114	.11
	Hydrogen		
131	57	0.029	0.036
146	98	.022	.037
337	294	.016	.045
386	327	.023	.045
	Chlorine		
300	50	0.114	0.045
301	144	.099	.045
350	155	.106	.045
527	342	.117	.045
	Water		
136	70	0.0816	0.036
151	14	.0781	.038
	Nitrous Oxide		
68	50	0.019	0.026
125	60	.017	.033
168	35	.017	.039
225	111	.022	.045
268[c]	101	.062	.089
	Benzene		
200	104	0.029	0.044
493	133	.035	.045
	Hexane		
108	54	0.052	0.031
164	82	.053	.039
	Carbon Tetrachloride		
256	192	0.033	0.045
260	130	.038	.045
308	231	.035	.045
	Nitric Oxide		
236	72	0.065	0.045
281	50	.057	.045
320	45	.055	.045
319	16	.046	.045
155[c]	30	.098	.089

[a] Results of H. A. Frediani. [b] 195°. [c] 185°.

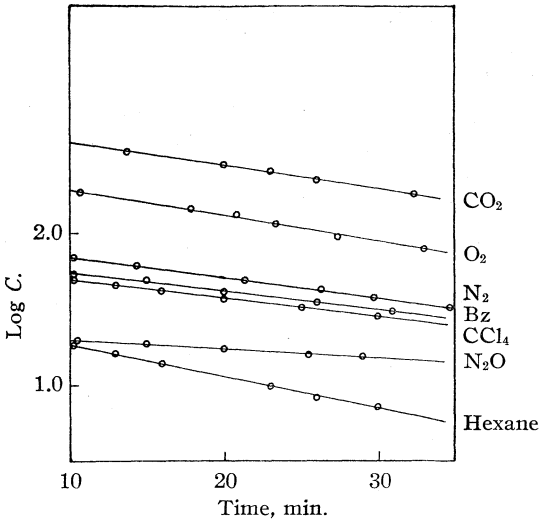


Fig. 1.

the reaction. It will be noted from Table I that the specific rate constant is more than doubled. The reaction definitely does not follow a first order rate over the first ten minutes. During this period the rate was more nearly second order with respect to the reactant. However, no good agreement for either was obtained over appreciable periods of time. Since the degree of catalysis does not seem to vary with the partial pressure of chlorine, one might conclude that the action takes place at the walls with adsorbed chlorine atoms acting as active centers. Thus a condition of saturated adsorption might govern the extent of catalytic action.

Ethyl chlorocarbonate is known to undergo both ammonolysis and hydrolysis. In the liquid state these reactions take place at the phase boundary, the reaction with aqueous ammonia proceeding quite rapidly and that with water at a much slower rate. At 175° the hydrolysis proceeds quite rapidly and the products slightly catalyze the thermal decomposition of any ethyl chlorocarbonate in excess. The presence of simultaneous reactions is apparent, and the initial stages can be described by neither a first nor second order rate. In view of the difficulty of separating these reactions the calculations of rate give at best a qualitative picture of the process, indicating principally the final effect of the bimolecular products upon the unimolecular reaction.

Inhibition by nitric oxide has been widely used as a test for one type of chain mechanism. Hinshelwood[3] has found low partial pressures quite

(3) Staveley and Hinshelwood, *J. Chem. Soc.*, 1568 (1937).

effective in suppressing the rates of a number of reactions proceeding through aliphatic free radical mechanisms. Pressures of nitric oxide of the order of 1 or 2 mm., suggested as being sufficient to seriously alter the reaction rate, were found to have no effect in the present case. As the partial pressure of nitric oxide was increased, however, a period of induction was observed. The length of the induction period varied with the partial pressure of nitric oxide (Fig. 2). At the end of the initial inhibition the reaction proceeded with a velocity greater than normal. Rate constants obtained for this region showed a consistent increase over normal values. Considering the high partial pressures of nitric oxide which caused this effect and the general unfavorable conditions for radical production, the indicated mechanism is some transient chemical interaction between the gas and the reactant. A catalytic effect of large partial pressures of nitric oxide has been observed in the decomposition of a number of compounds.[4,5,6]

In view of the difficulty of obtaining nitric oxide free from traces of nitrous oxide several runs were made with nitrous oxide to determine its effect on the reaction. Smooth curves were the result, with rates slightly depressed.

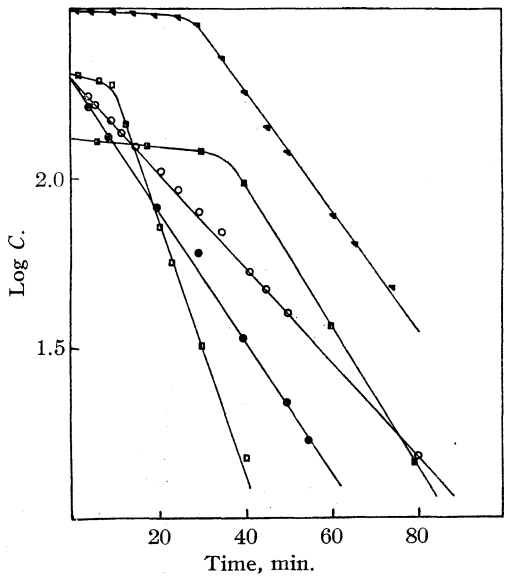


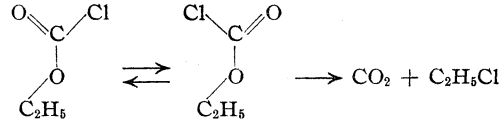
Fig. 2.—Effect of varying nitric oxide pressure; ◥, 95 mm.; □, 50 mm.; ■, 71.5 mm.; ●, 30 mm.; ○, 16 mm.

Discussion of Results

The observations cited above indicate a mechanism of extreme simplicity. This conclusion was first strongly implied by the quantitative decomposition of ethyl chlorocarbonate to carbon dioxide and ethyl chloride. Chemical analyses of these products have been further supported by spectrographic investigations.[7] No evidence of chlorine or phosgene could be obtained. Furthermore, ethyl chlorocarbonate does not absorb in the visible and the first appreciable ultraviolet absorption occurs with a continuum beginning in the region of 2500 Å.

The temperature at which decomposition takes place and the low energy requirement seems to preclude the possibility of an initial disruption into unstable fragments since the activation energy is lower by at least 40,000 cal. than any of the minimum bonding energies that might be involved. In addition to this the wall effects are negligible, the reaction proceeds smoothly over a wide range of pressures and in most cases there is no marked inert gas effect.

These facts seem to point to a mechanism involving an internal rearrangement with the elimination of carbon dioxide. The structure of ethyl chlorocarbonate as established by dipole measurements is in accord with such a mechanism.[8,9] The following resonating structures have been proposed by earlier investigators:



The work being carried on in this Laboratory, it is hoped, will be of value in establishing the significance of any structural changes insofar as they affect the decomposition.

Summary

The decomposition of ethyl chlorocarbonate has been investigated with regard to foreign materials. The products of the decomposition and a number of chemically inert gases are effective in maintaining the high pressure rate. The reaction is catalyzed by chlorine and, after a slight period of induction, by nitric oxide.

The kinetic results indicate a decomposition mechanism of a simple nature, probably involving an internal rearrangement with the elimination of carbon dioxide.

UNIVERSITY, LA. RECEIVED JANUARY 2, 1940

(4) Staveley and Hinshelwood, *Proc. Roy. Soc.* (London), **A154**, 335 (1936).
(5) Staveley and Hinshelwood, *J. Chem. Soc.*, 812 (1936).
(6) Daniels and Veltman, *J. Chem. Phys.*, **7**, 756 (1939).
(7) Unpublished data of C. H. Smith.
(8) Mizushima and Kubo, *Bull. Chem. Soc. Japan*, **13**, 174 (1938).
(9) Unpublished results of Robert E. Wood.

[CONTRIBUTION FROM THE STERLING CHEMISTRY LABORATORY, YALE UNIVERSITY]

Dialkylacetyl Biurets

BY ARTHUR J. HILL AND WILLIAM M. DEGNAN[1]

In spite of the considerable success of the hypnotics of the acetamide, acyl urea, and barbituric acid types, a need still exists for less toxic compounds with hypnotic properties. The structural features which appear to account for the pharmacological action of the above-mentioned compounds are two: one or more -CONH- groups, and branched-chain alkyl groups whose function is apparently to confer high lipoid-solubility on the molecules of which they are a part. Biuret, $NH_2CONHCONH_2$, has the significant -CONH- group repeated within its structure, and furthermore has been demonstrated to have a very low toxicity. It was to be expected, therefore, that acyl biurets containing branched-chain alkyl groups might combine high hypnotic effectiveness with low toxicity. Accordingly a number of dialkylacetyl biurets were prepared with a view to the study of their pharmacological properties. The dialkylacetyl groups were chosen for their demonstrated value in the acetamide and acyl urea series.

A survey of the literature shows that two approaches to the acyl biurets have been most extensively employed. Acetyl, benzoyl, and phenacetyl biurets have been prepared by the direct acylation of biuret with the acid chlorides[2,3,4,5] and benzoyl biuret has been prepared by the treatment of urea with benzoyl chloride in the presence of pyridine.[4,6] However, attempts to reproduce these results, and to extend the method to the preparation of dialkylacetyl biurets, were disappointing, the yields being very low. Attention was therefore directed to the development of a new synthesis of acyl biurets.

The work of Billeter[7] on the preparation of acyl isocyanates, and the reaction of these compounds with amines and alcohols, together with a number of patents[8,9,10,11] on the preparation of acyl ureas and acyl urethans by these reactions, suggested the possibility of carrying out the reaction

$$RCONCO + R'NHCONH_2 \longrightarrow RCONHCONHCONHR'$$

Accordingly, a series of dialkylacetyl isocyanates was prepared by the modification of Billeter's method patented by Baeyer and Co.,[12] and these isocyanates were allowed to react with urea, substituted ureas, and thiourea, in ether or benzene suspension, and the desired biurets were obtained in yields as high as 83% of the theoretical.

Experimental

Dialkylacetyl Chlorides.—The dialkylacetic acids used were prepared by the method of Levene and Cretcher,[13] with the exception of phenylethylacetic acid, which was prepared by the saponification and subsequent decarboxylation of phenylethylmalonic ester. The acids were converted to the corresponding acid chlorides by allowing them to stand with a 100% excess of thionyl chloride for twelve hours, then refluxing to complete the reaction. The acid chlorides were purified by distillation through a packed column under vacuum.

Dialkylacetyl Isocyanates.—The appropriate acid chloride was dissolved in five volumes of carefully dried diethyl ether and added slowly during stirring to a slight excess of freshly prepared silver cyanate suspended in dry ether. A round-bottomed flask fitted with a sealed stirrer and a reflux condenser carrying a calcium chloride tube was found to be convenient as a reaction vessel. In every case reaction commenced spontaneously and was completed by refluxing the reaction mixture gently for one to three hours. The suspension was then quickly filtered through a Büchner funnel to remove the silver chloride, and the ether was removed from the filtrate in the usual manner. The resi-

TABLE I[a]

Acyl isocyanate	B. p., °C.	Yield, %
Diethylacetyl[b]	59–61° at 31 mm.	90
n-Butylethylacetyl	78–85° at 20 mm.	81
s-Butylethylacetyl	55–56° at 11 mm.	59
Isoamylethylacetyl	100–105° at 30 mm.	82
Dibutylacetyl	68–73° at 12 mm.	74
Phenylethylacetyl	111–115° at 11 mm.	42
Allylethylacetyl	83–85° at 34 mm.	65
Ethyldimethylacetyl	65–70° at 10 mm.	70
Benzoyl[b]	88–91° at 20 mm.	50
Phenacetyl[b]	116–120° at 20 mm.	40

[a] By reason of the high reactivity of acyl isocyanates with atmospheric moisture, direct analysis of these compounds was impracticable. They were characterized through their derivatives with urea. [b] Previously reported.

(1) From a dissertation submitted by William M. Degnan to the Faculty of the Graduate School of Yale University in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

(2) Ostrogovich, *Ann.*, **288**, 318 (1895).

(3) Ostrogovich, *ibid.*, **291**, 377 (1896).

(4) Ostrogovich, *Bul. soc. stiinte Cluj*, **4**, 528 (1929).

(5) Ostrogovich and Tanislau, *Gazz. chim. ital.*, **64**, 800 (1934).

(6) Bloch and Sobotka, THIS JOURNAL, **60**, 1656 (1938).

(7) Billeter, *Ber.*, **36**, 3213 (1903).

(8) German Patent 271,682.

(9) German Patent 275,200.

(10) German Patent 316,902.

(11) U. S. Patent 1,424,236.

(12) German Patent 275,215.

(13) Levene and Cretcher, *J. Biol. Chem.*, **33**, 505 (1918).

due was then distilled under vacuum. The isocyanates must be carefully protected from moisture throughout the course of preparation and purification, as they react vigorously with water to give the corresponding acetamides and carbon dioxide. The yields in this preparation ranged from 40–90%. Table I lists the acyl isocyanates prepared.

Substituted Ureas.—Monoethyl and diethyl urea were prepared by the nitrourea dearrangement method of Davis and Blanchard.[14] Other ureas were prepared by the conventional treatment of the amine hydrochlorides with potassium cyanate.

Dialkylacetyl Biurets.—These compounds were prepared by the reaction of the appropriate isocyanate with urea or a substituted urea in diethyl ether or petroleum ether. The general technique employed was as follows: the urea was suspended (or dissolved where soluble) in dry ether or petroleum ether in an Erlenmeyer flask. Slightly less than one equivalent of the acyl isocyanate dissolved in dry ether was then added quickly. A reflux condenser carrying a calcium chloride tube was attached to the flask and the suspension (or solution) was refluxed gently until the characteristic odor of the isocyanate had disappeared. The heating time varied from three to forty-eight hours. When reaction was complete the suspension (or solution) was cooled and filtered if the product appeared only slightly soluble in cold ether, or the ether was removed by distillation if the product appeared appreciably soluble. The residue was then crystallized from hot water, hot alcohol, or hot dilute alcohol. Two recrystallizations usually sufficed.

Dialkylacetyl Thiobiurets.—It was found that the dialkylacetyl isocyanates reacted slowly or not at all with thiourea at the temperature of boiling ether, so reactions in this series were carried out in boiling benzene. Thiourea was suspended in dry benzene and exactly one equivalent of the isocyanate was added. The suspension was heated for twelve hours, during which time the thiourea disappeared and a clear yellow solution with a characteristic unpleasant odor was formed. This was cooled in an ice-bath to precipitate a jelly-like material which was filtered off with some difficulty. Attempts to crystallize this crude product from water, alcohol, dilute alcohol, benzene, and dilute acetone failed, amorphous solids being obtained in each case. The acyl thiobiurets were purified by dissolution in cold alcohol, followed by precipitation by the addition of an equal volume of cold water. Several repetitions of this operation gave products which melted sharply. The acyl thiobiurets were obtained as slightly yellow amorphous powders with marked pyroelectric properties. Yields in this series were low, due primarily to handling losses during purification.

Table II lists the acyl biurets prepared. Benzoyl biuret and phenacetyl biuret are not new, having been prepared primarily for comparison with the products reported by Ostrogovich and his co-workers.[3,5] Benzoyl biuret prepared from the isocyanate was shown by mixed melting point to be identical with a sample prepared by the direct benzoylation of biuret with benzoyl chloride.

(14) Davis and Blanchard, THIS JOURNAL, **51**, 1797 (1929).

TABLE II

Biuret	Yield, %	M. p., °C.	Nitrogen, % Calcd.	Found
Diethylacetyl	70	178	20.89	20.89
n-Butylethylacetyl	52	106	18.34	18.24
s-Butylethylacetyl	..	89	18.34	18.19
Isoamylethylacetyl	34	177	17.35	17.21
Dibutylacetyl	61	158	16.34	16.21
Phenylethylacetyl	83	154	16.83	16.90
Allylethylacetyl	..	106	19.71	19.56
Benzoyl[a]	33	233	20.20	20.29
Phenacetyl[a]	66	203	19.00	18.87
Ethyldimethylacetyl	..	171	20.89	20.95
1-Diethylacetyl-5-ethyl	..	245	18.34	18.30
1-Diethylacetyl-5,5-diethyl	20	104	16.34	16.39
1-Diethylacetyl-5-*p*-phenacetyl	79	127	14.14	14.20
1-Diethylacetyl-5,5-cyclopentamethylene	..	113	15.61	15.68
Ethylene-*bis*-diethylacetyl[b]	66	246	19.55	19.65
1-Diethylacetyl-4-thio-	..	132	19.20	19.35
1-Isoamylethylacetyl-4-thio-	..	123	16.22	16.36
1-Allylethylacetyl-4-thio-	..	123	18.34	18.40

[a] Previously reported. [b] Crystallized from glacial acetic acid.

Pharmacological Results

Preliminary pharmacological tests[15] indicate that these compounds compare favorably with sodium barbital in hypnotic effectiveness. They do not show any anesthetic (depressor) action. The toxicities of these compounds, with the exception of those of the thiobiurets, are remarkably low; doses as high as 500 mg./kg. have no permanent ill effects on the test animals. The presence of branched chains in the acyl radical increases effectiveness. Alkylation in the 5-position of the biuret chain also increases effectiveness, 1-diethylacetyl-5,5-cyclopentamethylene biuret being the most active of the compounds tested.

Summary and Conclusions

1. A series of acyl biurets, including dialkylacetyl biurets, 1-dialkylacetyl-5-alkyl biurets, alkylarylacetyl biurets, and 1-dialkylacetyl-4-thiobiurets, has been synthesized by the reactions of appropriate acyl isocyanates upon urea, substituted ureas, and thiourea.

2. Preliminary pharmacological investigation indicates that these compounds possess a moderate hypnotic activity, accompanied by extremely low toxicity. The high margin of safety afforded would indicate that members of this series should be valuable sedatives.

NEW HAVEN, CONN. RECEIVED APRIL 20, 1940

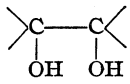
(15) The pharmacological tests were carried out by the Calco Chemical Co. Division of American Cyanamid and Chemical Corp.

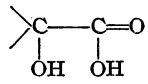
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, BANTING INSTITUTE, UNIVERSITY OF TORONTO]

Oxidative Cleavage of α-Keto Acids and α-Keto Alcohols by Means of Lead Tetraacetate

BY ERICH BAER

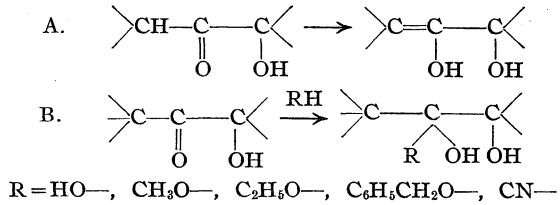
In 1930 and 1931 Criegee[1] reported the possibility of splitting glycols into aldehydes and ketones by oxidation with lead tetraacetate in absolutely dry solvents. The usefulness of this reaction has been considerably increased by the recent observation of Baer, *et al.*,[2] that, where the rate of reaction between glycol and oxidizing agent is sufficiently rapid, the same operation may be carried out successfully in water, or in organic solvents containing water. Nevertheless, the method was still confined to compounds which *already contained* a pair of adjacent hydroxyl groups as exemplified by glycols (I) or α-hydroxycarboxylic acids (II).


(I)


(II)

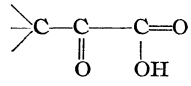
Very little has been published[3] however, concerning the extension of this technique to compounds which were not glycols, but whose structure would permit the formation of adjacent hydroxyl groups. Examples of such a type could be expected among compounds containing vicinal keto-hydroxyl groups which might be able to form the necessary hydroxyls either by enolization (reaction A) or, by addition to the keto group of water, alcohols (*e. g.*, methyl alcohol, ethyl alcohol, benzyl alcohol) or hydrocyanic acid, etc. (reaction B).

An indication of the possibility of such oxidative cleavage is to be found in two papers by Baeyer[4] in which are described the conversion of



keto-isocamphoronic acid into dimethyl tricarballylic acid, pinoyl-formic acid into pinic acid and homoterpenoyl-formic acid into homoterpenylic acid by oxidation with lead peroxide in the presence of acetic or sulfuric acid. These reactions are probably to be interpreted as oxidative cleavages induced by the intermediary formation of lead tetraacetate or plumbic disulfate.

From the great variety of compounds which could conceivably form two adjacent hydroxyl groups according to reaction A or B, a few representatives of the α-ketocarboxylic acids (III) and the α-keto alcohols (IV) (with aliphatic and aromatic substituents) have been chosen as experimental material.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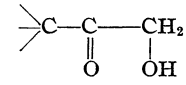

(IV)

The substances examined were pyruvic acid, phenylpyruvic acid, trimethylpyruvic acid, and phenylglyoxylic acid; acetyl-methylcarbinol, benzoylcarbinol, benzoin and anisoin. Their ability to enter into cleavage reactions with lead tetraacetate has been studied, and the results of the investigation constitute the subject matter of this paper.

After it had been established that under certain conditions all these substances are split by lead tetraacetate, an attempt was made to obtain a more detailed understanding of the reaction. The main point at issue was whether a pair of adjacent hydroxyl groups is actually necessary for cleavage. Secondly, if so, which of the above-mentioned possibilities (A or B) describes their formation? Finally, does the cleavage of the resulting "pseudoglycol" follow the same mechanism which Criegee postulated for the splitting of α-glycols?

(1) Criegee, *Ann.*, **481**, 275 (1930); *Ber.*, **64**, 260 (1931); *Angew. Chem.*, **50**, 153 (1937).

(2) E. Baer, J. Grosheintz and H. O. L. Fischer, THIS JOURNAL, **61**, 2607 (1939).

(3) The present investigation of the cleavage of α-keto alcohols was completed and nearly ready for publication when a paper entitled "Über durch Pervanadinsäure katalysierte Oxydationen" was published by W. Treibs (*Ber.*, **72**, 1194 (1939)) in which he mentioned, in support of his theory on the oxidation and cleavage of saturated cyclic ketones by H_2O_2, that he had succeeded in splitting an α-keto alcohol (benzoin) by lead tetraacetate into benzoic acid and benzaldehyde. However, he gave no experimental data in the above-mentioned paper. Apparently Treibs did not recognize the mechanism involved in the cleavage of α-keto alcohols and α-keto acids with lead tetraacetate, *viz.*, the necessity of forming a pair of new adjacent OH groups as the initial step in this reaction, when he asserts that α-keto acids are not cleavable by lead tetraacetate. Since considerable time has now elapsed and Treibs' experimental data have not yet appeared, it has been decided to publish the paper which was written at that time.

(4) A. Baeyer, *ibid.*, **29**, 1916, 1919, 2792 (1896).

The elucidation of the first two questions is closely connected and they have been investigated together. It is well-known that α-keto acids and α-keto alcohols may form enols or addition compounds, and therefore it seemed equally possible that the cleavage could occur through the enol forms or through the addition products of the keto forms.

To distinguish between these two possible reaction courses we were guided by the following considerations. If it can be shown that oxidative cleavage does not take place when conditions allow the formation of enol forms, but does occur as soon as substances capable of forming pseudoglycols by addition are supplied, the probability of the first alternative being correct may be considered very slight. The second alternative will be further supported if α-keto compounds which are unable to form enols because of their lack of an enolizable hydrogen atom adjacent to the keto group (*e. g.*, trimethylpyruvic acid, phenylglyoxylic acid) undergo an oxidative cleavage in the presence of glycol-forming substances, but not in their absence.

The experiments, therefore, were carried out so that in each case the α-keto acid or α-keto alcohol was dissolved in an indifferent solvent and brought into contact with lead tetraacetate in the absence of water or any other glycol-forming substance. If no significant amount of cleavage (*e. g.*, enol cleavage) or consumption of oxidizing agent had been detected after a definite time interval, then water, an alcohol, or hydrocyanic acid was added. The products of cleavage of the addition compound so formed were determined quantitatively where practicable or in other cases isolated as completely as possible and identified.

The investigation of the action of lead tetraacetate upon keto acids was particularly simple by reason of the ease with which one of the products of the reaction, carbon dioxide, could be determined quantitatively. For this operation, the keto acids were dissolved in glacial acetic acid, lead tetraacetate was added, and the carbon dioxide evolved was measured gravimetrically or volumetrically. All four of the keto acids examined yielded, with lead tetraacetate alone, only a trivial amount of carbon dioxide. The evolution of gas always came quickly to a complete standstill, and never amounted to more than 5–10% of the theoretical. It was probably caused by unavoidable traces of moisture in the solvents or the reagents, or adsorbed on the walls of the reaction vessel (see blank values in experiments II (1a, 2a, 3a); III (1a, 2a, 3a); IV (1a, 2a); V (1a). After a considerable time only a small amount of the keto acid and lead tetraacetate were used up. The addition of water, methanol, ethanol, benzyl alcohol, or hydrocyanic acid to the same mixture caused an almost instantaneous and complete cleavage of the α-keto acids. The cleavage reaction yielded 1 mole of carbon dioxide (Expt. II (1a, 2a, 3a); III (1a, 2a); IV (1a, 2a); V (1a)) for each mole of keto acid consumed and required 1 mole of lead tetraacetate (Expt. II (1c); III (1c); IV (1c); V (1c); VI (1b); VIII (1c); IX (1c)).

The compounds other than carbon dioxide resulting from the cleavage of the α-keto acids were determined by repeating the experiments as before, but using larger quantities so that the products could be isolated. According to the nature of the glycol-forming substance supplied the oxidative cleavage yielded either the free acid (Expt. III (1b); IV (1b); V (1b), its ester (Expt. II (3b); III (3); IV (2b)), or the nitrile of the original keto acid (Expt. IV (3)). These were in most cases easily isolated in good yield. However, the figures given in the experimental part obviously represent the lower limits of the actual quantities formed, because of some unavoidable losses in the isolation processes.

The presence of acetic acid arising from lead tetraacetate during the reaction made it difficult to detect the acetic acid or trimethylacetic acid expected as cleavage products of pyruvic acid and trimethylpyruvic acid, respectively. In these two cases the oxidative cleavage was carried out in benzene and in the presence of benzyl alcohol, so that instead of the free acids, their benzyl esters, which are easily isolated, resulted. These compounds as well as the silver salts, obtained by treatment of their saponification products with silver nitrate, served to identify the cleavage products as acetic or trimethylacetic acid, respectively.

The only exception to the normal course of the keto acid cleavage so far observed occurred in the case of phenylpyruvic acid. The cleavage product of this compound, to be analogous to those of the other keto acids, should have been phenylacetic acid. However, the cleavage required 2 moles of lead tetraacetate, and no crystal-

line product could be isolated. Since saponification gave mandelic acid, the original cleavage product was probably acetylmandelic acid. To explain its formation we may assume that the lead tetraacetate simultaneously effected the oxidative cleavage and an acetylation of the —CH_2— group, situated as it is between two strongly negative substituents. Similar acetylations caused by lead tetraacetate are already known, *e. g.*, that of acetoacetic ester.[5] Phenylpyruvic acid was the only keto acid of this type investigated. However, it may be expected that the cleavage of other acids of the same type will also yield derivatives of hydroxy acids. Since the hydroxy acids which would be obtained by saponification can easily be converted into aldehydes by a further oxidative reaction with lead tetraacetate, it is possible to obtain from this type of α-keto acids, aldehydes with two carbon atoms less (Equation C).

$$\text{(C)}\quad RCH_2COCOOH \xrightarrow[+\ \text{saponification}]{2Pb(OAc)_4} RCHOHCOOH \xrightarrow{Pb(OAc)_4} RCHO$$

The investigation of the α-keto alcohols was carried out as outlined above. Here, as before, the effect of lead tetraacetate on the keto compounds was first examined in dry solvents and in the absence of any glycol-forming substances. Contrary to the experience with keto acids, a slow consumption of oxidizing agent was observed. After the lead tetraacetate had completely disappeared, attempts to recognize the product of the reaction led to the isolation of the direct oxidation products of the keto alcohols—their diketones—which were obtained in good yields, but no more than traces of cleavage could be detected (see Expt. X (a, b, c)).

However, when the experiments were conducted so that the lead tetraacetate was added to the solutions of the α-keto alcohols in the presence of hydroxyl-forming substances (*e. g.*, water or alcohol) then the oxidative cleavage occurred at once and the two cleavage products, 1 mole of acid or its ester and 1 mole of aldehyde or ketone, could be isolated either as such or in the form of derivatives (see Expts. VI, VII, VIII, IX).

In the case of α-keto alcohols the oxidative cleavage and the direct oxidation tend to occur simultaneously. In the presence of glycol-forming substances the cleavage reaction predominates; in the absence of such substances the direct oxidation becomes the main reaction but proceeds far more slowly than does the above cleavage reaction.

The results of the experiments may be summarized thus. In the *absence* of hydroxyl-forming substances α-keto acids are not attacked by lead tetraacetate, while α-keto alcohols are oxidized slowly to their corresponding diketones. In the *presence* of hydroxyl-forming substances α-keto acids and α-keto alcohols undergo rapid oxidative cleavage.

These observations can probably be best interpreted as follows.

For the occurrence of oxidative cleavage of α-keto acids and α-keto alcohols the initial formation of a pair of adjacent hydroxyl groups is necessary. These glycols (or pseudoglycols) are formed by the addition of water, alcohols, or hydrocyanic acid to the keto group according to reaction B.

The oxidative cleavage of the keto compounds takes place, therefore, through their pseudoglycol forms and not, or only to an insignificant extent, through their enol form.

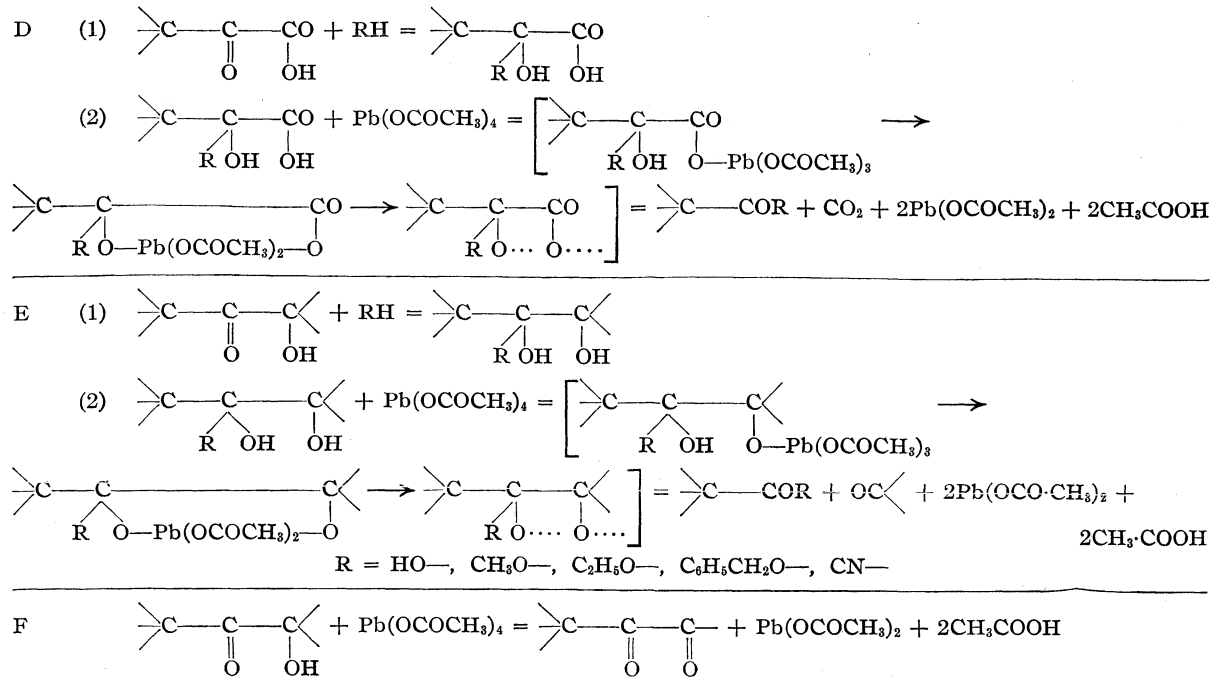
Further support for this view is the fact that trimethylpyruvic acid and phenylglyoxylic acid, which, by reason of their lack of enolizable hydrogen atoms cannot form an enol, are split by lead tetraacetate only in the presence of glycol-forming substances.

From the fact that the oxidative cleavage of α-keto acids and α-keto alcohols takes place only after the formation of a glycol, and from the nature of the resulting products, it may be assumed that the actual cleavage reaction is brought about by the same mechanism as the typical glycol cleavage produced by the action of lead tetraacetate. The fact that the cleavage products of pseudoglycols are in part different from those of true glycols does not invalidate the assumption as to the parallelism of the two reaction mechanisms, but is a natural consequence of the varying degrees of oxidation of the starting materials.

If one attempts to apply Criegee, Kraft, and Rank's[6] proposed reaction mechanism to formulate the course of the cleavage reaction following the initial formation of the two adjacent hydroxyl groups (D, 2; E, 2), a combination of the pseudoglycols with tetravalent lead must be assumed. According to Criegee these lead compounds induce the formation of biradicals which then

(5) O. Dimroth and R. Schweizer, *Ber.*, **56**, 1380 (1923).

(6) R. Criegee, L. Kraft and B. Rank, *Ann.*, **507**, 159 (1933).



decompose spontaneously into the end-products. The lead compounds assumed as intermediate stages are probably short-lived and have not yet been isolated. Their detection not only would have constituted a support for Criegee's scheme, but would have demonstrated also the close relationship between the two reactions. A substance which precipitated when lead tetraacetate was added to a solution of phenylglyoxylic acid in dry acetic acid, and which at first was suspected of being such an intermediate compound, was found later to be the plumbous salt of the starting material (Expt. IV (1)).

Even though the proof is lacking that the oxidative cleavage of pseudoglycols by lead tetraacetate proceeds through intermediate compounds similar to those postulated by Criegee for the cleavage of true glycols, the equations D and E include the assumed intermediary compounds which are placed in brackets.

The possible application of the use of lead tetraacetate to split α-keto acids and α-keto alcohols may simplify the solution of a number of problems concerning chemical constitution or tautomerism just as Criegee's glycol cleavage has proved very valuable for solving similar problems. An example of such an application where the use of lead tetraacetate would constitute a considerable simplification, is that of the tau- reactions of 1,2-ketols investigated by v. Auwers, Ludewig, Müller, Pötz and Noll.[7] In this case, the presence of substance I or II even in a mixture should be easy to detect and to determine on the basis of the cleavage products obtained by oxidation with lead tetraacetate in the presence of water as shown in equations G and H.

(G) $C_6H_5COCH(OH)CH_3$ (I) $\xrightarrow{Pb(OCOCH_3)_4,\ H_2O}$ $C_6H_5COOH + CH_3CHO$

(H) $C_6H_5CH(OH)COCH_3$ (II) $\xrightarrow{Pb(OCOCH_3)_4,\ H_2O}$ $C_6H_5CHO + CH_3COOH$

Another use of this reaction with lead tetraacetate is the detection of compounds which it is seldom possible to isolate. For example, the formation of addition products of water or alcohols with the keto group of α-keto alcohols and α-keto acids, which can be considered as hydrates or semiacetals, is often problematical. However if a mixture containing such components be subjected to an oxidative cleavage, the nature of the decomposition products will show whether or not formation of addition products has occurred.

A further practical application is the quantitative determination of α-keto acids by measurement of the carbon dioxide evolved during oxidative cleavage with lead tetraacetate.

The same reaction may be used to differentiate α-keto acids qualitatively from β-, γ-, etc., keto

(7) Von Auwers, H. Ludewig and A. Müller, *Ann.*, **526**, 143 (1936); v. Auwers, H. Pötz and W. Noll, *ibid.*, **535**, 219 (1938).

acids since in such an analogous series only the alpha-keto acids evolve carbon dioxide. To carry out this operation the acid is dissolved in as little water, or water-containing acetic acid, as possible and lead tetraacetate added. The evolution of carbon dioxide indicates the presence of an alpha-keto acid.

The investigation is being extended to other classes of compounds which should be capable of cleavage by application of the same principle.

Experimental

α-Keto Acids

I. Methods of Following Oxidative Cleavage

The cleavage reactions to be described give rise to carbonic acid and an organic acid or an acid derivative. The reactions may, therefore, be followed quantitatively by determining the carbon dioxide evolved, and qualitatively by identifying the second acid (or its derivative). The procedures used are described in detail below.

(1). Quantitative Determination of Carbon Dioxide (Gravimetric).[8]—The quantitative determination of carbon dioxide evolved during the oxidative cleavage was carried out by passing a slow current of dry, carbon dioxide-free air through the reaction flask to sweep the evolved gas into an absorption vessel. By means of gentle suction, air was drawn through a train assembled as follows: (1) a potassium hydroxide solution and calcium chloride tube; (2) the reaction vessel (a 125-cc. Erlenmeyer flask, with 3-holed rubber stopper, carrying a dropping funnel and the inlet and outlet tubes); (3) a U-tube filled with calcium chloride and kept at −10°; (4) a weighed absorption vessel for the quantitative determination of carbon dioxide. A weighed amount of the substance was placed in the dry reaction flask and absolutely water-free acetic acid and lead tetraacetate were added through the dropping funnel. The mixture was warmed to 50° while a slow stream of air was drawn through the apparatus. Since, for the establishing of the pseudoglycol theory, it was just as essential to prove the non-evolution of carbon dioxide in the absence of hydroxyl-forming substances as it was to determine the quantity of carbon dioxide produced in their presence, such a blank experiment always preceded the actual test run. The increase in weight of the carbon dioxide absorption vessel was measured after thirty minutes. The amount of carbon dioxide found in the absence of hydroxyl-forming substances was in all cases only a small per cent. of the total and was probably due to unremovable minute traces of moisture in the apparatus, in the substance, or in the solvent. After the apparatus was reassembled, water (or anhydrous hydroxyl-forming substances under investigation) was allowed to flow into the decomposition flask which was warmed to 50° while air was drawn through the apparatus until the weight of the carbon dioxide absorber remained fairly constant (forty to sixty minutes).

(2) Identification of the Second Acid.—It is impossible to describe a general procedure for the isolation and identification of the second product of the oxidative cleavage reactions. These will be dealt with under the individual headings which follow.

II. The Oxidative Cleavage of Pyruvic Acid in the Presence of Hydroxyl-forming Compounds

(1) Water as the Hydroxyl-forming Component.—**(a) Quantitative determination of carbon dioxide:** 0.3517 gram of water-free pyruvic acid (distilled several times) dissolved in 10 cc. absolutely dry acetic acid yielded, after addition of 2.8 g. of finely pulverized dry lead tetraacetate 11.8 mg. of carbon dioxide. Upon adding 10 cc. of water, oxidative cleavage occurred immediately as indicated by the visible evolution of carbon dioxide. The reaction was completed in a few minutes. After thirty minutes the increase in weight of the carbon dioxide apparatus was 169.8 mg. Calcd. amount carbon dioxide: 175.8 mg. Found: 181.6 mg., 103.2%.

(b) The second cleavage product, according to theory, would be acetic acid, which naturally cannot be detected in the presence of the large amount of acetic acid present as solvent.

(c) Determination of Lead Tetraacetate Required for the Cleavage of 1 Mole of Pyruvic Acid.—A mixture of 10 cc. of 0.1 *M* pyruvic acid (in glacial acetic acid), 30 cc. of 0.05 *M* lead tetraacetate (in glacial acetic acid) and 5 cc. of water or 5 cc. of methyl alcohol was kept at 50° for one hour. The decrease of lead tetraacetate was determined by back-titrating the excess of oxidizing agent with 0.1 *N* thiosulfate after addition of 75 cc. of a solution of potassium iodide and sodium acetate (20 g. of potassium iodide and 500 g. of sodium acetate made up to 1 liter); 21.5 cc. of 0.05 *M* lead tetraacetate solution was used up in the presence of water and 20.5 cc. in the presence of methyl alcohol, which is equivalent to 1.07 mole and 1.02 mole of lead tetraacetate, respectively, per 1 mole of keto acid oxidized.

(2) Methyl Alcohol as the Hydroxyl-forming Component.—(a) The oxidative cleavage of pyruvic acid in the presence of methyl alcohol was carried out in the same way as described in (II, 1a). 0.3651 gram of keto acid yielded 9.9 mg. of carbon dioxide; after addition of 10 cc. of water-free methyl alcohol a further 175.4 mg. of carbon dioxide was produced; total carbon dioxide, 185.3 mg. (101.5% of the theoretical).

(b) The isolation of the second product, methyl acetate, from a large excess of free acetic acid and methyl alcohol was not tried because of the obvious experimental difficulties.

(3) Benzyl Alcohol as the Hydroxyl-forming Component.—(a) The same method was used for the cleavage of pyruvic acid in the presence of benzyl alcohol: 0.3268 g. of pyruvic acid yielded 14.2 mg. of carbon dioxide. After addition of 0.8 g. of absolutely dry benzyl alcohol, a further 143.2 mg. of carbon dioxide was liberated in one hour; total, 157.4 mg. of carbon dioxide (96% of the theoretical).

(b) The isolation of the second product, benzyl acetate, was possible because of its high boiling point. By using

(8) If a Warburg apparatus is available the reaction may be followed by a volumetric measurement of the evolved carbon dioxide. The gas is liberated almost instantly. This volumetric procedure has the advantage that only very small quantities (about 0.5 mg.) of reactants are required; moreover, the time necessary for the determination is only a small fraction of that necessary for the gravimetric procedure.

anhydrous benzene as the solvent, it was possible to prove that the acid required by theory (acetic acid) is indeed the acid obtained by the oxidative cleavage of pyruvic acid.

To a solution of 1.76 g. (1/50 mole) of absolutely dry pyruvic acid[9] and 2.16 g. (1/50 mole) of absolutely dry benzyl alcohol in 50 cc. of water-free benzene[10] was added 9.3 g. (1/50 mole + 5%) of lead tetraacetate. The temperature of the solution rose from 24 to 40°, carbon dioxide was evolved and lead acetate precipitated. After one hour the lead tetraacetate was almost used up, carbon dioxide evolution had stopped and the mixture had returned to its initial temperature. After standing overnight the solution was decanted from the lead salt; the salt was washed with benzene and the combined benzene solutions were concentrated. The concentrate was diluted with ether, allowed to stand for a while, then filtered and concentrated again. The residue was fractionally distilled first *in vacuo* and then under normal pressure. The last distillation yielded two fractions: (1) b. p., 170–179°, *ca.* 0.3 g; (2) b. p., 202–212°, *ca.* 1.4 g., $n^{21}D$ 1.5150. Fraction (1) was identified as benzaldehyde by its b. p., odor and the m. p. of the *p*-nitrophenylhydrazone (192°). Fraction (2) judging by its b. p., refractive index and saponification number was fairly pure benzyl acetate. The corrected yield (1.2 g.) of benzyl acetate corresponds to 40% of the theoretical. Final proof of the identity of the acid formed from pyruvic acid in the oxidation was obtained by saponifying the benzyl ester (fraction 2) with aqueous alcoholic potassium hydroxide solution. After evaporation of the solvent the residue was acidified with sulfuric acid and the volatile acid was distilled over with the water. Water was added to the residue and the distillation was repeated until the distillate was no longer acid. The combined distillates were neutralized with barium hydroxide, concentrated *in vacuo* to a small volume and by addition of a concentrated silver nitrate solution, the silver salt of the acid was precipitated. The silver salt, recrystallized from water and dried in high vacuum, was found to contain 64.3% silver; calculated for silver acetate 64.6% silver. From 1.40 g. of fraction (2) was obtained 1.24 g. of silver acetate. In order to ascertain that the benzyl acetate (fraction 2) obtained in experiment II 3(b) was actually the product of the reaction between pyruvic acid, benzyl alcohol and lead tetraacetate, and not formed by the action of lead tetraacetate on benzyl alcohol, the experiment was repeated without pyruvic acid. After standing for forty-eight hours at room temperature, the mixture was worked up as described previously. After concentration of the solution by distilling off the ether and benzene, the residue obtained was separated into three fractions by distillation *in vacuo:* (1) b. p. (7 mm.) 62–64°, 0.45 g. (chiefly benzaldehyde, identified as *p*-nitrophenylhydrazone, m. p. 192–193°; (2) b. p. (7 mm.) 85–100°, 0.65 g. (chiefly unchanged benzyl alcohol containing a small amount of a benzyl ester); (3) a higher boiling residue which was not examined further.

The crude silver salt obtained from fraction 2 weighed 0.18 g., (which would correspond to 0.16 g. of benzyl acetate, *ca.* 5% of the theoretical). The silver content of this salt revealed it to be slightly impure silver acetate. The above blank showed, therefore, that in twice the time allowed in the experiment with pyruvic acid, the benzyl alcohol and lead tetraacetate did not yield at most more than 5% of benzyl acetate.

Therefore, in the main experiment the benzyl acetate obtained can only be a product of the reaction between pyruvic acid, benzyl alcohol and lead tetraacetate, thus proving that the reaction product of oxidative cleavage of pyruvic acid is acetic acid.

III. Oxidative Cleavage of Trimethylpyruvic Acid

(1) Oxidation in the Presence of Water. (a) Quantitative Determination of Carbon Dioxide.—The determination was carried out in the same way as described for pyruvic acid: 530.0 mg. of keto acid yielded 5.6 mg. of carbon dioxide in water-free medium (room temperature); addition of 10 cc. of water gave a further 168.9 mg. of carbon dioxide (temperature of reaction flask 40–45°). The total amount of carbon dioxide obtained was 174.5 mg. (97.5% of the theoretical).

(b) Isolation and Identification of the Second Cleavage Product.—1.30 grams (0.01 mole) of trimethylpyruvic acid was dissolved in 35 cc. of distilled water at 40° and 4.43 g. (0.01 mole) of finely pulverized lead tetraacetate was added in three portions with shaking. The oxidation took place immediately and was accompanied by a strong evolution of carbon dioxide. After thirty minutes 5 cc. of 5 *N* sulfuric acid was added and the solution extracted with ether in a continuous extractor for twenty-four hours. The ether extract, dried with sodium sulfate, was concentrated and the residue separated by fractional distillation under normal pressure into three fractions: (1) boiling up to 100°, (2) from 100–120° (1.89 g., mainly acetic acid), and (3) 120–160° (1.5 g.). Fraction 3 was separated again by fractional distillation into three fractions with b. p. ranges 118–125°, 126–148°, 148–165°. The last two fractions were only slightly soluble in water and possessed an odor similar to that of butyric acid. For the further purification and identification of the acid, an aqueous solution of the combined last two fractions, neutralized with barium hydroxide and concentrated to a small volume, was mixed with a concentrated aqueous solution of silver nitrate and the precipitated mixture of silver salts (acetate and silver trimethylacetate) separated by recrystallization from hot water. The silver trimethylacetate thus obtained was almost pure. Silver determination: calcd., for silver salt of trimethylacetic acid, Ag, 51.6. Calcd. for silver salt of acetic acid, Ag, 64.6. Found: Ag, 53.7.

(c) Lead Tetraacetate Required for Cleavage.—The determination was carried out as described in II (1c): 10 cc. of 0.1 *M* trimethylacetic acid required 19.2 cc. of 0.05 *M* lead tetraacetate in the presence of water and 20.1 cc. in the presence of methyl alcohol which is equivalent to 0.96 and 1.00 mole of lead tetraacetate, respectively, for the cleavage of 1 mole of trimethylacetic acid.

(2) Oxidation in the Presence of Methyl Alcohol.—(a) Quantitative Determination of Carbon Dioxide: 496.7 mg. of keto acid yielded 5.9 mg. of carbon dioxide in dry acetic acid; addition of 10 cc. of absolutely dry methyl alcohol gave a further 174.10 mg. of carbon dioxide (tem-

(9) Dehydrated by shaking for a long time with Drierite and centrifuged just before using.

(10) Dried with metallic sodium.

perature of reaction flask, 45–50°); total amount of carbon dioxide obtained, 180.0 mg. (107% of the theoretical.)

(3) Isolation and Identification of the Cleavage Product of Trimethylpyruvic Acid in the Presence of Benzyl Alcohol. (Benzyl Trimethylacetate as Intermediate Compound.)—To a solution of 1.30 g. (0.01 mole) of keto acid and 1.08 g. (0.01 mole) of absolutely dry benzyl alcohol in 20 cc. water-free benzene was added 4.43 g. (0.01 mole) of lead tetraacetate. The temperature of the solution rose in a short time from 24 to 37° with strong evolution of carbon dioxide. After the solution had cooled to its initial temperature and the evolution of carbon dioxide had stopped, the lead diacetate was centrifuged off, washed several times with benzene and ether and the wash solutions added to the supernatant. By carefully distilling off the ether and benzene and distillation of the residue *in vacuo*, 1.26 g. of a clear liquid boiling from 84–91° (at 7 mm.) was obtained. According to the saponification data, it contained 56% of benzyl trimethylacetate (0.374 g. of esterified trimethylacetic acid, 37% of the theoretical). The remainder apparently consisted of unesterified benzyl alcohol. The preparation of the silver salt of trimethylacetic acid from benzyl trimethylacetate was carried out as described for the preparation of silver acetate from benzyl acetate. The silver salt (crude product) obtained by this method contained 52.7% silver. Calculated for silver salt of trimethyl acetic acid, 51.6% of silver.

IV. Oxidative Cleavage of Phenylglyoxylic Acid

(1) Oxidation in the Presence of Water.—(a) Quantitative Determination of Carbon Dioxide.—0.4667 gram of absolutely dry phenylglyoxylic acid was dissolved in 10 cc. of absolutely dry acetic acid and a suspension of 4 g. of finely pulverized lead tetraacetate in 15 cc. of acetic acid was added. A bulky white, crystalline precipitate formed.[11] During the blank run the carbon dioxide liberated equalled 9.2 mg. After the addition of 15 cc. of water the precipitate dissolved again and an additional 120.8 mg. of carbon dioxide was obtained: total, 130.0 mg. (95% of the theoretical).

(b) Identification of the Second Cleavage Product.—To a solution of 1.5 g. of phenylglyoxylic acid in 50 cc. of 30% acetic acid was added a suspension of 4.48 g. of finely pulverized lead tetraacetate in 40 cc. of glacial acetic acid. The oxidative cleavage proceeded quickly and with slight warming. After the lead tetraacetate was used up the lead was precipitated by addition of the calculated amount of sulfuric acid. Concentration of the solution *in vacuo*, extraction of the residue with boiling ether and evaporation of the extract yielded 1.18 g. (96.7% of the theoretical) of pure benzoic acid, m. p. 122.5° (recrystallized from water); mixed m. p. with pure benzoic acid, 122.5°.

(c) Lead Tetraacetate Required for Cleavage.—The determination was carried out as described in II (1c). Ten cc. of 0.1 *M* phenylglyoxylic acid required 19.7 cc. of 0.05 *M* lead tetraacetate in the presence of water and 19.0 cc. in the presence of methyl alcohol, which is equivalent to 0.99 and 0.95 mole of lead tetraacetate, respectively, per mole of keto acid oxidized.

(11) The lead content of this precipitate (41%) agrees with that of plumbous phenylglyoxylate.

(2) Oxidation in the Presence of Ethyl Alcohol.—(a) Quantitative Determination of Carbon Dioxide.—0.5448 gram of phenylglyoxylic acid dissolved in 10 cc. of acetic acid yielded 7.8 mg. of carbon dioxide during the blank run. Addition of 5 cc. of ethyl alcohol liberated an additional 146.4 mg. of carbon dioxide; total, 154.2 mg. of carbon dioxide (96.5% of the theoretical).

(b) Isolation of Ethyl Benzoate from Cleavage in the Presence of Ethyl Alcohol.—To a solution of 1.5 g. of phenylglyoxylic acid and 10 cc. of absolutely dry ethyl alcohol in 30 cc. of absolutely dry benzene was added a solution of 4.43 g. of lead tetraacetate in 60 cc. of benzene and the mixture was kept at 45°[12] (carbon dioxide evolution). After one hour the lead acetate precipitate was centrifuged off and washed with ether. The combined benzene and ether solutions were extracted with 10% sodium bicarbonate solution to remove acetic acid, dried with solid potassium carbonate and concentrated. The residue, distilled *in vacuo*, yielded 1.2 g. (80% of the theoretical) of benzoic acid ethyl ester b. p. (756 mm.) 211–212°, $n^{26}D$ 1.5038.

(3) Isolation of the Cleavage Product in the Presence of Hydrogen Cyanide.—To a solution of 1.5 g. of phenylglyoxylic acid in 25 cc. of absolutely dry benzene was added a suspension of 4.43 g. of lead tetraacetate in 40 cc. of dry benzene and the mixture kept at 40–45°. The bright orange color which appeared immediately disappeared in a few minutes and the lead salt of the α-keto acid began to precipitate from the colorless solution. After forty-five minutes the solution was cooled in ice water, and about 5 cc. of anhydrous hydrogen cyanide was added, whereupon the lead salt of the α-keto acid redissolved quickly with simultaneous evolution of carbon dioxide and precipitation of lead acetate. The clear benzene solution was decanted and concentrated, using a fractionating column. In order to remove traces of lead salt the residue was dissolved in dry ether, filtered and again concentrated. The concentrate was distilled *in vacuo* and yielded 0.65 g. of phenylglyoxylic *nitrile* (50% of the theoretical), b. p. (9 mm.) 82°; b. p. (758 mm.) 208–210°; $n^{26}D$ 1.5303.

V. Oxidative Cleavage of Phenylpyruvic Acid

(1) Oxidation in the Presence of Water. (a) Quantitative Determination of Carbon Dioxide.[13]—0.492 gram of dry phenylpyruvic acid dissolved in 10 cc. of absolutely dry acetic acid yielded, after addition of 2.8 g. of finely pulverized lead tetraacetate, 13.2 mg. of carbon dioxide in the blank run. After addition of 10 cc. of water, a further 112.8 mg. of carbon dioxide was produced; total, 126.0 mg. of carbon dioxide (95% of the theoretical).

(b) The Identification of the Second Cleavage Product.—To 1.64 g. (0.01 mole) of phenylpyruvic acid dissolved in 30 cc. of glacial acetic acid was added 50 cc. of water and immediately afterward 9.3 g. (0.021 mole) of finely pulverized lead tetraacetate. The temperature of the solution rose very quickly from 27 to 39°. After ten minutes an additional 40 cc. of water was added and the mixture kept at room temperature for one hour. The lead

(12) The yield of benzoic acid ester does not differ when one adds the lead tetraacetate to the phenylglyoxylic acid in benzene first and the ethyl alcohol after thirty minutes.

(13) The experiment was carried out at room temperature except at the end when the reaction flask was warmed to 50°.

was removed by addition of 21 cc. of 2 *N* sulfuric acid and the precipitate extracted several times with alcohol and ether. The supernatant liquid combined with the alcohol and ether washings was evaporated to dryness *in vacuo*. Since attempts to isolate phenylacetic acid failed, it was obvious that secondary reactions had occurred (see theoretical part). The residue was dissolved in a mixture of 25 cc. of alcohol and 25 cc. of 2 *N* sodium hydroxide and warmed for one hour on the water-bath. After addition of 25 cc. of 2 *N* sulfuric acid the solution was evaporated again to dryness and the residue (I) exhaustively extracted with boiling ether. From the ether extract was obtained 500 mg. of fairly pure mandelic acid. Dissolving of residue (I) in a few cc. of dilute hydrochloric acid, evaporation to dryness and extraction with ether yielded a further 220 mg. of crude mandelic acid: total yield 0.77 g. of mandelic acid (50.6% of the theoretical); m. p. 118.5° after recrystallizing twice from chloroform. A mixed m. p. with mandelic acid showed no depression. The acid was readily soluble in water, gave an intense yellow color with ferric chloride and was oxidized to benzaldehyde by lead tetraacetate. The synthetically obtained mandelic acid by acetylation with acetic anhydride yielded acetylmandelic acid with the correct m. p., 54°.

(c) Lead Tetraacetate Required for Cleavage.—The determination was carried out as described in II (1c). Ten cc. of 0.1 *M* phenylpyruvic acid required 39.0 cc. of 0.05 *M* lead tetraacetate in the presence of water and 37.8 cc. in the presence of methyl alcohol which is equivalent to 1.95 and 1.90 moles of lead tetraacetate, respectively, for the cleavage of 1 mole of keto acid. The second mole of lead tetraacetate probably was used in the acetylation of the $-CH_2-$ group.

α-Keto Alcohols

Oxidative Cleavage of α-Keto Alcohols by Lead Tetraacetate in the Presence of Hydroxyl-forming Compounds.—The oxidative cleavage of α-keto alcohols by lead tetraacetate in the presence of hydroxyl-forming compounds leads to the formation of two products, one an acid, the other an aldehyde (or ketone, if the carbinol is tertiary in type). Both products of the cleavage of four α-keto alcohols have been identified (with one exception) as described below. The exception was in the case of acetylmethylcarbinol where the acid expected is acetic acid.

VI. Oxidative Cleavage of Acetylmethylcarbinol in the Presence of Water

(a) Identification of Acetaldehyde.—To 0.88 g. (0.1 mole) of freshly distilled acetylmethylcarbinol (b. p. 143.5–145°) dissolved in 20 cc. of 90% acetic acid was added 4.45 g. of lead tetraacetate. The solution became slightly warm. In order to avoid loss of acetaldehyde the process of oxidation was carried out in a closed vessel which was cooled occasionally. After twenty minutes the solution was cooled in ice and 50 cc. of water and 0.54 cc. of concentrated sulfuric acid were added. The lead sulfate was removed by centrifuging and the supernatant liquid added to a solution of lukewarm dilute hydrochloric acid containing 2.1 g. of 2,4-dinitrophenylhydrazine. The preparation was kept in ice for thirty minutes to ensure complete precipitation. After filtering with suction, the precipitate was washed with dilute hydrochloric acid and dried *in vacuo* over phosphorus pentoxide and potassium hydroxide; 2.13 g. (95% of the theoretical) of acetaldehyde 2,4-dinitrophenylhydrazone was obtained which melted at 162° after recrystallization from alcohol.

(b) Lead Tetraacetate Required for Cleavage.—The equivalent was determined as described in II (1c). The oxidative cleavage of 1 mole acetylmethylcarbinol required 1 mole of lead tetraacetate in the presence of water.

VII. Oxidative Cleavage of Benzoylcarbinol with Lead Tetraacetate

(1) In the Presence of Water. (a) Isolation of Benzoic Acid.—1.36 g. (0.01 mole) of benzoylcarbinol was dissolved in 25 cc. of 90% acetic acid and 4.84 g. (0.011 mole) of finely powdered lead tetraacetate added. The mixture was kept for twenty minutes at 50–55° with frequent shaking. After the cleavage was completed, the lead was precipitated as lead sulfate by addition of the calculated amount of concentrated sulfuric acid and removed by centrifuging. The acetic acid solution, evaporated *in vacuo*, yielded a residue out of which the benzoic acid was extracted with ether. On evaporation of the ether 0.96 g. (78.6% of the theoretical) of almost pure benzoic acid remained; m. p. after recrystallization from water was 122°. The mixed m. p. with benzoic acid showed no depression.

(b) The cleavage of the carbinol and isolation of aldehyde was carried out by procedures similar to those described for acetyl-methyl-carbinol. 1.36 g. (0.01 mole) of benzoylcarbinol yielded 1.75 g. (83% of the theoretical) of formaldehyde 2,4-dinitrophenylhydrazone which when purified by recrystallization from alcohol or petroleum ether had m. p. 154.5°.

(2) In the Presence of Ethyl Alcohol. Isolation of Ethyl Benzoate.—To a solution of 1.36 g. (0.01 mole) of absolutely dry benzoylcarbinol in a mixture of 25 cc. of absolute glacial acetic acid[14] and 5 cc. absolute ethyl alcohol 4.84 g. (0.011 mole) of finely powdered lead tetraacetate was added. The solution was heated to 50–55° and kept at this temperature for thirty minutes with frequent shaking. The preparation was diluted with 60 cc. of distilled water and the ethyl benzoate formed was extracted with ether under reflux. The ether extract was shaken with saturated sodium bicarbonate solution to remove free acid and was carefully concentrated. Distillation of the residue yielded 0.90 g. (60% of the theoretical) of benzoic acid ethyl ester, b. p. (747 mm.) 211–212°.

VIII. Oxidative Cleavage of Benzoin with Lead Tetraacetate

(1) In the Presence of Water. (a) Isolation of Benzoic Acid.—The cleavage of benzoin and isolation of the cleavage product, benzoic acid, were carried through in the same way as described for the cleavage of benzoylcarbinol (VII, 1a). However, before evaporation, the ether extract was shaken with saturated sodium sulfite solution for three hours to remove the benzaldehyde. From 2.12 g. (0.01 mole) of benzoin 0.9 g. (74% of the theoretical) of pure benzoic acid of m. p. 122.5° was obtained.

(b) Identification of Benzaldehyde as *p*-Nitrophenylhydrazone.—2.12 g. (0.01 mole) of benzoin was oxidized

(14) Glacial acetic acid and ethyl alcohol were dried by shaking for several days with Drierite and centrifuged before using.

with 4.5 g. of lead tetraacetate in 25 cc. of glacial acetic acid (VII, 1a). After removal of lead as sulfate, 2 g. of *p*-nitrophenylhydrazine was added and the solution warmed to 50°. After thirty minutes the preparation was diluted with a four-fold volume of water and kept at 0° for an hour. The crude hydrazone after recrystallization from ethyl alcohol yielded 1.8 g. (75% of the theoretical) of benzaldehyde-*p*-nitrophenylhydrazone with m. p. 192°.

(c) Lead Tetraacetate Required for Cleavage.—The equivalent was determined as described in II (1c) except that, due to the insolubility of benzoin in acetic acid, a 0.05 *M* solution was used. The mixture was kept at 50° for two and one-half hours. The oxidative cleavage of 1 mole of benzoin required 1.01 mole of lead tetraacetate in the presence of water and 1.01 mole in the presence of methyl alcohol.

(2) In the Presence of Ethyl Alcohol. Isolation of Ethyl Benzoate.—The cleavage of benzoin with lead tetraacetate in the presence of ethyl alcohol was carried out as described for benzoylcarbinol. After dilution with water the mixture was extracted with ether. The ether layer was shaken with saturated sodium bicarbonate solution to remove acids and with concentrated sodium bisulfite to remove benzaldehyde. After evaporation of the ether, the residue was distilled *in vacuo* and redistilled at atmospheric pressure.

From 2.12 g. (0.01 mole) of benzoin 1.26 g. (84% of the theoretical) of benzoic acid ethyl ester was obtained, b. p. (756 mm.) 212°. Hydrolysis of the ethyl ester yielded benzoic acid, m. p. 122.5°.

IX. Oxidative Cleavage of Anisoin by Lead Tetraacetate

(1) In the Presence of Water. (a) Isolation of Anisic Acid.—The cleavage of anisoin with lead tetraacetate was carried out by the same procedure as described for benzoylcarbinol. However, in this case, the anisic acid was separated from the ether extract by shaking with an aqueous solution of sodium bicarbonate. Acidification of the bicarbonate extract yielded anisic acid. From 2.72 g. (0.01 mole) of anisoin, 1.1 g. (76.8% of the theoretical) of anisic acid, m. p. 185° (recrystallized from water), was obtained.

(b) Isolation of Anisaldehyde as *p*-Nitrophenylhydrazone.—The ether extract (IX, 1a) freed of the anisic acid by the sodium bicarbonate solution was concentrated by distilling off the ether under ordinary pressure. The residue contained crystals which were isolated by taking up the residue in ethyl alcohol and filtering. The alcohol-insoluble material, yellow-green in color, weighed 0.15 g. (5% of the starting material), had a m. p. 133° and proved to be anisil.[15]

The alcoholic solution which contained the anisaldehyde was added to a warm solution of *p*-nitrophenylhydrazine in dilute hydrochloric acid; yield 2.12 g. (83% of the theoretical)[16] of *p*-nitrophenylhydrazone of anisaldehyde; m. p. after recrystallization from ethyl alcohol, 162°.

(c) Lead Tetraacetate Required for Cleavage.—The equivalent was determined as described in II (1c). The mixture was kept at 50° for four hours. The oxidative cleavage of 1 mole of anisoin required 0.93 mole of lead tetraacetate in the presence of water and 0.97 mole in the presence of methyl alcohol.

(2) In the Presence of Ethyl Alcohol. Isolation of the Anisic Acid Ethyl Ester.—The cleavage of anisoin in the presence of ethyl alcohol was carried out exactly as described for benzoin (VIII, 2). The residue obtained by evaporation of the ether extract contained a crystalline substance which was separated by taking up in alcohol and filtering. The isolated substance (0.45 g., 16.5% of the starting material) had a m. p. 133° and was found to be anisil. The alcoholic filtrate and wash solution were combined and concentrated and the residue distilled *in vacuo;* 2.72 g. (0.01 mole) of anisoin yielded 1.02 g. (68% of the theoretical) of anisic acid ethyl ester, b. p. (8 mm.) 125–130°; b. p. (750 mm.) 267–269°. The ester after saponification with alkali and acidification yielded anisic acid (m. p. 182°).

X. Oxidation of α-Keto Alcohols with Lead Tetraacetate in Absence of Hydroxyl-forming Compounds.[17]

(a) Diacetyl from Acetylmethylcarbinol.—0.88 gram (0.01 mole) of freshly distilled acetylmethylcarbinol and 4.43 g. (0.01 mole) of lead tetraacetate in 30 cc. of absolutely water-free benzene was kept at 50° for four hours. After cooling the solution to room temperature the lead salt was separated by centrifuging and washed several times with benzene. The combined benzene solutions were heated with a mixture of 30 cc. of 20% hydroxylamine chlorohydrate, 30 cc. of 20% sodium acetate and 30 cc. of 10% nickel chloride at 80° for one hour with frequent shaking. By distilling off the benzene, 0.60 g. of nickel dimethylglyoxime was obtained which corresponded to 0.358 g. of diacetyl (41.6% of the theoretical).

(b) Benzil from Benzoin.—To a solution of 2.12 g. (0.01 mole) of benzoin (dried in high vacuum) in 25 cc. of absolutely dry acetic acid was added 4.43 g. (0.01 mole) of finely pulverized lead tetraacetate and the mixture kept at 50° for twenty-four hours with occasional shaking and exclusion of moisture. The solution was evaporated to dryness *in vacuo* at about 40–45° bath temperature and the residue completely extracted with ether. After shaking the ether extract with saturated sodium bicarbonate solution and evaporating to dryness, 1.75 g. of benzil (83.4% of the theoretical) with m. p. 94–95° (recrystallized from carbon tetrachloride and ethyl alcohol) was obtained.

(c) Anisil from Anisoin.—The oxidation of anisoin to anisil was carried out exactly as described for benzoin: 2.72 g. (0.01 mole) of anisoin yielded 2.0 g. (74% of the theoretical) of anisil with m. p. 133° and 0.30 g. (20% of the theoretical) of anisic acid,[18] m. p. 184.5° (recrystallized from water).

Acknowledgment.—Grateful acknowledgment is made to Dr. C. C. Lucas for assistance in preparing this manuscript in English as well as to H. N. MacFarland for preparing some of the keto acids used in this investigation.

(15) This substance, which is here a by-product, becomes the main product when working in the absence of hydroxyl-forming compounds (see Xc).

(16) After deduction of the anisoin used up in the formation of anisil.

(17) In this and the following experiments, the solvents used must be absolutely dry to avoid oxidative cleavage.

(18) Obtained by acidification of the sodium bicarbonate extract of the ether solution.

Summary

1. Under certain conditions lead tetraacetate effects quantitative oxidative cleavage of α-keto acids and α-keto alcohols. The reaction seems to be one of general application.

2. This reaction occurs only after formation of a vicinal hydroxyl pair and therefore has to be considered as a glycol cleavage.

3. The formation of the "pseudoglycols" takes place by addition to the keto group. Water, alcohols (*e. g.*, methyl, ethyl and benzyl alcohols) and hydrocyanic acid were found capable of such an addition.

4. In the absence of substances forming pseudoglycols by addition no reaction takes place between lead tetraacetate and α-keto acids, whereas α-keto alcohols are oxidized in good yield to their diketones.

5. The nature of the cleavage products is determined by the glycol-forming substance added.

6. In the presence of water, alcohols or hydrocyanic acid the products are as follows: (a) from 1 mole of α-keto acid and 1 mole of lead tetraacetate are obtained 1 mole of carbon dioxide and 1 mole of acid (or ester or keto nitrile). (b) From 1 mole of α-keto alcohol and 1 mole of lead tetraacetate are obtained 1 mole of acid (or its ester) and 1 mole of aldehyde (or ketone).

7. The present use of lead tetraacetate to detect vicinal hydroxyl groups in compounds of unknown constitution may be extended to the detection of the α-keto acid and α-keto alcohol groups, if one compares the reaction of the substance with lead tetraacetate in dry solvents with the behavior in the presence of compounds capable of forming pseudoglycols, as explained above.

8. The method of oxidative cleavage may be employed not only to determine α-keto acids quantitatively by the carbon dioxide evolved but also to distinguish them qualitatively from other keto acids (β, γ, · · ·, etc.).

TORONTO, CANADA RECEIVED APRIL 8, 1940

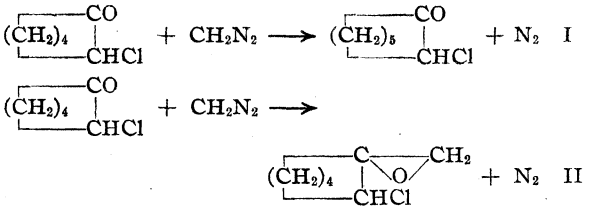
[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF HARVARD UNIVERSITY]

The Ring Enlargement of Two Cyclic Alpha-Chloroketones

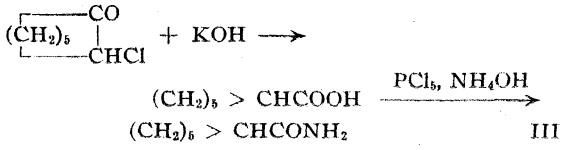
BY THOMAS R. STEADMAN[1]

A study of the reaction of diazomethane with cyclic α-chloroketones was undertaken in these laboratories in order that further light might be shed on the process of ring enlargement of cyclic systems. Giraitis and Bullock[2] have reported briefly on work similar in character to that described in the present paper. The present investigation has been confined to experiments based on Meerwein's mode of operation,[3,4] involving the introduction of nitrosomethylurethan at a suitable rate into a solution of the ketone in methanol containing a small amount of sodium carbonate. This is quite different from the method employed by Giraitis and Bullock,[2] who used diazomethane in ethereal solution.

The principal reactions in the case of α-chlorocyclohexanone may be represented by the following equations, although the actual intermediate may not be diazomethane



It is important to note that when the ring was enlarged, the methylene group entered the ring in such a manner that the chlorine atom remained alpha to the carbonyl group. This was shown by the fact that when the chloroketone was treated with alcoholic sodium hydroxide, cyclohexane carboxylic acid was obtained and identified by conversion to the amide:



This degradation was first recognized by Favorskii and Boshowski.[5]

(1) This investigation was begun by the author at the suggestion and under the direction of the late Prof. E. P. Kohler.

(2) Giraitis and Bullock, THIS JOURNAL, **59**, 951 (1937).

(3) Meerwein, *Chem. Zentr.*, **104**, II, 1758 (1933); German Patent 579,309.

(4) Kohler, Tishler, Potter and Thompson, THIS JOURNAL, **61**, 1057 (1939).

(5) Favorskii and Boshowski, *J. Russ. Phys.-Chem. Soc.*, **50**, 582-588 (1917); *C. A.*, **18**, 1476 (1924).

The possibility that β-chloroketones might also undergo the Favorskii degradation is considered unlikely. No evidence bearing directly on the point could be found in the literature, but such an eventuality would require that both the α- and the β-chloroketones should pass through a common intermediate, the α,β unsaturated ketone. This is an hypothesis difficult to accept. It is much more likely that the reaction is analogous to the benzilic acid rearrangement.

Attempts to secure a semicarbazone from the chloroketone proved futile, but it is common for α-halogen atoms to reduce the carbonyl activity of ketones in this respect.

The structure of 2-chloro-1-methylenecyclohexane oxide as formulated in Equation II above was proved by hydrogenation of the substance, thus forming cyclohexylcarbinol, which was readily identified as the phenylurethan.

From a typical experiment involving α-chlorocyclohexanone and diazomethane, there was obtained a 52% yield of pure α-chlorocycloheptanone and a 16% yield of pure 2-chloro-1-methylenecyclohexane oxide. It was estimated that the intermediate fractions from the distillation contained further yields of about 7.5% of the ketone and 8% of the oxide. Taking these materials into consideration, together with a distillation residue of 3%, it was possible to account for 86.5% of the ketone used. This compares favorably with the material balance reported by Kohler and his associates[4] for the reaction of cycloöctanone with diazomethane. The three to one ratio of ketone to oxide corresponds roughly with the similar ratio observed in the case of the unsubstituted cyclic ketone. However, it should be noted that the results of this experiment contrast sharply with the report by Giraitis and Bullock[2] that a quantitative yield of α-chlorocycloheptanone was obtained from α-chlorocyclohexanone and diazomethane in ethereal solution.

From the reaction of diazomethane with α-chlorocycloheptanone, three substances were isolated. One of them was recovered starting material, as indicated by its physical properties and an analysis. A second substance was tentatively identified as 2-chloro-1-methylenecycloheptane oxide. The third compound, α-chlorocycloöctanone, upon treatment with alcoholic alkali, gave cycloheptane carboxylic acid, which was identified as the amide.

After long standing in a stoppered flask under an atmosphere of air, the α-chlorocycloöctanone which had been obtained by careful fractional distillation under diminished pressure was found to contain a small amount of a white, crystalline compound. This was filtered off, washed free of α-chlorocycloöctanone with ether and then recrystallized from dilute hydrochloric acid. The recrystallized material proved to be suberic acid, as shown by an analysis and a mixed melting point determination with an authentic sample of suberic acid. Presumably suberic anhydride was formed by oxidation of the chloroketone and this transformed to the acid on recrystallization.

Despite the fact that a 10% excess of nitrosomethylurethan was used in the reaction with α-chlorocycloheptanone, 36.8% of the starting material was recovered in a good state of purity. The pure α-chlorocycloöctanone and the pure isomeric oxide were obtained in roughly equal amounts (the yields of ketone and oxide being 13 and 11.7%, respectively). The impure intermediate fractions were estimated to contain more of the starting material (15.4%) and further yields of α-chlorocycloöctanone (2.4%) and oxide (4.4%). These, together with distillation residues amounting to 10.8%, accounted for 94.5% of the starting material.

The work of Kohler and his associates[4] on the reaction of diazomethane with cycloöctanone and cyclononanone showed that these reactions were subject to steric hindrance due probably to both the lessened reactivity of the carbonyl group and the difficulty of introducing another methylene group into an already crowded ring system. Owing to the possibility of the interaction of several factors in the reactions studied in the present investigation, the interpretation of the experimental results is not easy. The fairly good yields of products obtained in the reaction of diazomethane with α-chlorocyclohexanone are comparable with those obtained under similar conditions in the case of cyclohexanone, demonstrating that α-chloro substitution has exercised no pronounced effect on the reactivity of the carbonyl group in this direction.

However, the lower yields of products resulting from the reaction of diazomethane with α-chlorocycloheptanone, when contrasted with the behavior of cycloheptanone under similar circumstances, lend support to the idea put forward by Stoll and Stoll-Comte[6] to explain by steric con-

(6) Stoll and Stoll-Comte, *Helv. Chim. Acta*, **13**, 1185 (1930).

siderations the difficulties encountered in synthesizing cycloalkanones with eight to thirteen ring members. The replacement of a hydrogen with a relatively larger chlorine atom in these ketones should tend to make more difficult the formation of rings of such size. This has been borne out by the finding that the reaction of α-chlorocycloheptanone with diazomethane gave rise to smaller yields of products and a lower ratio of ketone to oxide than resulted from the reaction of α-chlorocyclohexanone with diazomethane under similar conditions. The decrease in the yield of products may be ascribed to the lower degree of reactivity of the carbonyl group of α-chlorocycloheptanone as compared with that of α-chlorocyclohexanone. The decrease in the ratio of ketone to oxide is probably due to the steric hindrance offered to the introduction of a methylene group into the ring. An extension of the evidence offered herein would be highly desirable.

Experimental Part

α-Chlorocyclohexanone.—The chlorination of cyclohexanone in acetic acid solution according to directions by Bartlett and Rosenwald[7] resulted in 50–60% yields of α-chlorocyclohexanone, m. p. 22–23°.

α-Chlorocyclohexanone and Diazomethane.—In a 500-cc. three-necked, round-bottomed flask equipped with a thermometer, a dropping funnel, an outlet for nitrogen, and an efficient mechanical stirrer operated through a mercury seal, there was placed 133 g. (1 mole) of freshly distilled α-chlorocyclohexanone, 100 cc. of absolute methanol, and 1–2 g. of finely powdered anhydrous sodium carbonate. Over a period of about seven hours, 146 g. (1.1 moles) of nitrosomethylurethan was added dropwise to the well-stirred reaction mixture, which was cooled as necessary to maintain a temperature between 20 and 30°. When the evolution of nitrogen had ceased, the solution was filtered into a modified Claisen flask and the methanol, together with some methylethyl carbonate, removed by distillation at atmospheric pressure. By careful and repeated fractional distillations of the residue through an efficient column packed with three feet (91 cm.) of glass helices, it was possible to obtain 76.2 g. (52%) of α-chlorocycloheptanone, b. p. 87–88° (10 mm.), and 22.7 g. (16%) of 2-chloro-1-methylenecyclohexane oxide, b. p. 62–63° (10 mm.), m. p. −10 to −8°. The other fractions obtained in the final distillation (10 mm.) were: (1) 59–62°, 3.3 g.; (2) 63–64°, 3.6 g.; (3) 64–70°, 3.4 g.; (4) 70–80°, 3.0 g.; (5) 80–86°, 7.1 g.; (6) 86–87°, 2.4 g.; and a residue of 4.7 g. The ketone was a colorless, mobile liquid with a pungent odor, d^{20}_4 1.140 (Favorskii and Boshowski[5] reported d^{20}_4 1.133), $n^{20}D$ 1.4870.

Anal. Calcd. for $C_7H_{11}OCl$: Cl, 24.2. Found: Cl, 24.3.

By refluxing 15 g. (0.1 mole) of α-chlorocycloheptanone with alcoholic potassium hydroxide, approximately 4 g. (36% yield) of cyclohexane carboxylic acid was secured in a somewhat impure state. For purposes of identification, the liquid acid was treated with an excess of phosphorus pentachloride and the resulting acid chloride poured into concentrated ammonium hydroxide. After one treatment with active charcoal and two recrystallizations from water, white leaflets of cyclohexane carboxamide, m. p. 183–184° (uncor.), were obtained; reported,[8] 184°.

The oxide was also a colorless, mobile liquid with an odor much like that of the isomeric ketone, d^{20}_4 1.120, $n^{20}D$ 1.4763.

Anal. Calcd. for $C_7H_{11}OCl$: Cl, 24.2. Found: Cl, 24.1.

Hydrogenation of the oxide to cyclohexylcarbinol in 95% ethanol, using Raney nickel as catalyst, required much time. An equivalent amount of potassium hydroxide was used in the reaction mixture to absorb the hydrogen chloride formed. From 7.3 g. of oxide was obtained 3.15 g. of liquid, b. p. 81–86° (15 mm.), which was conclusively identified as cyclohexylcarbinol by conversion to a phenylurethan, m. p. 81.5–82.0° (cor.), mixed melting point with an authentic sample 81–82° (cor.). Since the phenylurethan of cycloheptanol has a melting point of 84–85°, it was thought advisable to perform a mixed melting point with an authentic sample of this phenylurethan: found, m. p. 78–80°.

α-Chlorocycloheptanone and Diazomethane.—Using the method outlined for α-chlorocyclohexanone, 143 g. (0.98 mole) of α-chlorocycloheptanone was treated with a 10% excess of nitrosomethylurethan. Three careful fractional distillations of the reaction mixture under diminished pressure permitted the separation of three products. The lowest boiling fraction was identified tentatively as 2-chloro-1-methylenecycloheptane oxide, 18.4 g. (11.7% yield), b. p. 84–86° (10 mm.), $n^{20}D$ 1.4848.

Anal.[9] Calcd. for $C_8H_{13}OCl$: Cl, 22.07. Found: Cl, 22.18.

The middle fraction was considered to be starting material, α-chlorocycloheptanone, 55 g. (38% recovered), b. p. 88–90° (10 mm.), $n^{20}D$ 1.4861.

Anal.[9] Calcd. for $C_7H_{13}OCl$: Cl, 24.22. Found: Cl, 24.18.

The highest boiling fraction proved to be α-chlorocyclooctanone, and was obtained in 13.0% yield (20.2 g.), b. p. 104–106° (10 mm.), $n^{20}D$ 1.4930, $n^{15}D$ 1.4952 (reported[10]: $n^{14.5}D$ 1.4938). The other fractions obtained from the final distillation (10 mm.) were: (1) 80–84°, 1.2 g.; (2) 86–87°, 2.6 g.; (3) 87–88°, 3.6 g.; (4) 90–91°, 7.4 g.; (5) 91–94°, 10.9 g.; (6) 94–101°, 2.3 g.; (7) 101–103°, 2.3 g.; (8) 103–104°, 2.3 g.; and distillation residues totalling 16.7 g.

Extension of the Favorskii degradation to α-chlorocyclooctanone confirmed the tentative identification. Treatment of the ketone with an excess of alcoholic sodium hydroxide gave cycloheptane carboxylic acid, which was readily identified by conversion to the amide, m. p. 192–193° (uncor.); reported,[11] m. p. 193–194°.

After standing for approximately six months in a stoppered flask under an atmosphere of air, the α-chlorocyclo-

(7) Bartlett and Rosenwald, THIS JOURNAL, **56**, 1990–1994 (1934).

(8) Aschan, *Ann.*, **271**, 264 (1892).

(9) Analysis by Mr. H. S. Wight.

(10) Godchot and Mousseron, *Bull. soc. chim.*, (4) **51**, 782 (1932).

(11) Zelinsky, *Ber.*, **35**, 2691 (1902).

octanone was found to contain a precipitate of a white, crystalline compound which was filtered off and washed free of α-chlorocycloöctanone with ether. Two recrystallizations of the substance from 5% hydrochloric acid resulted in a substance, m. p. 140.5–141°, which contained neither chlorine nor nitrogen. A mixed melting point determination with an authentic sample of suberic acid showed no depression of the melting point.

Anal.[9] Calcd. for $C_8H_{14}O_4$: C, 55.16; H, 8.11. Found: C, 55.28; H, 8.05.

Summary

Two alicyclic α-chloroketones have been found to undergo ring enlargement on treatment with diazomethane. From the yields of ketonic materials obtained, evidence has been adduced for the Stoll and Stoll-Comte[6] hypothesis regarding steric effects in certain alicyclic ring systems.

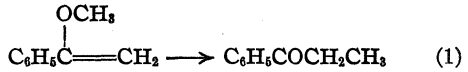
CAMBRIDGE, MASSACHUSETTS RECEIVED MARCH 23, 1940

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

The Condensation of α-Methoxystyrene with Halogen Compounds

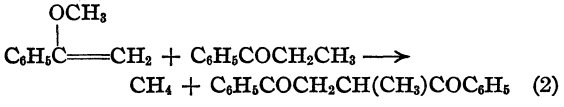
BY C. W. MORTENSON AND M. A. SPIELMAN

In addition to the normal rearrangement (1),[1]



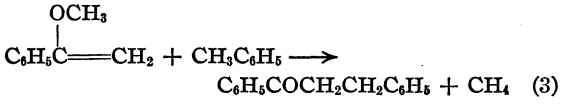
$$C_6H_5\overset{OCH_3}{\overset{|}{C}}{=}CH_2 \longrightarrow C_6H_5COCH_2CH_3 \quad (1)$$

α-methoxystyrene and a few similar enol ethers undergo a peculiar side reaction (2) in which the unchanged ether condenses with the rearrangement product to eliminate methane and form a γ-diketone. Later[2] it was discovered that at



$$C_6H_5\overset{OCH_3}{\overset{|}{C}}{=}CH_2 + C_6H_5COCH_2CH_3 \longrightarrow CH_4 + C_6H_5COCH_2CH(CH_3)COC_6H_5 \quad (2)$$

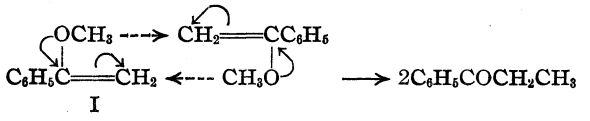
250° α-methoxystyrene also condenses with hydrocarbons such as toluene and cyclohexane (3).



$$C_6H_5\overset{OCH_3}{\overset{|}{C}}{=}CH_2 + CH_3C_6H_5 \longrightarrow C_6H_5COCH_2CH_2C_6H_5 + CH_4 \quad (3)$$

This reaction, so far as we know, has no analogy except, perhaps, in the recently discovered photolytic condensation of phosgene or oxalyl chloride with cyclohexane.[3] Only ethers capable of undergoing the rearrangement[4] also take part in the condensation, and it is evident that there is some common factor in the two reactions.

The hypothesis here advanced to account for the behavior of α-methoxystyrene is that both the rearrangement and the condensation involve the polarized hetero-enoid system in I. Collision, under the proper circumstances, of two such



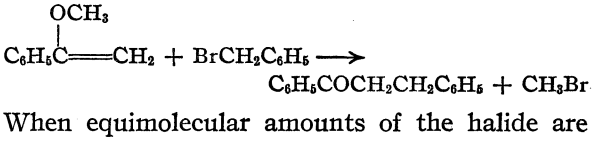
$$C_6H_5\overset{OCH_3 \dashrightarrow}{\overset{|}{C}}{=}\overset{\curvearrowleft}{CH_2}{=}CC_6H_5 \quad C_6H_5C{=}\overset{\curvearrowright}{CH_2} \dashleftarrow CH_3O \longrightarrow 2C_6H_5COCH_2CH_3$$

I

molecules leads to the so-called rearrangement which, in the light of such an interpretation, becomes an intermolecular alkylation. The mechanism explains why the reaction is of the second order and why the alkyl group on the oxygen atom of one molecule may, at the end of the reaction, turn up on the carbon atom of another.[1]

Collision of the polarized molecule I with a reactive but different molecular species leads to the condensation reaction. Attack should be at the anionoid center on the methylene carbon atom,[5] and in that event a reaction should take place with alkyl halides which are cationoid in their reactivity and definitely more polarized than hydrocarbons. A few typical halogen compounds of varying degrees of reactivity have been studied.

α-Methoxystyrene when heated with an eightfold excess of benzyl bromide yields β-phenylpropiophenone in 51% of the theoretical yield.



$$C_6H_5\overset{OCH_3}{\overset{|}{C}}{=}CH_2 + BrCH_2C_6H_5 \longrightarrow C_6H_5COCH_2CH_2C_6H_5 + CH_3Br$$

When equimolecular amounts of the halide are used, the yield is 35%, which is well above the 8% yield obtained from toluene under comparable conditions. *n*-Butyl bromide, containing a moderately active halogen atom, condenses in 28% yield, whereas bromobenzene does not react at all.

(1) Lauer and Spielman, THIS JOURNAL, **55**, 4923 (1933).

(2) Spielman and Mortenson, *ibid.*, **61**, 666 (1939).

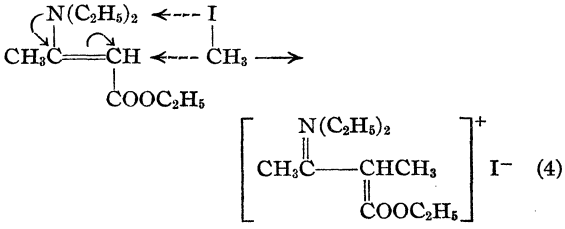
(3) Kharasch and Brown, *ibid.*, **62**, 454 (1940).

(4) The second order, intermolecular rearrangement of enol ethers (MacDougall, Lauer and Spielman, *ibid.*, **55**, 4089 (1933)) possesses only a formal similarity to the familiar first order, intramolecular rearrangement of allyl ethers (Kincaid and Tarbell, *ibid.*, **61**, 3085 (1939); Hurd and Schmerling, *ibid.*, **59**, 107 (1937)).

(5) The anionoid reactivity of α-methoxystyrene is shown by the avidity with which it adds water, alcohol, acids, etc. For terminology refer to Robinson, "Outline of an Electrochemical Theory of the Course of Organic Reactions," The Institute of Chemistry of Great Britain and Ireland, London, 1932.

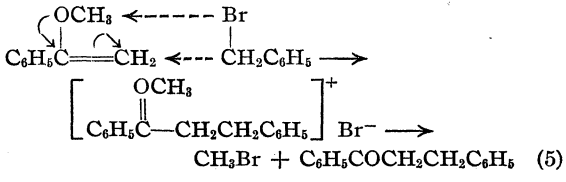
Ethyl chloroacetate yields 36% of ethyl β-benzoylpropionate and a trace of *sym*-triphenylbenzene. Benzoyl chloride heated with equimolecular amounts of α-methoxystyrene produces tribenzoylmethane in 9% yield; in large excess it gives 45% of the theoretical amount of *sym*-triphenylbenzene. The triphenylbenzene is the product of a side reaction and is not related to the condensation. It has its origin in the reaction of hydrogen chloride with α-methoxystyrene. Even at room temperature the ether gives triphenylbenzene in 54% yield simply on saturation with hydrogen chloride.

The condensation of α-methoxystyrene with alkyl halides has the appearance of a novel reaction, but in point of fact it has a close analogy in the addition of methyl iodide to ethyl β-diethylaminocrotonate (4).[6] The reaction between α-



(4)

methoxystyrene and benzyl bromide may be similarly formulated (5); the only real difference



(5)

is that in the former addition the nitrogen atom is sufficiently basic to form a stable salt, whereas the onium compound formed from α-methoxystyrene decomposes instantaneously.

Experimental Part

All condensations were carried out in Pyrex tubes heated in an electrical bomb furnace.

Condensation with Benzyl Bromide.—Ten grams of α-methoxystyrene and 76 g. of benzyl bromide were heated for seventeen hours at 220°. When the cooled bomb was opened, a slight pressure was evident. The unreacted benzyl bromide and the propiophenone formed by normal rearrangement were removed by vacuum distillation. An 8.3-g. fraction was collected at 150° (1 mm.). It soon solidified, and after one crystallization from alcohol yielded 8.0 g. of β-phenylpropiophenone; m. p. and mixed m. p. 72–73°.[7] No dibenzyl could be detected in the residues.

In order to identify methyl bromide as a reaction product a mixture of α-methoxystyrene and benzyl bromide was heated under a reflux while the effluent gas was passed into a boiling solution of sodium saccharin in butyl carbitol and water. N-Methylsaccharin separated on dilution; m. p. 132°.[8]

Condensation with *n*-Butyl Bromide.—A mixture of 4.6 g. of α-methoxystyrene and 105 g. of *n*-butyl bromide heated to 245° for thirty-six hours gave 1.7 g. of *n*-caprophenone boiling at 108–110° at 7 mm. It was characterized as the semicarbazone; m. p. and mixed m. p. 131–132°.[9]

Condensation with Ethyl Chloroacetate.—Ninety-seven grams of ethyl chloroacetate and 7.7 g. of α-methoxystyrene were heated to 200° for twenty-five hours. Fractionation yielded 90 g. of ethyl chloroacetate, 1.7 g. of acetophenone and 4.3 g. of ethyl β-benzoylpropionate; b. p. 143–145° at 6 mm. The semicarbazone melted at 138–139° and a mixed melting point was not depressed.

Anal. Calcd. for $C_{13}H_{17}O_3N_3$: N, 16.0. Found: N, 16.1.

The non-volatile residue upon treatment with ether gave 0.3 g. of *sym*-triphenylbenzene; m. p. and mixed m. p. 173–174°.[10]

Condensation with Benzoyl Chloride.—Equimolecular amounts of α-methoxystryene and benzoyl chloride (4.5 g. and 4.7 g., respectively) heated to 180° for seven hours gave 0.5 g. of a white solid, sparingly soluble in organic solvents. It melted at 210° and gave a ferric chloride color test. The melting point was not depressed by a synthetic sample of tribenzoylmethane.[11]

Similar heating of 5.2 g. of the ether with 134 g. of the acid chloride gave as the only identifiable substance 1.8 g. of *sym*-triphenylbenzene; m. p. and mixed m. p. 173–174°.[10]

Reaction between Hydrogen Chloride and α-Methoxystyrene.—Dry hydrogen chloride was passed into 2 g. of α-methoxystyrene for two hours. The reaction mixture solidified to a brown mass. Crystallization from alcohol–acetone gave 0.8 g. of triphenylbenzene; m. p. and mixed m. p. 173–174°.

Summary

α-Methoxystyrene condenses with benzyl bromide, *n*-butyl bromide, ethyl chloroacetate and benzoyl chloride, but not with bromobenzene. A methyl halide is eliminated and a phenacyl derivative is formed. An interpretation of the course of the reaction is presented.

MADISON, WISCONSIN RECEIVED MARCH 23, 1940

(6) Robinson, *J. Chem. Soc.*, **109**, 1038 (1916); Lauer and Lones, THIS JOURNAL, **59**, 232 (1937).

(7) Kohler, *Am. Chem. J.*, **42**, 391 (1909).

(8) Merritt, Levey and Cutter, THIS JOURNAL, **61**, 15 (1939).

(9) Schroeter, *Ber.*, **40**, 1603 (1907).

(10) Engler and Berthold, *ibid.*, **7**, 1123 (1874).

(11) Abell, *J. Chem. Soc.*, **101**, 998 (1912).

[CONTRIBUTION FROM THE INSTITUTO DE FISIOLOGÍA, FACULTAD DE MEDICINA, BUENOS AIRES]

Action of the Reagent Pyridine–Acetic Anhydride on *d*-α-Glucoheptose, *d*-Glucosamine and *l*-Fucose Oximes

BY E. RESTELLI DE LABRIOLA AND V. DEULOFEU

The action of pyridine–acetic anhydride on aldose oximes was studied first by Behrend[1] with glucose oxime. He obtained an oxime hexaacetate at low temperature and the *d*-gluconononitrile pentaacetate at a higher temperature. Wolfrom and Thompson[2] showed that Behrend's acetylated glucose oxime was a cyclic form and that another isomer could be obtained when working with Wohl's method. This isomer was an open-chain or *aldehydo*-glucose oxime hexaacetate and was an intermediate in the formation of the acetylated nitrile.

Deulofeu, Wolfrom and co-workers[3] subjected galactose oxime to the action of pyridine–acetic anhydride at low temperature and obtained a mixture of *aldehydo*-galactose oxime hexaacetate, galactononitrile pentaacetate and cyclic galactose oxime hexaacetate. This work showed that galactose oxime reacted in the open-chain form to give the first two compounds and in the ring or cyclic form to give the last-named substance. Deulofeu, Cattaneo and Mendivelzúa[4] subjected a series of aldose oximes to the same reagent and found that even at very low temperatures, *l*-arabinose, *d*-xylose, *l*-rhamnose and *d*-mannose oximes reacted in the *aldehydo* structure. The first three gave the acetylated nitriles. Above 30° mannose oxime gave the acetylated nitrile but below that temperature *aldehydo*-mannose oxime hexaacetate was obtained. Similar results were obtained by Wolfrom and Georges[5] with mannose oxime. The application of the method to cellobiose oxime by Wolfrom and Soltzberg[6] and to *d*-α-galaheptose oxime by Hann and Hudson[7] gave n both cases the acetylated open-chain form.

We have studied now the behavior of three other aldose oximes, *viz.*, *d*-glucosamine oxime, *d*-α-glucoheptose oxime and *l*-fucose oxime, when treated with pyridine–acetic anhydride. The first two always reacted in the open-chain form but only gave acetylated nitriles, even at −10°. No open-chain or cyclic acetylated oximes could be detected among the products of the reaction. A very different result was obtained with *l*-fucose oxime. At −10°, there was obtained an oxime pentaacetate, melting at 116°, which was identical with the compound isolated by Votoček[8] on preparing *l*-fuconononitrile tetraacetate by Wohl's method. A sample of this substance, which gave no nitrile reaction, was found to have a rotatory power of +44.9° (*l*-series).[9] This is a cyclic compound because on fusion or on treatment with acetic anhydride and sodium acetate, it does not change to a nitrile. Its rotatory power is also of the same order as that of the closely related derivative of galactose oxime, which rotates −27.5° (*d*-series). At higher temperatures, part of the oxime reacted in the open-chain form and *l*-fuconononitrile tetraacetate was easily isolated and was finally the main product. The acetylated nitrile rotated at −22.4°, a value lower than that established for *d*-galactononitrile pentaacetate (+43.2°). The sign of the rotation was in agreement with the rule formulated by Deulofeu[10] that when the acetoyl group on carbon two is on the left in the projection formula the rotation is in the *levo* direction.

It is a very difficult matter to correlate the results obtained with the different oximes. Hann and Hudson[7] have pointed out that there is a similarity between the stereochemical constitution of *d*-mannose and *d*-α-galaheptose, and the reaction of their oximes with pyridine and acetic anhydride. It is evident that according to the structure of the sugar, its oxime tends to react at low temperatures in a cyclic form (*d*-glucose); in the *aldehydo* structure (*l*-arabinose, *d*-xylose, *l*-rhamnose, *d*-α-galaheptose, *d*-α-glucoheptose and *d*-glucosamine); or in a mixed form (*d*-galactose and *l*-fucose). When reacting in the open-chain form, the acetylated nitrile or the acetylated

(1) R. Behrend, *Ann.*, **359**, 109 (1907).
(2) M. L. Wolfrom and A. Thompson, THIS JOURNAL, **53**, 622 (1931).
(3) V. Deulofeu, M. L. Wolfrom, P. Cattaneo, C. C. Christman and L. W. Georges, *ibid.*, **55**, 3488 (1933).
(4) V. Deulofeu, P. Cattaneo and G. Mendivelzúa, *J. Chem. Soc.*, 147 (1934).
(5) M. L. Wolfrom and L. W. Georges, THIS JOURNAL, **58**, 1781 (1936).
(6) M. L. Wolfrom and S. Soltzberg, *ibid.*, **58**, 1783 (1936).
(7) R. M. Hann and C. S. Hudson, *ibid.*, **59**, 1898 (1937).
(8) E. Votoček, *Ber.*, **50**, 37 (1917).
(9) All rotations are specific rotations measured in chloroform solution at room temperature.
(10) V. Deulofeu, *Nature*, **131**, 548 (1933).

aldehydo oxime can be obtained as products. If we apply to the oximes of the aldoses the known information concerning the reactivity of aldoximes, then the formation of the acetylated nitrile or of the acetylated *aldehydo* oxime must be determined by preferential existence of *syn* or *anti* forms of the oxime, the first stabilizing as the oxime acetate. If we consider only the low temperature reaction, we find that *l*-rhamnose, *d*-mannose, *d*-α-glucoheptose and *d*-α-galaheptose oximes react in the open-chain form and are configurationally related in part, as their first three hydroxyl groups have the same spatial configuration. From their mutarotation, it has always been accepted that the aldose oximes have, at least in part, a cyclic structure, but it is evident that the oxygen rings must open easily under the action of the reagents.

l-Fucose and *d*-galactose are closely related in their configuration and their oximes react in the same manner to give derivatives of both the cyclic and open-chain forms. It must be noted that the acetate of the *aldehydo*-fucose oxime is unstable as only the acetylated nitrile can be isolated. On the other hand, *aldehydo*-galactose oxime hexaacetate can be obtained. Another difference is that, with fucose, the cyclic form predominates at low temperatures, while with galactose, the open-chain form predominates. The elimination of the fifth carbon atom of galactose, as in arabinose, determines an exclusive reaction in the open-chain form.

It is more difficult to relate the remaining oximes. Their different manner of reacting is a proof of the sensibility of the path of the reaction to the spatial constitution of the aldose. Glucose reacts at 0° exclusively in the cyclic form and the oxime hexaacetate is obtained, but the introduction of a glucose residue on the fourth carbon atom, as in cellobiose, or the transformation of the first hydroxyl into an amino group, as in glucosamine, or the elimination of the fifth carbon atom, as in xylose, determines that the reaction takes place exclusively in the *aldehydo* form.

Experimental

d-α-Glucoheptose Oxime.—*d*-α-Glucoheptose (1 g.) prepared by reduction of *d*-α-glucoheptonolactone,[11] was dissolved in 1 cc. of water and added to 10 cc. of alcoholic hydroxylamine solution prepared according to Wohl and List.[12] As no crystalline oxime separated spontaneously, the solution was concentrated under reduced pressure (20°) and a sirup was obtained that could not be induced to crystallize by drying with alcohol or by standing over sulfuric acid in a vacuum. A semi-crystalline solid was the best material obtained and this could not be purified by employing different solvents. The solid material could be used with success for the preparation of the acetylated nitrile.

d-α-Glucoheptononitrile Hexaacetate.—The oxime from 1 g. of *d*-α-glucoheptose was treated with a mixture (1:1) of 10 cc. of pyridine and acetic anhydride. In the several experiments the temperature was varied from −10 to 20°. The oxime dissolved more rapidly with increasing temperature of reaction. The solution was evaporated in a desiccator over sulfuric acid and potassium hydroxide, and crystals began to appear that when dried melted at 110–112° without purification. Pure material was obtained on recrystallization from alcohol; yield 1.5 g. (69%, basis *d*-α-glucoheptose), m. p. 113–114°, spec. rot. +24.1 (20°, D-line, $CHCl_3$). Zemplén and Kiss[13] record the constants: m. p. 112.5–113.5°, spec. rot. +24.6° (D-line, $CHCl_3$).

d-Glucosamine Oxime Hydrochloride.—Although this compound has been prepared by Winterstein,[14] the following method gave better yields. An alcoholic solution of hydroxylamine was prepared by dissolving 15 g. of hydroxylamine hydrochloride in 8 cc. of water, adding 15 g. of sodium dissolved in 100 cc. of absolute ethanol, filtering the precipitated sodium chloride and washing with 20 cc. of absolute ethanol (washings combined with filtrate). Glucosamine hydrochloride (20 g.), dissolved in the minimum quantity of warm water, was added to the above solution and, after twenty-four hours of standing, crystallization was initiated by seeding; yield 15 g. (70%), m. p. 166°. Impure crystals could be recovered from the mother liquor.

d-Glucosaminonitrile Pentaacetate.—Glucosamine oxime hydrochloride (1 g.) was treated with 12 cc. of the pyridine–acetic anhydride (1:1) mixture. In the several experiments the temperature was varied from −10 to 20°. After solution of the oxime, the reaction mixture was concentrated in a desiccator at 20° and crystals separated; m. p. 120°. Long prisms were obtained on recrystallization from alcohol; yield 1.8 g., m. p. 126°, spec. rot. +20.5° (20°, D-line, *c* 4.7, $CHCl_3$, 2-dm.). Neuberg and Wolff,[15] who prepared this substance by Wohl's method, recorded the melting point of 118–119° but gave no rotation.

Anal. Calcd. for $C_{16}H_{22}O_9N_2$: N, 7.25. Found: N, 7.25.

Mild Acetylation of *l*-Fucose Oxime.—*l*-Fucose oxime was prepared according to Votoček,[8] who recorded the melting point 188–189°; yield 1.8 g. from 2 g. of fucose, m. p. 185°. For the acetylation, lots of 0.5 g. of *l*-fucose oxime were treated with 5 cc. of the pyridine–acetic anhydride (1:1) mixture at the temperatures indicated in Table I. The solution obtained was concentrated under reduced pressure at room temperature. Concentration was continued for a short time after the appear-

(11) L. H. Philippe, *Ann. chim. phys.*, [8] **26**, 316 (1912).
(12) A. Wohl and E. List, *Ber.*, **30**, 3101 (1897).
(13) G. Zemplén and D. Kiss, *ibid.*, **60**, 165 (1927).
(14) E. Winterstein, *ibid.*, **29**, 1392 (1896).
(15) C. Neuberg and H. Wolff, *ibid.*, **35**, 4017 (1902).

ance of crystals, after which these were removed by filtration. These were crystals of *l*-fuconitrile tetraacetate; m. p. 176–177°. On further concentration, material was obtained which began to melt at about 115° and was a difficulty separable mixture of the cyclic-*l*-fucose oxime pentaacetate and the acetylated nitrile. Acetylation at −10° did not give crystals melting at 176°, but the nitrile was always present as the material isolated gave a faint nitrile reaction. Table I records the results of several experiments operated at different temperatures.

TABLE I

MILD ACETYLATION OF *l*-FUCOSE OXIME (0.5 G.) AT VARIOUS TEMPERATURES

Temp., °C.		−10	3	15	37	100
Wt., g., m. p.	115°	0.8	0.62	0.5	0.5	0.30
Wt., g., m. p.	176°	..	.12	.32	.36	.48

l-Fuconitrile Tetraacetate.—The material from several of the preparations described above was combined and recrystallized from alcohol, from which it was obtained as rectangular plates; m. p. 177°, sp. rot. −22.4° (20°, D-line, *c* 5.0, $CHCl_3$, 2-dm.).

l-Fucose Oxime Pentaacetate.—The product obtained by acetylation at −10° as described above, gave the nitrile test. Crystallization from alcohol did not separate the nitrile and the method of Deulofeu, Wolfrom and coworkers[3] for the purification of galactose oxime hexaacetate was employed. The crude preparation (1.5 g.) was recrystallized once from alcohol and this material was then boiled with 500 cc. of water, a portion dissolving. The mixture was cooled to 5°, maintained at this temperature for one hour, filtered and the filtrate extracted with chloroform. The crystalline material (plates) obtained on chloroform removal and recrystallization from alcohol gave a negative nitrile reaction; m. p. 116° (unchanged on further recrystallization), spec. rot. +44.9° (25°, D-line, *c* 3.35, $CHCl_3$, 1.894-dm.).

The acetylated oxime on heating at 135° for five minutes gave a sirup that crystallized on the addition of alcohol. The crystals melted at 115–116° and were the original substance. Unchanged material (m. p. 116°) also was returned on refluxing for fifteen minutes with acetic anhydride and sodium acetate.

Summary

1. A study has been made of the action of the reagent pyridine–acetic anhydride on the oximes of *d*-α-glucoheptose, *d*-glucosamine hydrochloride and *l*-fucose.

2. *d*-α-Glucoheptose oxime and *d*-glucosamine oxime react in an open-chain form to give the acetylated nitriles, even at low temperatures.

3. *l*-Fucose oxime reacts at low temperature in a cyclic form and cyclic-*l*-fucose oxime pentaacetate predominates among the substances obtained. At higher temperatures one part reacts in an open-chain form and *l*-fuconitrile tetraacetate is produced and predominates at 100°.

BUENOS AIRES, ARGENTINE RECEIVED FEBRUARY 23, 1940

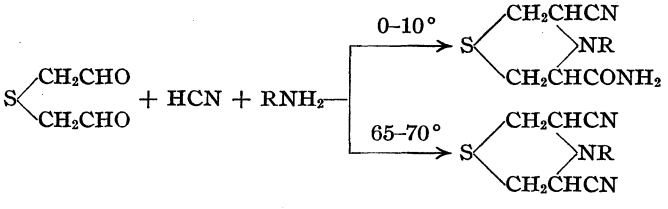
[CONTRIBUTION FROM THE STERLING CHEMISTRY LABORATORY, YALE UNIVERSITY]

Studies in the Thiamorpholine Series. II. N-Alkyl Substituted Derivatives

BY HELEN I. MINER,[1] EDWIN O. HOOK[1] AND ROBERT D. COGHILL[2]

In the first paper of this series was described the reaction between thiodiacetaldehyde, hydrocyanic acid and ammonia to produce the half-amide, half-nitrile of thiamorpholine 3,5-dicarboxylic acid. The use of the Strecker reaction in this fashion for ring-closure in the thiamorpholine series has now been extended by using various aliphatic amines in place of the ammonia.

During the course of a study of the original synthesis in order to determine better reaction conditions, it was found that by allowing the reaction to proceed at temperatures of 65–70° instead of 0°, the dinitrile of the acid was obtained rather than the nitriloamide. This situation was also found to hold when methyl- or ethylamine was substituted for the ammonia, the dinitriles being formed at the elevated temperatures. These reactions can be expressed by the equations



In the cases of other amines, benzylamine formed only the dinitrile, while *n*-butyl-, *n*-amyl-, isoamyl- and *n*-heptylamine produced the nitriloamides. To date it has not been found possible to cause either reaction to take place with aniline.

Attempts have been made to hydrolyze these compound products to the corresponding N-alkyl

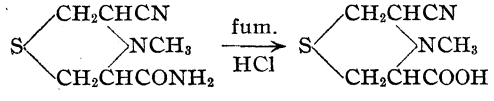
(1) This paper is constructed from the Dissertations of Helen I. Miner and Edwin O. Hook which were submitted in candidacy for the degree of Doctor of Philosophy at Yale University, June, 1939.

(2) Northern Regional Research Laboratory, U. S. Department of Agriculture, Peoria, Ill.

TABLE I

3,5-Dinitrilothiamorpholine	Formula	M. p., °C. corr.	Analyses, % C Calcd.	C Found	H Calcd.	H Found	N Calcd.	N Found	S Calcd.	S Found
N-Methyl-	$C_7H_9N_3S$	178	50.2	50.0	5.4	5.4	25.1	24.9	19.2	19.4
N-Ethyl-	$C_8H_{11}N_3S$	137	53.0	53.1	6.1	6.2	23.2	23.1	17.7	18.0
N-Benzyl-	$C_{13}H_{13}N_3S$	170	64.2	64.0	5.4	5.3	17.3	16.9		
Nitrilothiamorpholine-5-carboxamide										
N-Methyl-3-	$C_7H_{11}ON_3S$	208d	45.3	45.1	6.0	6.2	22.6	22.3	17.3	17.5
N-Ethyl-3-	$C_8H_{13}ON_3S$	177d	48.2	48.3	6.6	6.8	21.1	20.8	16.1	16.5
N-*n*-Butyl-3-	$C_{10}H_{17}ON_3S$	192d	52.8	52.7	7.5	7.7	18.5	17.3	14.1	14.5
N-*n*-Amyl-3-	$C_{11}H_{19}ON_3S$	174d	54.7	54.8	7.9	7.9	17.4	16.4	13.3	12.9
N-iso-Amyl-3-	$C_{11}H_{19}ON_3S$	192d	54.7	54.7	7.9	8.1	17.4	16.3	13.3	13.4
N-*n*-Heptyl-3-	$C_{13}H_{23}ON_3S$	181d	57.9	58.1	8.6	8.8	15.6	14.7	11.9	12.2

thiamorpholine-3,5-dicarboxylic acids, but so far with very meager success. The compounds are unstable and decompose under most of the reaction conditions used. The odor of hydrocyanic acid becomes quite pronounced and the material rapidly transforms into red or black tars. In one case, however, using cold fuming hydrochloric acid, the amide group of the N-methyl derivative was hydrolyzed to a carboxyl.



This nitrilo acid, when subjected to more strenuous conditions, also gave rise to colored tar-like products. Further attempts are being made to accomplish this hydrolysis in a satisfactory manner.

Experimental

All melting points are corrected.

3,5-Dinitrilothiamorpholine.—Fifty-three grams of acetalyl sulfide was hydrolyzed and the resulting solution of thiodiacetaldehyde concentrated to 100 cc. as previously described.[3] To this solution, held at a temperature of 0°, were added 4 drops of piperidine and 16 cc. of liquid hydrogen cyanide. After standing ten minutes 7 g. of ammonia gas was led in without cooling. The temperature rapidly rose to 70° and a crystalline material separated. This was filtered off, washed with ice-water and dried; yield, 13.9 g. or 43%. After recrystallization from 95% alcohol the product was obtained as four-sided plates which melted with decomposition at 214°.

(3) R. D. Coghill, THIS JOURNAL, **59**, 801 (1937).

Anal. Calcd. for dinitrile, $C_6H_7N_3S$: C, 47.0; H, 4.6; N, 27.4; S, 20.9. Found: C, 47.0; H, 4.5; N, 26.8; S, 21.0.

N-Alkyl Dinitrilothiamorpholines.—These were prepared as described above except for the substitution of methyl-, ethyl- and benzylamines for the ammonia. Table I portrays the melting points and analyses of these substances.

N - Alkyl - 3 - nitrilothiamorpholine - 5 - carboxamides.—These compounds were prepared as described for the dinitriles, except that during the addition of the amines the temperatures were kept below 10°. Liquid amines were added slowly from a dropping funnel. The melting points and analyses of these substances are given in Table I.

N-Methyl-3-nitrilothiamorpholine-5-carboxylic Acid.—Five grams of N-methyl-3-nitrilothiamorpholine carboxamide was dissolved in 50 cc. of cold fuming hydrochloric acid and allowed to stand for five days at 10° and an additional five days at room temperature. After removal of the hydrochloric acid *in vacuo* at low temperature the residue was taken up in 50 cc. of cold water, which dissolved the tarry material and left some crystals in suspension. These were filtered off, washed, and recrystallized from boiling water. They melted at 184–185° and decomposed aqueous sodium bicarbonate; yield, 0.6 g. (12%).

Anal. Calcd. for $C_7H_{10}O_2N_2S$: C, 45.15; H, 5.41. Found: C, 45.06; H, 5.35.

We gratefully acknowledge a grant from Sharp and Dohme which made possible a part of this work.

Summary

Several new N-alkyl substituted thiamorpholines have been prepared and described.

NEW HAVEN, CONN. RECEIVED APRIL 24, 1940

[CONTRIBUTION FROM THE STERLING CHEMISTRY LABORATORY, YALE UNIVERSITY]

Studies in the Thiamorpholine Series. III. Derivatives of Thiamorpholine-3,5-dicarboxylic Acid

BY EDWIN O. HOOK,[1] HELEN I. MINER,[1] AND ROBERT D. COGHILL[2]

A study of thiamorpholine-3,5-dicarboxylic acid with the view to the preparation of possibly pharmacologically active products has been in progress since the original synthesis of the parent substance, described in the first paper of this series.[3]

The thiamorpholine nucleus with acid groups in the 3,5-positions seems to be reasonably stable to ordinary reactions. The sulfur atom has been oxidized by peroxide to sulfoxide and the carboxyl groups themselves can be esterified readily. The NH group, being alpha to both carboxyls, is apparently somewhat sterically hindered, as the hydrogen is replaced with comparative slowness by such reagents as carbobenzoxy chloride and ethyl chlorocarbonate.

The action of acetic anhydride on the acid leads to a compound which seems to be the anhydride of the acetyl derivative. This would seem to indicate, but not necessarily prove, that the thiamorpholine-3,5-dicarboxylic acid previously described had the meso (*cis*) structure, rather than the racemic (*trans*).

A description of the derivatives prepared is given.

Experimental

All melting points are corrected.

1-Oxothiamorpholine-3,5-dicarboxylic Acid.—One gram of thiamorpholine-3,5-dicarboxylic acid, 20 cc. of acetic acid and 5 cc. of acetic anhydride were mixed in a round-bottomed flask and cooled in an ice–salt-bath. One gram of 30% hydrogen peroxide was then added slowly during vigorous stirring. The reaction was now allowed to stand at room temperature for five days, during which time crystals separated. These were filtered off, washed with water and recrystallized from water; m. p. 242° (dec.). The yield was 0.69 g. (64%).

Anal. Calcd. for $C_6H_9O_5NS$: C, 34.8; H, 4.4; N, 7.8; S, 15.5. Found: C, 34.8; H, 4.6; N, 6.1; S, 15.6.

N-Acetylthiamorpholine-3,5-dicarboxylic Acid Anhydride.—This compound was obtained by adding thiamorpholine-3,5-dicarboxylic acid to boiling acetic anhydride; m. p. 143° (dec.).

Anal. Calcd. for $C_8H_9O_4NS$: C, 44.6; H, 4.2. Found: C, 44.4; H, 4.5.

N - Carbobenzoxythiamorpholine - 3,5 - dicarboxylic Acid.—A mixture of 2 g. of thiamorpholine-3,5-dicarboxylic acid and 5 g. of sodium bicarbonate was dissolved in about 20 cc. of water. The solution was treated with 6 cc. of carbobenzoxy chloride, added in four portions over a period of two hours. Between additions the mixture was shaken in the shaking machine and shaking was continued overnight (fifteen hours) to complete the reaction. The solution was then extracted three times with ether to remove benzyl alcohol and any unchanged carbobenzoxy chloride, treated with Norite for an hour at room temperature, and filtered. Upon acidification of the filtrate with hydrochloric acid, the product separated as an oil, which after standing overnight in an oven at about 40° became crystalline; yield, 2 g. (59%). Upon slow evaporation of a water solution of this material, colorless rectangular prisms were obtained which melted at 149.5–150°.

Anal. Calcd. for $C_{14}H_{15}O_6NS$: C, 51.7; H, 4.6; S, 9.9. Found: C, 51.6; H, 4.6; S, 10.2.

Diethyl Ester of Thiamorpholine-3,5-dicarboxylic Acid.—A mixture of 10 g. of finely-powdered thiamorpholine-3,5-dicarboxylic acid, 200 cc. of absolute alcohol, and 5 cc. of concentrated sulfuric acid was refluxed for twenty-four hours in a 500-cc. 2-necked flask fitted with a dropping funnel and an efficient fractionating column equipped with a total-condensation variable take-off stillhead. Ten cc. of dry benzene was added through the dropping funnel and distilled from the flask, first as the ternary mixture with alcohol and water boiling at 64°, and later as the binary mixture with alcohol boiling at 68°, until the distillation temperature had risen to the boiling point of pure alcohol. This procedure was repeated after the eighth hour of refluxing. Little or none of the distillate came over below 68°. After four hours of refluxing, the sulfuric acid was neutralized by the cautious addition of 10 g. of calcium carbonate, after which the mixture was filtered and the precipitate washed by trituration with a small amount of 95% alcohol. The alcohol was distilled from the combined filtrate and washings under reduced pressure and the residual sirup taken up in 25–30 cc. of water. The solution was made basic with sodium bicarbonate and extracted four times with 20-cc. portions of ether. After drying of the extract and removal of the ether the product was distilled *in vacuo*. A light yellow oil boiling at 154–156° at 3 mm. was obtained; yield, 8.3 g. (64%); $n^{20}D$ 1.4924.

Anal. Calcd. for $C_{10}H_{17}O_4NS$: S, 12.96. Found: S, 12.90. The ester formed a hydrochloride, m. p. 148°.

Anal. Calcd. for $C_{10}H_{18}O_4NSCl$: Cl, 12.49. Found: Cl, 12.45.

β-Diethylaminoethyl Ester of Thiamorpholine-3,5-dicarboxylic Acid (Trihydrochloride).—To 3.3 g. of the diethyl ester of thiamorpholine-3,5-dicarboxylic acid were added 50 cc. of freshly distilled β-diethylaminoethanol and 0.2 g. of sodium. The mixture was then refluxed for one and one-half hours in a flask fitted with an efficient frac-

(1) This paper is constructed from the Dissertations of Helen I. Miner and Edwin O. Hook which were submitted in candidacy for the degree of Doctor of Philosophy at Yale University, June, 1939.

(2) Northern Regional Research Laboratory, U. S. Department of Agriculture, Peoria, Ill.

(3) R. D. Coghill, THIS JOURNAL, **59**, 801 (1937).

tionating column equipped with a total-condensation variable take-off stillhead. The ethyl alcohol formed in the alcoholysis was fractionated from the mixture at frequent intervals. About 1.5 cc. of material boiling below 150° was separated during the course of the reaction. The excess β-diethylaminoethanol was removed from the reaction mixture by distillation on the steam-bath under reduced pressure, and the residue was dissolved in a small amount of ice-water. The solution was extracted three times with ether and the extracts washed three times with ice-water and dried. On passing hydrogen chloride into the ether solution the product separated as a dark tar which was recrystallized from *n*-butyl alcohol; m. p. 208°, (dec.); yield, 1.3 g. (17%).

Anal. Calcd. for $C_{18}H_{38}O_4N_3SCl_3$: C, 43.3; H, 7.7; N, 8.4; S, 6.4; Cl, 21.3. Found: C, 43.9; H, 7.8; N, 8.5; S, 6.2; Cl, 20.3.

γ-Diethylaminopropyl Ester of Thiamorpholine-3,5-dicarboxylic Acid (Trihydrochloride).—This substance was prepared in the same general fashion as just described for the β-diethylaminoethyl ester; m. p. 215° (dec.).

Anal. Calcd. for $C_{20}H_{42}O_4N_3SCl_3$: N, 7.97. Found: N, 7.98, 7.71.

Thiamorpholine - 3,5 - di - (β - diethylaminoethyl) - carboxamide.—A mixture of 1 g. of the diethyl ester of thiamorpholine-3,5-dicarboxylic acid and 1.5 g. of β-diethylaminoethylamine was heated to 160–170° for twelve hours in an open test-tube supported in a Wood's metal bath. Excess amine was removed from the reaction mixture by distillation on the steam-bath under reduced pressure. The residue was dissolved in 50 cc. of dry ether and the product precipitated as the hydrochloride by adding an ethereal solution of hydrogen chloride. The material so obtained was a tan-colored, very hygroscopic, crystalline solid. It was purified by dissolving in hot absolute alcohol, adding ether to the point of turbidity, and allowing to cool. After four such recrystallizations a pure white, practically non-hygroscopic product was obtained which decomposed in the neighborhood of 245°, depending on the rate of heating; yield, 1.1 g. (55%).

Anal. Calcd. for $C_{18}H_{40}O_2N_5SCl$: C, 43.5; H, 8.1. Found: C, 43.0; H, 8.3.

We gratefully acknowledge a grant from Sharp and Dohme which made possible a part of this work.

Summary

Some new derivatives of thiamorpholine-3,5-dicarboxylic acid have been prepared, several of them having interesting pharmacological potentialities.

NEW HAVEN, CONN. RECEIVED APRIL 24, 1940

[CONTRIBUTION FROM THE HOSPITAL OF THE ROCKEFELLER INSTITUTE FOR MEDICAL RESEARCH]

The Structure of Trimethyl Glucurone

BY RICHARD E. REEVES[1]

Pryde and Williams[2] have prepared from glucurone a crystalline trimethyl derivative which they regard to be 1,2,4-trimethylglucurone (I). Although no evidence substantiating this structure has been presented, Marrack and Carpenter[3] also refer to the trimethylglucurone as having this structure. Such a substance on hydrolysis and oxidation might be expected to yield 2,4-dimethylsaccharic acid, which is wanted as a reference compound in this Laboratory.

When the trimethylglucurone, m. p. 129–130°, was prepared, its properties were found to resemble those of a methylfuranoside more than the methylpyranoside called for by structural formula I. On acid hydrolysis reducing sugar was liberated at the rapid rate characteristic of methylfuranosides.[4] Pryde and Williams have noted the rapid fall in rotation when trimethylglucurone is dissolved in methanol containing hydrogen chloride. It is now shown that this fall in rotation is accompanied by the formation of an isomeric trimethylglucurone, m. p. 90–91°, having a low rotation. This suggests the rapid mutarotation which Levene and Meyer[5] have observed for α- and β-methylfuranosides under similar conditions.

The high melting trimethylglucurone was hydrolyzed and oxidized to a dimethylsaccharic acid which was characterized as the crystalline diamide. When the crude dimethylsaccharic acid was esterified with cold ethereal diazomethane, no crystalline dimethylsaccharic acid esters or lactone esters were obtained; instead there was produced an unsaturated dimethyl lactone methyl ester (II) known to have its methyl groups on positions 2 and 5.[6] This

(1) Present address: Boyce Thompson Institute for Plant Research, Inc., Yonkers, N. Y.

(2) J. Pryde and R. T. Williams, *Biochem. J.*, **27**, 1205 (1933).

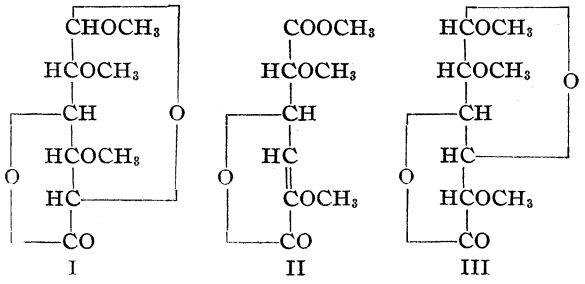
(3) J. Marrack and B. R. Carpenter, *Brit. J. Exptl. Path.*, **19**, 59 (1938).

(4) W. N. Haworth and E. L. Hirst, *J. Chem. Soc.*, 2615 (1930).

(5) P. A. Levene and G. M. Meyer, *J. Biol. Chem.*, **74**, 701 (1927).

(6) O. Th. Schmidt, H. Zeiser and H. Dippold, *Ber.*, **70**, 2402 (1937).

finding, together with the above-mentioned properties, make it appear that the furanoside structure III, 2,5-dimethyl-α-methylglycoside of glucurone, is probably the correct structure for the trimethylglucurone of Pryde and Williams. The low melting isomer and the diamide are regarded as 2,5-dimethyl-β-methylglycoside of glucurone and 2,5-dimethylsaccharic acid diamide, respectively.



Experimental Part

High-Melting Trimethylglucurone.—Pryde and Williams[1] report a 25% yield of this substance following three methylations of glucurone with silver oxide and methyl iodide. By the present procedure a 50% yield was obtained after one methylation. To 5.11 g. of glucurone was added 15 cc. of acetone and 20 cc. of methyl iodide. The vigorously stirred mixture was cooled in an ice-bath during the addition of 3 g. of silver oxide. The temperature was gradually raised to 45° with the addition of 27 g. of silver oxide during nine hours. Fifteen cc. of methyl iodide and 10 cc. of acetone were added and the mixture was then refluxed at 45–48° for five hours. The product was extracted with chloroform and crystallized from acetone by the addition of ether, a second and third crop being obtained from the mother liquors. After recrystallization 2.71 g. of 2,5-dimethyl-α-methylglycoside of glucurone, m. p. 129–130°, was obtained; sp. rot. (D-line) (24°) 151° (*c*, 0.4 in $CHCl_3$).

Low-melting Trimethylglucurone.—Trimethylglucurone, m. p. 129–130°, (372.6 mg.) was dissolved at 23° in 15 cc. of methanol containing 3.6% dry hydrogen chloride. After seventy minutes the rotation (1-dm. tube) became constant at −0.03°. The solution was evaporated to dryness *in vacuo* and, when the residue was redissolved in methanol and again taken to dryness, crystals formed in the distillation flask. Recrystallization from methanol and ether gave 270 mg. of 2,5-dimethyl-β-methylglycoside of glucurone, m. p. 90–1°, sp. rot. (D-line) (21°) 2.0° (*c*, 1.0 in H_2O); (24°) −2.3° (*c*, 0.9 in $CHCl_3$).

Anal. Calcd. for $C_9H_{14}O_6$: C, 49.53; H, 6.42; CH_3O, 42.6. Found: C, 49.24; H, 7.15; CH_3O, 42.85.

Kinetics of Hydrolysis.—Trimethylglucurone (94.6 mg.) m. p. 129–130° was refluxed in 50 cc. of 0.05 *N* hydrochloric acid and the reducing sugars were determined at intervals by the modified Hagedorn–Jensen procedure.[7] The results are given in cc. of 0.01 *N* thiosulfate required by 1 cc. of hydrolysate after refluxing for a stated length of time: 0 min., 0.11 cc.; 5 min., 1.76 cc.; 15 min., 3.91 cc.; 30 min., 4.65 cc.; 60 min., 4.49 cc. To minimize the effect of the gradual decomposition of reducing sugar a curve was drawn through the points and the velocity constant was calculated by the method of Guggenheim[8] for the first twenty minutes of the hydrolysis. The value was found to be $k = 1380 \times 10^{-5}$ min.$^{-1}$ for *N*/100 HCl at 100°, which is definitely within the range exhibited by most furanosides. When recalculated on the basis of natural logarithms the values found by Haworth and Hirst[4] for furanosides in 0.01 *N* acid at 100° range from 600×10^{-5} to $11{,}000 \times 10^{-5}$.

2,5-Dimethylsaccharic Acid Diamide.—Trimethylglucurone (100 mg.), m. p. 129–130°, was heated for four hours at 80–85° in 4 cc. of dilute nitric acid, sp. gr. 1.2. Nitric acid was removed by evaporating *in vacuo*, adding water and repeatedly evaporating to dryness *in vacuo*. The residue was then esterified by heating for three hours at 75° in a sealed tube with 4 cc. of methanol containing 2% dry hydrogen chloride. The hydrogen chloride was removed with silver carbonate. Attempts to obtain crystals from this ester both before and after vacuum distillation were unsuccessful. The sirup was dissolved in 2 cc. of methanol, cooled to 0°, and treated with ammonia gas. Crystals separated, and more were obtained by the addition of ether to the mother liquors; 43 mg. of crude material yielded 11 mg. of pure diamide, m. p. 169–170°, after three recrystallizations from ethanol.

Anal. Calcd. for $C_8H_{16}O_6N_2$: C, 40.68; H, 6.78; N, 11.88; CH_3O, 26.3. Found: C, 40.62; H, 6.77; N, 11.70; CH_3O, 26.46.

Unsaturated Saccharolactone Methyl Ester II.—Two hundred mg. of high-melting trimethylglucurone was hydrolyzed and oxidized with nitric acid as in the preparation of the diamide. The saccharic acid after removal of nitric acid and water was treated with 15 cc. of an 0.5 molar solution of diazomethane in ether, and allowed to stand at 0° for three days. The solution was filtered from a small flocculent precipitate, and concentrated to 3 cc. Forty mg. of crystals separated, which on recrystallization from acetone–ether melted at 85–86.5°. Mixed with the unsaturated lactone ester, m. p. 87–88°, prepared from saccharolactone methyl ester[9] the melting point was 86–87°.

Summary

Evidence is presented which indicates that the trimethylglucurone prepared by Pryde and Williams is the 2,5-dimethyl-α-methylglycoside of glucurone.

NEW YORK, N. Y. RECEIVED MARCH 29, 1940

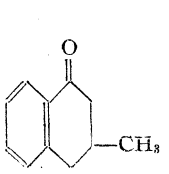
(7) C. S. Hanes, *Biochem. J.*, **23**, 99 (1929).
(8) E. A. Guggenheim, *Phil. Mag.*, [7] **2**, 538 (1926).
(9) R. E. Reeves, THIS JOURNAL, **61**, 664 (1939).

NOTES

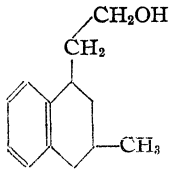
The Preparation of 3-Methyl-1-tetralone and β-[1-(3-Methyl-1,2,3,4-tetrahydronaphthyl)]-ethyl Alcohol

By W. E. Bachmann and W. S. Struve

In the course of an investigation β-[1-(3-methyl-1,2,3,4-tetrahydronaphthyl)] - ethyl alcohol (II) was required. The starting material for the preparation was γ-phenyl-β-methylbutyric acid, which was prepared from 1-allylbenzene according to the procedure of Carter.[1] Cyclization of the acid through its acid chloride by means of aluminum chloride gave 3-methyl-1-tetralone (I), whose structure was established by its conversion to β-methylnaphthalene by Clemmensen reduction and subsequent dehydrogenation of the product. By means of the Reformatsky reaction with methyl bromoacetate and subsequent dehydra-



I



II

tion of the resulting hydroxy ester, the ketone was converted into what is probably the methyl ester of 1-(3-methyl-3,4-dihydronaphthyl)-acetic acid, although the position of the double bond was not established. Reduction of the ester by means of sodium and alcohol yielded the desired alcohol (II). The alcohol reacted with phosphorus tribromide to give the corresponding bromide.

Experimental

3-Methyl-1-tetralone.—A mixture of 25.5 g. of γ-phenyl-β-methylbutyric acid, 20 cc. of thionyl chloride, and 5 drops of pyridine was allowed to stand at room temperature for a half hour. The thionyl chloride was evaporated under reduced pressure, 150 cc. of carbon disulfide was added and the solution was cooled in an ice–salt mixture. Twenty-two grams of aluminum chloride was added in portions and the mixture was refluxed for ten minutes. After hydrolysis of the complex with ice and hydrochloric acid, the organic layer was separated, the carbon disulfide was evaporated, and the residue was dissolved in benzene. The benzene solution was washed with dilute ammonium hydroxide and with water and the benzene was evaporated. The 3-methyltetralone distilled under reduced pressure as a colorless liquid at 94–96° at 0.3 mm.; weight, 16.7 g. (73%).

Anal. Calcd. for $C_{11}H_{12}O$: C, 82.5; H, 7.5. Found: C, 82.4; H, 7.4.

The **oxime** crystallizes from dilute alcohol as colorless needles; m. p. 122.5–123.5°.

Anal. Calcd. for $C_{11}H_{13}NO$: N, 8.0. Found: N, 7.8.

A mixture of 5 g. of the above ketone, 25 g. of amalgamated zinc, 50 cc. of concentrated hydrochloric acid, 25 cc. of water, and 2.5 cc. of acetic acid was refluxed for twenty-four hours, an additional 50 cc. of concentrated hydrochloric acid being added in portions over this time. The oil was extracted with ether, the ether extract was dried with anhydrous sodium sulfate, and the residue obtained by evaporation of the ether was distilled at 12 mm. pressure. The colorless distillate was heated for four hours at 200–220° with 2.3 g. of powdered sulfur. A small amount of copper bronze was then added and the heating was continued for ten minutes more. The mixture was extracted with ether, the filtered ether solution, after having been dried with anhydrous sodium sulfate, was evaporated, and the residue was distilled at 10 mm., giving 2.0 g. of colorless distillate which solidified on cooling to room temperature; m. p. 29–30.5°. After being purified through the picrate, the hydrocarbon melted at 34–35°. The mixed melting point with authentic β-methylnaphthalene gave no depression. The picrate melted at 115–116.5° and the mixed melting point with authentic β-methylnaphthalene picrate gave no depression.

Methyl 1-(3-Methyl-3,4-dihydronaphthyl)-acetate.—A mixture of 20 g. of 3-methyl-1-tetralone, 14.4 cc. of methyl bromoacetate, 48 g. of zinc, 480 cc. of dry ether, 480 cc. of dry benzene, and a small amount of iodine was refluxed for four hours, additional zinc and iodine being added at the end of each hour and an additional 14.4 cc. of methyl bromoacetate being added at the end of the second hour. The complex was decomposed with ice and hydrochloric acid, the organic layer was washed with ammonium hydroxide and then with water, and the benzene and ether were evaporated. The hydroxy ester was dehydrated by heating with 100 cc. of anhydrous formic acid on a steam-bath for fifteen minutes; water was added and the ester was extracted several times with benzene. The benzene extract was washed with dilute sodium carbonate solution and then with water, the benzene was evaporated, and the residue was distilled under reduced pressure, the yellowish liquid distilling at 130–133° at 0.4 mm. being collected; weight, 23 g. (85%).

Anal. Calcd. for $C_{14}H_{16}O_2$: C, 77.8; H, 7.4. Found: C, 77.6; H, 7.6.

β - [1 - (3 - Methyl - 1,2,3,4 - tetrahydronaphthyl)]-ethyl Alcohol.—To a boiling solution of 25 g. of the above ester in 125 cc. of absolute methanol was added 21.3 g. of sodium metal over a period of fifteen minutes. After the vigorous reaction had subsided, another 50 cc. of methanol was added. When all of the sodium had reacted, 100 cc.

(1) Carter, *J. Biol. Chem.*, **108**, 622 (1935).

of water was added and the mixture was refluxed for three hours. The mixture was cooled, acidified with dilute sulfuric acid, and extracted several times with benzene. The benzene extracts were extracted with 2 *N* sodium carbonate solution and with water, the benzene was evaporated, and the residue was distilled under reduced pressure, the colorless viscous liquid distilling at 134–137° at 0.4 mm. being collected; weight, 12.4 g. (57%).

Anal. Calcd. for $C_{13}H_{18}O$: C, 82.1; H, 9.5. Found: C, 81.8; H, 9.4.

The acid obtained by acidification of the alkaline washings was esterified with methanolic hydrochloric acid, purified by distillation (7 g., b. p. 128–133° at 0.4 mm.), and this recovered ester could be used in subsequent reductions.

β - [1 - (3 - Methyl - 1,2,3,4 - tetrahydronaphthyl)]-ethyl Bromide.—A mixture of 5.0 g. of the above alcohol and 2 cc. of phosphorus tribromide was heated on a steam-bath for two hours. The mixture was taken up in benzene and washed with 2 *N* sodium carbonate solution and then with water. The residue obtained by evaporation of the benzene was distilled, the colorless liquid distilling at 137–140° at 0.4 mm. being collected; weight, 5.2 g. (75%).

Anal. Calcd. for $C_{13}H_{17}Br$: Br, 31.6. Found: Br, 31.8.

CHEMISTRY LABORATORY
UNIVERSITY OF MICHIGAN
ANN ARBOR, MICHIGAN RECEIVED APRIL 6, 1940

The Preparation of Pentaacetyl-*d*-gluconyl Chloride

BY CHARLES E. BRAUN, S. H. NICHOLS, JR., J. L. COHEN AND THEIS E. AITKEN

In the course of work being carried out in these laboratories a method has been developed for the preparation of pentaacetyl-*d*-gluconyl chloride in quantity. This new procedure, based upon that of Major and Cook,[1] involves much less manipulation and gives consistently good results. The details are presented here for those interested.

Anhydrous pentaacetylgluconic acid[2] (25 g. or 0.062 mole) was dissolved in 185 cc. of anhydrous ethyl ether and an excess of phosphorus pentachloride (15 g. or 0.072 mole) was added without cooling. The reactants were allowed to stand at room temperature from four to twelve hours (usually overnight). The excess phosphorus pentachloride was then filtered off on a sintered glass funnel, and the ethereal filtrate concentrated to about one-half of its volume *in vacuo* at room temperature. The concentrated solution was kept at zero degrees or below[3] for fifteen to twenty-four hours. The mother liquor was then decanted, *care being taken not to break up or disturb the crystals which had formed on the bottom of the flask.* The crystalline mass was next broken up, mechanically removed and filtered on a sintered glass funnel. After thorough washing with petroleum ether (Eastman Kodak Company, practical, b. p. 35–55°), the crystalline acid chloride was preserved *in vacuo* over calcium chloride and potassium hydroxide at room temperature.

The decanted mother liquor, after being concentrated *in vacuo* at room temperature to one-half of its volume, was allowed to stand at zero degrees or below for another twenty-four hours. The second crop of crystals thus obtained was treated as described above. The concentrated mother liquor which contained all of the phosphorus oxychloride was usually discarded. By this procedure pentaacetyl-*d*-gluconyl chloride was produced as large colorless crystals; m. p. 68–71°; $[\alpha]^{21}D$ +1.71° (alcohol-free chloroform, *c*, 4.38).

Anal. Calcd. for $C_{16}H_{21}O_{11}Cl$: Cl, 8.35. Found: Cl, 8.20.

The yields obtained in five typical preparations were 83%, 86%, 92%, 88% and 93%, or an average yield of 88.4%.

DEPARTMENT OF CHEMISTRY
THE UNIVERSITY OF VERMONT
BURLINGTON, VERMONT RECEIVED MARCH 25, 1940

(1) Major and Cook, THIS JOURNAL, **58**, 2477 (1936).

(2) Major and Cook, *ibid.*, **58**, 2475 (1936).

(3) At higher temperatures the yields are decreased appreciably due to the increase in solubility of the acid chloride in the anhydrous ether.

Additional Observations on the Vitamin K Activity of Quinones

BY ERHARD FERNHOLZ, H. B. MACPHILLAMY AND S. ANSBACHER

Several months ago we reported that phlorone (2,5-dimethyl-1,4-benzoquinone) has vitamin K activity,[1] an observation recently confirmed by H. J. Almquist.[2] In this connection it seemed of interest to investigate whether 2-methyl-5,6,7,8-tetrahydro-1,4-naphthoquinone possesses the great potency of the parent substance. The hydrogenated quinone, first synthesized by Chuang and Han,[3] was prepared by catalytic hydrogenation of 2-methyl-1,4-naphthoquinone. It was found to be active at 1 mg., a degree of activity which should be considered practically negligible, since it is common to a great number of quinones.

We have also studied the analogous hydrogenation product of vitamin K_1 (β,γ,5,6,7,8-hexahydrovitamin K_1). It showed no vitamin K activity, not even in a dose of 2 mg. In contrast to this, Fieser, Tishler, and Sampson[4] reported it to have slight activity, although the dosage is not indicated.

We wish to point out that we have prepared and assayed the naphthotocopherol and its quin-

(1) Ansbacher and Fernholz, *J. Biol. Chem.*, **131**, 399 (1939).

(2) 52nd Annual Meeting, Am. Physiol. Soc., New Orleans, May 16 (1940).

(3) Chuang and Han, *Ber.*, **68**, 876 (1935).

(4) Fieser, Tishler and Sampson, THIS JOURNAL, **62**, 996 (1940).

oid oxidation product recently mentioned by Fieser, *et al.*[4] The latter authors gave no biological data for the oxidation product and stated that the tocopherol was active at 0.3 mg. We found that 1 mg. of the tocopherol was totally inactive, but the oxidation product was fully active at that dose.[5]

Experimental

2 - Methyl - 5,6,7,8 - tetrahydro - 1,4 - naphthoquinone.—A solution of 1.72 g. of 2-methyl-1,4-naphthoquinone in glacial acetic acid was completely hydrogenated using platinum oxide catalyst. The reaction mixture was decanted from the catalyst, diluted with water and extracted with ether. The ethereal solution was washed, dried and the solvent evaporated. The quinone was obtained by steam distilling a suspension of the crude hydroquinone in a ferric chloride solution. The distillate was extracted with ether, the extract dried and the solvent evaporated. The residue after recrystallization from light petroleum ether yielded 1.6 g. (94%) of quinone melting at 58–59°.

Anal. Calcd. for $C_{11}H_{12}O_2$: C, 74.97; H, 6.87. Found: C, 74.95; H, 6.71.

β,γ-5,6,7,8-Hexahydro Vitamin K_1.—One gram of the synthetic vitamin was hydrogenated as described above. The hydroquinone was oxidized with silver oxide in dry ether. The yield was 0.95 g. (95%) of yellow oil giving with alcoholic alkali a pink color which darkened to brown on standing.

Anal. Calcd. for $C_{31}H_{52}O_2$: C, 81.52; H, 11.47. Found: C, 81.17; H, 11.60.

Naphthotocopherol.—A mixture of 3.5 g. of 2-methyl-1,4-naphthoquinone, 5 g. of phytol, 5 g. of anhydrous zinc chloride and 50 cc. of xylene[6] was refluxed for twenty-four hours. The solvent was removed *in vacuo* and the residue taken up in ether. The ethereal solution was washed repeatedly with 2% potassium hydroxide solution containing hydrosulfite and finally with dilute hydrochloric acid and water. After drying and removal of the solvent, the remaining brown oil was taken up in petroleum ether (b. p. 40–60°), and extracted with Claisen alkali. The small amount of yellow oil obtained on working up the soluble portion gave the typical Dam–Karrer reaction for vitamin K_1.

The petroleum ether portion was washed, dried and the solvent evaporated. The residue was purified by chromatographic adsorption on activated alumina in petroleum ether solution. The yield was about 1.0 g. (13% based on phytol), of reddish-brown oil which strongly reduced an alcoholic silver nitrate solution in the cold.

Anal. Calcd. for $C_{31}H_{48}O_2$: C, 82.24, H, 10.70. Found: C, 82.48; H, 10.72.

Oxidation of Naphthotocopherol.—Two hundred milligrams of the above tocopherol was oxidized with ferric chloride in alcoholic solution. The reaction mixture was diluted with water, extracted with ether, and the ethereal solution washed, dried and concentrated. The residue was purified by chromatographing in petroleum ether solution on activated calcium sulfate. About 100 mg. (48%) of dark orange oil was obtained.

Anal. Calcd. for $C_{31}H_{48}O_3$: C, 79.43; H, 10.30. Found: C, 79.42; H, 10.03.

THE SQUIBB INSTITUTE FOR MEDICAL RESEARCH
DIVISION OF ORGANIC CHEMISTRY
NEW BRUNSWICK, N. J. RECEIVED APRIL 22, 1940

(5) Reported by the senior author in a lecture at Columbia University on December 4, 1939.

(6) Jacob, Sutcliffe and Todd, *J. Chem. Soc.*, 331 (1940), report an unsuccessful attempt to effect this condensation in boiling decalin. In our experience the tocopherol is destroyed at that temperature.

Collidine Treatment of 2-Bromocholestanone

BY ROBERT P. JACOBSEN

In the course of preparation of certain steroids for photochemical study, the author has had occasion to employ the collidine method of Butenandt, *et al.*,[1] for the splitting of hydrogen bromide from 2-bromocholestanone to form 1-cholestenone. On refluxing a collidine solution of the bromo compound for two hours, these workers obtained the α,β-unsaturated ketone (m. p. 95°, $[\alpha]_D$ + 64.5°) in 77% yield. Butenandt and Wolff[2] had earlier reported the preparation of 1-cholestenone (m. p. 111–112°, $[\alpha]_D$ −32.1°; oxime, m. p. 146–147°), in poor yield by the potassium acetate–acetic acid treatment of 2-bromocholestanone. This latter compound the German workers now call "hetero-Δ^1-cholestenone" and state that the "normal Δ^1-ketone" is the substance melting at 95°.

In the experience of the author, the collidine reaction appears to follow a less straightforward course than that indicated by Butenandt and his collaborators. 2-Bromocholestanone (m. p. 169°) was refluxed in collidine[3] for two, four, or six hours without effecting the complete fission of hydrogen bromide. After twelve hours of boiling, a non-homogeneous, crystalline, halogen-free product (m. p. 89–92° to a sludge which cleared at about 100°) was obtained in 74% yield. By repeated crystallization from methanol this gave a very small amount of material, m. p. 126–127.5° (nearly pure cholestanone), which showed no selective absorption[4] in the ultraviolet region between 2200 and 2600 Å. No pure 1-cholestenone could be obtained from the intermediate fractions by crystallization, although some sam-

(1) Butenandt, Mamoli, Dannenberg, Masch and Paland, *Ber.*, **72**, 1617 (1939).

(2) Butenandt and Wolff, *ibid.*, **68**, 2091 (1935).

(3) Obtained from the Research Department of the Barrett Company, 90% of the material boiling in the range 170.7–171.9°.

(4) Ultraviolet absorption measurements by Dr. P. A. Cole and Mr. C. Z. Nawrocki of this Laboratory.

ples[5] which melted at 93–96° showed an ultraviolet absorption maximum at 2275 Å. (log ϵ 4.07, cyclohexane). By brominating the combined intermediate fractions (0.5 g.) in cold acetic acid (5 cc.) there was obtained 0.20 g. of impure 1-cholestenone dibromide (effervesces at 85°). On allowing the filtrate to stand for a few minutes, hydrogen bromide was evolved and there separated 0.095 g. of needles, m. p. 152–156°. The dibromide liberated iodine on warming in an alcoholic sodium iodide solution but the needles did not. The latter on crystallization from methyl acetate melted at 169° and mixed with 2-bromocholestanone showed no depression. The crude dibromide was debrominated with sodium iodide or zinc dust in alcohol, or potassium iodide in 80% acetone, to give the corresponding unsaturated ketone, m. p. 102–104°. By repeating the purification through the dibromide, pure 1-cholestenone, crystallizing as a hydrate from 98% methanol or aqueous acetone, m. p. 107–108° ($[\alpha]^{24}D$ +65°).

These observations indicate that the collidine treatment of 2-bromocholestanone, under the conditions specified, gives principally a mixture of 1-cholestenone and cholestanone. The formation of the latter compound is not surprising in view of the work of Schwenk and Whitman,[6] who obtained cholestanone as the principal product of the treatment of 2-bromocholestanone with dimethylaniline.

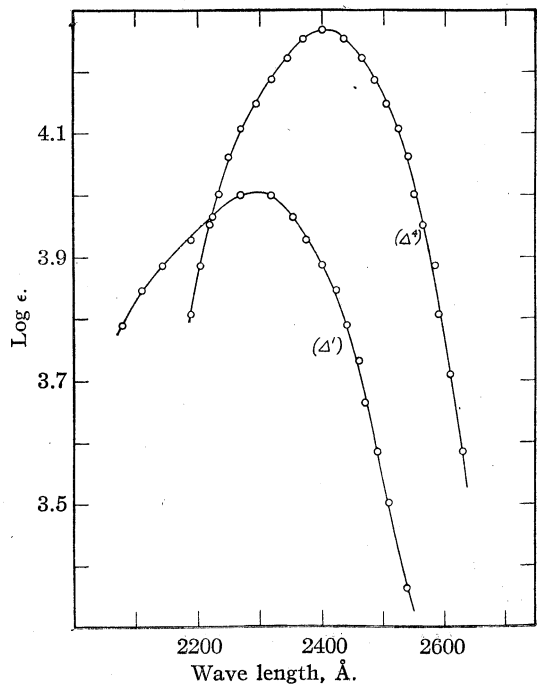


Fig. 1.

The ultraviolet absorption in alcohol of 1-cholestenone hydrate (calculated on the anhydrous basis) in the region of the maximum is compared with that of the Δ^4-isomer in Fig. 1.

The preparation of 1-cholestenone will be detailed later in connection with a report of photodehydrogenation studies now in progress.

(5) These properties correspond closely to those of the product (m. p. 95°) of Butenandt, *et al.*, who reported a maximum at 230 mμ (log ε 4.03).

(6) Schwenk and Whitman, THIS JOURNAL, **59**, 949 (1937).

WASHINGTON BIOPHYSICAL INSTITUTE
BETHESDA, MARYLAND RECEIVED APRIL 27, 1940

The Behavior of Certain Substituted Allenes toward the Meinel Color Test[1]

BY F. B. LAFORGE AND FRED ACREE, JR.

A method for the detection of conjugated double bonds has been proposed by Meinel[1a] based upon the treatment of the compound to be tested with one molecular equivalent of bromine in methanol solution. The isolated reaction product is then treated with a suspension of silver thiocyanate containing ammonium ferric sulfate. The formation of a red color of variable intensity depending upon the compound is indicative of the presence of a conjugated system of double bonds.

Conant and Jackson[2] have reported the formation of dibromo compounds along with the methyl hypobromite addition products when bromine in methanol solution is allowed to react on an unsaturated compound. Thus, while Meinel indicated that the methyl hypobromite addition product is responsible for the reaction with silver thiocyanate, there also is the possibility that the dibromo addition product might be the influencing factor in the reaction.

Meinel subjected a number of compounds to the test but did not include any that possessed a cumulated system of double bonds.

In studying the reaction of halogens[3] on compounds of this class it was of interest to determine whether or not they would also respond to the color test.

It was found that 1-phenyl-1,2-butadiene, 2,3-pentadiene, 1-cyclohexyl-2,3-pentadiene, and pyrethrone gave a positive reaction. When com-

(1) Not subject to copyright.

(1a) K. Meinel, *Ber.*, **70B**, 429 (1937).

(2) J. B. Conant and E. L. Jackson, THIS JOURNAL, **46**, 1727 (1924).

(3) Fred Acree, Jr., and F. B. LaForge, *J. Org. Chem.*, (in press).

pared with myrcene, 1-pentene and styrene dibromide, the approximate speed and the intensity of the color formation were greatest in the case of the 1-phenyl-1,2-butadiene and decreased in the order named with the other compounds.

Since compounds possessing a cumulated system of double bonds respond to the Meinel tests, the method is not specific for the conjugated system.

BUREAU OF ENTOMOLOGY AND PLANT QUARANTINE
U. S. DEPARTMENT OF AGRICULTURE
WASHINGTON, D. C. RECEIVED APRIL 10, 1940

Preparation of Phenylacetone

BY J. PHILIP MASON AND LEWIS I. TERRY

Phenylacetone has been prepared by several methods.[1] We have obtained it in a 32% yield from benzene, chloroacetone and anhydrous aluminum chloride.

Experimental

Forty-one grams (0.31 mole) of anhydrous aluminum chloride and 100 ml. of anhydrous benzene (free from thiophene) were put in a 500-ml. three-necked flask which was equipped with a mercury-sealed stirrer, a reflux water condenser and a small addition funnel. The top of the condenser was connected to a sulfuric acid trap and this trap was connected to a gas absorption bottle. The mixture was stirred, heated to refluxing on a steam-bath and 13.9 g. (0.15 mole) of chloroacetone was allowed to drop in slowly during a period of thirty minutes. After refluxing for five hours, the mixture was practically black. After cooling to room temperature, the reaction mixture was decomposed by adding water slowly through the addition funnel, stirring during the addition. When no more hydrogen chloride was evolved, 20 ml. of water and 20 ml. of concentrated hydrochloric acid were added. The benzene layer was separated and the aqueous layer extracted with four 25-ml. portions of benzene. All of the benzene solutions were combined and filtered. The benzene was distilled and the remaining viscous oil was distilled under reduced pressure. Nine grams of liquid boiling below 123° (20–22 mm.) was obtained. Approximately 10 g. of high-boiling liquid was left in the distilling flask.

Phenylacetone was recovered from the distillate by making the sodium bisulfite addition product, filtering, decomposing the addition product with sodium carbonate solution and steam distilling as long as any oil distilled. The distillate was extracted with ether, the ether solution dried over anhydrous magnesium sulfate and the ether distilled on a steam-bath. The phenylacetone was distilled under reduced pressure, b. p. 108–114° at 20–22 mm.; yield, 6.5 g. or 32%. The semicarbazone melted at 188°.[2]

Several variations of this procedure were tried in an effort to increase the yield. The yield was decreased by (a) decreasing the time of refluxing to one or two hours after the addition of the chloroacetone, (b) lowering the temperature of the reaction and allowing a longer time for its completion, (c) adding the aluminum chloride in small portions over a period of two hours to a boiling mixture of benzene and chloroacetone, and then refluxing for two hours. No change in the yield occurred when (a) the ratio of chloroacetone and aluminum chloride to benzene was increased, or (b) the ratio of aluminum chloride was increased from two equivalents to 2.5 equivalents.

CHEMISTRY LABORATORY
BOSTON UNIVERSITY
BOSTON, MASSACHUSETTS RECEIVED MARCH 14, 1940

(1) Herbst and Manske, "Organic Syntheses," Vol. XVI, 1936, p. 47. Additional references on p. 50.
(2) Pickard and Kenyon, *J. Chem. Soc.*, **105**, 1124 (1914).

Vapor Pressures of Trimethylphosphine, Trimethylarsine and Trimethylstibine

BY E. J. ROSENBAUM AND C. ROGER SANDBERG

We prepared pure samples of the methyl derivatives of phosphorus, arsenic and antimony for an investigation of their Raman spectra. Because of the paucity of data on the physical constants of these compounds we have measured their vapor pressures. Phosphorus methyl and antimony methyl were prepared from methylmagnesium iodide and the corresponding trichloride.[1] The crude phosphorus methyl was purified by precipitation with silver iodide,[2] washing thoroughly and heating gently in a vacuum to regenerate the phosphorus methyl. Arsenic methyl was prepared by a modification of the method of Renshaw and Holm.[3] A small amount of arsenic trichloride was condensed on zinc methyl cooled by a carbon dioxide–acetone bath, which was slowly removed until the reaction was complete. Then the bath was replaced and more arsenic trichloride was condensed. This procedure was repeated until all of the reagents were used up. The resulting double salt was decomposed with sodium hydroxide solution, forming arsenic methyl.

In all cases the products were dried over phosphorus pentoxide and fractionated many times, the final fractionation being in a vacuum. The vapor pressures of head and tail fractions agreed to within 1 part in 500. The Raman spectra of these compounds showed no lines which could not be attributed to the compounds themselves. This, of course, is not a very sensitive criterion of purity.

The vapor pressures were measured in the range −25 to +25° with a mercury manometer and a cathetometer. The temperatures were measured

(1) Hibbert, *Ber.*, **39**, 160 (1908).
(2) Mann, Wells and Purdie, *J. Chem. Soc.*, 1828 (1937).
(3) Renshaw and Holm, THIS JOURNAL, **42**, 1468 (1920).

with a type K potentiometer and a copper–constantan thermocouple calibrated against a thermometer which had been calibrated by the Bureau of Standards. The molecular weights were determined by the vapor density method.

The measured vapor pressures could all be represented by an equation of the conventional form: $\log p = A/T + B$. The values of the constants, the average deviation of the observed from the calculated vapor pressures and the values of certain derived quantities and of the molecular weights are given in the table.

Compd.	$P(CH_3)_3$	$As(CH_3)_3$	$Sb(CH_3)_3$
A	−1518	−1456	−1697
B	7.7627	7.3936	7.7068
Av. dev., %	1	1.5	<1
B. p., °C.	37.8[a]	49.5[b]	78.5[c]
$\Delta H_{vap.}$ cal.	6943	6660	7760
Trouton's constant, cal./T	22.3	20.6	22.1
Mol. wt. Obsd.	75.5	119.0	....
Mol. wt. Calcd.	76.10	120.03	....

[a] Previous recorded value, 40–42° (Cahours and Hofmann, *Ann.*, **104**, 29 (1857)). [b] Previous recorded values, 51.9° (Renshaw and Holm, THIS JOURNAL, 42, 1468 (1920)); 51–53° (Dyke and Jones, *J. Chem. Soc.*, 2426 (1930)); 68–73° (G. Natta, *Chem. Zentr.*, 98, I, 416 (1927)); 74° (Paneth and Loleit, *J. Chem. Soc.*, 366 (1935)). [c] Previous recorded values, 82° (Paneth and Loleit, *ibid.*, 366 (1935)); 80.6° (Landolt, *J. prakt. Chem.*, 84, 329 (1861)).

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF CHICAGO
CHICAGO, ILL.

RECEIVED MARCH 18, 1940

Hydrogen Fluoride as a Condensing Agent. XI. The Reaction of Alcohols and Ethers with Benzene[1]

BY J. H. SIMONS AND S. ARCHER

Hydrogen fluoride has been found[2] to be an effective catalyst for alkylations in which aliphatic alcohols and ethers are used. We have now made additional studies of this reaction using primary, secondary, and tertiary alcohols and their ethers. Good yields were obtained with secondary and tertiary compounds at room temperature; but with primary compounds except benzyl alcohol and ether, 100° was necessary to obtain appreciable yields. *n*-Butyl alcohol and *n*-butyl ether both gave *s*-butylbenzene in about 20% yield. Benzyl alcohol and benzyl ether both gave a 65–70% yield of diphenylmethane at room temperature. From the reaction of isopropyl alcohol with benzene in a mole ratio of about one to seven, four compounds were isolated: isopropylbenzene, 1,4-diisopropylbenzene, 1,2,4-triisopropylbenzene, and 1,2,4,5-tetraisopropylbenzene, in yields of 22.4, 14, 26, and 28%, respectively. The ether gave the same products in yields of 26, 24, 25, and 8%. *t*-Butyl alcohol and *t*-amyl alcohol reacted with benzene, when the mole ratios were about one to seven, to give about 40% monoalkylated and 50% dialkylated products.

Several items of interest are noted from the above experimental results. Alcohols react more readily, *i. e.*, give a good yield at lower temperature, than the corresponding chlorides. For example, secondary chlorides reacted very slowly to give low yields in a twenty-four hour reaction time at room temperature, whereas secondary alcohols or ethers gave high yields at the same temperature. Although the mechanism of the reaction is unknown, one fact is obvious and may be a contributing factor when it is known. When the chlorides are used, hydrogen chloride is evolved; and for reactions at atmospheric pressure its thermodynamic activity in the reaction mixture must equal that for the gas at one atmosphere. When alcohols or ethers are used, water is a product of the reaction; and it remains in solution in the hydrogen fluoride. Its activity in this solution is very much lower than liquid water at the same temperature. For certain mechanisms this difference would contribute to the driving force of the reaction.

The other point of interest lies in the fact that when aluminum chloride is used as the condensing agent, the chlorides react more readily than the alcohols. Reasoning from this and also from the fact that chlorides can be made from the alcohols by treatment with aluminum chloride, the formation of the chloride may be postulated as the first step in the reaction. As the ease of reaction is in the opposite order when hydrogen fluoride is used, the reaction in this case may proceed through a different mechanism.

The ease of reaction of benzyl alcohol is a strong argument against the hypothesis that an olefin is an intermediate in the reaction. Such a mechanism has been postulated by McKenna and Sowa[3] for reactions between alcohols and benzene

(1) For the previous paper see Simons, Archer and Randall, THIS JOURNAL, **62**, 485 (1940).

(2) (a) Calcott, Tinker and Weinmayr, *ibid.*, **61**, 1010 (1939); (b) Simons, Archer and Passino, *ibid.*, **60**, 2956 (1938).

(3) McKenna and Sowa, *ibid.*, **59**, 470 (1937).

in which boron trifluoride was employed. The formation of mesitylene from toluene and methanol in the presence of aluminum chloride reported by Norris and Ingraham[4] also supports this argument.

Calcott, Tinker, and Weinmayr[2a] reporting condensation reactions catalyzed by hydrogen fluoride state, "Dibenzyl ether gave benzyl isocyclic compounds while benzyl alcohol polymerized to 1,2,3,4,5,6-hexaphenylcyclohexane." In our hands, both the alcohol and the ether reacted to give diphenylmethane when treated with benzene and hydrogen fluoride. At room temperature and at 100° alkylation rather than polymerization was the only reaction.

(4) Norris and Ingraham, THIS JOURNAL, **60**, 1421 (1938).

SCHOOL OF CHEMISTRY AND PHYSICS
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STATE COLLEGE, PA. RECEIVED JANUARY 13, 1940

Hydrogen Fluoride as a Condensing Agent. XII. Reactions of Methyl, Ethyl and Phenyl Compounds with Benzene and its Derivatives[1]

BY J. H. SIMONS AND H. J. PASSINO

The use of hydrogen fluoride to promote alkylations has been shown in recent publications from this Laboratory. We are now reporting a study of its use in conjunction with a variety of reagents of potential value for methylation, ethylation, and phenylation. An alcohol, ester and halide were used in investigating each alkylation, and other reagents were used in some cases. Ethylation proceeded with a variety of substances, namely: ethyl alcohol, ethyl iodide, ethyl chlorocarbonate, ethyl acetate, and ethyl ether. Ethyl alcohol and benzene at 200° gave very high yields of ethyl- and diethylbenzenes, while the other reagents gave varying yields with benzene and toluene. Ethylene was tried at 0°, but although indications of the formation of ethylbenzene were observed no product was isolated; and the reaction was not attempted at higher temperatures. Methyl alcohol, methyl acetate, and methyl iodide failed, however, to react with benzene, toluene, or phenol to give methylated products at temperatures up to 200°. The reaction between phenol and methyl alcohol resulted in the formation of anisole, instead of alkylated phenol. Phenol, phenyl acetate, chlorobenzene, and diphenyl ether all failed to give phenylated products, when treated with hydrogen fluoride and an aromatic compound at temperatures up to 200°. Acylation occurred when phenyl acetate was caused to react with benzene at 200° and some acetophenone and phenol were formed.

The formation of anisole led to the attempt at similar reactions. From a reaction between ethyl alcohol and phenol no phenetole was isolated although ethylation occurred, and phenol heated alone at 200° with hydrogen fluoride failed to give diphenyl ether. When diphenyl ether was heated alone with hydrogen fluoride at 210°, some splitting did occur as a small amount of phenol was isolated. The stability of the phenyl ethers is in marked contrast to the ease of reaction of the aliphatic ethers. Anisole has previously been made by the condensation of phenol and methyl alcohol using boron fluoride as the condensing agent.[2]

The failure of hydrogen fluoride to effect methylations is in contrast to the use of aluminum chloride for these reactions. Investigators[3] have recently been able to methylate using methyl alcohol and aluminum chloride. Methylations by means of methyl chloride in the presence of aluminum chloride are well known.

Very little tar formation was experienced with reactions at 200° with the exception of a few experiments in which phenol was used as a reagent.

(1) For the previous paper of this series see Simons and Archer, THIS JOURNAL, **62**, 1623 (1940).

(2) Sowa, Hennion and Nieuwland, *ibid.*, **57**, 709 (1935).

(3) Norris and Ingraham, *ibid.*, **60**, 1421 (1938); Tsukervanik and Vikhrova, *J. Gen. Chem.* (*U. S. S. R.*), **7**, 632–636 (1937).

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Saponins and Sapogenins. XV. The Interrelationship of Echinocystic Acid and Oleanolic Acid

BY DAVID TODD, G. H. HARRIS AND C. R. NOLLER

Previous work[1] has indicated that echinocystic acid is closely related to other triterpenoid sapogenins but no derived products identical with those from other triterpenoids have been obtained in which the carbon skeleton remained intact. It has now been found that Clemmensen reduction of norechinocystenone or norechinocystendione gives a hydrocarbon which is identical

(1) Bergsteinsson and Noller, THIS JOURNAL, **56**, 1403 (1934); Noller, *ibid.*, **56**, 1582 (1934); White and Noller, *ibid.*, **61**, 983 (1939).

as determined by melting and mixed melting points, optical rotation and crystal form with oleanene III, obtained by Winterstein and Stein[2] from oleanolic acid. Inasmuch as the preparation of both hydrocarbons involves a Clemmensen reduction which Winterstein and Stein[2] have shown results in a molecular rearrangement in the case of oleanene III, and both hydrocarbons are decarboxylated derivatives, it is not possible to state that echinocystic acid and oleanolic acid have exactly the same skeletons but the possibility that such is the case is very likely.

Experimental

A solution of 0.132 g. of norechinocystenone in 250 cc. of 95% ethyl alcohol was added to 5 g. of amalgamated zinc. The mixture was boiled under a reflux condenser and a slow stream (2–3 bubbles per second) of dry hydrogen chloride was passed in for thirty-six hours. The solution was poured into an equal volume of water and evaporated to 50 cc. After dilution with water to 100 cc. the mixture was extracted with ether. The ether layer was washed with dilute hydrochloric acid, sodium hydroxide and water and dried over anhydrous sodium sulfate. After removal of the ether the residue was crystallized from methyl alcohol in which it is only slightly soluble, and then from acetone to a constant melting point of 224–225°; $[\alpha]^{25}D$ +31.3 ± 3°; c = 1.408 in toluene, l = 0.5 dm.

Anal. Calcd. for $C_{29}H_{48}$: C, 87.80; H, 12.20. Found: C, 87.79; H, 12.12.

The same product as determined by melting and mixed melting points was obtained on reducing norechinocystendione by the above procedure.

Oleanylene II and oleanene III were prepared from oleanolic acid[3] according to the procedures of Winterstein and Stein.[2] The oleanene III was crystallized twice from glacial acetic acid and then from acetone until its melting point was 216.5–220.5°[4]; $[\alpha]^{25}D$ +30.7 ± 3°; c = 2.082 in toluene, l = 0.5 dm.

A mixture with an equal part of the hydrocarbon obtained from norechinocystenone, m. p. 218–221.5°[4], melted at 216.5–221°. The melting points of the mixture and of the two pure products were taken simultaneously in the same bath. Slow evaporation of solutions of the hydrocarbons from both sources gave well formed hexagonal plates which were indistinguishable under a lens. The properties of oleanene III recorded by Winterstein and Stein[2] are m. p. 225–226°; $[\alpha]^{20}D$ +30.1, c = 1.76 in chloroform.

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RECEIVED FEBRUARY 14, 1940

(2) Winterstein and Stein, *Ann.*, **502**, 223 (1933).

(3) We are indebted to Dr. C. N. Anderson of Lever Brothers Company, Cambridge, Mass., for a supply of crude barium oleanolate derived from clove oil residues.

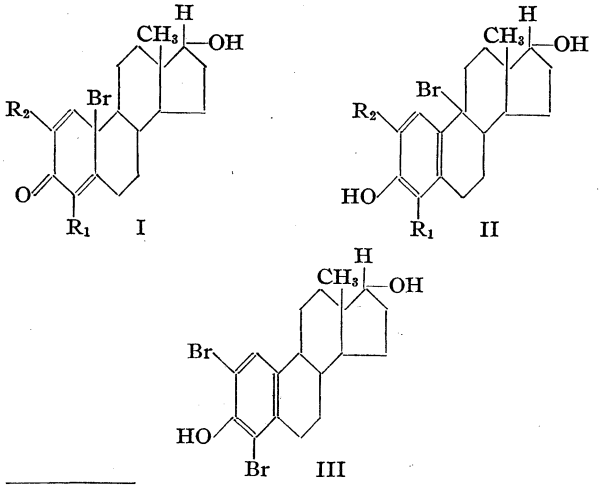
(4) The maximum melting point of 224–225° is obtained only with difficulty and large losses, so that the lower melting product was used for comparison purposes.

2,4-Dibromo-α-oestradiol

BY ROBERT BURNS WOODWARD

As evidenced by the investigations of Doisy,[1] Butenandt,[2] and Marrian,[3] the phenolic sex hormones are extensively halogenated under the conditions obtaining in the determination of the iodine number with the Rosenmund–Kuhnmann reagent. The number of halogen atoms consumed by one mole of the hormone varied widely with the conditions. Although both Butenandt and Doisy isolated halogen-containing products, these were insufficiently characterized and until further investigation must be regarded as of equivocal nature. Only in the case of equilenin has a definitely pure halogen-substituted hormone been prepared, *viz.*, monobromoequilenin, prepared by Girard, *et al.*,[4] likewise by the action of the Rosenmund–Kuhnmann reagent. On the other hand, Marrian and Haslewood[3] found that the methyl ethers of the hormones consumed approximately one mole of halogen quite smoothly in the iodine number determinations, and this result was confirmed by the isolation of monobromoestrone methyl ether and monobromoestriol methyl ether.

In the course of a related investigation, we have found that α-oestradiol is converted smoothly and almost quantitatively into a dibromoestradiol on standing overnight in alcohol solution with the theoretical quantity of N-bromoacetamide. Since no halogen was removed on treatment with alcoholic silver nitrate or potassium hydroxide, the product was not 2-(*or* 4)-10-dibromo-$\Delta^{1,4}$-oestra-



(1) Thayer, Levin and Doisy, *J. Biol. Chem.*, **91**, 791 (1931).

(2) Butenandt, Störmer and Westphal, *Z. physiol. Chem.*, **208**, 149 (1932).

(3) Marrian and Haslewood, *J. Soc. Chem. Ind.*, **51**, 277T (1932).

(4) Girard, Sandulesco, Fridenson and Rutgers, *Compt. rend.*, **195**, 981 (1932).

dienon-3-ol-17 (I, R_1 *or* R_2 = H *or* Br), nor the corresponding pseudo-bromide, 2-(*or* 4)-9-dibromo-α-oestradiol (II, R_1 *or* R_2 = H *or* Br). Consequently our product has the only alternative structure, 2,4-dibromo-α-oestradiol (III).

It is highly probable that the introduction of bromine by bromoacetamide will be of service in the case of other phenolic compounds which defy clean-cut halogenation by the more usual methods.

Experimental

One-half gram of α-oestradiol and 0.54 g. of recrystallized N-bromoacetamide were dissolved in 40 cc. absolute alcohol and the reaction mixture was allowed to stand at room temperature for about eighteen hours. By this time the originally faintly yellow solution had become almost colorless. The alcohol solution was evaporated on the hot plate to about one-third of its volume and allowed to cool, when the brominated product was precipitated by the addition of water. On crystallization from alcohol–water, 0.54 g. of 2,4-dibromo-α-oestradiol was obtained as beautiful colorless rosets of needles, melting at 215.5–216.5° (cor.) to an emerald-green liquid, with gas evolution. From the filtrate another 0.2 g. of the product was obtained by dilution with water and recrystallization.

Anal.[5] Calcd. for $C_{18}H_{22}O_2Br_2$: C, 50.20; H, 5.14. Found: C, 50.10; H, 5.13.

No turbidity developed when an alcoholic silver nitrate solution of the substance was allowed to stand for twenty hours, and the material was recovered unchanged after solution for an hour in alcoholic potassium hydroxide.

(5) Analysis by D. M. Bowen.

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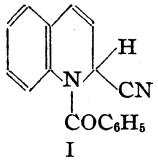
HARVARD UNIVERSITY
CAMBRIDGE, MASSACHUSETTS RECEIVED APRIL 13, 1940

The Formation of Reissert's Compounds in Non-aqueous Media

BY ROBERT BURNS WOODWARD

By shaking quinoline with benzoyl chloride and an aqueous solution of potassium cyanide, Reissert[1] prepared 1-benzoyl-1,2-dihydroquinaldonitrile (I).



I

This compound was remarkable in that it split on hydrolysis into benzaldehyde and quinaldinic acid. The availability of a considerable number of substances differing from Reissert's original compound only in the nature of the acyl group would afford the possibility of a new general method for the reduction of carboxylic acids to aldehydes. However, the ready hydrolysis of many aliphatic acid chlorides vitiates Reissert's original method.

In an attempt to surmount this difficulty, we have investigated the formation of Reissert's compound in non-aqueous media. Dieckmann and Kämmerer[2] observed the formation of the substance in unstated amount while investigating the action of quinoline and other tertiary bases in accelerating the formation of benzoyl cyanide from benzoyl chloride and hydrogen cyanide in ether solution. We found that the formation of acyl cyanide was largely preponderant when benzoyl chloride was used and exclusive in the case of acetyl chloride, either on conducting the reaction in ether or other inert solvents, or on using quinoline as its own solvent. No reaction was observed when acetonitrile, benzonitrile, ether, dioxane, acetone or chloroform was substituted for water in the original procedure of Reissert.

On the other hand, quinoline and potassium cyanide reacted smoothly with either benzoyl or cinnamoyl chloride[3] in liquid sulfur dioxide to give the corresponding aroyl dihydroquinaldonitrile in excellent yield. The use of acetyl chloride, however, led to the formation of intractable dark mixtures from which no pure product could be isolated.

The striking difference in this case between liquid sulfur dioxide and the organic solvents is in consonance with the probable ionic character of the reaction.

Experimental

1-Benzoyl-1,2-dihydroquinaldonitrile.—Ten grams of benzoyl chloride, 10 g. of quinoline (freshly distilled *in vacuo*) and 7 g. of potassium cyanide were placed in a pressure bottle. After approximately 35 cc. of liquid sulfur dioxide had been added, the bottle was sealed and allowed to stand with occasional shaking for twenty-four hours. The sulfur dioxide was then allowed to evaporate, and the residue washed successively with water, dilute hydrochloric acid and ether. On crystallization from alcohol of the white powder so obtained, 16 g. of 1-benzoyl-1,2-dihydroquinaldonitrile separated as glistening needles, m. p. 154–155°, of a very faint greenish tinge which was lost on two further crystallizations.

(1) Reissert, *Ber.*, **38**, 1610 (1905).

(2) Dieckmann and Kämmerer, *ibid.*, **40**, 3737, Note 2 (1907).

(3) *Cf.* Sugasawa and Tsuda, *J. Pharm. Soc. Japan*, **56**, 557 (1936); *C. A.*, **32**, 5836 (1938). The original is here incorrectly reported as appearing on p. 103.

1-Cinnamoyl-1,2-dihydroquinaldonitrile was prepared from 12 g. of freshly made cinnamoyl chloride in exactly the same manner as the benzoyl compound; needles from alcohol, m. p. 149–150°; yield, 16 g.

Anal. Calcd. for $C_{19}H_{14}ON_2$: C, 79.75; H, 4.93; N, 9.73. Found: C, 79.62; H, 5.02; N, 9.80.

CONVERSE MEMORIAL LABORATORY
HARVARD UNIVERSITY
CAMBRIDGE, MASS. RECEIVED APRIL 17, 1940

COMMUNICATIONS TO THE EDITOR

ELECTROPHORETIC ISOLATION OF CONSTITUENTS OF RAGWEED POLLEN EXTRACTS*

Sir:

Dialyzed extracts of giant ragweed pollen were studied with the Tiselius[1] moving boundary technique at approximately *p*H 7.4 and 1.5°. Employing the Philpot–Svensson[2] cylindrical lens system to visualize the boundaries, we have found a major constituent which is negatively charged, unpigmented and migrates more slowly than the pigmented constituents. The latter are also negatively charged. The major unpigmented constituent may constitute as much as 75% of the material in fresh extracts when estimated by the criterion of the integration of the Philpot–Svensson curves. Similar Longsworth[3] diagrams have been obtained. The unpigmented fraction is highly skin reactive in individuals with ragweed hay fever. It may be introduced into the skin by electrophoresis in these cases by the positive pole even though the substance is negatively charged at the *p*H employed. The electrical mobility of the unpigmented constituent is 0.5×10^{-5} cm. sec.$^{-1}$ in 0.05 *M* phosphate buffer at *p*H 7.0.[4] Variations have been observed in the pigmented portions of the electrophoretic diagrams and apparently depend on the extent and nature of the dialysis as well as the age and treatment of the pollen grains.

COLUMBIA UNIVERSITY AND THE MOUNT SINAI HOSPITAL, NEW YORK CITY, AND THE BIOLOGICAL LABORATORIES, COLD SPRING HARBOR
H. A. ABRAMSON
D. H. MOORE
H. GETTNER
J. GAGARIN
L. JENNINGS

RECEIVED MAY 17, 1940

* This investigation has been aided by a grant from the Josiah Macy, Jr., Foundation.

(1) A. Tiselius, *Trans. Faraday Soc.*, **33**, 524 (1937).

(2) H. Svensson, *Kolloid-Z.*, **87**, 190 (1939).

(3) L. G. Longsworth and D. A. MacInnes, *Chem. Rev.*, **24**, 271 (1939).

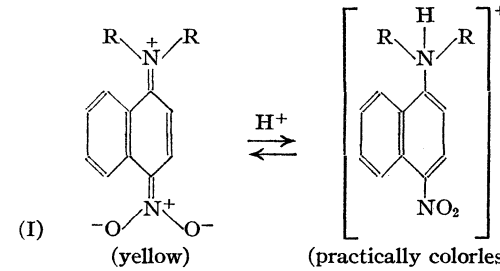
(4) H. A. Abramson, A. Sookne and L. S. Moyer, *J. Allergy*, **10**, 317 (1939); H. A. Abramson and M. H. Gorin, *Chem. Prod.*, **3**, 37 (1940).

THE STERIC INHIBITION OF RESONANCE

Sir:

It has been shown recently[1] that the concept of the steric inhibition of resonance offers an adequate explanation for the differences in acidity observed with trinitrotriphenylmethanes.

Using exactly the same reasoning, we have attacked this problem from a different point of view, *i. e.*, by a consideration of the basic strengths of substituted 4-nitro-1-naphthylamines.



The electron pair of the amino nitrogen atom (upon which depends the basicity of the molecule) is no longer present in the resonance isomer I. If the alkyl groups in I are large, they will inhibit the ability of the group R_2N- and the benzene ring to become coplanar. The result of this must be a diminution in resonance. This reduction in resonance by steric hindrance should result in an increase in the electron density at the amino nitrogen atom and thus lead to an increase in basicity. We have shown that the basicity of the substituted amine (I, R = CH_3) is much greater than that of the unsubstituted amine (I, R = H) and that this difference is far too great to be explained by an inductive effect of the methyl groups.

The decrease in resonance reduces the polar character of these molecules[2] and should consequently lower the melting points (if other crystal

(1) Wheland and Danish, THIS JOURNAL, **62**, 1125 (1940).

(2) Birtles and Hampson, *J. Chem. Soc.*, 10 (1937).

structure factors remain essentially constant). The values in Table I show that the melting points decrease markedly with increasing size of the alkyl groups.

TABLE I

MELTING POINTS OF VARIOUS ALKYLATED AMINO NITRO COMPOUNDS

Substance	M. p., °C.
Nitroaminodurene	161
Nitrodimethylaminodurene	90
1-Amino-4-nitronaphthalene	191
1-Methylamino-4-nitronaphthalene	184
1-Ethylamino-4-nitronaphthalene	176
1-Benzylamino-4-nitronaphthalene	156
1-Dimethylamino-4-nitronaphthalene[a]	65
1-Diethylamino-4-nitronaphthalene[a]	Liquid

[a] There is no chance for a preferred position of the alkyl groups in this case.

SCHOOL OF CHEMISTRY
UNIVERSITY OF MINNESOTA
MINNEAPOLIS, MINNESOTA
RICHARD T. ARNOLD
GEO. PEIRCE
R. A. BARNES

RECEIVED MAY 16, 1940

THE BIOLOGICAL ACTIVITY OF SYNTHETIC PANTOTHENIC ACID

Sir:

The lactone of the "acid fragment" of pantothenic acid has been identified as α-hydroxy-β,β-dimethylbutyrolactone by Stiller, Keresztesy and Finkelstein.[1] The coupling of the synthetic *dl*-lactone with β-alanine in 50% yields, as determined by microbiological assay, and assuming the inactivity of one isomer, has been reported by Weinstock and co-workers.[2] In the present investigation the yield from the coupling reaction was 88%, and definite evidence was found for the inertness of the unnatural isomer.

When equimolecular amounts of 1 *N* sodium hydroxide, β-alanine and the lactone[3] are mixed at 0°, 50% coupling takes place almost immediately as determined by a Sörensen formol titration for free amino nitrogen. Upon standing no further coupling occurs. Instead, the remaining hydroxide ion disappears during the course of an hour, due probably to the saponification of the uncoupled lactone. If instead of equimolecular amounts, the ratio of lactone to β-alanine to 1 *N* sodium hydroxide is made 3:1:1, a 55% coupling occurs immediately, again followed by the disappearance of hydroxide ion. If now to this same solution an amount of 10 *N* sodium hydroxide equivalent to the amount of free β-alanine remaining is added, 51% of this remainder likewise couples. Upon repetition of the procedure, the % of the remainder of the β-alanine which couples falls off rapidly. The results of a typical experiment are summarized in Table I.

(1) As reported by Williams and Major, *Science*, **91**, 246 (1940).
(2) Weinstock, Arnold, May and Price, *ibid.*, **91**, 411 (1940).
(3) Prepared according to the directions of Kohn and Neustadter, *Monatsh.*, **39**, 295 (1918).

TABLE I

	Milliequivalents of				Total % conversion
	β-alanine	hydroxide ion	Lactone	*dl*-pantothenic acid	
Present at start	540	540	1680	0	..
Present after 1 hr.	235[a]	< 1[b]	..	305[c]	55
Added at end of 1 hr.	0	235	0	0	..
Present at end of 2 hr.	115[a]	< 1[b]	..	425[c]	79
Added at end of 2 hr.	0	115	0	0	
Present at end of 3 hr.	78[a]	< 1[b]	..	462[c]	85
Added at end of 3 hr.	0	100	0	0	
Present at end of 4 hr.	68[a]	< 1[b]	..	472[c]	88

[a] By Sörensen formol titration. [b] Acid to phenolphthalein. [c] By difference.

At the end of the experiment, the solution was biologically assayed with chicks,[4] and found to contain 3,680,000 chick filtrate factor units, corresponding to 36 units per mg. of *dl*-pantothenic acid. Natural pantothenic acid has been stated to contain 71 chick units per mg.[5] This points to the inactivity of one enantiomorph in the synthetic preparation.

At the same time a mixture of 10 g. of the *dl*-lactone and 7 g. of β-alanine was incorporated in 1000 g. of heated diet and biologically assayed. Slight but definite activity was observed, calculated to correspond roughly to a coupling *in vivo* of 0.06% of the mixture. This indicates that none of the activity of the pantothenic acid solution at the level fed (corresponding to 2.1 mg. of *dl*-pantothenic acid per 100 g. of diet) may be attributed to the presence of unchanged starting materials.

(4) Jukes, *J. Biol. Chem.*, **117**, 11 (1937).
(5) Jukes, *ibid.*, **129**, 225 (1939).

DIVISIONS OF CHEMISTRY AND POULTRY HUSBANDRY
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DAVIS, CALIFORNIA
S. H. BABCOCK, JR.
T. H. JUKES

RECEIVED MAY 20, 1940

NAPHTHOQUINONE OXIDES

Sir:

Since 2-methyl-1,4-naphthoquinone oxide can be converted very easily and efficiently [Fieser, *J. Biol. Chem.*, **133**, 391 (1940)] into the isomer phthiocol, it was somewhat surprising to discover

that the substance surpasses phthiocol by far in vitamin K activity. The observation that the pure oxide [Fieser, Campbell, Fry and Gates, THIS JOURNAL, **61**, 3216 (1939)] is fully effective in the chick assay at a dosage of 5 γ prompted the investigation of other oxides of 2-alkyl and 2,3-dialkyl 1,4-naphthoquinones, and it was found that the hydrogen peroxide procedure [Fieser, *et al.*, *loc. cit.*] provides a convenient route to a number of substances of both types. Farnesylnaphthoquinone oxide [found: C, 78.88; H, 8.16] and phytylnaphthoquinone oxide [found: C, 79.91; H, 9.76] were obtained as nearly colorless oils showing, respectively, very weak and weak (500 γ) antihemorrhagic activity. These substances are cleaved by alkali to a mixture of 2-hydroxy-1,4-naphthoquinone and its 3-alkyl derivative. Crystalline oxides were obtained from 2,3-dimethyl-1,4-naphthoquinone [m. p. 104–104.5°, found: C, 71.26; H, 5.09; active at 25 γ] and 2-methyl-3-cinnamyl-1,4-naphthoquinone [m. p. 85–86°, found: C, 78.94; H, 5.47].

Vitamin K_1 was converted in nearly quantitative yield into the 2,3-oxide, which was obtained as an almost colorless oil [found: C, 79.85; H, 9.69]. Any uncertainty as to the structure is eliminated by the observation that the absorption spectrum corresponds closely with that of 2,3-dimethyl-1,4-naphthoquinone oxide. The K_1 oxide shows antihemorrhagic activity of about the same order as the vitamin (1.5 γ) and gives no purple-blue color with alcoholic alkali. The properties of the oxide are of interest in connection with the reports of Fernholz, Ansbacher and coworkers [THIS JOURNAL, **61**, 1613 (1939); *Proc. Soc. Exptl. Biol. Med.*, **42**, 655 (1939)] stating that they have isolated from alfalfa concentrates a nearly colorless substance of high potency which does not give the Dam–Karrer color test characteristic of vitamins K_1 and K_2. However, in our hands, there is no great difference in the ratio of the effective dose of the oxide and of vitamin K_1 when assayed by the six and eighteen hour method.

We have found that the oxides of vitamin K_1 and of methylnaphthoquinone can be reduced smoothly to vitamin K_1 hydroquinone and methylnaphthohydroquinone with sodium hydrosulfite in aqueous alcohol, even at room temperature. This lends plausibility to the hypothesis that the high potency of the oxides is due to a reduction in the organism to the corresponding quinones or hydroquinones; possibly the 2-methyl oxide is converted in part into the comparatively inactive phthiocol.

CONVERSE MEMORIAL LABORATORY L. F. FIESER
HARVARD UNIVERSITY
CAMBRIDGE, MASS.
RESEARCH LABORATORIES,
MERCK AND CO., INC., AND M. TISHLER
MERCK INSTITUTE FOR THERAPEUTIC RESEARCH
RAHWAY, NEW JERSEY W. L. SAMPSON

RECEIVED APRIL 20, 1940

MISCIBILITY OF CARBON DIOXIDE AND WATER UNDER HIGH PRESSURE

Sir:

Wiebe and Gaddy [THIS JOURNAL, **62**, 815 (1940)] report the solubility of carbon dioxide in water and make the following statement: "The compositions of the gas and liquid phases at 12° and 600 atm. were identical." My understanding of the behavior of carbon dioxide–water systems is that compression at 12° to about 47.7 atm. will change the phases from a gas (predominantly carbon dioxide) and liquid (mostly water) to a gas (mostly carbon dioxide), a liquid (mostly carbon dioxide), and a liquid (mostly water). Further attempts to compress the system will cause the gas phase to change to a liquid (mostly carbon dioxide) phase and leave at its disappearance two liquids, one predominantly water and the other predominantly carbon dioxide.

Their data show that compression of the two phases increases the carbon dioxide content of the water phase only from 0.03 mole fraction to less than 0.04 mole fraction. Lowry and Erickson [*ibid.*, **49**, 2729 (1927)] indicated that the water concentration in the liquid carbon dioxide was much lower than the above concentration of carbon dioxide in the water phase. Wiebe and Gaddy [*ibid.*, **61**, 315 (1939)] state the mutual solubility of water and carbon dioxide as liquid–liquid system is affected by pressure to only a slight extent.

These statements appear contradictory to the above quotation of identical phases. Any critical phenomena in this region would be of the liquid–liquid critical solution type and not of the type reported by Kuenen [*Commun. Phys. Lab. Univ. Leiden*, **4** (1892)] for the carbon dioxide–methyl chloride system. To become mutually soluble, it is normally expected that the two phases approach each other in composition. A consideration of the probable behavior of these two phases upon compression indicates a possible explanation of the above contradictions. At 10 to 20°,

carbon dioxide is relatively close to its critical temperature and is more compressible than water. At low pressures the predominantly water phase is the more dense but the increase of pressure to about 200 atm. and about 500 atm. at 10 and 20°, respectively, would cause the two immiscible fluids to reach the same density.

I know no reason to believe that the same density makes the two phases miscible but the formation of a relatively uniform suspension of the two phases might occur. Unless the possibility of this reversal in the positions of the two phases in the equilibrium cell were recognized, experimental results might indicate a critical state had been reached. Details of the manipulation of the equilibrium cell and quantitative results at the high pressures in the reported region of complete miscibility should show whether the proposed explanation of the unusual results is tenable.

DEPARTMENT OF CHEMICAL ENGINEERING
UNIVERSITY OF MICHIGAN
ANN ARBOR, MICHIGAN D. L. KATZ

RECEIVED APRIL 18, 1940

REDISTRIBUTION REACTIONS

Sir:

Recently Calingaert and co-workers[1] have described a "hitherto unrecognized type of intermolecular exchange of organic radicals" which they term "redistribution reactions." These reactions are characterized by equilibrium constants which are independent of temperature through the temperature range employed, and which have values that agree with the idea of a random distribution of the exchanging radicals to within the precision of the data obtained.

In view of the large amount of experimental work done by these authors already, it seems justifiable to point out that, while such reactions have not hitherto been recognized as a type, their existence need not surprise one; and, furthermore, given any of the reactions so far studied, the *equilibrium* results obtained could have been predicted about as closely as the experiments justify the idea of random exchange of radicals.

The significance of these reactions lies, first, in the fact that, to the precision to which a modified Redgrove[2] rule would apply, values of ΔH would be zero in all cases. Thus in every type of exchange studied certain bonds are broken and others are formed, but the latter are always identical with the former except for slight steric effects. For $\Delta H = 0$, $K = e^{\Delta S^0/R}$, and ΔS^0 for random distribution should be measured by the relative external symmetry numbers of the molecules involved in the equilibrium; *e. g.*, in the type reaction

$$\underset{\sigma = 12}{R_4M} + \underset{12}{R'_4M} \rightleftharpoons \underset{2}{2R_2R'_2M} \qquad (1)$$

$$\Delta S^0_\sigma = R \ln \frac{12^2}{2^2} = 7.11 \text{ units or } K = 36$$

where σ is the external symmetry number. By the nature of the reactions studied, the only remaining appreciable contributions to ΔS^0 would lie in the effect of the redistribution of mass on the translational entropies, and on the redistribution of principal moments of inertia on the possible rotational entropies. Based on six specific redistributions from systems typified by the left-hand side of equation 1, the former of the two mentioned contributions (*i. e.*, mass redistribution) averages 0.076 entropy unit (a heat effect of about 27 small calories at 350°K.); and, assuming stretched molecules and free rotation, the average of the upper limit of the second contribution to ΔS^0 mentioned above is, for the same six reactions, 0.86 entropy units (a heat effect of about 300 small calories at 350°K.).

It is therefore not surprising that the controlling factor in determining the equilibrium state for such reactions is the value of ΔS^0_σ, or randomness of distribution.

UNIVERSITY OF MISSOURI
COLUMBIA, MISSOURI ALLEN E. STEARN

RECEIVED MARCH 11, 1940

THE ISOMERIZATION EQUILIBRIUM OF *n*-BUTANE AND *i*-BUTANE AND THE THIRD LAW OF THERMODYNAMICS

Sir:

Recently complete measurements in this Laboratory of the thermal properties of the two butanes from 11°K. to their respective boiling points furnish values for the entropies of the gases at their normal boiling points. For *n*-butane $S^\circ_{272.66°K.} = 72.05 \pm 0.2$ e. u.; for *i*-butane $S^\circ_{261.44°K.} = 67.54 \pm 0.2$ e. u. These values, together with available heat capacity data on the gas, yield a value of $\Delta S^\circ_{298.1} = -3.7 \pm 0.3$ e. u. for the reaction

n-butane(g) ⟶ *i*-butane(g)

(1) Calingaert and Beatty, THIS JOURNAL, **61**, 2748 (1939); Calingaert, Beatty and Neal, *ibid.*, **61**, 2755 (1939); Calingaert and Soroos, *ibid.*, **61**, 2758 (1939); Calingaert Beatty and Hess, *ibid.*, **61**, 3300 (1939).

(2) Redgrove, *Chem. News*, **116**, 37 (1917).

The work of Moldavskii and Nizovdima[1] upon the equilibrium constant for this reaction from 70–150°, combined with the measurement of Montgomery, McAteer and Franke[2] at 27° furnishes an independent value for the entropy difference of the two isomers. Two of these equilibrium measurements, at 27° (Montgomery) and at 70° (Moldavskii) were made in the liquid phase at pressures of about 3 and 10 atmospheres, respectively. The constants were calculated to the gas phase with fugacity data for *n*-butane[3] and *i*-butane[4] reported by Sage, Webster and Lacey. The assumption that the liquid follows Raoult's law is in accord with the results of Montgomery, *et al.*[2] The other equilibrium measurements were made in the gas phase by a flow method. The heat of isomerization -2200 ± 200 cal./mole was obtained from the slope of a $\log K - \frac{1}{T}$ plot. Essentially a straight line was obtained, which indicates that over the temperature range in question ΔH is constant to within a small fraction of the experimental error in the equilibrium values. This constancy of ΔH has been confirmed by statistical mechanical calculation.

From the equilibrium data two values of ΔS°_{298} for the isomerization reaction may be obtained, one using the measured heat[5] (A), the other using the heat of isomerization from the slope of the plot (B). These two values are compared with our experimental value of ΔS°_{298} (C) in Table I.

TABLE I

n-C_4H_{10} (g) = i-C_4H_{10} (g)

ΔS°_{298} cal./deg./mole	Source of data
-2.1 ± 0.6	Equilibrium measurement (Montgomery, *et al.*[2])
	Heats of combustion (Rossini[5])
-3.7 ± 0.3	Thermal data to 11 °K. *n*-butane submitted for publication in THIS JOURNAL
	i-butane, unpublished data
-4.0 ± 0.8	Temperature coefficient of equilibrium constant. Montgomery *et al.*,[2] and Moldavskii and Nizovdima.[1]

The agreement between (B) and (C) is well within experimental error. There is thus at present no reason to doubt[6] the practical applicability of the third law of thermodynamics to these compounds.

The assistance of the Standard Oil Development Company in portions of this work is gratefully acknowledged.

(1) Moldavskii and Nizovdima, *Compt. rend. acad. sci. U. R. S. S.*, **23**, 919–20 (1939); *Chem. Abs.*, **34**, 931 (1940).

(2) Montgomery, McAteer and Franke, THIS JOURNAL, **59**, 1768 (1937).

(3) Sage, Webster and Lacey, *Ind. Eng. Chem.*, **29**, 1188 (1937).

(4) Sage and Lacey, *ibid.*, **30**, 673 (1938).

(5) Rossini, *J. Chem. Phys.*, **3**, 438 (1935).

(6) Kassel, THIS JOURNAL, **59**, 2745 (1937).

SCHOOL OF CHEMISTRY AND PHYSICS
THE PENNSYLVANIA STATE COLLEGE
STATE COLLEGE, PENNSYLVANIA
G. H. MESSERLY
J. G. ASTON
R. M. KENNEDY

RECEIVED MAY 6, 1940

NEW BOOKS

Die exakten Methoden der Mikromassanalyse. (The Exact Methods of Titrimetric Microanalysis.) By Dipl.-Ing. JOSEF MIKA. (Die chemische Analyse. Edited by WILHELM BÖTTGER, Hannover. XLII. Band.) Ferdinand Enke Verlag, Hasenbergsteige 3, Stuttgart W, Germany, 1939. xii + 180 pp. 19 figs. 16.5 × 25 cm. Price, RM. 18; bound, RM. 19.60.

The author limits himself to a discussion of such titrimetric methods as can be applied to samples of approximately 10 microequivalents, *i. e.*, 1 to 10 milligrams of material. As a rule it is tried to attain a relative precision of 1 part in a thousand. Methods giving a relative precision of 10 parts in a thousand are included, however, if they offer practical advantages. Hundredth normal standard solutions are suggested for the use with burets of approximately 1 ml. total capacity, which permit delivery and determination of volume with a precision o 0.001 to 0.0001 ml.

In the general part are discussed: the recognition of the end-point with the use of colorimetric, potentiometric, and conductometric methods; the concentration of the standard solutions and the determination and accuracy of their titer; burets, pipets, and aliquot partition; storing of standard solutions; containers for the titrated solutions, stands for titration; apparatus for potentiometric and conductometric titrations; and the testing for purity of the reagents and the water used as solvent. The special part comprises: neutralimetry with the use of dyestuff indicators and of potentiometric and conductometric indication of the end-point; oxidimetry, redox indicators, and electrometric indication; titrations based on the formation of precipitates or complexes with the use of colori-

metric, potentiometric, and conductometric indication. Author index and subject index complete the book.

The treatment of the subject is critical and the problems arising in the small scale performance of titrations are properly emphasized. The book is highly recommended to those interested in the field. Even if the reader should not be willing to agree with the author in all points, he will be compensated by the stimulating originality of the presentation of the subject. The author is a student of Friedrich Emich and he has dedicated the book to his teacher.

A. A. BENEDETTI-PICHLER

Essentials of College Chemistry. By G. H. WHITEFORD, Ph.D., Professor of Chemistry, and R. G. COFFIN, M.S., Associate Professor of Chemistry, Colorado State College. Second edition. The C. V. Mosby Company, 3523 Pine Blvd., St. Louis, Missouri, 1939. 534 pp. 32 figs. 14.5 × 22 cm. Price, $4.00.

Teachers who do not wish to overwhelm the beginner with discouragingly large reference texts will be interested in this book. At first sight it seems to be an expanded form of carefully prepared lecture notes. The order is the conventional one and the assignments (chapters) are of such length as to encourage further readings. Most of the references are to material in the *Journal of Chemical Education* or *Industrial and Engineering Chemistry*. Historical material and factual data are minimized, allowing each instructor to present material of his own selection during the class and lecture hours or by use of references.

The book has an unusual feature in the inclusion of three chapters entitled "General Review." These review chapters take the form of a series of questions followed by groups of terms under various titles such as "Laws, Theories, Topics, Terms." Many instructors present material of this kind in mimeographed form but this is the first instance that has come to the reviewer's attention, where this type of review is included in the text. The review chapters correspond to the three-term academic year. The authors have included numerous exercises, a 6-page glossary, no photographs, 96 drawings on 32 plates, a 3-table appendix, and a 19-page 2-column index.

C. R. CONARD

Volumetric and Phase Behavior of Hydrocarbons. By BRUCE H. SAGE, Assistant Professor of Chemical Engineering, and WILLIAM N. LACEY, Professor of Chemical Engineering, California Institute of Technology. Stanford University Press, Stanford University, California, 1939. xli + 299 pp. 188 figs. 16 × 23.5 cm. Price, $5.00.

In this book, which is admirable in its self-sufficiency, the authors have presented a qualitative treatment of the fundamental principles relating to the volumetric and phase behavior of hydrocarbons. Separate chapters are devoted to the behavior of single, two, three and multi-component systems. Other chapters cover such subjects as: the phase rule, partial quantities, fugacities, ideal and non-ideal solutions, and the retrograde phenomena.

The omission of the concept of the pseudo-critical point weakens the chapter on multi-component systems. The inclusion of a chapter dealing with the computation of the isothermal pressure correction to such thermodynamic properties as the entropy and the enthalpy from volumetric behavior data would have added to the value of the book.

No quantitative data or correlations that can be used in making volumetric or phase behavior calculations are presented. This will no doubt be a disappointment to many. However, the fundamental principles presented in this volume will be quite helpful to the physical chemist and chemical engineer in developing such correlations from data already available and in revising them as new data become available. In this respect the book should prove to be of much industrial and academic value.

W. C. EDMISTER

Lecture Demonstrations in General Chemistry. By PAUL ARTHUR, Assistant Professor of General and Analytical Chemistry, Oklahoma Agricultural and Mechanical College. McGraw-Hill Book Co., Inc., 330 West 42nd Street, New York, N. Y., 1939. xvi + 455 pp. 113 figs. 14.5 × 21 cm. Price, $4.00.

A lecture demonstrator of long years of experience may be able to dispense with a guide in conducting experiments in general chemistry before large classes. An interested, gifted person may even devise new and unusual experiments and in time become renowned for his accomplishments. Time to gain experience and unusual aptitude are gifts seldom afforded the young man charged with such duties. To him, "Lecture Demonstrations in General Chemistry," by Paul Arthur, substitutes the years of Dr. Arthur's experience for an apprenticeship that in most cases is a trying one.

Within the compass of four hundred and fifty pages, the author presents complete instructions for conducting over one thousand experiments. Demonstrations are provided illustrating all principles that would commonly be included in a comprehensive course in inorganic chemistry. The principle to be illustrated is set forth under each experiment, followed by explicit quantitative details regarding the procedure to be employed. Abundant references are provided in each instance, including publications almost as recent as the date of publication of the book. The inclusion of so much modern material justifies the recommendation of the purchase of this volume by either the experienced demonstrator or the untutored novice.

H. S. LUKENS

Handbook of Chemical Microscopy. By ÉMILE MONNIN CHAMOT, B.S., Ph.D., Professor of Chemistry, Emeritus, and CLYDE WALTER MASON, A.B., Ph.D., Professor, Chemical Microscopy and Metallography, Cornell University. Volume II. Chemical Methods and Inorganic Qualitative Analysis. Second edition. John Wiley and Sons, Inc., 440 Fourth Avenue, New York, N. Y., 1940. xi + 438 pp. 233 figs. 15 × 23.5 cm. Price, $5.00.

The subject of chemical microscopy, unlike some branches of microchemistry, has grown to maturity and its

principles and procedures have been well-established and thoroughly tested over a period of years.

The revision of Volume II reflects this maturity in that the changes have not been extensive. The first two chapters dealing with manipulative methods and methods of applying reagents have some new material and new references added. The number of cuts has been increased by about fifty, with the result that twenty-seven new pages have been added. The chapters on the separation and qualitative detection of specific elements and groups have been brought up to date by adding recent references and making necessary changes in the text. The authors have continued their critical attitude toward the many new tests which have been published, and take the view that, in many cases, the methods have not been adequately studied from the standpoint of interfering ions. New tests under such conditions can often lead to erroneous conclusions when applied to an unknown mixture. Hence, the volume continues to be a thoroughly workable and practical guide in the application of the microscope in qualitative analysis, and not merely a compendium of isolated tests. The mature microscopist in his work on problems in his field should seek new methods and tests, but he will do well to evaluate his methods and technique by the criteria set forth in this volume.

Because of the proper balance between the academic and practical side of microscopy, this handbook continues to be an excellent text for teaching the subject.

L. T. HALLETT

Handbuch der Lebensmittelchemie. A. BÖMER, A. JUCKENACK and J. TILLMANS. Vierter Band. **Fette und Öle. Lipoide, Wachse, Harze, Ätherische Öle.** (Handbook of Food Chemistry. Vol. IV. Fats and Oils. Lipoids, Waxes, Resins, Ethereal Oils.) Editorial direction of J. GROSSFELD. Verlag von Julius Springer, Linkstrasse 22–24, Berlin W 9, Germany, 1939. xxi + 966 pp. 247 figs. 17.5 × 26 cm. Price, RM. 135; bound, RM. 138.60.

Sponsored by an editorial board headed by J. Grossfeld and including besides A. Juckenack, E. Bames, B. Bleyer and J. Grossfeld, there has appeared another volume, the eighth in order of completion, of the "Handbuch der Lebensmittelchemie." In its general pattern and excellence of quality it follows its predecessors; the combined efforts of a group of specialists are concentrated within its covers.

Approximately one-half of this volume had been written by the one time dean of German fatty oil chemists, the late A. Bömer, J. Grossfeld collaborating. A long chapter on general methods for the examination of edible fats (326 pp.), followed in turn by one on the preparation of fats and their constituents (54 pp.) and another on the occurrence, recovery and properties of the food fats (278 pp.), is the contribution of this pair to this volume. The latter chapter is divided into three parts, *viz.*, the occurrence, recovery, properties and composition of individual vegetable fats and oils; animal fats and oils treated in a somewhat similar manner; and artificially altered, or processed, fats. These chapters are up to date with respect to time of publication, and include among other topics that of the preparation of fatty acids by oxidation of the paraffin hydrocarbons.

The remaining chapters of this volume are devoted to the microscopical examination of oil-bearing seeds and fruits (44 p.), the contribution of C. Griebel; the lipoids (51 p.) (fat-soluble vitamins) by Wm. Halden; waxes, resins, ethereal oils and fruit essences (Fruchtäther) (94 p.) by R. Grau; the German laws pertinent to fat production (37 p.) by H. Holthöffer with a brief Austrian supplement by E. Bames who also wrote the section on foreign laws (13 p.). A table summarizing the simpler physical and chemical constants of 424 fatty oils and nine others pertinent to the analysis and technology of fatty oils complete this volume.

This volume, in particular the first half, may be regarded in a sense as a memorial to the late Prof. A. Bömer. It is an invaluable and authoritative aid not only to those working in the field of fatty oil chemistry itself but in the larger one of food chemistry.

H. A. SCHUETTE

Semimicro Qualitative Analysis. By WILLIAM LLOYD EVANS, ALFRED BENJAMIN GARRETT and LAURENCE LARKIN QUILL, The Ohio State University. Ginn and Company, 15 Ashburton Place, Boston, Massachusetts, 1940. 245 pp. 30 figs. 20.5 × 27.5 cm. Price, $2.00.

This is another addition to the rapidly increasing number of text-books and manuals on semi-micro qualitative analysis. The authors are to be commended for presenting their material in a logical, well-arranged fashion. They have obviously adopted a conservative policy and have deliberately set out to follow as closely as possible the usual macro-qualitative scheme of analysis.

In general each group is covered in the laboratory by a series of precipitation and separation reactions, confirmatory reactions, and supplementary reactions. Then the group is studied as a whole. Finally, numerous review and supplementary questions are given. Most of the equations are given both in the molecular and ionic forms. In regard to the ionic equations, it is the opinion of the reviewer that it would have been better if the authors had adopted the convention of writing ions for only those substances that furnish a high concentration of ions. Thus, $Cd^{++} + H_2S \rightleftarrows CdS + 2H^+$ is preferable to $Cd^{++} + S^{--} \rightleftarrows CdS$ in the precipitation of sulfides by hydrogen sulfide from acid solution. Similarly, precipitations with ammonium hydroxide are better expressed by ionic equations in which the NH_4OH is written in the molecular form. That the authors are not always consistent in this respect is shown in several instances, for example the dissolving of cadmium sulfide in nitric acid (p. 47) and the less satisfactory equation for dissolving copper sulfide in nitric acid (p. 170).

Throughout the book the authors have attempted to be concise and yet clear. This object has been attained by careful arrangement of the material, by the use of numerous charts, diagrams and flow-sheets, and by the use of cross references. The last quarter of the book is devoted to an adequate discussion of theoretical principles. The book is bound in loose-leaf form which has the obvious advantage of lying flat on the laboratory bench and of facilitating the removal of report sheets which are in-

cluded in the volume. At the same time durability is necessarily sacrificed, for, unless handled carefully, the book will undoubtedly suffer badly in physical condition during a semester's work. It is unfortunate that such an excellent work should be a "one year" book.

Instructors who favor the semi-micro method of teaching qualitative analysis will find in this book a well-presented course, flexible enough to be adaptable to varying conditions of available time and equipment.

STEPHEN G. SIMPSON

The Chemists' Yearbook 1939. Founded by F. W. ATACK, M.Sc.Tech., D.Sc. (Manc.), B.Sc. (Lond.), Fellow of the Institute of Chemistry. Edited by E. HOPE, M.A. (Oxon), D.Sc. (Manc.), Fellow of Magdalen College, Oxford. Chemical Publishing Co. of New York, Inc., New York, N. Y., 1939. 1257 pp. 10 × 15.5 cm. Price, $6.00.

In this edition of the Yearbook the sections dealing with general properties of inorganic and organic compounds have been enlarged, the chapter on crystallography revised, the atomic weights brought up to date and the table of alkaloids improved. A comparison with the 1923 copy of the same book shows that while some new topics have been added and old ones changed, yet, by and large the book has remained the same in size and subject matter. In fact many pages have been transposed without change into the later editions.

About one-third of the book is text material. This includes detailed instructions for analyses and examination of many substances ranging from the usual inorganic qualitative analysis scheme to discussions of fuels, clays, tobacco, hydrogen ion, essential oils, milk products, etc. Approximately 3000 organic and 1500 inorganic compounds are listed. This is to be compared with 4400, 4950 and 5000, 4000, respectively, for two comparable American handbooks. The Yearbook contains very little of the data of Physics and the mathematical section is quite brief. A number of sections are included which are not found in similar American handbooks. Among these are: Patent Law and Chemical Invention, Notable Dates in the History of Chemistry, Tobacco, Coal Tar, Cellulose and Paper, Leather Analysis, Lubricants, Tanning Materials, Paints and Pigments, Identification of Dyestuffs, Agricultural Chemistry, Textile Fibers, Analysis of Clays, Firebricks and Silica Material, Analysis of Portland Cement.

Unfortunately the price is out of line with that of the corresponding American books.

ROBERT TICHENOR

BOOKS RECEIVED

April 10, 1940 to May 10, 1940

CHARLES F. H. ALLEN, Editor. "Organic Syntheses." Vol. 20. John Wiley and Sons, Inc., 440 Fourth Avenue, New York, N. Y. 113 pp. $1.75.

FRANK BAMFORD. "Poisons. Their Isolation and Identification." The Blakiston Co., 1012 Walnut St., Philadelphia, Pa. 344 pp. $4.00.

HAROLD SIMMONS BOOTH AND VIVIAN RICHARD DAMERELL. "Quantitative Analysis." McGraw-Hill Book Co., Inc., 330 West 42d St., New York, N. Y. 246 pp. $2.25.

CARLETON ELLIS. "Printing Inks. Their Chemistry and Technology." Reinhold Publishing Corporation, 330 West 42d St., New York, N. Y. 560 pp. $7.00.

LOUIS P. HAMMETT. "Physical Organic Chemistry." McGraw-Hill Book Co., Inc., 330 West 42d St., New York, N. Y. 404 pp. $4.00.

C. N. HINSHELWOOD. "The Kinetics of Chemical Change." Oxford University Press, 114 Fifth Avenue, New York, N. Y. 270 pp. $4.50.

JOSEPH REILLY AND WILLIAM NORMAN RAE. "Physico-Chemical Methods." Volume I. "Measurement and Manipulation." Volume II. "Practical Measurements." D. Van Nostrand Co., Inc., 250 Fourth Avenue, New York, N. Y. 686 and 580 pp. $17.50.

ARTHUR K. SOLOMON. "Why Smash Atoms?" Harvard University Press, Cambridge 38, Mass. 174 pp. $2.50.

"Effect of Sulphur Dioxide on Vegetation." Prepared for the Associate Committee on Trail Smelter Smoke of the National Research Council of Canada, Ottawa, Canada. 447 pp. $15.00.

"Index of Research Projects." Volume III. Works Progress Administration, 1734 New York Avenue NW., Washington, D. C. 243 pp.